Nanotechnology — early lessons from early warnings

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Preface

An investment in knowledge pays the best interest
— Benjamin Franklin '*The Way to Wealth*' (1758).

There is something profoundly wrong with the way we are living today. There are corrosive pathologies of inequality all around us — be they access to a safe environment, healthcare, education or clean water. These are reinforced by short-term political actions and a socially divisive language based on the adulation of wealth. A progressive response will require not only greater knowledge about the state of the planet and its resources, but also an awareness that many aspects will remain unknown. We will need a more ethical form of public decision-making based on a language in which our moral instincts and concerns can be better expressed. These are the overall aims of Volume 2 of *Late lessons from early warnings*.

Volume 1 of *Late lessons from early warnings* was published at a time when the world was experiencing an economic slowdown, China had joined the World Trade Organization and western Europe was still a 15-member Union. Global grain production had declined for the third time in four years due mainly to droughts in North America and Australia, and the world saw major recalls of contaminated meat, foot and mouth disease and bovine spongiform encephalopathy (mad cow disease). Global temperatures continued to climb and many bird populations were in decline, but the United States of America had rejected the Kyoto Protocol. We were seeing ourselves through the lens of the first human genome sequence, yet we were trying to manage chemicals known to be harmful to humans and ecosystems, through international conventions and treaties such as the Basel Convention to deal with toxic waste dumping in the developing world; the OSPAR/HELCOM Conventions to reduce the discharges, emissions and the loss of hazardous substances into the sea and the Montreal Protocol, to phase out ozone-depleting substances. The destruction of the World Trade Center had just happened.

Since then, we have witnessed a period of extraordinary hubris. Most visibly, the financial profligacy of the first decade of the century led inexorably to the crises of 2007–2009 whereby the major components of the international financial system were weakened to the extreme by indebtedness, mispriced products, lax monetary policies and mis-engineered protection against risks and uncertainty. The world experienced more not less volatility. Political systems became silted up by vested interests and a determination by citizens to protect assets accumulated in easier times, and beneath it all lay a deeper environmental crisis epitomised by climate change and biodiversity loss.

There was also a collapse of trust, not only in financial institutions but in big companies, as they abandoned staff, pensions and health care schemes. Recent evidence from social psychology has shown that despite rising levels of education and innovation in products and services, people trust only those they know and not strangers. As Stephen Green said in *Good value: reflections on money, morality, and an uncertain world* in 2009:

> 'There has been a massive breakdown of trust: trust in the financial system, trust in bankers, trust in business and business leaders, trust in politicians, trust in the media, trust in the whole process of globalisation — all have been severely damaged, in rich countries and poor countries alike'.

The scientific elites have also been slowly losing public support. This is in part because of the growing number of instances of misplaced certainty about the absence of harm, which has delayed preventive actions to reduce risks to human health, despite evidence to the contrary.

Suddenly, our problems have grown into what Charles W. Churchman in 1967 termed *wicked problems* — difficult or impossible to solve because of incomplete, contradictory and changing requirements, difficult to recognize, resistant to resolution because of the complexity of their interdependencies and needing to be tackled not by one but via many forms of social power. Solving

them requires a new combination of hierarchical power, solidarity and individualism.

What could this mean, for example, for the 100 thousand chemicals currently in commercial use?

To begin with we have more conventions and treaties in place than a decade ago: the 2004 Rotterdam Convention on the Prior Informed Consent (PIC) Procedure covering international trade of 24 pesticides, four severely hazardous pesticide formulations and 11 industrial chemicals; the 2004 Stockholm Convention on Persistent Organic Pollutants to protect human health and the environment from substances which are highly toxic, persistent, bio-accumulative and move long distances in the environment, such as DDT, PCBs, various industrial chemicals, and a set of unintentional chemical by-products such as dioxin. But these conventions only address the top-down hierarchical approach to power.

At the same time Europe has put in place legislation to achieve a global regulatory influence including the EU Cosmetic Directive banning the use of chemicals known or strongly suspected of being carcinogens, reproductive toxins, or mutagens causing cancer, mutation or birth defects; the EU Restriction of Hazardous Substances Directive, which restricts the use of hazardous materials in the manufacture of various types of electronic and electrical equipment including lead, mercury, cadmium, hexavalent chromium, the flame retardents polybrominated biphenyls and polybrominated diphenyl ethers, and which encourages the substitution to safe/or safer alternatives in the electric and electronic equipment industry; the closely linked 2006 EU Waste Electrical and Electronic Equipment Directive for collection, recycling and recovery of electrical goods; the 2006 Strategic Approach to International Chemicals Management (SAICM); and the 2007 EU Registration, Evaluation and Authorisation of Chemicals, widely known as REACH, to assign greater responsibility to industry to manage the risks from chemicals and to provide safety information on substances. The effects of these regulatory tools are described in different chapters, but once again point to the main economic actors rather than communities or individuals.

One thing that has become clearer over the past decade is that certain chemical substances are highly stable in nature and can have long-lasting and wide ranging effects before being broken down into a harmless form. The risk of a stable compound is that it can be bio-accumulated in fatty tissues at concentrations many times higher than in the surrounding environment. Predators, such as polar bears, fish and seals, are known to bio-magnify certain chemicals in even higher concentrations with devastating consequences for both humans and ecosystems. So exposure to toxic chemicals and certain foodstuffs are at risk of causing harm, especially to vulnerable groups such as foetuses in the womb or during childhood when the endocrine system is being actively built. Even with small dose exposures, the consequences can in some instances be devastating with problems ranging from cancer, serious impacts on human development, chronic diseases and learning disabilities. Here the power to act could be more properly set by well-informed individuals and communities.

The relationship between knowledge and power lies at the heart of Volume 2. In many chapters, the implicit links between the sources of scientific knowledge about pollutants, changes in the environment and new technologies, and strong vested interests, both economic and paradigmatic, are exposed. A number of authors also explore in greater depth, the short-sightedness of regulatory science and its role in the identification, evaluation and governance of natural resources, physical and chemical hazards. By creating a better understanding of these normally invisible aspects, it is hoped that this volume will enable communities and people to become more effective stakeholders and participants in the governance of innovation and economic activities in relation to the associated risks to humans and the planet.

Much of what we are able to learn from the histories of past environmental and public health mistakes is also directly applicable to the better regulation and governance of global institutions and financial and economic risks. Robin G. Collingwood argued in his *Autobiography* (1939), that:

> 'History can offer something altogether different from [scientific] rules, namely insight. The true function of insight is to inform people about the present…we study history in order to see more clearly into the situation in which we are called upon to act… the plane on which, ultimately, all problems arise is the plane of 'real' life: that to which they are referred for their solution is history.'

In this volume, we go further. Whilst still drawing lessons from such widely accepted tragedies as leaded petrol, mercury poisoning in Japan's

Minamata Bay and older pesticides which sterilised many men who used it, we have ventured into the uncertainties of potential yet contested harm, from genetically modified products; nanotechnologies; chemicals such as Bisphenol A; new pesticides and mobile phones. There is also an examination of the 80 or so potential 'false positives' where there had been indications of harm but where it was subsequently claimed that there were in fact no risks to prevent: these cases too can provide information that can help to improve future decision-making about innovation and emerging technologies.

A major part of effective decision-making lies in the way issues are framed. In the case of climate change, the first order question is whether it is worth worrying about at all. US Vice President Al Gore chose to make the question a matter of choice between believers and sceptics. However, problems arose when the public was asked to make a scientific decision when too few people had the qualifications to make any kind of reasoned judgement. They were in fact asked to make a false choice. Instead the question should have been framed around which areas should people and governments make decisions and which should be delegated to experts.

In the end there are few certain and enduring truths in the ecological and biological sciences, nor in the economics, psychologies, sociologies and politics that we use to govern them. One, however, comes from the work of Elinor Ostrom, a late and widely missed colleague, who showed from her work on managing fisheries and ecosystems that complex problems can be solved if communication is transparent and open, visions are shared, trust is high and communities are activated to work from the bottom-up as well as from the top down.

As we navigate the Anthropocene, the epoch named in recognition of our impact on the planet, we will need to encourage more people to become involved in solving the wicked problems of our times. Whether through gathering local information or becoming more aware of the many uncertainties and unpredictabilities in our surroundings, the power structures of knowledge will need to change. And if we are to respond more responsibly to the early warning signals of change, we will need to re-design our style of governance to one which reflects a future defined by the local and specific rather than only the global and the average. We hope that Volume 2 of *Late lessons from early warnings* with its many lessons and insights can help us all meet such a challenge.

Professor Jacqueline McGlade,
Executive Director

1 Introduction

Why further late lessons from early warnings?

The 2013 *Late lessons from early warnings* report is the second of its type produced by the European Environment Agency (EEA) in collaboration with a broad range of external authors and peer reviewers.

Volume 1 of *Late lessons from early warnings: the precautionary principle 1896–2000* published in 2001, looked at the history of a selection of occupational, public health and environmental hazards and asked whether we could have been better at taking action early enough to prevent harm. Twelve key lessons for better decision-making were drawn from cases where public policy was formulated against a background of scientific uncertainty and 'surprises' — and where clear evidence of hazards to people and the environment was often ignored (see box on page 11).

The 14 case studies and 12 key lessons from the 2001 report remain highly pertinent today, and underline four main reasons for a second report. The first relates to expanding the late lessons approach to consider long-known, important additional issues with broad societal implications such as lead in petrol, mercury, environmental tobacco smoke and DDT, as well as issues from which lessons have emerged more recently such as the effects of the contraceptive pill on feminisation of fish and the impacts of insecticides on honeybees.

The second concerns filling an acknowledged gap in the 2001 report, by analysing the issue of false positives where government regulation was undertaken based on precaution but later turned out to be unnecessary. Most of the cases examined in the *Late lessons from early warnings* reports are 'false negatives' — instances where early warnings existed but no preventive actions were taken.

The third reason is to address the rapid emergence of new society-wide challenges such as radiation from mobile phones, genetically-modified products, nanotechnologies and invasive alien species as well as if, how and where precautionary actions can play a role.

The final reason relates to how precautionary approaches can help manage the fast-changing, multiple, systemic challenges the world faces today, what new insights can be drawn in this context and how these can underpin opportunities for sustainable innovations and, supported by information technologies, greater public participation in their selection.

Overall approach

As for Volume 1, the approach in Volume 2 has been to include a wide range of relevant case studies produced by external authors along with chapters written by members of the report's editorial team (see acknowledgements section for details). The relevant topics for case study treatment were selected on the basis of advice from the editor, in collaboration with the editorial team and an advisory board, members of the EEA Scientific Committee and the Collegium Ramazzini ([1]).

The chapters in Volume 2 are grouped into five parts: A. Lessons from health hazards; B. Emerging lessons from ecosystems; C. Emerging issues; D. Costs, justice and innovation; and E. Implications for science and governance.

The chapters have been written by authors who, to varying degrees, have had substantial involvement in the subject area being addressed. Indeed they would not have been approached if

([1]) The Collegium Ramazzini is an independent, international academy founded in 1982 by Irving J. Selikoff, Cesare Maltoni and other eminent scientists. Its mission is to advance the study of occupational and environmental health issues and to be a bridge between the world of scientific discovery and the social and political centers, which must act on the discoveries of science to protect public health.

they had not already extensively studied the case that they were asked to write about. All of them, as respected experts in their fields and in line with their professional scientific training, were expected to be as objective as possible in answering the questions put to them by EEA. To support this, and to develop consistency between chapters, the authors were provided with seven structuring questions to be followed when building their chapter.

The case studies have been peer-reviewed by recognised experts in the respective fields who gave of their time freely and provided their feedback within a set of editorial guidelines provided by the EEA.

Scope

The report has been designed, structured and written in order to, inter alia, help politicians, policymakers and the public to:

i understand better the ways in which **scientific knowledge** is financed, created, evaluated, ignored, used and misused in taking timely and precautionary decisions about how to reduce harms, whilst stimulating benign innovations and generating useful employment;

ii learn from some **very expensive 'mistakes' in the past** so as to help societies make fewer mistakes now, and in the future, especially with some of the relatively new, largely unknown, yet already widespread technologies like nanotechnology and mobile phones;

iii be aware of less visible, important factors such as the skewed ways in which the **costs of actions and inactions** for hazardous technologies have been estimated, and the role that **some businesses** have played in ignoring early warnings and in manufacturing doubt about the science supporting such warnings;

iv consider how the law, or administrative arrangements, could be better used to deliver **justice, to those people (and ecosystems) that have been, or could be, harmed** by poorly designed, or badly deployed, innovations;

v explore how best to **engage the public** in helping to make **strategic choices over innovations**, and their technological and social pathways, as well as their involvement in **ecosystems management** and in long term monitoring through **citizen science**.

Part A of the report commences with an analysis of 'false positives' showing that these are few and far between as compared to false negatives and that carefully designed precautionary actions can stimulate innovation, even if the risk turns out not to be real or as serious as initially feared. The remaining nine chapters address false negatives — lead in petrol, perchlorethylene contaminated water, Minamata disease, occupational beryllium disease, environmental tobacco smoke, vinyl chloride, dibromochloropropane (DBCP), Bisphenol A and dichlorodiphenyltrichlorethane (DDT) — from which three common themes emerge: there was more than sufficient evidence for much earlier action; slow and sometimes obstructive behaviour by businesses whose products endangered workers, the public and the environment; and the value of independent scientific research and risk assessments.

Part B focuses on emerging lessons from the degradation of natural systems and their wider implications for society — booster biocides, the pill and the feminisation of fish, climate change, floods, insecticides and honeybees as well as ecosystem resilience more broadly. It considers, like its predecessor, the issues of scientific evidence as the basis for action/inaction, the multiple, often complex factors and feedback loops in play, many of which are not fully understood, as well as the interfaces between science, policy and society and how all actors can move together towards necessary actions in the context of heightened systemic risks, and substantial unknowns.

Part C analyses some newly emerging and large-scale products, technologies and trends, which potentially offer many benefits but also potentially much harm to people and ecosystems and thereby ultimately economic development. Cases addressed include the Chernobyl and Fukushima nuclear accidents; genetically modified agricultural crops and agroecology; the growing threat of invasive alien species; mobile phones and the risk of brain tumours; and nanotechnologies. There is often little science, and very little direct hindsight, to assist in the management of these emerging technologies but the lessons from the historical case studies need to be applied if hazards are to be avoided.

The evidence from the chapters in Part C is that, by and large, societies are not making the most use of the costly lessons that can be gleaned from their histories. A key question is how this can be improved given the many reasons identified from the case studies why taking actions have been delayed including: the novel

and challenging nature of the issues themselves; poorly or inconsistently evaluated information; strong opposition by the corporate and scientific establishments of the day; and the tendency by the decision making institutions, practices and cultures to favour the status quo and the short term perspective. This section also illustrates the value of bottom up as well as top down approaches to innovations in ensuring that the directions of technological pathways, the equitable distributions of benefits, costs and knowledge ownership, and the diversity of locally sensitive technological options are relevant to the food, energy and ecosystems crises.

The historical chapters illustrate numerous harms which for the most part have been caused by irresponsible corporations. This fact, coupled with shortcomings in how decisions are made by governments on when to act on early warnings, and in the law when it comes to compensating victims of harm, are analysed in three chapters in Part D of the report. Each chapter analyses the reasons behind prevailing practice and then goes on to offer insights, for example, on how cost calculation methods can be improved; on how insurance schemes could be used to compensate future victims of harm; and on the reasons why businesses frequently ignore early warnings.

The cases in Parts A–D form the basis for considering in Part E the governance implications for science, public policy and public engagement, and how current practices could be improved to enable society to maximise the benefits of innovations while minimising harms. The main insights are that science could be more relevant for precautionary decision-making; that the wider use of the precautionary principle can avert harm and stimulate innovation; and that the late lessons of history and precautionary approaches are highly pertinent to today's multiple and inter-connected crises — such as those arising from finance, economics, the use of ecosystems, climate change, and the use and supply of energy and food.

Finally, many of the historical and recent case studies illustrate the value of engaging the public in broadening the knowledge base and stimulating robust innovations.

Twelve late lessons

Based on the case studies of Volume 1 of *Late lessons from early warnings* (EEA, 2001), twelve key lessons for better decision-making were drawn:

1	Acknowledge and respond to ignorance, as well as uncertainty and risk, in technology appraisal and public policymaking
2	Provide adequate long-term environmental and health monitoring and research into early warnings
3	Identify and work to reduce 'blind spots' and gaps in scientific knowledge
4	Identify and reduce interdisciplinary obstacles to learning
5	Ensure that real world conditions are adequately accounted for in regulatory appraisal
6	Systematically scrutinise the claimed justifications and benefits alongside the potential risks
7	Evaluate a range of alternative options for meeting needs alongside the option under appraisal, and promote more robust, diverse and adaptable technologies so as to minimise the costs of surprises and maximise the benefits of innovation
8	Ensure use of 'lay' and local knowledge, as well as relevant specialist expertise in the appraisal
9	Take full account of the assumptions and values of different social groups
10	Maintain the regulatory independence of interested parties while retaining an inclusive approach to information and opinion gathering
11	Identify and reduce institutional obstacles to learning and action
12	Avoid 'paralysis by analysis' by acting to reduce potential harm when there are reasonable grounds for concern

Source: EEA, 2001, *Late lessons from early warnings: the precautionary principle 1986–2000,* Environmental issues report No 22, European Environment Agency.

2 The precautionary principle and false alarms — lessons learned

Steffen Foss Hansen and Joel A. Tickner

Most of the cases examined in the *Late lessons from early warnings* reports are 'false negatives' — instances where early warnings existed but no preventive actions were taken. In debates surrounding the precautionary principle it is often claimed that widespread application of the principle will lead to a large number of regulatory false positives — over-regulation of minor risks and regulation of non-existent risks, often due to unwarranted public 'fears'. Understanding and learning from past false positives as well as false negatives is essential for improving decision-making about public health and the environment.

This chapter reviews incidents of 'false positives', where government regulation was undertaken based on precaution but later turned out to be unnecessary. In total 88 cases were identified to be alleged false positives, however, following a detailed analysis most of them turned out to be either real risks, or cases where 'the jury is still out', or unregulated alarms, or risk-risk trade-offs, rather than false positives.

The analysis revealed four regulatory false positives: US swine flu, saccharin, food irradiation, and Southern leaf corn blight. Numerous important lessons can be learned from each, although there are few parallels between them in terms of when and why each risk was falsely believed to be real. This is a lesson in itself: each risk is unique, as is the science and politics behind it and hence a flexible approach is therefore needed, adapted to the nature of the problem. The costs of the false positives identified were mainly economic, although the actions taken to address swine flu in 1976 did lead to some unintended deaths and human suffering, and diverted resources from other potentially serious health risks. Determining the net costs of mistaken regulatory action, however, requires a complete assessment of the impacts of the regulation, including the costs and benefits of using alternative technologies and approaches.

Overall, the analysis shows that fear of false positives is misplaced and should not be a rationale for avoiding precautionary actions where warranted. False positives are few and far between as compared to false negatives and carefully designed precautionary actions can stimulate innovation, even if the risk turns out not to be real or as serious as initially feared. There is a need for new approaches to characterising and preventing complex risks that move debate from the 'problem' sphere to the 'solutions' sphere. By learning from the lessons in this chapter, more effective preventive decisions can be made in the future.

The scarcity of genuine false positives compared to the large number of 'mistaken false positives' could partly be the result of a deliberate strategy in risk communication. Several references and leaked documents have shown that some regulated parties have consciously recruited reputable scientists, media experts and politicians to call on if their products are linked to a possible hazard. Manufacturing doubt, disregarding scientific evidence of risks and claiming over-regulation appear to be a deliberate strategy for some industry groups and think tanks to undermine precautionary decision-making.

3 Lead in petrol 'makes the mind give way'

Herbert Needleman and David Gee

This chapter addresses the widespread use of lead in petrol. It focuses on the period 1925–2005, when leaded petrol was first widely marketed in the US and then spread to the rest of the world before being gradually phased out from the 1970s. In Europe, the Aarhus Protocol (www.unece.org/env/pp/treatytext.html) initiated the phase-out of leaded petrol in the period 1998–2005.

The neurotoxic effects of lead were recognised as far back as Roman times. And in 1925, at the 'one day trial' of leaded petrol in the US, many experts warned of the likely health impacts of adding lead to petrol. Yet, despite the availability of an equally effective alcohol additive which was assessed by experts to be cleaner, the leaded route to fuel efficiency was chosen in the US and then exported to the rest of the world.

For several decades after the introduction of leaded petrol, virtually no independent research was carried out and the main source of information was industry and industry-sponsored researchers. Not until the 1960s and 1970s did independent scientists from outside this group show, for example, that body burdens of lead arising from human activities were not 'normal', as industry claimed, but were hundreds of times higher than before the industrial revolution and were therefore likely to be harmful.

At its peak in the mid-1970s, leaded petrol released about 200 000 tonnes of lead into the atmosphere annually in both the US and Europe. Following the subsequent phase-out, blood lead levels in children (the most sensitive group exposed) quickly fell, in line with the decrease in air concentrations. The lessons nevertheless remain relevant globally today. Although nearly all countries worldwide had phased out leaded petrol by 2012, lead concentrations in soils and sediments remain high. Meanwhile, electronic wastes containing lead and other contaminants also cause elevated blood lead levels.

Supplementary panel texts focus on the events leading up to the US choice of leaded petrol as the primary fuel source in 1925 and more recent accounts of EU policymaking on lead in petrol and the road to phase-outs in Germany and the United Kingdom.

4 Too much to swallow: PCE contamination of mains water

David Ozonoff

PCE (perchlorethylene, also known as 'perc' or tetrachloroethylene), was used in the production of plastic linings for drinking water distribution pipes in the late 1960s and 1970s. This new and relatively untested type of distribution pipe was used in over 700 miles of New England's water distribution systems. Not until 1976 was it discovered that PCE had been leaching into the water from the pipe lining, causing widespread contamination of water supplies that still today require continuous remediation.

Before the pipes were put into production there was a substantial amount of scientific information available about the potential hazards of PCE. This did not include current concerns about PCE's carcinogenicity, teratogenicity and other health consequences of relatively low-level exposure upper most among today's concerns, but many early warnings suggested the need for caution in introducing PCE-based mains pipe linings.

PCE had been used to treat hookworm and data on side effects were in the literature, while later a variety of occupational users were studied, including aircraft workers, small companies in countries where biological monitoring was required, and dry-cleaning firms. Several environmental studies were also conducted to see if drinking water contaminated with PCE or its close relative, TCE (trichloroethylene), was associated with cancer. Results were mixed and the chemical industry consistently denied that PCE was a human carcinogen.

This case study explores the early (pre 1970) history researching the toxicity of the chemical. It also focuses on the failure of one manufacturer, Johns-Manville Corporation, to recognise the warning signals about using a suspected toxic substance. It examines why a new product was deployed without thought to the public health consequences and why evidence of the potential hazard was ignored.

The science has not been hidden. It has been ineffective in guiding and catalysing action. Whether the problem is a failed duty of care or a lack of clarity about what evidence will trigger action, the contemporary argument over how to interpret the scientific evidence is irresolvable within science itself. There are no overarching criteria from the philosophy of science that can dictate a solution.

This chapter also includes two supplementary texts. A panel that analyses the differences between the conclusions of risk assessments based on the same data, focusing in particular on assessments of PCE and TCE. A further panel describes the opportunities to switch to wet-cleaning technologies to reduce the current use of PCE in dry cleaning.

5 Minamata disease: a challenge for democracy and justice

Takashi Yorifuji, Toshihide Tsuda and Masazumi Harada

Minamata disease, which can induce lethal or severely debilitating mental and physical effects, was caused by methylmercury-contaminated effluent released into Minamata Bay by Chisso, Japan's largest chemical manufacturer. It resulted in widespread suffering among those who unknowingly ate the contaminated fish. This chapter documents the story in three phases.

The disease first came to prominence in the 1950s. It was officially identified in 1956 and attributed to factory effluent but the government took no action to stop contamination or prohibit fish consumption. Chisso knew it was discharging methylmercury and could have known that it was the likely active factor but it chose not to collaborate and actively hindered research. The government concurred, prioritising industrial growth over public health. In 1968 Chisso stopped using the process that caused methylmercury pollution and the Japanese government then conceded that methylmercury was the etiologic agent of Minamata disease.

The second part of the story addresses the discovery that methylmercury is transferred across the placenta to affect the development of unborn children, resulting in serious mental and physical problems in later life. Experts missed this at first because of a medical consensus that such transfer across the placenta was impossible.

The third phase focuses on the battle for compensation. Initially, Chisso gave token 'sympathy money' under very limited criteria. In 1971 the Japanese government adopted a more generous approach but after claims and costs soared a more restrictive definition was introduced in 1977, justified by controversial 'expert opinions'. Legal victories for the victims subsequently made the government's position untenable and a political solution was reached in 1995–1996. In 2003, the 'expert opinions' were shown to be flawed and the Supreme Court declared the definition invalid in 2004.

In September 2011 there were 2 273 officially recognised patients. Still, the continuing failure to investigate which areas and communities were affected means that the financial settlement's geographic and temporal scope is still not properly determined. Alongside deep-seated issues with respect to transparency in decision-making and information sharing, this indicates that Japan still faces a fundamental democratic deficit in its handling of manmade disasters.

This chapter is followed by three short updates on the effects of mercury poisoning since Minamata; on attempts to contain it, including the 2009 global agreement to phase mercury out of economic activity; and on the need for better information about contaminant exposures to enable policymakers to make informed choices that balance the benefits of fish consumption against the assumed adverse effects of low-level methylmercury exposures.

6 Beryllium's 'public relations problem'

David Michaels and Celeste Monforton

Scores of workers employed in nuclear weapons production have been diagnosed with chronic beryllium disease (CBD), a progressive and irreversible inflammatory lung disease. This chapter presents a history of knowledge and public policy about preventing beryllium-related disease, focusing primarily on the United States beryllium industry's role in shaping US regulatory policy.

Over several decades increasingly compelling evidence accumulated that CBD was associated with beryllium exposure at levels below the existing regulatory standard. The beryllium industry had a strong financial incentive to challenge the data and decided to be proactive in shaping interpretation of scientific literature on beryllium's health effects. It hired public relations and 'product defence' consulting firms to refute evidence that the standard was inadequate. When the scientific evidence became so great that it was no longer credible to deny that workers developed CBD at permitted exposure levels, the beryllium industry responded with a new rationale to delay promulgation of a new, more protective exposure limit.

This case study underscores the importance of considering the hazards from toxic materials throughout the entire product life cycle. While primary producers of beryllium products may be able to control exposures in their own facilities, it is unlikely that many secondary users and recyclers have the expertise, resources and knowledge necessary to prevent beryllium disease in exposed workers and residents in nearby communities.

The primary lessons of this chapter are widely applicable to many environmental health controversies. In particular, it illustrates the practice of 'manufacturing uncertainty' — a strategy used by some polluters and manufacturers of hazardous products to prevent or delay regulation or victim compensation.

This chapter is followed by an analysis of the rationale for corporate behaviour in the regulation of beryllium. It is argued that the availability of occasional and limited opportunities for companies to change course without suffering onerous consequences would encourage them to rethink their position and create an obligation on shareholders to take the responsible course. Although this may be perceived as letting them 'get away with it', the end result may be better public policy and corporate responsibility.

7 Tobacco industry manipulation of research

Lisa A. Bero

This chapter differs in some ways from the others in Volume 2 of *Late lessons from early warnings*. The history of 'second hand', 'passive' or 'environmental tobacco smoke' (ETS), to which non-smokers are exposed overlaps with the history of active smoking. Those affected include the partners and children of smokers, and the bartenders and other workers who have to work in smoky environments.

The focus in this chapter is on the strategies used by the tobacco industry to deny, downplay, distort and dismiss the growing evidence that, like active smoking, ETS causes lung cancer and other effects in non-smokers. It does not address the history of scientific knowledge about tobacco and how it was used or not used to reduce lung cancer and other harmful effects of tobacco smoke. There is much literature on this and a table at the end of the chapter summarises the main dates in the evolution of knowledge in this area.

The chapter concentrates on the 'argumentation' that was used to accept, or reject, the growing scientific evidence of harm. Who generated and financed the science used to refute data on adverse health effects? What were the motivations? What kind of science and information, tools and assumptions were used to refute data on the adverse health of tobacco?

The release of millions of internal tobacco industry documents due to law suits in the US has given insights into the inner workings of the tobacco industry and revealed their previously hidden involvement in manipulating research. However, this insight is not available for most corporate sectors. The chapter discusses the possibilities of 'full disclosure' of funding sources and special interests in research and risk assessment in order to secure independence and prevent bias towards particular viewpoints.

While smoking bans are now being introduced in more and more countries, other industries are drawing inspiration from tobacco company strategies, seeking to maintain doubt about harm in order to keep hazardous products in the marketplace.

The chapter also includes a summary of the tobacco industry's role in shaping risk assessment in the US and Europe to serve its own interests.

8 Vinyl chloride: a saga of secrecy

Morando Soffritti, Jennifer Beth Sass, Barry Castleman and David Gee

This chapter is about how early warnings in the 1950s and 1960s concerning the short-term harm of vinyl chloride (VC) to the skin and bones of workers, and to the livers of laboratory animals, were initially hidden from other workers and regulators. This was despite some early misgivings by company experts whose advice was initially ignored by their employers. This pattern was repeated when the later, more devastating news of a rare liver cancer in workers was revealed by long-term animal studies and by an attentive and concerned company physician.

Unlike many other histories, however, this story features a very prompt response from the global chemical industry to the publication of the liver cancer evidence, a response that included funding cancer testing and later compliance with a large reduction in the permissible exposure limits. The case also provides early evidence of reproductive effects of vinyl chloride monomer (VCM).

Other features of this story presage the later and common responses of the corporate world to heightened public awareness and pressure from non-governmental organisations (NGOs) and trade unions, including greatly exaggerated estimates of the likely costs of complying with tighter pollution controls; a frequent mismatch between the position of the trade association and that of many, more progressive companies within the association; but also some relatively quick corporate responses to public, NGO and regulatory pressure.

The chapter also features two legal aspects, which, though more common in the US, are also valuable for Europeans. First, the potentially positive role that judicial review of regulatory proposals can play in providing a societal judgement about the behaviour of corporations. This can embrace not just moral judgements but also judgements about the state of the science and what society should do with it.

Second, the role that document discovery in legal compensation cases can play in revealing the real and until then secret activities of corporations. Any proposals to promote justice for victims of environmental and health harms via no fault administrative arrangements need to be accompanied by other measures to extract information about corporate behaviour.

The chapter is followed by a panel analysing the value of animal testing for identifying carcinogens.

9 The pesticide DBCP and male infertility

Eula Bingham and Celeste Monforton

Dibromochloropropane (DBCP) is a pesticide used against nematodes (roundworms or threadworms) that damage pineapples, bananas and other tropical fruits. It was introduced into US agriculture in 1955 and approved for use as a fumigant in 1964. By 1961 laboratory experiments had shown that it made the testicles of rodents shrink and significantly reduced the quantity and quality of sperm. Nonetheless, the compound was widely marketed and became a commercial success.

In 1977, workers at a production plant became worried that they were unable to father children. An emergency study by a US government agency discovered that in many cases the workers were suffering from deficient or absent sperm. While controls were improved at US facilities, the product continued to be marketed and sprayed in Latin America, the Philippines, some African countries, and elsewhere.

By the 1990s, tens of thousands of plantation workers in these countries had allegedly suffered adverse reproductive effects from DBCP use.

The story continues today with contentious legal claims for compensation, contamination of drinking water and industry attempts to prevent a Swedish documentary on the issue from being screened.

This chapter looks at the knowledge available about the hazards and the actions taken, or not taken, to avert them. The DBCP story is significant as it is the first clear example of reproductive damage to workers who manufactured and used a synthetic chemical. This is one of many examples supporting the growing concerns about increasing rates of reproductive and developmental disease, and about the endocrine disrupting chemicals that seem to be playing a role in these disorders.

Protecting production workers, users, consumers and the environment from chemicals that may damage reproduction demands closer integration of scientific disciplines, as well as government action. The lessons of DBCP may help in ensuring timely protection from harm, based on precautionary approaches to scientific evidence.

10 Bisphenol A: contested science, divergent safety evaluations

Andreas Gies and Ana M. Soto

Bisphenol A (BPA) is currently one of the world's best-selling chemicals and primarily used to make polycarbonate plastics. It is widely used in common products such as baby bottles, household electronics, medical devices and coatings on food containers. BPA is known to mimic the female hormone oestrogen and has been found to leach from the materials where it is used.

Studies have suggested that even exposure to low doses of BPA may cause endocrine disrupting effects. As with other hormones, it appears that an organism is most sensitive during development but that effects are often not observed until much later in the lifecycle. This means that at the time when the effects become detectable, the chemical exposure has vanished. This makes it extremely difficult to link exposure to effects in humans.

This chapter maps some of the findings in studies of rodents and humans. It also discusses the challenges of evaluating scientific findings in a field where industry-sponsored studies and independent scientific research seem to deviate strongly. The authors offer suggestions for ways to uncouple financial interests from scientific research and testing.

A widely used and dispersed industrial chemical like Bisphenol A is a controversial example of an endocrine disrupting substance that has implications for policymakers. Different approaches to risk assessment for BPA by US and European authorities are presented. It throws light on the ways in which similar evidence is evaluated differently in different risk assessments and presents challenges for applying the precautionary principle.

The intense discussion and scientific work on BPA have slowly contributed to a process of improving test strategies. While traditional toxicology has relied on a monotonic increasing dose-response relationship as evidence that the effect is caused by the test agent, studies on BPA and other endocrine disruptor chemicals (EDCs) have demonstrated the limitations of this approach and adjustments have been made in some cases.

It has also been widely accepted that effects cannot be predicted by simply thinking of BPA as a weak oestrogen and extrapolating from what is observed for more potent endogenous oestrogens. This lesson is particularly evident in the intense pharmaceutical interest in selective oestrogen response modifiers (SERMs).

The chapter is followed by a panel analysing the value of animal testing for identifying carcinogens.

11 DDT: fifty years since *Silent Spring*

Henk Bouwman, Riana Bornman, Henk van den Berg and Henrik Kylin

'There was a strange stillness. The birds for example — where had they gone? Many people spoke about them, puzzled and disturbed. The feeding stations in the backyards were deserted. The few birds seen anywhere were moribund: they trembled violently and could not fly. It was a spring without voices ... only silence lay over the fields and woods and marsh.'

The book *Silent Spring* by Rachel Carson is mainly about the impacts of chemicals (in particular dichlorodiphenyltrichlorethane also known as DDT) on the environment and human health. Indeed, the close association between humans and birds remains very apt. Representing the only two warm-blooded groups of life on Earth, mammals and birds share the same environments and threats.

Carson's claim that she lived in 'an era dominated by industry, in which the right to make a dollar at whatever cost is seldom challenged' still resonates strongly with the problems that societies face all over the world. One chapter heading, 'The obligation to endure', derived from the French biologist and philosopher Jean Rostand's famous observation that, 'the obligation to endure gives us the right to know'. United States President John F. Kennedy responded to the challenge posed by Carson by investigating DDT, leading to its complete ban in the US. The ban was followed by a range of institutions and regulations concerned with environmental issues in the US and elsewhere, driven by public demand for knowledge and protection.

DDT was the primary tool used in the first global malaria eradication programme during the 1950s and 1960s. The insecticide is sprayed on the inner walls and ceilings of houses. Malaria has been successfully eliminated from many regions but remains endemic in large parts of the world. DDT remains one of the 12 insecticides — and the only organochlorine compound — currently recommended by the World Health Organization (WHO), and under the Stockholm Convention on Persistent Organic Pollutants, countries may continue to use DDT. Global annual use of DDT for disease vector control is estimated at more than 5 000 tonnes.

It is clear that the social conscience awakened by Rachel Carson 50 years ago gave momentum to a groundswell of actions and interventions that are slowly but steadily making inroads at myriad levels. Chapter 17 of her book, 'The other road' reminds the reader of the opportunities that should have been seized much earlier. With more than 10 % of bird species worldwide now threatened in one way or another, it is clear that we missed early warnings or failed to act on them. Will we continue to miss signposts to 'other roads'? Are our obligations to endure met by our rights to know? As Carson said 50 years ago: 'The choice, after all, is ours to make.'

12 Booster biocide antifoulants: is history repeating itself?

Andrew R. G. Price and James W. Readman

Tributyltin (TBT) was widely used as an effective antifouling agent in paints for ships and boats until the European Community restricted its use in 1989 because of its proven harm to the environment and shellfisheries. Thereafter, booster biocides were introduced to enhance the performance of antifouling paints. They were believed to be less damaging to aquatic life than TBT. Subsequently, however, it has been established that booster biocides can also create significant environmental risks.

This chapter outlines the background to booster biocide use, the early warnings about their potential physiological and ecological impacts on non-target species, and the actions taken in response. The science that set some alarm bells ringing is described, along with lessons that could influence the future of an industry still searching for less environmentally invasive solutions.

Booster biocide antifouling agents threaten a variety of habitats — from coral reefs and seagrass beds to open moorings — within the EU and globally. Their primarily herbicidal properties mean that coral zooxanthellae, phytoplankton and periphyton are particularly vulnerable. Compared to TBT, an antifouling agent with a quite specific action, booster biocides have more broad-spectrum impacts. The wider ecological effect of shifting to booster biocides remain poorly understood but of considerable concern because they may affect the base of marine food chains.

From a toxicological viewpoint, booster biocides do not threaten to have endocrine disrupting properties similar to TBTs. At current environmental concentrations, however, some can damage primary producers and some are persistent. While legislation has been introduced to control their use, the rigour of regulations varies between countries. These geographical disparities need to be addressed, and future biocidal products and novel approaches to antifouling should be better appraised.

For policymakers, the challenge is to protect non-target biological communities from selective change resulting from booster biocide use. Persistence, bioaccumulative and toxic (PBT) criteria can be used to evaluate the relative potential impact from the available biocides, and consequently target appropriate legislation. Nevertheless, lateral thinking, aiming to identify novel materials and strategies to address antifouling, could pay dividends in the future.

13 Ethinyl oestradiol in the aquatic environment

Susan Jobling and Richard Owen

Many decades of research have shown that when released to the environment, a group of hormones known as oestrogens, both synthetic and naturally occurring, can have serious impacts on wildlife. This includes the development of intersex characteristics in male fish, which diminishes fertility and fecundity. Although often sublethal, such impacts may be permanent and irreversible.

This chapter describes the scientific evidence and regulatory debates concerning one of these oestrogens, ethinyloestradiol (EE2), an active ingredient in the birth control pill. First developed in 1938, it is released to the aquatic environment via wastewater treatment plants. Although it is now clear that wildlife species are exposed to and impacted by a cocktail of endocrine disrupting chemicals, there is also reasonable scientific certainty that EE2 plays a significant role, and at vanishingly low levels in the environment.

In 2004 the Environment Agency of England and Wales accepted this, judging the evidence sufficient to warrant consideration of risk management. In 2012, nearly 75 years after its synthesis, the European Commission proposed to regulate EE2 as a EU-wide 'priority substance' under the Water Framework Directive (the primary legislation for protecting and conserving European water bodies). This proposal was subsequently amended, delaying any decision on a regulatory 'environmental quality standard' until at least 2016.

This is in part because control of EE2 will come at a significant price. Complying with proposed regulatory limits in the environment means removing very low (part per trillion) levels of EE2 from wastewater effluents at considerable expense.

Is this a price we are willing to pay? Or will the price of precautionary action be simply too high — a pill too bitter to swallow? To what extent is society, which has enjoyed decades of flexible fertility and will also ultimately pay for the control and management of its unintended consequences, involved in this decision? And what could this mean for the many thousands of other pharmaceuticals that ubiquitously infiltrate our environment and which could have sublethal effects on aquatic animals at similarly low levels?

14 Climate change: science and the precautionary principle

Hartmut Grassl and Bert Metz

The first scientifically credible early warning about the possible dangers of climate change due to carbon dioxide (CO_2) emissions from burning fossil fuels came in 1897. While the basic physical principles of global warming are simple, however, the more detailed science of climate change is exceedingly complicated. Even now, more than a hundred years since the first early warning, many important details of climate change cannot be predicted with certainty. It is therefore unsurprising that the science of climate change and questions about the true value of burning fossil fuels have fostered sustained scientific and political controversy.

When the first volume of *Late lessons from early warnings* was drafted there appeared to be too much legitimate controversy about climate change for the issue to be included. A case study could have led to arguments that distracted attention from the valuable and robust lessons from more established issues such as asbestos, polychlorinated biphenyls (PCBs), chlorofluorocarbons (CFCs) and the ozone-hole, X-rays and acid rain. This decision was taken despite the then widespread acceptance that 'the balance of evidence suggests a discernible human influence on global climate' (*Contribution of Working Group I to the Second Assessment Report of the Intergovernmental Panel on Climate Change,* IPCC, 1995).

Over a decade later and after two more reviews by the Intergovernmental Panel on Climate Change (IPCC) of a much greater volume of climate change science it seemed appropriate to include climate change in this volume, despite some continuing controversy. The evidence that human activities are having a dangerous impact on the climate has strengthened since 1995. By 2007, the IPCC was able to conclude with 'very high confidence that the global net effect of human activities since 1750 has been one of warming'. Given the size and irreversibility (on human time scales) of many of the harmful effects of human-induced climate change, there is an urgent need for action to reduce CO_2 emissions and other greenhouse gases. Some contrarian views persist, however, as the authors illustrate.

This chapter summarises the history of growing knowledge about human-induced climate change and of the main actions, or inactions that accompanied it. Like many other chapters, it reflects the lifelong commitment of both authors to trying to understand and mitigate the effects of human-induced climate change. It concludes with some lessons and insights that are relevant to many other environmental and health issues.

Also included is a panel text describing how the IPCC's approach to assessing uncertainty evolved between its first to its fifth assessment reports.

15 Floods: lessons about early warning systems

Zbigniew W. Kundzewicz

Floods are an increasingly acute problem. Intense precipitation has become more frequent and more intense, growing manmade pressure has increased the magnitude of floods that result from any level of precipitation, and flawed decisions about the location of human infrastructure have increased the flood loss potential.

Unlike most other case studies presented in this report, this chapter focuses on flooding as a phenomenon and the requirements for effective early warning systems, rather than addressing a particular event and the lessons that can be learned.

Flooding cannot be wholly prevented. The occurrence of a flood need not be considered a 'failure' and, conversely, minimisation of losses may constitute a 'success'. There are lessons to be learned from every flood and it is important to use them in preparing for the next flood. Once we accept that no flood protection measures can guarantee complete safety, a general change of paradigm is needed to reduce human vulnerability to floods. The attitude of 'living with floods' and accommodating them in planning seems more sustainable than hopelessly striving to eradicate them.

Flood forecasting and warning systems fail because links in the chain perform poorly or fail completely. A single weak point in a system that otherwise contains excellent components may render the overall system performance unsatisfactory. A successful system requires sufficient integration of components and collaboration and coordination between multiple institutions.

The chapter deals primarily with the challenges of fluvial (river) floods. It is complemented by three short supplementary texts. The first highlights the complex, dynamic and diverse ecosystems of river floodplains, which are often degraded during construction of flood defences. Despite their huge economic value, near-natural floodplains are among the most threatened ecosystems globally.

The second discusses uncertainties in anticipating rainfall patterns and intensity, and their relationship to flood levels during extreme flows. Such uncertainties present challenges for scientists and decision-makers alike.

The third addresses the increasing risks of coastal flooding due to factors such as climate change and sea-level rise, and reviews European experience with precautionary action.

16 Seed-dressing systemic insecticides and honeybees

Laura Maxim and Jeroen van der Sluijs

In 1994 French beekeepers began to report alarming signs. During summer, many honeybees did not return to the hives. Honeybees gathered close together in small groups on the ground or hovered, disoriented, in front of the hive and displayed abnormal foraging behaviour. These signs were accompanied by winter losses.

Evidence pointed to Bayer's seed-dressing systemic insecticide Gaucho®, which contains the active substance imidacloprid. This chapter presents the historical evolution of evidence on the risks of Gaucho® to honeybees in sunflower and maize seed-dressing in France, and analyses the actions in response to the accumulating evidence regarding these risks.

The social processes that ultimately lead to application of the precautionary principle for the ban of Gaucho® in sunflower and maize seed-dressing are described, with a focus on the ways in which scientific findings were used by stakeholders and decision-makers to influence policy during the controversy.

Public scientists were in a difficult position in this case. The results of their work were central to a social debate with high economic and political stakes. In certain cases their work was not judged according to its scientific merit but based on whether or not it supported the positions of some stakeholders. This situation tested the ability and courage of researchers to withstand pressure and continue working on imidacloprid.

Other European countries also suspended neonicotinoid seed-dressing insecticides. Evidence of the toxicity of neonicotinoids present in the dust emitted during sowing of coated seeds supported such decisions. Most important, the French case highlighted the major weaknesses of regulatory risk assessment and marketing authorisation of pesticides, and particularly neonicotinoids. These insights were recently confirmed by work by the European Food Safety Authority.

From this case study eight lessons are drawn about governance of controversies related to chemical risks. The study is followed by two additional texts. A first panel presents Bayer Crop Science's comments on the analysis in this chapter. A second contains the authors' response to the Bayer comments.

17 Ecosystems and managing the dynamics of change

Jacqueline McGlade and Sybille van den Hove

A decade after Rachel Carson's *Silent Spring* was published, describing the toxic legacy of the twentieth century, Annie Dillard in her Pulitzer prize winning book *Pilgrim at Tinker Creek*, opened up a different way of looking at the world. It presaged a twenty first century in which the global economy would be based on a more thorough understanding of nature, its functioning and material wealth. Wholly descriptive, yet increasingly relevant, her book captured the very essence of what this chapter is about: that amongst the observations which routinely help to predict the evolution of the natural world are the seeds of surprise — surprise of the unusual and surprise as a portent of future change. Our systemic failure to anticipate such surprises forms the core of this chapter. A series of case studies from fisheries, forests, savannah and aquatic systems are used to underline how early warnings about changes in these natural systems emerged but were not used.

The chapter highlights how the division of knowledge into political, disciplinary and geographic silos has led to the 'recurring nightmares' of short-term interests outcompeting long-term vision; situations where competition replaces co-operation; fragmentation of values and interest; fragmentation of authority and responsibility; and fragmentation of information and knowledge leading to inadequate solutions or even additional problems. In addition, the lack of institutional fit has often confounded the effectiveness of the stewardship of ecosystem services, and led to unexpected surprises, excessive rent seeking and high transaction costs.

Using counterfactual thinking (i.e. the dependence of *whether, when* and *how* one event occurs on *whether, when* and *how* another event occurs and the possible alteration of events), built around the four interconnected concepts of *planetary boundaries, tipping points, panarchy* and *resilience*, the chapter provides an analytical lens through which to explore why many of the warning signals were not seen. The chapter concludes by suggesting why ecosystems are likely to be even more at risk in the future and why we will need to observe and interpret the dynamics of both nature and institutions ever more closely if we are to avoid sudden irreversible ecological changes.

18 Late lessons from Chernobyl, early warnings from Fukushima

Paul Dorfman, Aleksandra Fucic and Stephen Thomas

The nuclear accident at Fukushima in Japan occurred almost exactly 25 years after the Chernobyl nuclear accident in 1986. Analysis of each provides valuable late and early lessons that could prove helpful to decision-makers and the public as plans are made to meet the energy demands of the coming decades while responding to the growing environmental costs of climate change and the need to ensure energy security in a politically unstable world.

This chapter explores some key aspects of the Chernobyl and Fukushima accidents, the radiation releases, their effects and their implications for any construction of new nuclear plants in Europe. There are also lessons to be learned about nuclear construction costs, liabilities, future investments and risk assessment of foreseeable and unexpected events that affect people and the environment.

Since health consequences may start to arise from the Fukushima accident and be documented over the next 5–40 years, a key lesson to be learned concerns the multifactorial nature of the event. In planning future radiation protection, preventive measures and bio-monitoring of exposed populations, it will be of great importance to integrate the available data on both cancer and non-cancer diseases following overexposure to ionising radiation; adopt a complex approach to interpreting data, considering the impacts of age, gender and geographical dispersion of affected individuals; and integrate the evaluation of latency periods between exposure and disease diagnosis development for each cancer type.

Given the degree of uncertainty and complexity attached to even the most tightly framed and rigorous nuclear risk assessment, attempts to weight the magnitude of accident by the expected probability of occurrence have proven problematic, since these essentially theoretical calculations can only be based on sets of pre-conditioning assumptions. This is not an arcane philosophical point but rather a very practical issue with significant implications for the proper management of nuclear risk. With its failure to plan for the cascade of unexpected beyond design-base accidents, the regulatory emphasis on risk-based probabilistic assessment has proven very limited. An urgent reappraisal of this approach and its real-life application seems overdue.

Whatever one's view of the risks and benefits of nuclear energy, it is clear that the possibility of catastrophic accidents and consequent economic liabilities must be factored into the policy and regulatory decision-making process. In the context of current collective knowledge on nuclear risks, planned pan-European liability regimes will need significant re-evaluation.

19 Hungry for innovation: from GM crops to agroecology

David A. Quist, Jack A. Heinemann, Anne I. Myhr, Iulie Aslaksen and Silvio Funtowicz

Innovation's potential to deliver food security and solve other agriculture-related problems is high on the agenda of virtually all nations. This chapter looks at two different examples of food and agricultural innovation: genetically modified (GM) crops and agroecological methods, which illustrate how different innovation strategies affect future agricultural and social options.

GM crops are well suited to high-input monoculture agricultural systems that are highly productive but largely unsustainable in their reliance on external, non-renewable inputs. Intellectual property rights granted for GM crops often close down, rather than open up further innovation potential, and stifle investment into a broader diversity of innovations allowing a greater distribution of their benefits.

Science-based agroecological methods are participatory in nature and designed to fit within the dynamics underpinning the multifunctional role of agriculture in producing food, enhancing biodiversity and ecoystem services, and providing security to communities. They are better suited to agricultural systems that aim to deliver sustainable food security than high external input approaches. They do, however, require a broader range of incentives and supportive frameworks to succeed. Both approaches raise the issue of the governance of innovation within agriculture and more generally within societies.

The chapter explores the consequences of a 'top-down transfer of technology' approach in addressing the needs of poor farmers. Here innovation is often framed in terms of economic growth in a competitive global economy, a focus that may conflict with efforts to reduce or reverse environmental damage caused by existing models of agriculture, or even deter investment into socially responsible innovation.

Another option explored is a 'bottom-up' approach, using and building upon resources already available: local people, their knowledge, needs, aspirations and indigenous natural resources. The bottom-up approach may also involve the public as a key actor in decisions about the design of food systems, particularly as it relates to food quality, health, and social and environmental sustainability.

Options are presented for how best to answer consumer calls for food quality, sustainability and social equity in a wide sense, while responding to health and environmental concerns and securing livelihoods in local small-scale agriculture. If we fail to address the governance of innovation in food, fibre and fuel production now, then current indications are that we will design agriculture to fail.

20 Invasive alien species: a growing but neglected threat?

Sarah Brunel, Eladio Fernández-Galiano, Piero Genovesi, Vernon H. Heywood, Christoph Kueffer and David M. Richardson

Biological invasions are one of the five major causes of biodiversity loss as global human travel and trade have moved, and continue to move, thousands of species between and across continents. Some species of alien origin have a high probability of unrestrained growth which can ultimately lead to environmental damage.

An alien species — animal, plant or microorganism — is one that has been introduced, as a result of human activity, either accidentally or deliberately, to an area it could not have reached on its own. A common definition of the term 'invasive' focuses on its (negative) impact, while other definitions consider only rate of spread and exclude considerations of impact.

Despite the growing amount of legislation being adopted at the global scale, biological invasions continue to grow at a rapid rate, with no indication yet of any saturation effect. Decision-making in this area is very challenging. The overall complexity of the problem, its interdisciplinarity, the scientific uncertainties and the large number of stakeholders that need to be informed and involved, together demand governance actions that are difficult to see emerging at the regional scale (as in the EU), let alone globally.

It is widely agreed that preventing biological invasions or tackling them at a very early stage is the most efficient and cost-effective approach. Harmless species can be confused with harmful invasive species, however, leading to a waste of resources. Even more seriously, harmful invaders can be mistaken for innocuous species — so-called 'invaders in disguise' — and no appropriate action may be taken to counter the threats they pose.

Even with a very good risk assessment system, new outbreaks of invasive alien species could still occur, necessitating a system of rapid early warning and effective eradication response. The decision on where to draw the line on the acceptable environmental risks versus the introduction of new species or new communities that may carry invasive alien species then becomes a value judgement.

There is lively debate within the scientific community regarding the most appropriate strategies for managing invasive alien species. Governments and institutions charged with making decisions have access to considerable knowledge on the topic, but the lack of rules of interactions between multiple parties regularly thwarts effective decision-making.

21 Mobile phones and brain tumour risk: early warnings, early actions?

Lennart Hardell, Michael Carlberg and David Gee

In 2011 the World Health Organization's International Agency for Research on Cancer (IARC) categorised the radiation fields from mobile phones and other devices that emit similar non-ionizing electromagnetic fields (EMFs), as a Group 2B i.e. 'possible' human carcinogen. Nine years earlier IARC gave the same classification to the magnetic fields from overhead electric power lines.

The IARC decision on mobile phones was principally based on two sets of case-control human studies of possible links between mobile phone use and brain tumours: the IARC Interphone study and the Hardell group studies from Sweden. Both provided complementary and generally mutually supportive results. This chapter gives an account of the studies by these two groups — and others coming to different conclusions — as well as reviews and discussions leading up to the IARC decision in 2011. The chapter also describes how different groups have interpreted the authoritative IARC evaluation very differently.

There are by now several meta-analyses and reviews on mobile phones and brain tumours, which describe the challenges of doing epidemiology on this issue, the methodological limitations of the major studies published so far and the difficulties of interpreting their results.

It has been suggested that national incidence data on brain tumours could be used to qualify or disqualify the association between mobile phones and brain tumours observed in the case-control studies. However, in addition to methodological shortcomings, there might be other factors that influence the overall incidence rate such as changes in exposure to other risk factors for brain tumours that are unknown in descriptive studies. Cancer incidence depends on initiation, promotion and progression of the disease. As the mechanism for radiofrequency electromagnetic fields carcinogenesis is unclear, it supports the view that descriptive data on brain tumour incidence is of limited value.

The chapter points to mobile phone industry inertia in considering the various studies and taking the IARC carcinogenic classification into account and a failings from the media in providing the public with robust and consistent information on potential health risks. The IARC carcinogenic classification also appears not to have had any significant impact on governments' perceptions of their responsibilities to protect public health from this widespread source of radiation.

The benefits of mobile telecommunications are many but such benefits need to be accompanied by consideration of the possibility of widespread harms. Precautionary actions now to reduce head exposures would limit the size and seriousness of any brain tumour risk that may exist. Reducing exposures may also help to reduce the other possible harms that are not considered in this case study.

Evidence is increasing that workers with heavy long-term use of wireless phones who develop glioma or acoustic neuroma should be compensated. The first case in the world was established on 12 October 2012. The Italian Supreme Court affirmed a previous ruling that the Insurance Body for Work (INAIL) must grant worker's compensation to a businessman who had used wireless phones for 12 years and developed a neuroma in the brain.

22 Nanotechnology — early lessons from early warnings

Steffen Foss Hansen, Andrew Maynard, Anders Baun, Joel A. Tickner and Diana M. Bowman

Nanotechnology is the latest in a long series of technologies heralded as ushering in a new era of technology-driven prosperity. Current and future applications of nanotechnology are expected to lead to substantial societal and environmental benefits, increasing economic development and employment, generating better materials at lower environmental costs, and offering new ways to diagnose and treat medical conditions. Nevertheless, as new materials based on nanoscale engineering move from the lab to the marketplace, have we learnt the lessons of past 'wonder technologies' or are we destined to repeat past mistakes?

This chapter first introduces nanotechnology, clarifies the terminology of nanomaterials and describes current uses of these unique materials. Some of the early warning signs of possible adverse impacts of some nanomaterials are summarised, along with regulatory responses of some governments. Inspired by the EEA's first volume of *Late lessons from early warnings*, the chapter looks critically at what lessons can already be learned, notwithstanding nanotechnology's immaturity.

Nanotechnology development has occurred in the absence of clear design rules for chemists and materials developers on how to integrate health, safety and environmental concerns into design. The emerging area of 'green nanotechnology' offers promise for the future with its focus on preventive design. To gain traction, however, it is important that research on the sustainability of materials is funded at levels significant enough to identify early warnings, and that regulatory systems provide incentives for safer and sustainable materials.

Political decision-makers have yet to address many of the shortcomings in legislation, research and development, and limitations in risk assessment, management and governance of nanotechnologies and other emerging technologies. As a result, there remains a developmental environment that hinders the adoption of precautionary yet socially and economically responsive strategies in the field of nanotechnology. If left unresolved, this could hamper society's ability to ensure responsible development of nanotechnologies.

23 Understanding and accounting for the costs of inaction

Mikael Skou Andersen and David Owain Clubb

In political decision-making processes, the burden of proof is often distributed such that policymakers only respond to early warning signals from environmental hazards once the costs of inaction have been estimated.

This chapter revisits some key environmental issues for which estimates of costs of inaction have been carefully developed over many years of research. The aim is to consider the methodological challenges involved in producing estimates that are credible and appropriate rather than present specific estimates for these costs.

The case studies also provide insights into how early warning signals might provide a basis for estimating the costs of inaction, when the science base is less consolidated. For example, the case of nitrates in drinking water illustrates that a precautionary approach to the costs of inaction is quite conceivable. The phase-out of ozone-depleting substances, where early-warning scientists successfully alerted the world to the damaging effects of chlorofluorocarbons (CFCs), provides another important case because additional impacts for global warming actually cause the costs of inaction to be considerably higher than initially believed. This is a reminder that figures for the costs of inaction have often been grossly underestimated.

Finally, in the case of air pollution, making use of different estimates for mortality risk avoidance will help decision-makers to see that there are higher- and lower-bound estimates for the costs of inaction. Even if the lower-bound estimates are perhaps too conservative, with a bias towards health effects, they will in many situations encourage more rather than less abatement effort. Reducing emission loads will also tend to bring relief for the intangible assets of biodiversity and nature.

Making the best use of environmental science and modelling helps to make environmental protection and precaution a priority. Producing cost estimates should not be left to economists alone, but should rather be seen as a starting point for a broader discussion, featuring also the relevant expertise in health, ecology, demography, modelling and science. Well researched estimates, based on interdisciplinary collaboration, can strengthen some of those scattered and diffuse interests, which during the ordinary processes of policy-making have difficulty making their voices heard.

24 Protecting early warners and late victims

Carl Cranor

Many *Late lessons from early warnings* chapters provide examples of early warning scientists who were harassed for bringing inconvenient truths about impending harm to the attention of the public and regulators. There is also some evidence that young scientists are being discouraged from entering controversial fields for fear of such harassment. In addition, where warnings have been ignored and damage has ensued, it has often proven difficult in the past to achieve prompt and fair compensation for the victims. Some ideas for reform, building on some current institutional models are explored here.

This chapter first explores the idea of extending whistleblowing laws to help encourage and protect early-warning scientists and others who identify evidence of impending harm. Complementary measures, such as greater involvement of professional societies and the use of recognition awards, as for example in Germany, could also be helpful.

Next, the chapter explores improved mechanisms for compensating victims of pollution and contamination. The chapter on the Minamata Bay disaster provides an extreme example of long delays in getting adequate compensation for the victims of methylmercury poisoning. It was almost fifty years, between 1956 and 2004, before the victims attained equitable levels of compensation and legal recognition of responsibility. Other case studies illustrate similar examples of long delays in receiving adequate compensation.

Options are examined for providing justice to any future victims of those emerging technologies such as nanotechnology, genetically modified crops and mobile phone use, which currently can provide broad public benefits but potentially at a cost to small groups of victims. The potential for widespread exposure and uncertain science could justify 'no-fault' administrative schemes that provide more efficient and equitable redress in situations where the benefit of scientific doubt would be given to victims. The use of anticipatory assurance bonds to help minimise and meet the costs of future environmental damage from large scale technologies is also explored.

A supplementary panel text describes cases of asbestos and mesothelioma, where the senior courts in the United Kingdom have developed innovative ways of dealing with both joint and several liability, and the foreseeability of subsequent asbestos cancers, after the initial recognition of the respiratory disease, asbestosis. Such legal developments in the field of personal injury could illustrate the future direction of long-tail liability in both environmental damage and personal injury.

25 Why did business not react with precaution to early warnings?

Marc Le Menestrel and Julian Rode

In the past, companies have frequently neglected early warning signals about potential hazards for human health or the environment associated with their products or operations. This chapter reviews and analyses relevant interdisciplinary literature and prominent case studies — in particular those documented in both volumes of *Late lessons from early warnings* — and identifies main factors responsible for the disregard of early warning signals.

The chapter shows how economic motives often drive non-precautionary business decisions. In virtually all reviewed cases it was perceived to be profitable for industries to continue using potentially harmful products or operations. However, decisions are also influenced by a complex mix of epistemological, regulatory, cultural and psychological aspects. For instance, characteristics of the research environment and the regulatory context can provide business actors with opportunities to enter into 'political actions' to deny or even suppress early warning signals. Also, business decision-makers face psychological barriers to awareness and acceptance of the conflicts of values and interests entailed by early warning signals. Cultural business context may further contribute to the denial of conflicts of values.

The chapter concludes with a set of reflections on how to support more precautionary business decision making. A prominent policy response to the conflicting interests of business and society is introducing regulations that attempt to steer business rationality towards internalising external effects. Innovative solutions such as assurance bonding should be considered.

There is a need to better understand and expose why business actors do not respond voluntarily to early warning signals with precautionary actions. Blaming business, in particular with hindsight, tends to be common reaction that may not always be constructive. It often misses the complex or even contradictory set of motives and drivers that business actors face.

Public institutions could support progressive business by analysing and publically disclosing the dilemmas and temptations entailed by early warning signals, for example for different industries and for the specific societal and regulatory context of decisions. Rigorous and explicit exposition of the dilemmas will create further incentives for responsible actors to share and communicate their precautionary responses.

An additional reflection centres on the role of political actions of business actors, in particular those actions aimed at suppressing early warning signals. Regulatory efforts that make the political actions of business more transparent can help to sustain a sound balance of power, thereby maintaining our ability to benefit from early warning signals and reducing the likelihood of health and environmental hazards.

26 Science for precautionary decision-making

Philippe Grandjean

The goals of academic researchers may differ from those of regulatory agencies responsible for protecting the environment. Thus, research must take into account issues such as feasibility, merit and institutional agendas, which may lead to inflexibility and inertia.

A large proportion of academic research on environmental hazards therefore seems to focus on a small number of well studied environmental chemicals, such as metals. Research on environmental hazards should therefore to a greater extent consider poorly known problems, especially the potential hazards about which new information is in particular need.

Misinterpretation may occur when results published in scientific journals are expressed in hedged language. For example, a study that fails to document with statistical significance the presence of a hazard is often said to be negative, and the results may be misinterpreted as evidence that a hazard is absent. Such erroneous conclusions are inspired by science traditions, which demand meticulous and repeated examination before a hypothesis can be said to be substantiated.

For prioritising needs for action, research should instead focus on identifying the possible magnitude of potential hazards. Research is always affected by uncertainties and many of them can blur a real association between an environmental hazard and its adverse effects, thereby resulting in an underestimated risk. Environmental health research therefore needs to address the following question: are we sufficiently confident that this exposure to a potential hazard leads to adverse effects serious enough to initiate transparent and democratic procedures to decide on appropriate intervention?

The choice of research topics must consider societal needs for information on poorly known and potentially dangerous risks. The research should be complementary and extend current knowledge, rather than being repetitive for verification purposes, as required by the traditional science paradigm. Research findings should be openly available and reported so that they inform judgments concerning the possible magnitude of suspected environmental hazards, thereby facilitating precautionary and timely decision-making.

27 More or less precaution?

David Gee

Despite its presence in a growing body of EU and national legislation and case law, the application of the precautionary principle has been strongly opposed by vested interests who perceive short term economic costs from its use. There is also intellectual resistance from scientists who fail to acknowledge that scientific ignorance and uncertainty, are excessively attached to conventional scientific paradigms, and who wait for very high strengths of evidence before accepting causal links between exposure to stressors and harm.

The chapter focuses on some of the key issues that are relevant to a more common understanding of the precautionary principle and to its wider application. These include different and confusing definitions of the precautionary principle and of related concepts such as prevention, risk, uncertainty, variability and ignorance; common myths about the meaning of the precautionary principle; different approaches to the handling of scientific complexity and uncertainty; and the use of different strengths of evidence for different purposes.

The context for applying the precautionary principle also involves considering the 'knowledge to ignorance' ratio for the agent in focus: the precautionary principle is particularly relevant where the ratio of knowledge to ignorance is low, as with emerging technologies.

A working definition of the precautionary principle is presented that aims to overcome some of the difficulties with other definitions, such as their use of triple negatives; a failure to address the context of use of the precautionary principle; no reference to the need for case specific strengths of evidence to justify precaution; and overly narrow interpretations of the pros and cons of action or inaction.

The chapter also points to the need for greater public engagement in the process of framing and decision-making about both upstream innovations and their downstream hazards, including the specification of the 'high level of protection' required by the EU treaty. A precautionary and participatory framework for risk analysis is proposed, along with some 'criteria for action' to complement criteria for causation.

The capacity to foresee and forestall disasters, especially when such action is opposed by powerful economic and political interests, appears to be limited, as the case studies in *Late lesson from early warnings* illustrate. The chapter argues that with more humility in the face of uncertainty, ignorance and complexity, and wider public engagement, societies could heed the lessons of past experience and use the precautionary principle, to anticipate and minimise many future hazards, whilst stimulating innovation. Such an approach would also encourage more participatory risk analysis; more realistic and transparent systems science; and more socially relevant and diverse innovations designed to meet the needs of people and ecosystems.

28 In conclusion

The first volume of *Late lessons from early warnings* highlighted the difficulties of balancing precaution with technological innovation and ended with a call to action for policymakers. How much progress has been made since then?

First, there is growing evidence that precautionary measures do not stifle innovation, but instead can encourage it, in particular when supported by smart regulation or well-designed tax changes. Not only has the body of knowledge become richer since 2001, but also the number of stakeholders involved in decision-making has become larger and more diverse. There has also been increasing attention to communicating scientific uncertainty, especially in the fields of climate change, food safety, and emerging risks.

However, there has been less progress in other areas: for example, many of the political and scientific 'bureaucratic silos' still remain, despite frequent calls for policy integration and inter-departmental coordination. This has led to the unintended destruction of stocks of natural capital in some parts of the world and in other instances, the global spread of technologies, despite warnings of impending hazards. The result has been widespread damage, with most polluters still not paying the full costs of pollution.

Yet, more encouragingly, new transformative approaches are emerging to manage the systemic and interconnected challenges the world faces e.g. economic/financial, climate/energy, ecosystems/food. These relate, inter alia, to the increasing use of digital communications and networking by consumers, citizens and shareholders to demand and foster increased participation, more social responsibility, greater levels of accountability and higher transparency, especially in determining future pathways for energy and food production. There is a greater understanding of the complexity of the environment, of scientific ignorance and uncertainties, the irreversibility of many harmful impacts and on the broader risks to the long term interests of society if political and financial institutions remain unchanged. Also some corporations are fundamentally embracing sustainable development objectives in their business models and activities.

The case studies across both volumes of *Late lessons from early warnings* cover a diverse range of chemical and technological innovations, and highlight a number of systemic problems. These include a lack of institutional and other mechanisms to respond to early warning signals; a lack of ways to correct market failures either caused by misleading market prices or where costs and risks to society and nature are not properly internalised; and the fact that key decisions on innovation pathways are made by those with vested interests and/or by a limited number of people on behalf of many. The insights and lessons drawn from the case histories certainly provide the seeds for some of the answers. They also provide knowledge for a series of key actions that are outlined below.

Of course, many questions remain. For example: how can the precautionary principle be used further to support decision-making in the face of uncertainties and the inevitable surprises that come from complex systems?; how can societies avoid a lack of 'perfect' knowledge being used as a justification for inaction in the face of 'plausible' evidence of serious harm?; how can conflicting interests be balanced during the phases of development and use?; and how can the benefits of products and technologies be more equitably distributed?

Reduce delays between early warnings and actions

The majority of the case studies in *Late lessons from early warnings* Volumes 1 and 2 illustrate that if the precautionary principle had been applied on the basis of early warnings, justified by 'reasonable grounds for concern' many lives would have been saved and much damage to ecosystems avoided. It is therefore very important that large scale emerging technologies, such as biotechnologies, nanotechnologies and information

and communication technologies, apply the precautionary principle based on the experiences and lessons learned from these and other case studies.

Precautionary actions can be seen to stimulate rather than hinder innovation; they certainly do not lead to excessive false alarms. As the analysis in Volume 2 shows, of 88 cases of claimed 'false positives', where hazards were wrongly regulated as potential risks, only four were genuine false alarms. The frequency and scale of harm from the mainly 'false negative' case studies indicate that shifting public policy towards avoiding harm, even at the cost of some false alarms, would seem to be worthwhile, given the asymmetrical costs of being wrong in terms of acting or not acting based on credible early warnings.

However, the speed and scale of today's technological innovations can inhibit timely action. This is often because by the time clear evidence of harm has been established, the technology has been modified, thereby allowing claims of safety to be subsequently re-asserted. Even where the technological change has been marginal, the large, often global, scale of investment can lead to widespread technological lock-in, which is then difficult and expensive to alter.

These features of current technological innovation strengthen the case for taking early warning signals more seriously and acting on lower strengths of evidence than those normally used to reach 'scientific causality'. Most of the historical case studies show that by the time such strong evidence of causality becomes available, the harm to people and ecosystems has become more diverse and widespread than when first identified, and may even have been caused by much lower exposures than those initially considered dangerous.

The case studies have also shown that there are many barriers to precautionary action, including: the short-term nature of most political and financial horizons; the existence of technological monopolies; the conservative nature of the sciences involved, including the separate 'silos' within which they operate; the power of some stakeholders; and the cultural and institutional circumstances of public policymaking that often favour the status quo.

Acknowledge complexity when dealing with multiple effects and thresholds

Increasing scientific knowledge has shown that the causal links between stressors and harm are more complex than was previously thought and this has practical consequences for minimising harm. Much of the harm described in Volumes 1 and 2, such as cancers or species decline, is caused by several co-causal factors acting either independently or together. For example, the reduction of intelligence in children can be linked to lead in petrol, mercury and polychlorinated biphenyls (PCBs) as well as to socio-economic factors; bee colony collapse can be linked to viruses, climate change and nicotinoid pesticides; and climate change itself is caused by many complex and inter-linked chemical and physical processes.

In some cases, such as foetal or fish exposures, it is the timing of the exposure to a stressor that causes the harm, not necessarily the amount; the harm may also be caused or exacerbated by other stressors acting in a particular timed sequence. In other cases, such as radiation and some chemicals such as bisphenol A (BPA), low exposures can be more harmful than high exposures; and in others, such as asbestos with tobacco, and some endocrine disrupting substances, the harmful effects of mixtures can be greater than from each separate stressor. There are also varying susceptibilities to the same stressors in different people, species and ecosystems, depending on pre-existing stress levels, genetics and epigenetics. This variation can lead to differences in thresholds or tipping point exposures, above which harm becomes apparent in some exposed groups or ecosystems but not others. Indeed there are some harmful effects which occur only at the level of the system, such as a bee colony, which cannot be predicted from analysing a single part of the system, such as an individual bee.

Our increased knowledge of complex biological and ecological systems has also revealed that certain harmful substances, such as polychlorinated biphenyls (PCBs) and dichlorodiphenyltrichlorethane (DDT) can move around the world via a range of biogeochemical and physical processes and then accumulate in organisms and ecosystems many thousands of kilometres away.

The practical implications of these observations are threefold. First, it is very difficult to establish very strong evidence that a single substance or stressor 'causes' harm to justify timely actions to avoid harm; in many cases only reasonable evidence of co-causality will be available. Second, a lack of consistency between research results is not a strong reason for dismissing possible causal links: inconsistency is to be expected from complexity. Third, while reducing harmful exposure to one co-causal factor may not necessarily lead to a large reduction in the overall harm caused by many other

factors, in some cases the removal of just one link in the chain of multi-causality could reduce much harm.

A more holistic and multi-disciplinary systems science is needed to analyse and manage the causal complexity of the systems in which we live.

Rethink and enrich environment and health research

Environment and health research overly focuses on well-known rather than unknown hazards at the expense of emerging issues and their potential impacts. For example the ten most well-known substances, such as lead and mercury, account for about half of all articles on chemical substances published in the main environmental journals over the last decade. Over the past decade, public research funding in the European Union on nanotechnology, biotechnology as well as Information and Communications Technology (ICT) is heavily biased towards product development with about 1 % being spent on their potential hazards. A more equal division of funding between known and emerging issues, and between products and their hazards, would enrich science and help avoid future harm to people and ecosystems and to the long term economic success of those technologies.

Funding more holistic systems science would also help achieve a greater integration among the different branches of science and counteract problems such as: peer review predominantly within and not across disciplines; short-term interests outcompeting long-term vision; competition replacing cooperation because of conflicts of interest; contradictions amongst paradigms; fragmentation of values and authority; as well as fragmentation of information and knowledge. These can all lead to inferior solutions and provide increased opportunities for those with vested interests to manufacture doubt.

Scientific methods can also be improved. For example, much higher strengths of evidence are required overall before causality is accepted, compared to the evidence being used to assert safety. The assertion that there is *no evidence of harm* is then often assumed to be *evidence of no harm*, even though the relevant research is missing. Historically there has been an over-reliance on the statistical significance of point estimates compared to confidence limits based on multiple sampling. There has also been a bias towards using models that grossly simplify reality rather than using long-term observations and trend data of biological and ecological systems. These approaches have sometimes led to the production of false positives. More importantly the governance of scientific ignorance and unknown unknowns has been neglected.

Finally, many case studies highlight the problems faced by early warning scientists who have been harassed for their pioneering work, including bans on speaking out or publishing, loss of funding, legal or other threats, and demotion. One obvious conclusion is that scientists in these situations should receive better protection either via an extension of 'whistle blowing' and discrimination laws, or by independent acknowledgement of the value of their work.

Improve the quality and value of risk assessments

The majority of the case studies in *Late lessons from early warnings* indicate that risk assessment approaches need to better embrace the realities of causal and systems complexity (rather than use a narrow conception of 'risk') with the inevitable features of ignorance, indeterminacy and contingency. In a number of case studies, for example BPA, where low doses are more harmful than high doses, or tributyltin antifoulants (TBT) and synthetic oestrogen diethylstilboestrol (DES) where the timing of the dose is what makes it harmful, simplistic assumptions are inadequate. Variability in exposures and varying susceptibilities in populations and species exposed also need to be more realistically factored into risk assessments.

This is equally true for technological risk assessments. As the Fukushima Investigation Committee concluded in 2011:

> '…the accidents present us with crucial lessons on how we should be prepared for 'incidents beyond assumptions'. With its failure to plan for the cascade effects beyond design–base accidents 'the regulatory emphasis on risk based probabilistic risk assessment has proven very limited'.

In other words, narrow risk assessment approaches are now outstripped by the realities which they cannot address, recognise and communicate. Too often this contributes to the effective denial of those risks that do not fit the risk assessment frame. It is therefore urgent that risk assessment practices

be transformed to make them broader-based, more inclusive, transparent and accountable. There should also be more communication on the diversity of scientific views, especially on emerging issues where ignorance and uncertainties are high and genuine differences of scientific interpretations are likely, desirable, and defensible. In this sense, recognising the pedigree of knowledge, i.e. the consistency of views amongst peers and the level of convergence coming from different branches of research, is essential for effective decision making and action to support the wellbeing of people and the environment.

The case studies show that evaluations of evidence in risk assessments can be improved by including a wide range of stakeholders when framing the risks and options agenda; broadening the scope and membership of evaluation committees; increasing the transparency of committee approaches and methods, particularly in identifying uncertainties and ignorance; and ensuring their independence from undue influence through using appropriate funding sources and applying robust policies on conflicts of interest.

Public confidence would be increased if all the evidence used in risk assessments was made publicly accessible and open to independent verification, including data submitted by industries to authorities.

As experiences from mercury, nuclear accidents, leaded petrol, mobile phones, BPA, and bees show, there can be a significant divergence in the evaluations of the same, or very similar, scientific evidence by different risk assessment committees. In such instances, differences in the choice of paradigm, assumptions, criteria for accepting evidence, weights placed on different types of evidence, and how uncertainties were handled, all need to be explained. Risk assessors and decision makers also need to be aware that complexity and uncertainty have sometimes been misused to shift the focus away from precautionary actions by 'manufacturing doubt' and by waiting for 'sound science' approaches that were originally developed by the tobacco industry to delay action.

Foster cooperation between business, government and citizens

Policy formulation should start from a broad concept of technological innovation to include non-technological, social, institutional, organisational and behavioural innovation. In this framework, governments have at least three roles: providing direction by putting in place smart regulations and consistent market signals; ensuring that the distributional consequences of innovations are balanced between risks and rewards across society, fostering a diversity of innovations so that the wider interests of society; and take precedence over narrower interests.

Numerous case studies show that decisions to act without precaution often come from businesses. There are, however, several impediments to businesses acting in a precautionary manner, including a focus on short-term economic value for shareholders alongside psychological factors that lead to a so-called 'ethical blindness' or a 'self-serving bias' whereby people largely interpret ambiguous situations in their own interests. Governments and businesses could collaborate more with citizens on publicly disclosing the potential value conflicts entailed in acting on early warning signals. A culture of transparency can in turn promote positive business attitudes and innovations.

Involving the public can also help in choosing between those innovation pathways to the future; on prioritising relevant public research; on providing data and information in support of monitoring and early warnings; improving risk assessments; on striking appropriate trade-offs between innovations and plausible health and environmental harms; and, making decisions about risk-risk trade-offs.

Correcting market failures using the polluter pays and prevention principles

When evidence of initial harm emerges, the costs should be internalised retroactively into the prices of polluting products, via taxes and charges, in line with the polluter pays principle and emerging practice across the world. The revenues could then be devoted partly to stimulating research into less hazardous alternatives, and partly to reform tax systems by reducing taxes and charges on 'societal goods' like employment.

The pollution taxes/charges would rise or fall in line with new scientific knowledge about increasing/decreasing harm, and this would help to level the playing field for less-polluting alternative products. Tax shifts from employment to pollution and the inefficient use of resources can bring multiple benefits such as increased employment, a stimulus to innovation, a more stable tax base in the light of expected demographic changes, and a more efficient tax collection system.

More broadly, firms and governments need to extend their economic accounting systems to incorporate the full impacts of their activities on people's health and on ecosystems. Governments need to anticipate this in their policies, by providing the right blend of fiscal instruments to both protect the public and ensure that firms internalise the true costs of potential harm.

A number of case studies also demonstrate the long time lags between evidence of harm and the additional injustice and time of forcing victims to pursue their cases through civil compensation claims. Prompt and anticipatory no-fault compensation schemes and assurance bonds, could be set up and financed in advance of potential harm by the industries that are producing novel and large-scale technologies, thereby helping to offset any potential market failure. Such schemes can also be designed to increase the incentives for innovating companies to carry out more *a priori* research into the identification and elimination of hazards.

Governance of innovation and innovation in governance

The *Late lessons from early warnings* reports demonstrate the complexities of developing not only the right kind of science and knowledge but also handling the interactions between the many actors and institutions involved — governments, policymakers, businesses, entrepreneurs, scientists, civil society representatives, citizens and the media.

Alongside many other analyses produced across the world today, the reports also stress the need to act to transform our ways of thinking and of doing, and urgently so in the face of unprecedented global changes, challenges and opportunities. Many lessons have been learnt, yet have not been acted upon. Any calls for action will need to reflect on today's global socio-economic setting and support, among other things, the drive to:

- rebalance the prioritisation of economic and financial capital over social, human and natural capitals through the broader application of the policy principles of precaution, prevention and polluter-pays, and environmental accounting;

- broaden the nature of evidence and public engagement in choices about key innovation pathways by directing scientific efforts more towards dealing with complex, systemic challenges and unknowns and complementing this with professional, lay, local and traditional knowledge; and,

- build greater adaptability and resilience in governance systems to deal with multiple systemic threats and surprises, through strengthening institutional structures and deploying information technologies in support of the concept of responsible information and dialogues.

The governance of innovation will remain at the level of good intentions unless it is translated into innovations in science practices, institutional arrangements and public engagements as well as transformations in prevailing business attitudes, practice and influence. These are the tasks that lie ahead.

In memory of Masazumi Harada, 1935–2012

Masazumi Harada, a physician involved for many years in the study of the mercury poisoning Minamata disease, died in June 2012 of acute myelocytic leukemia at his home in Kumamoto City. He was 77.

Harada conducted medical examinations on the disease's sufferers for the first time in the summer of 1961 in Minamata city in Kumamoto Prefecture while he was a student at Kumamoto University's graduate school.

Shocked by their miserable lives, Harada devoted himself to the study of the disease from that time. Harada published a thesis on congenital Minamata disease in 1964. The work had a significant impact as it disproved the conventional belief at the time that the placenta does not pass poisons. He received an award from the Japanese Society of Psychiatry and Neurology for the thesis in 1965.

He then established the Open Research Center for Minamata Studies at the university in 2005, becoming the center's head. He continued to lead the disease's research from non-medical perspectives as well. Harada visited Brazil, China and native Indian communities in Canada to discover those suspected of suffering from the disease.

Author of many books, Harada wrote 'Minamata Byo' (Minamata Disease), which raised awareness on the issue around the world.

Dr. Masazumi Harada first came to Asubpeeschoseewagong (Grassy Narrows) and Wabaseemoong (White Dog) First Nations in Canada in the early 1970s. Harada's death comes at the end of River Run 2012, five days of actions by members and supporters of Grassy Narrows in Toronto, who are seeking to have Minamata disease recognized in Canada and Ontario. Harada's final report for the Grassy Narrows community was released on 4 June 2012 after 30 years of research, showing mercury deposited in the river by the Dryden paper mill in the 1970s is impacting those who were not yet born when the dumping ceased.

In memory of Poul Harremoës, 1934–2003

Poul Harremoës was a key player in environmental issues in Denmark and internationally for more than 30 years until his death, at 69, in 2003. In that time, those who worked closely with him benefited from a continuous, almost daily flow of excellent ideas for new research projects.

He was a member of the Danish Pollution Council, which prepared the first framework national law on environmental protection and advised on the establishment of a Ministry of Environment from 1971. He was a key participant in numerous settings, including the first Scientific Committee of the European Environment Agency from 1995.

He had a civil engineering degree from the Technical University of Denmark. He specialised early on in geo-technics and constructed dams on the Faroe Islands. While teaching geo-technics he wrote a textbook that was used for more than 40 years. However, he was able to quickly change his research direction and develop new areas of excellence. So, for example, he got a grant to study at Berkeley, California, from where he received a M.Sc. degree in environmental engineering.

In 1972, he became professor in environmental engineering at the Technical University of Denmark where he originally worked with wastewater discharge to the sea and the biological processes of wastewater treatment. He became a world leading scientist in the theories of biofilms for removal of organics and nitrogen from wastewater before turning to sewer design and modelling. In 2000, Poul was awarded the *Heineken prize for Environmental Sciences* for his contributions to the theory of biofilm kinetics in relation to biological waste water treatment and for his successful organisation of the international scientific community in water pollution research and control.

As a result of his work with sewers and storm water he went into the area of risk analysis and the role of the precautionary principle. In a short time he became an international expert in this field and was highly demanded for lectures in all parts of the world. A key outcome of his interest was his contributions as chairman of the editorial team for the first volume of *Late lessons from early warnings* published in 2001.

Part A Lessons from health hazards

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2 The precautionary principle and false alarms — lessons learned

Steffen Foss Hansen and Joel A. Tickner

Most of the cases examined in the *Late lessons from early warnings* reports are 'false negatives' — instances where early warnings existed but no preventive actions were taken. In debates surrounding the precautionary principle it is often claimed that widespread application of the principle will lead to a large number of regulatory false positives — over-regulation of minor risks and regulation of non-existent risks, often due to unwarranted public 'fears'. Understanding and learning from past false positives as well as false negatives is essential for improving decision-making about public health and the environment.

This chapter reviews incidents of 'false positives', where government regulation was undertaken based on precaution but later turned out to be unnecessary. In total 88 cases were identified to be alleged false positives, however, following a detailed analysis most of them turned out to be either real risks, or cases where 'the jury is still out', or unregulated alarms, or risk-risk trade-offs, rather than false positives.

The analysis revealed four regulatory false positives: US swine flu, saccharin, food irradiation, and Southern leaf corn blight. Numerous important lessons can be learned from each, although there are few parallels between them in terms of when and why each risk was falsely believed to be real. This is a lesson in itself: each risk is unique, as is the science and politics behind it and hence a flexible approach is therefore needed, adapted to the nature of the problem. The costs of the false positives identified were mainly economic, although the actions taken to address swine flu in 1976 did lead to some unintended deaths and human suffering, and diverted resources from other potentially serious health risks. Determining the net costs of mistaken regulatory action, however, requires a complete assessment of the impacts of the regulation, including the costs and benefits of using alternative technologies and approaches.

Overall, the analysis shows that fear of false positives is misplaced and should not be a rationale for avoiding precautionary actions where warranted. False positives are few and far between as compared to false negatives and carefully designed precautionary actions can stimulate innovation, even if the risk turns out not to be real or as serious as initially feared. There is a need for new approaches to characterising and preventing complex risks that move debate from the 'problem' sphere to the 'solutions' sphere. By learning from the lessons in this chapter, more effective preventive decisions can be made in the future.

The scarcity of genuine false positives compared to the large number of 'mistaken false positives' could partly be the result of a deliberate strategy in risk communication. Several references and leaked documents have shown that some regulated parties have consciously recruited reputable scientists, media experts and politicians to call on if their products are linked to a possible hazard. Manufacturing doubt, disregarding scientific evidence of risks and claiming over-regulation appear to be a deliberate strategy for some industry groups and think tanks to undermine precautionary decision-making.

In debates surrounding the precautionary principle it is often claimed that widespread application of the principle will lead to a large number of regulatory false positives — over-regulation of minor risks and regulation of non-existent risks, often due to unwarranted public 'fears'. Critics of the precautionary principle argue that this means losing economic, environmental and human health benefits associated with the over-regulated activities (Smith, 1997 and 2000; Within Worldwide, 2000; Bate, 2001; Bergkamp, 2002; Sunstein, 2002; Graham, 2004). The literature is replete with case studies in which researchers claim excessive or unnecessary environmental and health regulation (see for instance Claus and Bolander, 1977; Whelan, 1985 and 1993; Bast et al., 1994; Wildavsky, 1995; Lieberman and Kwon, 1998; Sanera and Shaw, 1999; Bailey, 2002).

The case studies in the first volume of *Late lessons from early warnings* (EEA, 2001) were all false negatives, where early warnings existed but no preventive action was taken. In preparing the first volume, the editorial team queried the existence of 'false positives' and invited industry representatives to submit examples of instances where action was taken on the basis of a precautionary approach that turned out to be unnecessary. No suitable examples emerged and the false positive were therefore not addressed. To address this shortfall, the present chapter contains a thorough review of the issue.

2.1 'False alarms', 'regulatory abuse' and 'regulatory false positives'

The terminology regarding false positives varies. Lieberman and Kwon (1998) call their cases of overreaction 'unfounded health scares', whereas others use terms like 'environmental hoaxes and myths' (Martin, 1990), 'eco-myths' (Bailey, 2002), 'regulatory abuse' (Cohen and Giovanetti, 1999) and 'false alarms' (Mazur, 2004). Each of these researchers uses a different set of criteria — often not clearly outlined — to define when such cases of overreaction have occurred.

Most often, the authors cited above have included any case where concerns were raised over the safety of an activity, and where they deem that these concerns were later shown to be unfounded. The mere fact that concerns were raised does not, however, imply that regulatory measures were taken. The present analysis focuses on the extent to which applying the precautionary principle leads to over-regulation and it is therefore important that regulatory measures were actually taken to mitigate the suspected risk as a result of public and scientific concerns. Clearly, concerns raised by the media or public entities can lead to changes in markets or companies ceasing activities because of concerns over, for example, liability. The present chapter focuses, however, on false positives in terms of government regulation.

Similarly, for a case to be classified as a 'false positive', scientific evidence must exist showing that a perceived risk is actually non-existent and this evidence must be generally accepted in the scientific and regulatory communities. Using the Intergovernmental Panel on Climate Change (IPCC) sliding scale for assessing the state of knowledge on climate change (Moss and Schneider, 2000; Table 2.1), we argue that there should at least be a 'high confidence' (67–95 %) in the scientific evidence indicating no harm before a case can reasonably be claimed to be a false positive. This is consistent with the strength of evidence often sought in regulatory policy before preventive actions are taken, and with the classification systems of international bodies. For example, the International Agency for Research on Cancer requires that strict criteria be applied in concluding that there is no evidence of carcinogenicity as it is often difficult to rule out the possibility of effects.

For the purpose of this analysis, regulatory false positives are defined as:

> 'Cases where (i) regulatory authorities suspected that an activity posed a risk, and acted upon this suspected risk by implementing measures aimed at mitigating this risk, and (ii) that there is at least 'high confidence' in the scientific evidence that later became available indicating that the activity regulated did not pose the risk originally suspected' (Hansen et al., 2007a).

Thus, in the absence of preventive regulatory (mandated) action and high confidence in the scientific evidence about an activity's risk, a case

Table 2.1 IPCC scale for assessing the state of knowledge

95–100 %	Very high confidence
67–95 %	High confidence
33–67 %	Medium confidence
5–33 %	Low confidence
0–5 %	Very low confidence

Source: Moss and Schneider, 2000.

cannot be considered a regulatory false positive. All types of regulatory measures — including bans, labelling requirements and restrictions — fall under the definition of preventive measures. Contrastingly, decisions to study a suspected risk further or non-regulatory actions (e.g. including a substance on a list of chemicals of concern) are not considered regulatory measures for the purposes of this chapter, although some might consider government agency programmes or statements to be *de facto* regulation.

2.2 Identifying regulatory false positives

In order to identify regulatory false positives, we followed a two-step approach.

First, we conducted a detailed literature review to identify examples of regulatory false positives in the environmental and human health fields. The search terms used included 'false positives', 'over-regulation', 'health scares' and 'false alarms'. The review involved detailed literature searches and cross-referencing, and scrutiny of relevant websites. We also interviewed experts from academia, industry, non-governmental organisations and independent think tanks. Based on the review, we compiled a list of 88 case studies that claimed to be regulatory false positives (listed in full in Table 2.3 at the end of this chapter). A limited number of references provided the majority of these cases (Mazur, 2004; Wildavsky, 1995; Lieberman and Kwon, 1998; Milloy, 2001).

In the second part of the study, we analysed the literature on each of these examples to determine whether the case could indeed be considered a regulatory false positive. This was assessed based on the definition of a regulatory false positive elaborated in the previous section and current scientific knowledge. The analysis of the literature on each of the examples was performed as follows:

1. first, scientific opinions and reviews conducted by international consensus panels or bodies such as the World Health Organization (WHO), the United Nations Environment Programme (UNEP), European Commission Scientific Committees, and the IPCC, were consulted;

2. if no recent international reviews were available, we consulted up-to-date, recent reviews conducted by national governmental institutions such as the US Food and Drug Administration (FDA), and national environmental protection agencies such as the US National Academy of Sciences or Britain's Royal Society;

3. in cases where neither international nor national reviews were available, we performed literature reviews of peer-reviewed journals.

When reviewing the cases, emphasis was first placed on whether the conclusions reached in the scientific literature and by the different scientific panels and agencies were in conflict. Differing conclusions by various scientific panels, agencies, and scientists would tend to lead to dismissing the case as a false positive, whereas consistent conclusions would tend to lead to accepting the case. In cases of conflicting conclusions between different scientific panels, agencies and scientists, however, we investigated the scientific literature to identify possible explanations for those differing viewpoints. If a reasonable explanation was identified to support the claim that a case was a false positive and the explanation was found to be scientifically valid by most scientists (some dissenting scientific views were accepted) in the field, the case was accepted as an authentic false positive.

For each case, we investigated what regulatory action had been taken to mitigate the risk in question, when and why, in order to determine whether the action taken could be considered to be unnecessary or disproportionate. In the event that a case was not considered to be a false positive, which occurred frequently, the reason for this was identified.

2.3 Mistaken false positives

Following a detailed analysis of each of the 88 cases, we developed a series of 'categories' of mistaken false positives including: real risks; 'the jury is still out'; unregulated alarms; 'too narrow a definition of risk'; and risk-risk trade-offs. The criteria used to assign cases to each category are set out in Table 2.2, and Hansen et al. (2007a) present additional examples that illustrate the key characteristics of each category.

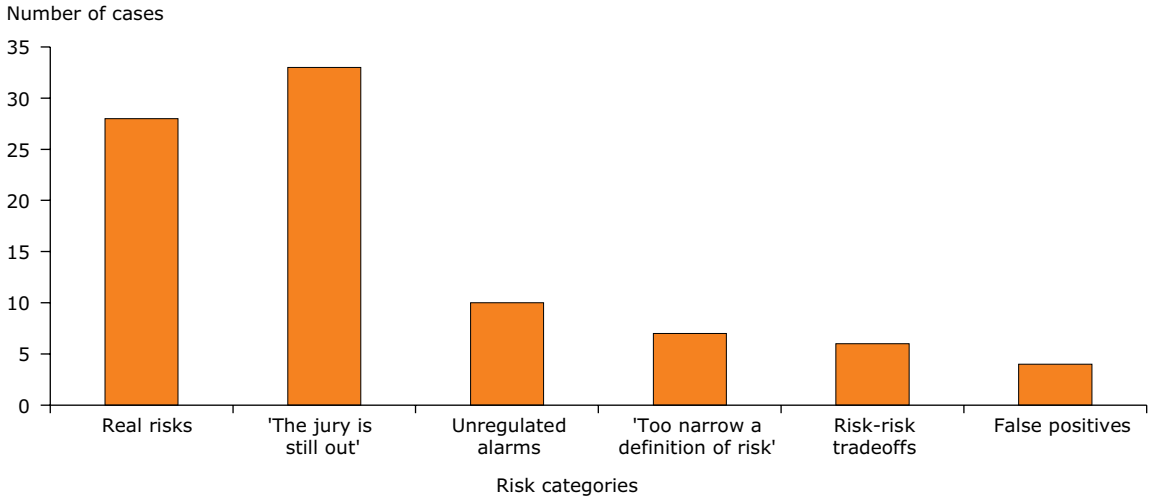
Figure 2.1 presents the distribution of cases in categories of false positives and mistaken false positives.

A detailed written analysis of each case is beyond the scope of this chapter. For a rationale for the categorisation of the cases into false positive and mistaken false positive categories, see Hansen (2004). Below, the categories are summarised.

Table 2.2 Categories of mistaken false positives and criteria for inclusion

	Criterion 1		Criterion 2		Criterion 3	Conclusion
Real risks	Hazard	and	exposure			Not a false positive
'The jury is still out'	Uncertain hazard	or	uncertain exposure	or	disputed evidence	
Unregulated alarms	Alarm raised	and	no action taken			
'Too narrow a definition of risk'	Other hazard	and	exposure			
Risk-risk trade-offs	Target risk	and	countervailing risk	and	action taken	

Figure 2.1 Distribution of 88 proclaimed false positives



2.3.1 Real risks

In about one third of the 88 cases proclaimed to be false positives, scientific evidence is available indicating that the activity in question posed a real risk. In these cases, a lack of regulatory intervention could have (and in some cases has) led to adverse effects on human health or the environment.

An example of such a case is acid rain. When exposed to bright sunshine, human emissions of sulphur dioxide and nitrogen oxides can be converted into sulfate and nitrate molecules. These particles can then interact with water vapour to form sulphuric or nitric acids, which return to Earth in rain, snow or fog. Concern was raised in the 1980s that acid rain might injure human health and the environment but according to Bast et al. (1994) and Wildavsky (1995) acid rain poses little or no threat to forests, crops, human health or lakes in America.

In response to the claims about damage caused by acid rain, the US Congress authorised a ten-year research effort called the National Acid Precipitation Assessment Program (NAPAP) (Bast et al., 1994). NAPAP acts as a coordinating office between six federal agencies including the National Oceanic and Atmospheric Administration (NOAA), the Environmental Protection Agency (EPA), and the National Aeronautics and Space Administration (NASA) (NAPAP, 2011).

In 1996 NAPAP published an integrated assessment of costs, benefits and effectiveness of acid rain controls. NAPAP found that, although most forest ecosystems were not then known to be adversely impacted by acid deposition, sulphur and nitrogen deposition had caused adverse impacts on certain highly sensitive forest ecosystems, especially high-elevation spruce-fir forests in the eastern United States. These adverse effects might develop in more forests if deposition levels were not reduced (NAPAP, 1996). Because acid deposition has had adverse impacts on certain highly sensitive forest ecosystems in the eastern United States, this case is considered a real risk. See Semb (2001) for a discussion of sulphur dioxide and acid rain in the European context.

2.3.2 *'The jury is still out'*

In another third of the 88 cases, there is not a 'high confidence' in the scientific evidence of no harm from the activity in question. These could be categorised as cases for which 'the jury is still out' — instances where the scientific data are uncertain or disputed and no final conclusion has yet been reached.

In these cases, lack of evidence of harm has been misinterpreted as evidence of safety. This may be due to numerous factors, including the length of time the hazard has been studied, clear disagreements in the scientific literature, or limited human studies. For example, for the International Agency for Research on Cancer (IARC) to classify a chemical as 'probably not carcinogenic to humans', there is a need for 'strong evidence that it does not cause cancer in humans'. Only one substance has been listed as such.

An example of a case where 'the jury is still out' is the health risks of mobile phones (see also Chapter 21). Lieberman and Kwon (1998) argue that there is no evidence of serious health effects from routine use of cellular phones. Graham (2004) also mentions cell phones and brain cancer as a scare where qualified scientists did not replicate early studies suggesting danger. Several reviews of the scientific literature have been conducted by both international and national bodies such as the UK's Independent Expert Group on Mobile Phones (IEGMP, 2000), the British Medical Association (BMA, 2001), the Health Council of the Netherlands (2002), the Swedish Radiation Protection Authority's Independent Expert Group on Electromagnetic Fields (2003), the UK's National Radiological Protection Board (NRPB, 2003), Sweden's Research Council for Worklife and Social Science (FAS, 2003), WHO (2004) and the Scientific Committee on Emerging and Newly Identified Health Risks (SCENIHR, 2009). Although most reviews conclude that cellular phones probably do not constitute a health hazard after less than ten years of use, many still advise a 'precautionary approach' and recommend further research into the long-term effects on health because of the prolonged latency period of many chronic diseases (SCENIHR, 2009; WHO, 2010a and 2010b). A recent book compiling the scientific evidence on cell phone health risks (Davis, 2010), found that the there is strong enough evidence on health risks to warrant immediate action to redesign cell phones to make them safer.

According to the IEGMP (2000), the US FDA (cited in US GAO, 2001), the Danish Health Agency (2000), the Royal Society of Canada (RSC, 1999) and SCENIHR (2009), there is not enough information to conclude that cellular phones are without risk after long-term use (more than 10 years), although research to date does not show that mobile phones have adverse effects after short-term use (less than 10 years).

Several factors make it difficult to draw definitive conclusions from existing studies (US GAO, 2001; SCENIHR, 2009). Existing epidemiological studies on the health effects of radiofrequency in general have focused on short-term exposure of the entire body, not long-term exposure to the head. No studies on mobile and cordless phone use among children and adolescents have been completed so far. Additionally, most research has been conducted on the use of analogue phones instead of digital phones, which have become the standard technology. Finally, most research investigates the health effects at different frequencies than those used in mobile phones, and it is not clear how impacts from one frequency on the radiofrequency spectrum relate to other frequencies (US GAO, 2001; SCENIHR, 2009).

Studies on animal and human cells and tissues have shown that radiofrequency emissions can produce measurable responses, although it is not known whether or not these responses are harmful (Bast et al., 1994; RSC, 1999; ICNIRP, 2001). IEGMP (2000) found evidence to suggest that radiofrequency radiation might influence the ion channels and other membrane proteins of neurons in the brain under normal conditions but the significance of such effects for human health is uncertain. According to the US FDA (cited in US GAO, 2001), one type of test known as the micronucleus assay has shown changes in the genetic material, which is a common precursor to cancer. The US FDA therefore calls for additional research into the safety of mobile phones emissions. Numerous national and international research projects have been initiated across the globe to study the health risks (BMA, 2004).

The IARC has an electromagnetic field (EMF) project under way to coordinate and stimulate research and scientific discussion that can provide the basis for its reviews. IARC (2008) has established a series of multinational case-control studies (known as the Interphone study) that will potentially deliver more conclusive data on the possible health effects of mobile phones than previous research. Several studies from the Interphone study have been published (IARC, 2008) and a majority of these have found no association between cellular phone use and the risk of brain cancer. A number of small, long-term

studies did, however, find a slightly increased risk for certain types of brain tumours after long-term use of cellular phones (Lönn et al., 2004 and 2005; Hours et al., 2007; Klaeboe et al., 2007). After pooling data from Nordic countries and the United Kingdom, Lahkola et al. (2007) and Schoemaker et al. (2005) reported finding a significant increased risk of glioma on the side of the head where the tumour developed after at least 10 years of using cellular phones (IARC, 2008). See Chapter 21 on mobile phone use and brain tumour risk for an updated evaluation of this evidence.

There are a number of reasons why this case falls into the category 'the jury is still out'. First, several factors make it hard to evaluate existing epidemiological studies, as previously noted. Second, although the significance for human health is unknown, different effects on cells and tissues have been observed when exposed to radiofrequency radiation. Third, there is a vast amount of research currently under way as a result of lingering scientific concerns and uncertainties.

2.3.3 Unregulated alarms

In a number of cases, a given substance, technology or procedure was proclaimed to be a risk but no regulatory action was ever taken to mitigate it. Concerns could be raised as a result of a scientific study (which later turns out to be a scientific false positive) or public or political concern. Since the cases have not been regulated, they are not considered false positives from a regulatory point of view. Examples of cases that fall into this category include the claimed links between coffee and pancreatic cancer, between fluoridated water and associated health effects, and between the measles-mumps-rubella (MMR) vaccine and autism.

There has been great public concern about the safety of the measles-mumps-rubella (MMR) vaccine since Wakefield et al. (1998) published a small study in *The Lancet* suggesting an association between the vaccine and bowel problems and autism in 12 children. In the study, parents or doctors recalled that the first signs of autism had started within two weeks after the MMR vaccination and the researchers wondered whether these two were connected. They never claimed, however, to have conclusively demonstrated this association (IOM, 2001a). The culprit was suspected to be a vaccine preservative known as thimerosal, which contains mercury (Fields, 2004).

According to Bate (2001), this research made some pressure groups argue that a precautionary approach should be taken and that the vaccines should be withdrawn, which could lead to new disease outbreaks with severe public health consequences. According to Bate (2001) 'Precautionary vaccination propaganda that results in individual and government action harms, and sometimes even kills, children.' Guldberg (2000) calls this case an obvious example of scare-mongering and argues that damage has been done because many parents decided not to take the one-in-a-million chance of a serious reaction to the vaccine. According to Guldberg (2000) this led to falling vaccination rates in the United Kingdom, which could lead to a measles epidemic. Marchant (2003) also mentions the MMR vaccine as a case in which excessive precaution was taken.

Extensive efforts have been made to confirm the findings of Wakefield et al. (1998). A number of small studies have supported the results, whereas a series of large-scale studies have found no association between MMR vaccines and autism (e.g. Taylor et al., 1999; Meldgaard Madsen et al., 2002; DeStefano et al., 2004; Smeeth et al., 2004; Hornig et al., 2008). A number of literature reviews have also been published that have all concluded that the epidemiological evidence does not support the hypothesis of an association between the MMR vaccine and autism. These reviews further conclude that the epidemiological studies that do support an association have significant flaws in their design that limit the validity of their conclusions (CSM, 1999; IOM, 2001a, 2001b and 2004; WHO, 2003a; Parker et al., 2004). In 2004, 10 of the 12 authors of the original article by Wakefield et al. (1998) retracted their support for the findings in the study (Murch et al., 2004).

Despite the public concern about MMR vaccine and actions by many advocacy groups and parents, no regulatory action was ever taken to stop parents from getting their children MMR vaccinated. On the contrary, health agencies all over the world strongly recommended MMR vaccines at the time concerns were raised and still do (NACI, 2003; CDC, 2004; UK Department of Health, 2004; WHO, 2001 and 2003b). Therefore, this case falls into the 'unregulated alarm' category.

It is correct that the controversy about the safety of MMR vaccines led to decreasing numbers of children being vaccinated in the United Kingdom but according to the UK Department of Health (2003) the numbers are increasing again. There has been an outbreak of mumps in England and Wales but the agency has emphasised that this outbreak could not be attributed to the drop in MMR

Photo: © istockphoto/Josef Mohyla

vaccinations caused by fears of a link to autism. The outbreak was actually largely due to young adults that missed out on the MMR programme, which began in 1988 (see Medical News Today, 2004).

2.3.4 'Too narrow a definition of risk'

Some cases proclaimed as false positives focus only on one aspect of the potential risks from a hazard. This can happen, for example, when only the human health effects of a particular hazard are examined and not the known environmental effects. Another example could be claims that a given substance is a false positive because it has been shown not to cause one type of cancer, when there is documented evidence that it increases the risk of other kinds of cancer. Examples of cases in this category include the links between hair dyes and certain cancers, and between second-hand smoke and breast cancer.

Nuclear power is another example, with some authors arguing that precautionary decisions to halt nuclear plant construction were not justified by the risks to those living near plants or the risks of accidents at the plants. For example, Graham (2004) notes that on the basis of precautionary considerations there has been a *de facto* moratorium ([1]) on the construction of new nuclear power plants in the US since the 1979 Three Mile Island incident. As a consequence, he argues that the US has become deeply dependent on fossil fuels for energy and 'now precaution is being invoked as a reason to enact stricter rules on use of fossil fuels'.

Bast et al. (1994) have further argued that the public is overly fearful of nuclear power and has been since the Three Mile Island incident. They further argue that low doses of radiation are not harmful and that nuclear power is a safe and clean technology, although they admit that accidents can happen. More recently, some have argued that nuclear power poses no risk of cancer based on a 2011 UK Committee on Medical Aspects of Radiation in the Environment (COMARE) 30 year study which found no increased risk of leukemia among children in the proximity of nuclear power plants in the United Kingdom (Ross, 2011; COMRE, 2011).

In fact, concerns about at least two other types of issues need to be considered in discussions

([1]) Since the moratorium has only been *de facto*, this case can also be discounted as a regulatory false positive because it constitutes an 'unregulated alarm'.

about risks from nuclear plants: the cost of nuclear-generated electricity and radioactive waste. Before considering them, however, it is worth asking whether the risks to those living near nuclear plants are, indeed, insufficient to justify a precautionary moratorium. There is little doubt, for example, that a major reactor accident could release large amounts of radiation into the environment, as was demonstrated during the nuclear disasters at Chernobyl, Ukraine, in 1986 and more recently at Fukushima, Japan, in 2011. Dispute seems to centre on the likelihood of such an event and there seems to be a significant disagreement between expert and lay perceptions of risk.

In 1975, the Rasmussen report assessed reactor safety in US commercial nuclear power plants. It found that the probability of having an accident like the Three Mile Island is anywhere from 1 in 250 to 1 in 25 000 reactor-years. These estimates did not take (among other factors) the possibility of human errors into consideration. US Nuclear Regulatory Commission data indicate that there is a 50 % chance of another accident occurring equal in size to Three Mile Island or larger (Shrader-Frechette, 1993).

These findings suggest that a precautionary moratorium on plant construction based on concerns about accidents and radiation leaks alone might not have been irrational. As noted, however, other factors played a role, including concerns about financial risks. Orders to construct nuclear plants had begun to decline sharply even before the Three Mile Island accident. By September 1974, 57 of 191 nuclear plants under construction, under licensing review, on order, or announced by utilities had been delayed by a year or more and a few had been cancelled altogether. Fourteen months later, 122 of the 191 projects had been deferred and nine had been cancelled. Between 1975 and 1978, US utilities ordered only 11 nuclear units. Utilities cut back on both coal and nuclear projects, but the blow fell disproportionately on builders of nuclear units because of higher capital costs (Walker, 2004). This was only partly due to public opposition.

The energy crisis of the early seventies sharply and quickly drove up the price of oil and other fuels that utilities purchased to run their plants. This again drained their financial resources. Adding to this, the serious problem of inflation greatly increased the cost of borrowing money for plant construction. An economic slump and increasing unemployment also curtailed demand for electricity, which grew at a substantially slower rate than experts had anticipated (Walker, 2004). As Giere (1991) states 'The accidents at Three Mile Island and Chernobyl dramatised the dangers of nuclear power, but the immediate cause of the demise of the nuclear power industry in the United States has been economic'. Supporting Giere's statement, the costs of nuclear-generated electricity quadrupled in the 1980s alone, and 2001 data from the US Department of Energy show that nuclear fission is more expensive per kilowatt-hour than coal, natural gas, wind, and solar thermal (Shrader-Frechette, 1993). According to Shrader-Frechette (2003) this is just another reason that no new nuclear plant has been ordered since the seventies.

In addition to accidents, radiation leaks and doubts about the financial viability of nuclear power, concerns also focused on the risks associated with radioactive waste produced as a by-product of power generation. During the 1980s radioactive waste doubled and there is still controversy surrounding how to deal with it. Although large-scale nuclear accidents might be rare, several accidents have occurred at nuclear storage facilities causing the death of hundreds of people. Clean-ups will cost hundreds of billions of dollars (Shrader-Frechette, 1993).

The example of nuclear power demonstrates that in assessing whether a decision is based on a false perception of risk, it is essential to examine all the factors motivating that decision. In this case, claims that the US moratorium represents (*de facto*) over-regulation based on disproportionate fears about accidents and radiation leaks do not bear up to scrutiny.

2.3.5 Risk-risk trade-offs

Risk-risk trade-offs can be defined as cases where efforts to combat a 'target risk' of concern unintentionally create 'countervailing risks' (also known as 'side-effects' or 'unintended consequences') (Graham and Wiener, 1995). Addressing risk-risk trade-offs (ensuring that regulatory actions do not create new risks) is an important concern in regulatory policy and several authors have written about this subject (see Tickner and Gouveia-Vigeant, 2005). The situation differs, however, from precautionary over-regulation.

One example of such a case is the use of nitrites in meat preservation. Nitrites have been used to cure meat, such as bacon, ham, hot dogs and other sausages, for several centuries. Besides enhancing

colour and flavour, nitrites inhibit the growth of *Clostridium botulinum* and other toxins. *Clostridium botulinum* causes botulism, a rare but often fatal form of food poisoning (McCutcheon, 1984). Since 1899 there have been only seven outbreaks of botulism poisoning in commercially cured meat products in the US and Canada, resulting in nine deaths. The excellent safety record of cured meat has been largely attributed to the use of nitrites (Pierson and Smoot, 1982).

In the late 1970s there was a discussion about whether or not to ban nitrites in the US. Concerns were raised after scientists found that nitrites react in the body with other food agents to form nitrosamines, which are known carcinogens (IPCS, 1978). Since attempts to discover a single alternative preservative with all the properties of nitrites have been unsuccessful, banning nitrites could result in a risk-risk trade-off between the risk of nitrosamine-induced cancers and increased risk of botulism. This argument was used by the US Food and Drug Administration (FDA) and the US Department of Agriculture (USDA) and as a result nitrites were not banned (Wildavsky, 1995; Lieberman and Kwon, 1998).

Lieberman and Kwon (1998) have described the arguments against nitrites as one of the 'greatest unfounded health scares of recent times' fuelled by application of the precautionary principle. But the fact that a ban on nitrites could itself have created certain risks is not evidence that concerns about nitrites were unfounded. Indeed, the measured response of government and the food industry that ensued looks like smart management of risks, rather than over-regulation.

In 1978 the USDA required that the level of nitrite be reduced and that nitrite be used in combination with sodium ascorbate or erythorbate. Sodium ascorbate (vitamin C) or erythorbate (chemically similar to vitamin C) block or inhibit the formation of nitrosamines from nitrite (Institute of Food Technologists, 1998). The USDA took forceful steps to ensure that bacon was in compliance with the new regulations and began an extensive three-phase monitoring programme. The intent of the programme was not to stop bacon production but rather to produce bacon according to the new requirements. Plants in violation of the requirements were allowed to correct their procedures to reduce nitrosamines, and USDA offered technical assistance to plants with potential problems. The food industry responded by tightening its own quality control and nearly all bacon was free from confirmable levels of nitrosamines within one year of the start of the three-phase monitoring programme (McCutcheon, 1984).

Beyond bacon, the food industry generally made substantial changes to the cured meat manufacturing process. It stopped using sodium nitrate in major meat processes; it reduced the use of nitrite in the processing of cured meats; and it increased the use of ascorbate and erythorbate in the curing process. As a result, the food industry was able to eliminate the addition of nitrite to foods, reducing residual nitrite levels in cured meat products five-fold without compromising antibotulinal effects. Today the average level of residual nitrite is one-fifth of the amount present 20 years ago (Institute of Food Technologists, 1998). Indeed, there is a growing market for non-preserved meats due to concerns about the health implications of nitrites and antibiotics in traditional processed meats with no known safety implications to date.

2.4 Identified false positives

Of 88 cases of alleged over-regulation, only four cases fulfilled the definition of a regulatory false positive (Hansen et al., 2007a). These are the cases of:

- **Southern corn leaf blight:** the US Department of Agriculture decision in 1971 to plant more corn in the mistaken anticipation that Southern corn leaf blight would return and destroy a large part of the harvest (Lawless, 1977; Mazur, 2004; Hansen 2004);
- **saccharin:** the 1977 decision requiring saccharin to be labelled in the US because it was believed to be a human carcinogen;
- **swine flu:** the US Department of Health, Education, and Welfare decision in 1976 to mass immunise the entire American population in the mistaken anticipation of a return of swine flu (US GAO, 1977; Neustadt and Fineberg, 1978);
- **food irradiation impacts on consumer health:** the reluctance of the US Food and Drug Administration to allow food irradiation that could help reduce a large number of food pathogens and increase shelf life (WHO, 1981; 1999; SCF, 2003).

The latter two cases are presented below in greater detail. An in-depth analysis of the first two cases can be found in Hansen (2004). In the discussion that

follows, however, all four cases are referred to in drawing policy relevant lessons for decision-makers.

Each case was analysed in order to understand:

- when and why precautionary regulatory action was taken;
- when and why it was realised that this precautionary action was unnecessary;
- what the resulting cost and benefits were.

These factors are emphasised differently in each of the cases, as each has a unique historical and scientific basis. Literature is very scarce on Southern corn leaf blight, which makes it impossible to analyse and answer all of the questions in depth.

2.5 Swine flu

In late January 1976, twelve soldiers at Fort Dix in New Jersey became sick with an upper respiratory infection. One of the soldiers died after participating in a forced march. The cause of the infection was a new strain of the flu virus dubbed 'swine flu', which was antigenetically similar to the Spanish flu that had caused 40–50 million deaths worldwide in 1918–1919 (US GAO, 1977; Potter, 1998; Reid et al., 1999). Influenza epidemics result in about three to five million cases of severe illness annually and about 250 000 to 500 000 deaths, primarily among the elderly (WHO, 2010c).

Photo: © istockphoto/Sean Locke

US President Ford decided to immunise the entire American population against swine flu, dedicating USD 135 million to the production of vaccines (US GAO, 1977). The immunisation programme suffered a number of setbacks in the implementation phase, however, and only 40 million Americans (out of 200 million) were inoculated. The widespread swine flu outbreak feared by decision-makers never occurred. On this basis, the mass immunisation program appears to have been unnecessary.

2.5.1 Responses to early warnings

The initial outbreak at Fort Dix was taken very seriously by the Center for Disease Control (CDC) and other agencies for a number of reasons. Among them:

- Scientists had observed that when a new strain of the flu emerged, it would typically appear in low levels towards the end of a flu season — just as swine flu did at Fort Dix — and then return in epidemic proportions the following flu season.
- A hypothesis at the time suggested that major flu epidemics took place at regular intervals of eleven years. Because the US had experienced epidemics in 1946, 1957 and 1968, it seemed plausible that a new one would occur in 1977.
- Another theory suggested that virulent flu strains recycled themselves at intervals of sixty or seventy years. Almost sixty years had elapsed since the Spanish flu epidemic of 1918–1919 and it seemed reasonable that the swine flu virus was in the process of re-emerging.
- A new strain of flu virus had never before appeared without it leading to a major epidemic (Boffey, 1976; Colin, 1976; USDHEW, 1976; Neustadt and Fineberg, 1978; Wecht, 1979; Silverstein, 1978; Bernstein, 1985).

Knowing this, government officials held a series of emergency meetings and decided that the CDC should begin preparing to produce large amounts of swine flu antibodies. Special attention was

paid to informing the public to prevent the media portraying the Fort Dix outbreak as a 'gloom and doom' scenario (Neustadt and Fineberg, 1978; Silverstein, 1978).

Little new information on the Fort Dix outbreak was available when the CDC's Advisory Committee on Immunization Practices (ACIP) held its annual meeting in March, 1976 to review the vaccine recommendations for the next flu season. Most of the participants were in favour of recommending mass production of swine flu vaccine and inoculation of the American population as soon as possible.

One member of ACIP suggested producing the vaccine and then stockpiling it until a clearer signal of a flu pandemic emerged. According to the records, he felt that one should always be careful about putting foreign material into the human body, especially when the number of bodies approached 200 million (Neustadt and Fineberg, 1978; Silverstein, 1978). According to the minutes of the meeting, the possibility of stockpiling vaccines was never really discussed. According to some experts (Wecht, 1979), however, the option was discussed by Dr Sencer, Director of the CDC, and a few other committee members during one of the breaks of the meeting. They did not consider the option viable due to the amount of time required to distribute and administer the vaccines. Too many people could get sick and perhaps die in the time it would take for the vaccine to find its way through the delivery pipeline. The basis for not discussing this option openly during the ACIP meeting was later attributed by some to Dr Sencer's eagerness to act immediately (US GAO, 1977; Neustadt and Fineberg, 1978; Silverstein, 1978; Bernstein, 1985).

Based on the ACIP recommendations, Dr Sencer prepared a memorandum presenting the pros and cons of four courses of action:

1. No action: leave it to private drug manufacturers to produce vaccines in response to their estimates of demand, and let consumers make their own decisions on whether to get vaccinated.

2. Minimum response: the federal government would advise the drug industry to produce sufficient vaccine to immunise the general population and would undertake a public awareness programme.

3. Government programme: the federal government would advise vaccine manufacturers to embark on full scale production with the expectation of a federal government purchase of up to 200 million doses. The health authorities would carry out an immunisation programme designed to reach 100 % of the population.

4. Combined approach: the federal government would advise vaccine manufacturers to embark on full-scale production and purchase 200 million doses. However, they would leave it to state health agencies to develop plans for immunisation (USDHEW, 1976).

The memorandum recommended the 'combined approach' for a number of reasons. Previous experiences with widespread flu pandemics in 1957 and 1968 indicated that the vaccine should be produced, distributed and administered as fast as possible. In 1957 the flu outbreak came earlier than expected and only about a quarter of the vaccine doses were administered before massive outbreaks occurred, and ultimately only about half of the doses were administrated. Efforts to contain the flu pandemic of 1968 were hampered by the fact that it was realised too late that a new strain of flu had appeared, rendering vaccines in use ineffective.

A combined approach was considered be the only way to immunise the whole population successfully before the next flu season. Furthermore full public funding was the only means of ensuring the availability of vaccines to all citizens. The cost of approximately USD 135 million would be small in comparison with the human and economic costs of past pandemics (USDHEW, 1976; Wade, 1976; Neustadt and Fineberg, 1978; Dowdle, 1997). The 1957 and 1968 pandemics caused about 45 and 50 million cases of influenza and resulted in the loss of about 70 000 and 33 000 lives, respectively. The total economic cost due to death and disease, health care costs and loss of productivity was USD 7 billion in 1957 and USD 3.9 billion in 1968 (US GAO, 1977; Silverstein, 1978; Bernstein, 1985).

The White House Office of Management and Budget (OMB) prepared a briefing paper for President Ford. It raised three main questions, relating to the probability that swine flu would reappear, the seriousness of the epidemic should it come, and whether the scientific community fully agreed with the recommendation made in Dr Sencer's memorandum (Neustadt and Fineberg, 1978; Silverstein, 1978).

Before announcing his decision on 24 March, President Ford requested a meeting with the nation's top influenza and public health experts. Many of

the scientists at the meeting thought that the vaccine was safe, that there was little to lose and that it was 'better to be safe than sorry' (Neustadt and Fineberg, 1978). Consequently, the experts voted unanimously in favour of proceeding with the immunisation campaign. Immediately after the meeting, President Ford requested Congress to appropriate USD 135 million for producing vaccines to inoculate the entire US population (US GAO, 1977; Neustadt and Fineberg, 1978; Bernstein, 1985). Later the President stated:

> 'I think you ought to gamble on the side of caution. I would rather be ahead of the curve than behind it' (Neustadt and Fineberg, 1978).

Congress approved the funds with little debate, and the final bill was signed some four months after the initial outbreak of swine flu at Fort Dix (Neustadt and Fineberg, 1978; Silverstein, 1978; Reitze, 1986).

There are some indications that the consultation process leading up to President Ford's decision did not give proper attention to alternative options and dissenting opinions. Many of the scientists consulted by President Ford noted that the discussions felt *pro forma* and that President Ford seemed already to have reached a decision (Boffey, 1976; Silverstein, 1978).

There was little doubt that Congress would respond positively to the President's request to appropriate money for producing vaccines in the face of unknown dangers (Silverstein, 1978). However, Bernstein (1985) argues that the hearings in Congress were carefully staged and that dissent was excluded. Only a few voices questioned the programme during hearings in the House of Representatives. For instance consumer advocate Ralph Nader's Health Research Group claimed that everyone was being overly alarmist, and hinted at some sort of federal-scientific plot to waste taxpayers' money. Democratic congressmen Henry Waxman of California and Andrew Maguire of New Jersey also spoke critically, implying that a potential 'rip-off' might be in the making, giving huge profits to the vaccine manufacturers (Silverstein, 1978; Garrett, 1994).

Two studies had also become available, indicating that the swine flu virus was not as virulent as had been feared. In England, Beare and Craig (1976) had injected six volunteers with the virus and only four had developed minor symptoms. They concluded that the virus was not especially contagious, a pandemic was very unlikely, and mass immunisation was unnecessary.

These results were supported by a study in the US on monkeys, which suggested that the virus would cause only a 'mild disease' (Silverstein, 1981; Neustadt and Fineberg, 1978; Edsall, 1979). According to *Medical World News* (1977), the results of the British study were known to the programme scientists, and according to Dr Sencer the programme was reconsidered three times: after the field trials; just before the President's push for money; and finally when the programme was suspended (Neustadt and Fineberg, 1978).

2.5.2 *Evidence of a false positive*

Although the mass immunization programme got off to a good start, the programme soon ran into a series of setbacks that delayed the inoculation process. Eventually, concerns over a possible link between the swine flu vaccination and an outbreak of a rare neurological disease, Guillain-Barré Syndrome (GBS), led the CDC to suspend the programme after only a fraction of the vaccine had been administered. By mid-December 1976, the CDC had received reports of 107 cases of GBS, including six deaths. The evidence indicated that the incidence of the disease was higher in the part of the population that had received the swine flu vaccine (one case in 100 000–200 000) compared to those who had not (one case in more than a million). An option was left open to resume immunisation if the swine flu pandemic in fact occurred in the US but swine flu did not reappear anywhere in the world during the winter of 1976–1977. The media's verdict on the swine flu immunisation programme was harsh, and allegations of incompetence and mismanagement of public funds were common (Neustadt and Fineberg, 1978; Silverstein, 1978; Dowdle, 1997; Reitze, 1986).

2.5.3 *Costs and benefits*

Besides the non-monetary costs in life and personal injuries due to the vaccine's side effects, the US Department of Health, Education and Welfare spent over USD 100 million on the mass immunisation programme, and state and local agencies are estimated to have spent USD 24 million (US GAO, 1977; Silverstein, 1978). In addition to these direct costs, the federal government had to pay settlements and legal fees related to the over 4 100 lawsuits that followed in the wake of the immunisation programme. Most of these lawsuits either alleged that the swine flu vaccine had caused GBS, or that it was responsible for various other illnesses including rheumatoid arthritis and multiple

sclerosis. The indemnities paid by the government totalled USD 83 million which, when added to the administrative and legal costs associated with the law suits, probably equalled the USD 100 million spent directly on the immunisation programme (Kurland et al., 1984; Reitze, 1986; Christoffel and Teret, 1991).

On a positive note, much was learned about the preparation, standardisation and administration of vaccines, as well as adverse reactions, whole and split vaccines and the adjustment of dosage according to age. Besides these benefits, some of the more puzzling findings from previous vaccine studies were clarified (Dowdle, 1997). After the events of 1976, research was initiated on the causes and possible treatment of GBS in medical institutions throughout the US (Silverstein, 1978), and a nationwide disease surveillance system was established (Neustadt and Fineberg, 1978).

2.6 Food irradiation and consumer health

Food irradiation was first applied on strawberries in Sweden in 1916 and the first patents were taken on this technology in 1921 in the US. Three kinds of radiation are typically used to sterilise food: gamma rays, X-rays and electron beams. And there are three main purposes for irradiating food: killing insects and other pests in grain, fruit, and spices; delaying ripening of fruit and vegetables; and reducing bacterial contamination of meat, chicken, seafood and spices (SOU, 1983; MAFF, 1986; WHO, 1981, 1999; SCF, 2003).

Gamma irradiation uses radioactive elements, whereas X-rays and electronic beams use ordinary electricity. However, all three perform a similar function (Environmental Nutrition, 2000; Pothisiri et al., 1991; WHO, 1993). Over the years, the FDA has issued a number of clearances to use this technology on food but in the late 1960s concerns were raised about the safety of food irradiation and no additional approvals were given for the next twenty years. At the beginning of the 1980s, the FDA authorised irradiation for several different kinds of foods, despite consumer reluctance to buy irradiated food (Meeker-Lowry and Ferrara, 1996; Adams, 2000). Consumer resistance is seen by many as the main reason why food irradiation is not widely applied (Thorne et al., 1991).

The failure of regulatory agencies to approve and accept food irradiation, despite evidence of its safety for consumers, constitutes a false positive. Similar evidence of safety was not identified for either the potential risks to worker health and safety from irradiating food, or the potential increased threat of terrorism that could follow from implementing large-scale food irradiation. Since these concerns cannot be ruled out, the perspective of this case is limited to consumer health.

2.6.1 Responses to early warnings

Serious progress in developing food irradiation technology first began in the 1950s when President Eisenhower announced his 'Atoms for Peace' programme, and extensive research and funding went into food irradiation from the US Department of Defence. Irradiation was approved for use in inhibiting potato sprouting and disinfecting wheat in 1963. Irradiation of can-packed bacon was approved in 1963 but this permission was subsequently withdrawn in 1968, after a review of the research found adverse effects in animals fed irradiated food, such as fewer surviving offspring (Webb et al., 1987).

2.6.2 Evidence of a false positive

Several international and national committees have evaluated the safety and 'wholesomeness' of food irradiation since the beginning of the 1980s, and all have concluded that irradiated foods are safe for consumers (SOU, 1983; MAFF, 1986; WHO, 1981, 1999; SCF, 1998, 2003; US FDA, 1986; NFA, 1986). However, this has not led to a general acceptance of food irradiation, and a variety of concerns have been raised through the years.

One of these concerns is about so-called radiolytic products, which form in irradiated food. Some of these radiolytic products are unique for irradiation (SOU, 1983; US FDA, 1986). Opponents of food irradiation argue that some of these chemical changes are known to be mutagenic and carcinogenic, and that free radicals — believed to be cancer promoters — are produced during irradiation (Webb et al., 1987; Public Citizen and Grace, 2002; Epstein, 2002).

Numerous toxicity studies have been performed on a range of animals, using a wide variety of different kinds of irradiated food, and examining different doses and endpoints. According to the World Health Organization, these studies have not provided evidence of harmful effects (WHO, 1981, 1994 and 1999). A number of highly controversial studies have indicated changes in the number

of polyploid cells in rats, monkeys and even malnourished Indian children fed freshly irradiated wheat (US FDA, 1986; WHO, 1994; Thayer, 1990; Vijayalaxmi and Rao, 1976; Bhaskaram and Sadasivan, 1975; Vijaylaxmi, 1975 and 1978). The WHO (1994) states, however, that 'No effects were seen showing any consistent pattern or trend, and the studies were overwhelmingly negative indicating that the consumption of irradiated food … had no toxicological effect'.

The WHO (1981, 1994 and 1999) and a British Government Advisory Committee on Irradiated and Novel Foods (MAFF, 1986) concluded that virtually all the radiolytic products found in both low- and high-dose irradiated food were either naturally present in food or produced in thermally processed food. In the US, radiation doses of up to 1 kilogray (kGy) have been approved on the basis that the concentration of radiolytic products is too small to be of toxicological significance (US FDA, 1986).

Others have argued, however, that irradiated food has never been rigorously tested (Bloomfield and Webb, 1990). It was originally thought that the radiolytic compounds could and should be tested according to the accepted protocols for food additives. This would require, however, that all of the chemicals be identified, isolated and fed separately to laboratory animals. Because of the difficulties of isolating and purifying the numerous radiolytic products, this approach is simply impossible (Bloomfield and Webb, 1990; WHO, 1994). Attempts to apply a safety margin by giving animals food irradiated at high radiation doses were also unsuccessful because the animals simply refused to eat the unpalatable food (US FDA, 1986; Bloomfield and Webb, 1990). Because of these problems testing has been done without safety margins, which may miss underlying or long-term safety hazards, according to Webb et al. (1987).

Concerns have also been raised that food irradiation could benefit irradiation-resistant bacteria, which would then grow exponentially after the food has been irradiated. It has been argued that the consequences of this are unknown (Murray, 1990; Tritsch, 2000). However, the WHO (1981, 1994 and 1999), MAFF (1986) and the Scientific Committee on Food (SCF) (2003) have all found no evidence of selective destruction and potential development of mutations. On the contrary both the WHO (1994) and the SCF (2003) state that irradiation has been found to cause loss of virulence and infectivity, as mutants are usually less competitive and less adapted.

Discussion about the safety of food irradiation has focused in particular on the chemical class of cyclobutanones and the question of whether or not they are carcinogens (Public Citizen and Grace, 2002; Epstein, 2002). Cyclobutanones are created only when fat-containing food is radiated (Delincée and Pool-Zobel, 1998; Delincée et al., 2002). Reports by both the FDA and the WHO have been criticised heavily for ignoring the issue of cyclobutanones (Public Citizen and Grace, 2002; Epstein, 2002). Concern was originally raised after studies by Delincée and Pool-Zobel (1999) and Delincée et al. (1999) found that 2-Dodecylcyclobutanone (DCB) was genotoxic. The identity and purity of the compound had not been verified prior to the studies, however, which the authors argue cast doubts on the results originally obtained (Delincée and Pool-Zobel, 1998).

A further concern relates to reducing the nutritional value of foods. Irradiation treatment does not significantly alter the nutrient value and digestibility of fatty acids and macronutrients, such as proteins, fats and carbohydrates (MAFF, 1986; WHO, 1981, 1999; Bloomfield and Webb, 1990) but loss of micronutrients does increase with radiation doses. The rate of loss differs substantially depending on the food and nutrients. Therefore these losses must be assessed for each food and for each vitamin specifically. According to the WHO (1981), thiamine (B1) is the only vitamin that should be considered in terms of dietary intake because it is radiation sensitive and the main sources of thiamine in the diet (e.g. pork) are candidates for high-dose irradiation.

In 1981, the World Health Organization (WHO) conducted a review of the studies performed with doses below 10 kGy and found that irradiated food has been conclusively demonstrated to be safe from the standpoint of toxicological, nutritional or microbiological risks to human health. This document has later been described as the culmination and turning point in the scientific evaluation of the safety of irradiated foods (WHO, 1993; 1994; Urbain, 1993). Following this report, the FDA began a systematic review of the over 400 toxicological studies on mice, rats, dogs, pigs and monkeys available up to 1982. Only five studies were considered to have been properly conducted in accordance with 1980 toxicological standards and were able to stand alone in support of safety (US FDA, 1986; WHO, 1994). Despite several years of consumer reluctance to eat irradiated food, the FDA decided to allow irradiation of spices and seasonings in 1983 while requiring that irradiated whole foods be labelled

as such. Since then the FDA has further allowed irradiation of fruits, vegetables, pork, poultry, red meat and eggs (Meeker-Lowry and Ferrara, 1996; Webb et al., 1987; US FDA, 1997; USDA, 1999a, 1999b; Epstein and Hauter, 2001).

2.6.3 Costs and benefits

Complete estimates of cost and benefits of irradiated food are not available. The costs of food-borne diseases in health and economic terms, and the potential role of food irradiation in reducing those costs, are not well documented (WHO, 1993). Robert and Murrell (1993) estimated that the economic losses in the US from food-borne pathogenic diseases are up to USD 5.3 billion annually. A number of factors affect these cost estimates, however, such as the number of estimated cases and estimated deaths, the severity of the illness and the type of food-borne disease (Todd, 1993). Cost-benefit estimates done by the US Department of Agriculture indicate that the benefits would be likely to exceed costs by a ratio of 2.2–2.8 to 1 and that the irradiation of just 10 % of poultry production would produce annual savings in the US of up to USD 50 million (WHO, 1993).

Several cost-benefit analyses have assessed the feasibility of using irradiation in developing countries. Most have indicated large potential benefits, especially with regard to increased shelf life and reduced post-harvest losses (Grünewald, 1973; Al-Bachir et al., 1993; Kahn, 1993; Moretti, 1993; Neketsia-Tabire et al., 1993). A number of challenges would have to be addressed, however, before developing countries can benefit from food irradiation. For the technology to be used efficiently requires, for instance, that the necessary infrastructure be established (WHO, 1993; Hackwood, 1991).

One of the frequently cited benefits of food irradiation is that it reduces the use of chemicals, for example use of ethylene dibromide in controlling insects and mould infestation in grain (WHO, 1993; Grünewald, 1973; Piccioni, 1987). The plausibility of this argument is, however, unclear (Webb et al., 1987; EC, 2002a and 2002b; Piccioni, 1987).

Nestlé (2007) has voiced concerns that extensive irradiation could reduce attention to the sources of pathogenic contamination of food and primary prevention. On the other hand, it could be argued that public reluctance to accept food irradiation may actually focus greater attention on improved sanitation in manufacturing and food preparation. It is unclear, however, whether or not this has been the case.

2.7 Discussion

This chapter aims to identify false positives and investigate lessons that could be learned to improve future decision-making — to minimise both false positives and false negatives. In this final section, we discuss the results of our analysis, focusing on:

1. when and why precautionary regulatory action was taken;
2. when and why it was realised that this precautionary action was unnecessary;
3. the resulting cost and benefits.

Finally, we discuss what lessons can be learned about false positives, why we were only able to identify four false positives, and the policy implications of our analysis.

2.7.1 False positives and early warnings

There are few parallels between the four cases in terms of when and why each perceived risk was falsely believed to be real. This is a lesson in itself: each risk is unique, as is the science and politics behind it. A flexible approach to science and policy is therefore needed, adapted to the nature of the problem.

In the swine flu case, concern was mainly raised because an 'early warning' of an outbreak fitted perfectly into three widely held theories about influenza cycles. Perhaps too much faith was placed on the ability of science to foresee the impending outbreak in this case. Even with hindsight, however, it is not at all obvious that the decision to mass immunise the American population was the wrong decision or an over-reaction considering the scientific understanding at the time and the stakes involved. Much contemporary scientific knowledge indicated that swine flu could return and had it done so it could potentially have killed millions. Even with the benefit of current knowledge, the science behind predicting flu epidemics remains very uncertain. One lesson from this case could be the need to be open to dissenting opinions and to discuss their validity before making decisions. Swine flu did not return and this was recognised almost immediately after the flu season, reducing the negative impact of this false positive.

In the case of saccharin, concern was triggered by new scientific knowledge indicating that saccharin causes bladder cancer in rats. There is now a general

scientific consensus that saccharin does not have the same effect on humans, although some minority opinions still exist. While it proved unnecessary, it would be wrong to say that the decision to label saccharin as a cause of cancer in laboratory animals was unjustified at the time preventive action was taken. For instance there is no way decision-makers could have known that rats would be the only species in which saccharin causes bladder cancer. Nor could they have known that scientific evidence would emerge indicating that the mechanisms by which it operates in rats appear to be irrelevant in humans. Only the often slow evolution of our scientific understanding gave decision-makers reasons to eliminate the labelling requirements for saccharin.

In both of these cases, it was virtually impossible for scientists, regulatory agencies or decision-makers to know or foresee that the potential risk was not real. The mechanism by which saccharin causes cancer in rats is so specific to this one laboratory animal that no one could have known that it would be irrelevant for humans; even today these mechanisms are disputed. Similarly, no one could know whether the swine flu would reappear or was smouldering in sub-clinical form in the public and would return in epidemic proportions when the flu season began.

The situation was similar with respect to Southern corn leaf blight (SCLB). In that case, the USDA correctly anticipated that the SCLB would return but could not have anticipated that it would not have the same devastating effect as the year before, probably due to a change in weather conditions.

Food irradiation stands out because the publication of a WHO review of existing literature in 1981 created a general consensus regarding the safety of the technology. Even before that, the WHO and others had endorsed and used food irradiation and there had been general consensus about its safety for some time. Nevertheless, the decision to withdraw permission to irradiate can-packed bacon seems completely reasonable in view of the fact that studies had found adverse effects in animals fed irradiated food. At that time there was a serious need for scientific studies investigating the safety of food irradiation.

It is also noteworthy that the false positive of food irradiation had little impact on consumers because alternatives were available to achieve the same outcome, such as improved sanitation in the manufacturing processes and good hygiene. Hence it seems that the availability of alternatives can minimise the total impact of a false positive.

2.7.2 The costs of false positives

The costs of the false positives identified were mainly economic, although the actions taken to address swine flu did lead to some unintended deaths and human suffering, and diverted resources from other potentially serious health risks. Clearly, however, determining the **net costs** of mistaken regulatory action requires a complete assessment of the positive and negative impacts of the regulation, including the costs and benefits of using alternative technologies and approaches.

The case of irradiation illustrates this point. There is no doubt that society could benefit substantially from preventing the numbers of food-borne illnesses but it is not obvious that food irradiation is the right answer. An alternative could be improving animal welfare to reduce pathogenic contamination, improving sanitation and conditions in manufacturing processes, and good hygiene (which manufacturers and governments should already be enforcing). Indeed, food irradiation provides an obvious opportunity to cover bad practices. Poor hygiene practices in food production have been widely documented (Webb et al., 1987; Bloomfield and Webb, 1990; Epstein and Hauter, 2001). And since existing regulations and requirements should guarantee that the public receives safe food even without the use of irradiation, the public would have no immediate benefit from food irradiation but would suffer the adverse health impacts if any existed (Tritsch, 2000; Begley and Roberts, 2002). Addressing the root causes of pathogenic contamination in food supply would probably lead to more sustainable prevention actions.

2.7.3 The precautionary principle, science and technological innovation

Opponents of the precautionary principle often argue that the principle stifles technological innovation (e.g. Wildavsky, 1995; Mazur, 2004). It appears, however, that the four false positives identified actually sparked innovation within industry and within government.

Innovation experts have noted that regulation may result in technological innovation because stringent regulations indirectly cause dramatic changes in technology and often allow new firms or entrants, thereby displacing dominant technologies (Ashford et al., 1985; Ashford, 1993; Porter, 1991). This phenomenon can be observed in the case of saccharin, whose existence was a major deterrent to

the development of other, more costly non-caloric sweeteners.

The mistaken actions to address swine flu likewise resulted in an unprecedented nationwide disease surveillance programme and the government learned how to mobilise resources quickly in the face of an apparent public health threat (Reitze, 1986). Such knowledge is particularly important in the context of new concerns related to bioterrorism.

In all the four cases, regulatory action indirectly sparked a large amount of research in previously unexplored fields of science. Saccharin and food irradiation are often mentioned as being some of the most tested hazards ever, and the swine flu case generated new and far better understanding of GBS — a disease that was previously little understood. The SCLB case sparked research concerning gene diversity and gene vulnerability.

Hrudey and Leiss (2003) state that:

> 'If a hazard is important enough to invoke precaution as a justification to prioritise action, it must also be important enough to understand better'.

This definitely seems to have been the case in these four cases.

2.7.4 Why so few false positives?

Given the vast amount of literature raising concerns that precautionary and preventive policies lead to false positives, it is surprising that so few were identified.

Clearly, interpreting scientific literature includes some level of subjectivity. Employing the definitions used in this study, different researchers might come up with slightly different categorisations of the 88 cases reviewed and the number of false positives could differ from analysis to analysis. But other studies might also adopt different definitions. For example, some analysts might argue that the concept of a false positive includes situations where an agency conducts a high-profile investigation, makes a public statement or runs an advocacy campaign and this results in concerns that lead to unnecessary actions.

Analysts may also vary in their interpretation of the difference between categories such as 'the jury is still out' and 'false positive', as well as in terms of the types of evidence they review and how they value uncertainties. The science informs decisions about whether a risk is real or not (does it cross some threshold of 'acceptable risk'?). But these are partly policy judgements, based on considerations such as levels of uncertainty and the economic consequences of acting or not acting.

Similarly, the question of whether a regulation is excessive to address a certain risk is a controversial and highly subjective question and difficult to characterise. For example, in current science-policy debates some scientists argue that precautionary regulation of phthalates in children's products or bisphenol-A (BPA) in items that come into contact with food may represent 'over-regulation' based on current understanding. Assessing politically defined 'safe' levels of exposure is incredibly complex given the subtle nature of many product-based exposures, lack of understanding of cumulative and interactive exposures, limited information about exposure pathways and human epidemiological data, and inadequate understanding about critical windows of vulnerability. Given significant uncertainties in such cases, a qualitative synthesis that considers the totality of the evidence of potential exposure (from body burden studies), hazard information, and information on potentially safer alternatives, may be the soundest approach to science for addressing complex risks and sufficient to spur innovation in safer materials (Sarewitz, et al., 2010).

To address concerns about subjectivity, we have attempted in this chapter to make our categorisation and evaluation as transparent as possible so that other researchers can repeat the analysis with these or other cases. Given the large number of cases examined, however, we feel confident in our core findings: that many of the cases identified as false positives are in fact 'mistaken false positives' and that the number of genuine regulatory false positives identified in the literature is small. Cox (2007) and Hansen et al. (2007b) discuss this issue in more detail. In examining the regulatory landscape, the analysis also suggests that common concerns about over-regulation are not justified, based on empirical evidence. As such, a more nuanced approach to policy analysis is needed.

The scarcity of genuine false positives compared to the large number of 'mistaken false positives' could also be the result of a deliberate strategy in risk communication. Several references and leaked documents (e.g. Martin, 2003) have shown that some regulated parties have consciously recruited reputable scientists, media experts and politicians to call on if their products are linked to a possible hazard. As an automatic response or first barrier of defence, these experts are then sent to different news

sources to denounce any risk or to manufacture uncertainty about the risk, regardless of whether the risk is real or not (Barnes and Bero, 1998; Rampton and Stauber, 2001; Michaels, 2005). Manufacturing doubt, disregarding scientific evidence of risks and claiming over-regulation appear to be a deliberate strategy for some industry groups and think tanks to undermine precautionary decision-making.

A complementary explanation could be that current decision-making processes in public health and environmental regulation have focused on minimising false positives, which increases the probability of false negatives. Shrader-Frechette (1991) argues that this preference for false negatives arises because it appears to be more consistent with scientific practice. Furthermore, many risk assessments and impact analyses are conducted by those with a vested interest in a particular technology. In such cases, Shrader-Frechette argues that assessors typically underestimate risk probabilities at least in part because it is difficult to identify all hazards and because unidentified risks are usually assumed to be zero.

According to Ozonoff and Boden (1987), institutional reasons also explain why agencies tend to favour not responding to identified effects. First, acknowledging an effect means that the public would expect the agency to do something and might even accuse the agency of not doing enough about the situation in the first place. Second, the solutions to the problem often conflict with other interests, such as economic development. Third, agencies know that affected industries may challenge the agency, accusing it of creating hysteria or negatively impacting business (Ozonoff and Boden, 1987).

In addition to the scientific and political reasons limiting false positives, several aspects of legal and regulatory decision-making in the US and EU, such as judicial review or cost-benefit analysis, greatly influence the steps that agencies must fulfil before taking precautionary actions and how much precaution can be applied. The slow pace of the regulatory process often precludes swift precautionary action on uncertain hazards, unless they pose imminent risks of severe harm. The pace is determined both by regulatory requirements and, especially in the US, by court interpretations of federal policies. The regulatory process has become more rigid and burdensome since the 1970s, leading to the 'ossification' of rule-making (McGarity, 1990).

While avoiding false positives is important, we believe that too little attention is being paid to avoiding false negatives in regulatory decision-making. Decision-makers often worry about taking too much precaution but seem to lack similar concerns about not taking enough. This tendency has developed despite evidence that the costs of not taking precautionary action are substantial — both economically and socially (e.g. EEA, 2001) and despite the many identified benefits of preventive regulation with regards to health, safety and the environment (Ashford, 1993; Ackerman and Heinzerling, 2004). Furthermore, compared to false negatives, the impact of false positives may be more short term (over-regulation can be quickly caught) and affect a relatively small number of actors.

A decision to act on limited knowledge about a hazard may ultimately turn out to have been due to a false positive. But if it spurs innovations, stimulates new economic forces, and raises awareness about sustainability then it may still be judged to have been worthwhile. As a result, there is a need to develop more nuanced policy analysis methods that give equal weight to avoiding both false negatives and false positives. Combining a more precautionary approach with proper assessment of impacts and alternatives in a more flexible management process could minimise the number of false positives and negatives and maximise society's benefits from false positives.

2.7.5 Lessons learned

Understanding and learning from past mistakes is essential for improving decision-making about public health and the environment. Numerous important lessons can be learned from each of the false positives identified. Some are specific to the case and cannot easily be transferred to other risk situations. The focus here is on experience that is applicable to other cases and can be generalised. These lessons are important to avoid both false positives and false negatives.

Lesson 1: the cases of swine flu and saccharin show how important it is to **be open and honest about disagreement and not suggest that there is consensus when there is not**. Even though scientists and others might think that reaching consensus is a goal in itself, disagreement can help provide the decision-maker with a broad picture of alternative explanations of the science, what is at stake and which options and alternatives are available before making a decision.

Lesson 2: following on the previous lesson, it is important to **be transparent about what is known or not known and about uncertainties and make sure that these are apparent in communication** between scientists, regulatory authorities, politicians and the public. Alternative courses of action should be

considered with an open mind and limits should not be placed on the range of alternatives in advance.

Lesson 3: the cases of food irradiation and saccharin indicate that **the availability of options minimises the total impact of false positives**. An alternatives assessment that considers the pros and cons of other courses of action (including no action) is critical to avoid risk-risk trade-offs. To reduce the potential negative impact of committing false positives, adequate resources should be made available to consider alternative courses of action. In conducting assessments attention must be paid to defining 'safer' alternatives.

Lesson 4: **particular care is needed when introducing a new substance or technology at a large scale** because of the risk of 'unknown unknowns'. In two of the four cases (swine flu and Southern leaf corn blight), the precautionary action initially taken had unintended consequences because of events that could not have been anticipated and had severe consequences because of its widespread application.

Lesson 5: **initiating and funding research to increase understanding and reduce uncertainties should supplement other risk-reducing regulatory measures** and not be seen as a regulatory measure in itself. In none of the cases could more scientific research have prevented the false positives from happening; indeed, in some of the cases too much trust was put on the capability of science to demonstrate effects.

Lesson 6: **precautionary actions (both necessary and unnecessary) can lead to innovation in science, policy and technology**. Decision-makers should take this into consideration when they consider regulating a potentially harmful technology and choose regulatory measures that can spark innovation even if the precautionary action proves unnecessary.

Lesson 7: it is necessary to **be flexible in decision-making processes**. The decision-making process should be designed with re-evaluation as a key component, so that decisions can be altered in the light of new knowledge. It is also important that the regulators are prepared to alter their initial decisions about risks.

In conclusion, the analysis has shown that fear of false positives should not be a rationale for avoiding precautionary actions where warranted. False positives are few and far between as compared to false negatives and carefully designed precautionary actions can stimulate innovation, even if the risk turns out not to be real or as serious as initially feared. Overall, the analysis has demonstrated the need for new approaches to characterising and preventing complex risks that move debate from the 'problem' sphere to the 'solutions' sphere (Sarewitz, et al., 2010). By learning from the lessons above, more effective preventive decisions can be made in the future.

Table 2.3 Overview — the 88 case studies claimed to be regulatory false positives

	Subject	Risk category
1	Acid rain (Bast et al., 1994, Wildavsky, 1995)	Real risk
2	Acrylamide (Löfstedt, 2003)	'The jury is still out'
3	Aflatoxins (Majone, 2002)	Real risk
4	Agent Orange (Milloy, 2001)	Real risk
5	Air pollution in the USA (Whelan, 1993)	Real risk
6	Alar (Fumento, 1990; Wildavsky, 1995; Lieberman and Kwon, 1998)	Risk-risk trade-off
7	Amalgam dental fillings (Lieberman and Kwon, 1998)	Unregulated alarm
8	Antibiotics cause breast cancer (Kava et al., 2004)	'The jury is still out'
9	Asbestos in hair dryers (Lieberman and Kwon, 1998)	Unregulated alarm
10	Asbestos in schools (Lieberman and Kwon, 1998)	Real risk
11	BAM (From, 2004)	'The jury is still out'
12	Ban of Coca Cola (Whelan, 1999)	'The jury is still out'
13	Bendectin (Marchant, 2003)	Unregulated alarm
14	Benzene in Perrier Water (Lieberman and Kwon, 1998)	Real risk
15	Bovine Somatotropin (bST) (Lieberman and Kwon, 1998)	'The jury is still out'
16	Breast implants (Fumento, 1996; Milloy, 2001)	'The jury is still out'
17	BSE and vCJD (Adams, 2000)	'The jury is still out'
18	Busy streets and childhood cancer (Milloy, 2001)	'The jury is still out'
19	Cellular phones (Lieberman and Kwon, 1998; Graham, 2004)	'The jury is still out'
20	Cheeseburgers and Cardiovascular Disease (Kava et al., 2004)	Too narrow a definition of risk
21	Chemical Mace (Mazur, 2004)	Unregulated alarm
22	Chemicals in cosmetics (Kava et al., 2004)	'The jury is still out'
23	Chlormequat and Cerone (IMV, 2003)	'The jury is still out'
24	Coffee and pancreatic cancer (Lieberman and Kwon, 1998)	Unregulated alarm

Table 2.3 Overview — the 88 case studies claimed to be regulatory false positives (cont.)

25	Cyclamates (Lieberman and Kwon, 1998)	'The jury is still out'
26	DDT and malaria (Wildavsky, 1995; Lieberman and Kwon, 1998)	Real risk
27	DEHP (Milloy, 2001)	'The jury is still out'
28	DES in Beef (Lieberman and Kwon, 1998)	Real risk
29	Destruction of the ozone layer (Bast et al., 1994)	Real risk
30	Dioxin (Gough, 1994)	Real risk
31	Electric Blankets (Lieberman and Kwon, 1998)	'The jury is still out'
32	Electromagnetic fields (Lieberman and Kwon, 1998)	'The jury is still out'
33	Endocrine disrupting chemicals (Maxeiner and Miersch, 1998)	'The jury is still out'
34	Ethylene dibromide (Lieberman and Kwon, 1998)	Risk-risk trade-off
35	Fen-Phen and heart value disease (Milloy, 2001)	Real risk
36	Fluoridated water (Lieberman and Kwon, 1998)	Unregulated alarm
37	Food irradiation (Lieberman and Kwon, 1998)	False positive
38	Formaldehyde (Maxeiner and Miersch, 1998)	Real risk
39	Functional food (Marchant and Mossman, 2002)	'The jury is still out'
40	Genetically Modified Organisms (Miller and Conko, 2001)	'The jury is still out'
41	Global warming (Bast et al., 1994; Wildavsky, 1995)	Real risk
42	Hair dyes and cancer (Lieberman and Kwon, 1998)	Too narrow a definition of risk
43	Homocysteine causing Atheroschlerosis (Milloy, 2001)	Real risk
44	Hormone replacement therapy and breast cancer (Milloy, 2001)	Real risk
45	Hypoxia: dead zones in the Gulf of Mexico (Avery, 1999)	Real risk
46	Laundry detergents (Mazur, 2004)	Unregulated alarm
47	Love Canal (Wildavsky, 1995; Lieberman and Kwon, 1998)	Real risk
48	4-MBC in sun-lotion (Politiken, 2001)	Risk-risk trade-off
49	Mercury in fish (Mazur, 2004)	Real risk
50	MMR vaccines (Bate, 2001)	'The jury is still out'
51	Monarch butterfly and Bt corn (Marchant, 2003)	'The jury is still out'
52	Monosodium Glutamate (MSG) (Mazur, 2004)	Real risk
53	Nightlights and leukemia (Kava et al., 2004)	'The jury is still out'
54	Nitrilotriacetic acid in detergents (Mazur, 2004)	Risk-risk trade-off
55	Nitrites (Sodium Nitrite) (Lieberman and Kwon, 1998)	Risk-risk trade-off
56	Nuclear power (Bast et al., 1994; Graham, 2004)	Too narrow a definition of risk
57	Oral contraceptive pill scare (Adams, 2000)	Real risk
58	Perce in a Harlem School (Lieberman and Kwon, 1998)	'The jury is still out'
59	Pesticides (Whelan, 1993)	Real risk
60	Phenolphthalein (Milloy, 2001)	'The jury is still out'
61	Polybrominated biphenyls (Whelan, 1993)	'The jury is still out'
62	Polychlorinated biphenyls (Whelan, 1993)	Real risk
63	PVC blood bags and cancer (Milloy, 2001)	'The jury is still out'
64	Radon gas in houses poses a health risk (Miloy, 2001)	Real risk
65	Red Dye Number 2 (Lieberman and Kwon, 1998)	'The jury is still out'
66	Saccharin (Lieberman and Kwon, 1998)	False positive
67	Second hand smoke and breast cancer (Milloy, 2001)	Too narrow a definition of risk
68	Second hand smoke and lung cancer (Matthews, 2000)	Real risk
69	Second hand smoke causing hearing problems (Milloy, 2001)	'The jury is still out'
70	Soda causes esophageal cancer (Kava et al., 2004)	'The jury is still out'
71	Spermicides and birth defects (Mills, 1993)	Unregulated alarm
72	Superfund's abandoned hazardous waste sites (Milloy, 2001)	Real risk
73	2,4,5-T (Lieberman and Kwon, 1998)	'The jury is still out'
74	Taconite pollution (Mazur, 2004)	Too narrow a definition of risk
75	Teflon causes health problems in humans (Kava et al., 2004)	'The jury is still out'
76	The 'Cranberry Scare' of 1959 (Wildavsky, 1995; Lieberman and Kwon, 1998; Mazur, 2004)	'The jury is still out'
77	The baby bottle scare (Kamrin, 2004)	'The jury is still out'
78	The Dalkon Shield (Milloy, 2001)	Unregulated alarm
79	The Peruvian outbreak of cholera (Bate 2001; Milloy, 2001)	'The jury is still out'
80	The Southern leaf corn blight (Lawless, 1977)	False positive
81	The swine flu (Marchant, 2003)	False positive
82	Three Mile Island (Lieberman and Kwon, 1998; Graham, 2004)	Too narrow a definition of risk
83	Times beach, Missouri (Wildavsky, 1995; Lieberman and Kwon, 1998)	Real risk
84	Toxins in breast milk causing harm to babies (Ross, 2004)	Risk-risk trade-off
85	Trichloroethylene (TCE) (Jaeger and Weiss, 1994)	Real risk
86	Tris (Lieberman and Kwon, 1998)	Unregulated alarm
87	Video display terminals (Lieberman and Kwon, 1998)	Too narrow a definition of risk
88	Water contamination in Sydney (Clancy, 2000)	Real risk

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3 Lead in petrol 'makes the mind give way'

Herbert Needleman and David Gee ([1])

This chapter addresses the widespread use of lead in petrol. It focuses on the period 1925–2005, when leaded petrol was first widely marketed in the US and then spread to the rest of the world before being gradually phased out from the 1970s. In Europe, the Aarhus Protocol (UNECE, 1998) initiated the phase-out of leaded petrol in the period 1998–2005.

The neurotoxic effects of lead were recognised as far back as Roman times. And in 1925, at the 'one day trial' of leaded petrol in the US, many experts warned of the likely health impacts of adding lead to petrol. Yet, despite the availability of an equally effective alcohol additive which was assessed by experts to be cleaner, the leaded route to fuel efficiency was chosen in the US and then exported to the rest of the world.

For several decades after the introduction of leaded petrol, virtually no independent research was carried out and the main source of information was industry and industry-sponsored researchers. Not until the 1960s and 1970s did independent scientists from outside this group show, for example, that body burdens of lead arising from human activities were not 'normal', as industry claimed, but were hundreds of times higher than before the industrial revolution and were therefore likely to be harmful.

At its peak in the mid-1970s, leaded petrol released about 200 000 tonnes of lead into the atmosphere annually in both the US and Europe. Following the subsequent phase-out, blood lead levels in children (the most sensitive group exposed) quickly fell, in line with the decrease in air concentrations. The lessons nevertheless remain relevant globally today. Although nearly all countries worldwide had phased out leaded petrol by 2012, lead concentrations in soils and sediments remain high. Meanwhile, electronic wastes containing lead and other contaminants also cause elevated blood lead levels.

Supplementary panel texts focus on the events leading up to the US choice of leaded petrol as the primary fuel source in 1925 and more recent accounts of EU policymaking on lead in petrol and the road to phase-outs in Germany and the United Kingdom.

([1]) Authors would like to thank Gerald Markowitz and David Rosner for their detailed history of the leaded petrol story in Deceit and denial: the deadly politics of industrial pollution.

Dr Yandell Henderson, Professor of Physiology at Yale, told the conference that lead was as serious a public health menace as infectious diseases. He foresaw that:

> 'conditions will grow worse so gradually, and the development of lead poisoning will come on so insidiously ... that leaded petrol will be in nearly universal use ... before the public and the government awakens to the situation' (USPHS, 1925).

3.1 Introduction

There were 50–70 years between Henderson's prescient early warning about the long-term, low-level poisoning from leaded petrol, when it was introduced in 1925, and its phase out in the US and then Europe in the 1970s and mid-1980s. This long history is rich in lessons about the science, economics, and politics of identifying and controlling the hazards of toxic substances.

The focus of this chapter is lead in petrol and its damage to children (Box 3.1). However, the even longer histories of lead in pots and paints weave in and out of the leaded petrol saga, both complicating the search for the causes of lead poisoning in children, and creating a ubiquitous stock of lead in people and their environments that persists today in soils, sediments, plants, house dust and old paint. Such exposures affect adults too and recent research emphasises the increasing evidence linking lead with hypertension, heart disease and kidney disease (Navas-Acien et al., 2007; EFSA, 2010).

Most of Europe and North America now has lead free petrol but the lessons from this chapter are relevant for controlling most toxic chemicals. They may also be useful for the millions of people, including children, who are still exposed to leaded petrol or

Box 3.1 Children and lead: health impacts

At high levels of chronic exposure, lead attacks the brain and central nervous system, causing coma, convulsions and even death. Children who survive acute lead poisoning are typically left with grossly obvious mental retardation and behavioural disruption. At lower levels of exposure that cause no obvious symptoms and that were previously considered safe, lead is now known to produce a spectrum of harm involving diminished cognition, shortened attention span, disruptive behaviour, dyslexia, attention deficit disorder, hypertension, renal impairment, immunotoxicity and toxicity to the reproductive organs. For the most part, these effects are permanent and largely untreatable.

The major sources of children's exposure to lead are:

- lead from active industries, such as mining (especially in soils);
- lead-based paints and pigments;
- lead solder in food cans;
- ceramic glazes;
- drinking-water systems with lead solder and lead pipes;
- lead in products, such as herbal and traditional medicines, folk remedies, cosmetics and toys;
- lead released by incineration of lead-containing waste;
- lead in electronic waste (e-waste);
- lead in the food chain, via contaminated soil;
- lead contamination as a legacy of historical contamination from former mining and industrial sites.

Acute lead poisoning still occurs today and is most common among children in low-income countries and marginalised populations or in children living on lead-polluted sites of old lead factories or mines.

Recent research indicates that lead is associated with neurobehavioural damage at concentrations in the blood of 5 µg/dl and even lower. There appears to be no threshold level below which lead causes no injury to the developing human brain (see Box 3.11).

The biology of childhood lead poisoning is similar everywhere and the results of lead studies in one country are largely relevant to children in other countries.

Source: WHO, 2010.

Box 3.2 Ancient lead poisoning

Analysis of the Greenland ice core covering the period from 3 000 to 500 years ago — the Greek, Roman, Medieval and Renaissance eras — shows that from about 500 B.C. to 300 A.D. lead was present at concentrations four times greater than natural values. Greek and Roman lead mining and smelting clearly polluted the northern hemisphere long before the industrial revolution, which initiated the modern era of lead poisoning from about from 1750 onwards. Cumulative lead fallout to the Greenland ice sheet during those eight centuries was as high as 15 % of that caused by use of lead alkyl additives in petrol since the 1930s.

Source: Hong, Candelone et al., 1994.

other sources of lead, such as from old lead works, paint and toys, in many countries of the world.

3.2 Lead toxicity: some early warnings

The neurotoxic properties of lead were first noted during the first century AD by Dioscerides, a physician in Nero's army. In his book *Materia Medica* he observed that 'Lead makes the mind give way'. Exposure came from the leaded glaze on pots and from using lead in winemaking to counteracted the harsh acidity of the grapes (lead plates were dipped into the wine during fermentation and the lead acetate, which is also called 'sugar of lead', sweetened the taste). Centuries later, toddlers who chewed the leaded paint on cradles, beds and verandas found that it tasted like lemon drops.

Lead continued to be used in wine-making and epidemics of lead colic were common in Europe and the Americas. One of the earliest public health laws in the US was passed in 1723 to protect rum drinkers from what was called 'the dry gripes'. The law banned the use of leaden 'worms' (condensing coils) in the distilling process. A penalty of 100 pounds was imposed on law breakers, half being distributed to the poor and half to the person who informed the authorities about the breach of law. This was an early attempt to reward and protect 'whistleblowers' — an issue taken up in Chapter 24.

In early-18th century England, a severe outbreak of colic was reported each autumn in Devon. The disease was strictly limited to particular areas while neighbouring shires escaped. The physician Sir George Baker identified the source of the epidemic as the leaden keys in the millstones used in pressing cider apples. His paper to the Royal College of Physicians showed that Devonshire cider contained lead (Baker, 1768). Rather than receiving praise for his incisive work, Baker was condemned by the clergy, by mill owners and by fellow physicians: cider was Devon's main export.

Baker suffered the fate of many 'early warning' scientists whose inconvenient truths are not welcomed by supporters of the status quo ([2]).

During his European travels, Benjamin Franklin had also noted how long it took for 'useful truths' about health hazards to be acted on (Box 3.3).

The UK pottery manufacturer, Josiah Wedgewood, also experienced the long delay between 'useful truths' and regulatory actions. He was sufficiently moved by accidents and lead poisoning in his factories, and concerned about the unfair competition that arose from other, less scrupulous, employers, that he asked the British government to extend the recent Factories Act of 1833 from the textiles industries to the potteries industries so that he could share a 'level playing field' with his competitors. Opposition from other pottery manufacturers meant, however, that Wedgewood had to wait some 30 years before legal controls on lead were established in the Potteries Regulations of 1867.

These early warnings about occupational and consumer lead toxicity largely went unheeded. The use of lead for pots, paints, pipes and toys greatly

([2]) Such 'shooting the messenger' is well illustrated by Ibsen's play 'An enemy of the people'. The play chronicles the gradual downfall of the town physician who discovers pollution in the river caused by the local leather factory: a discovery that is initially welcomed by the mayor, the media and the public, but then rejected, as the economic implications for local industry begin to emerge. Many public health advocates in similar circumstances to Baker have taken comfort from Ibsen's play, such as Dr Hosakowa of the Chisso Company Japan, which polluted Minimata Bay with mercury. He, like Ibsen's Doctor Stockmann, was told to suppress his early discovery that sewage from Chisso caused the mercury poisoning (see Chapter 5 on the Minamata disaster).

Box 3.3 The 'useful truths' about lead poisoning in French painters, potters and plumbers

In 1818, Benjamin Franklin, while ambassador to France, described the 'dangles' of wrist drop, and the 'dry gripes' of stomach aches in painters, potters and plumbers who were widely known to suffer from lead poisoning. But he also observed two other trades that suffered similarly but seemed not to be obviously exposed to lead: stonecutters and soldiers. Pursuing this puzzle, he found that the stonecutters used lead to set metal rails in stone, and that soldiers found part time employment as painters' assistants. This provided an early example of the value of detailed job and life exposure histories in identifying occupational and environmental hazards.

Franklin concluded: 'this mischievous effect from lead is at least 60 years old; and you will observe with concern how long a useful truth may be known and exist, before it is generally received and practiced on' (Franklin, 1818).

expanded in the 19th and 20th centuries (Hunter, 1975), accompanied by widespread lead poisoning that could sometimes take years to appear:

> 'Lead poisoning develops insidiously' often years after the exposure, deranging the functions and structure of the cells, 'so that life is gradually brought to a close by the intervention of disease of organs, such as the kidney or nervous system' (Oliver, 1911).

This 'insidious' nature of lead poisoning would later be noted by some of the medical experts who assessed the likely risks from lead in petrol when it was introduced in the 1920s. Children were particularly at risk (Box 3.4).

Box 3.4 The early poisoning of children by leaded paint, and current poisoning from paint and battery plants in Asia

Children face increased risk of lead poisoning compared to adults because they can be exposed during pregnancy; they take in more food, drink and air relative to their weight; they have more hands-to-mouth activity; and they are more likely to have nutritional deficiencies that can increase lead absorption (WHO, 2010).

In 1892 an Australian doctor observed the link between the lead-based paints used on porches, verandas, and window frames, and lead poisoning in 10 children who chewed the flakes of paint and swallowed the dust and chips on the floor where they crawled and played (Gibson, 1904).

In 1914 in the US, the first childhood lead poisoning case was reported with a death from lead poisoning in a child who had chewed lead paint from his crib railings (Thomas and Blackfan, 1914).

By 1925 there was much scientific evidence in the US, Europe and elsewhere showing that infants and children were poisoned by lead in the paint that they found in their daily environments. But their eventual protection from this source of lead came via regulations to protect painters, which led to the widespread banning of lead in paint in Europe and Australia between 1909 and the 1930s.

The US, however, only banned leaded paint for interior surfaces in 1971. As a result, government authorities are still dealing with the legacy of lead poisoning in the poorer areas of the US where the housing remediation costs, and associated legal cases over who is to pay remediation, still consume much time and money.

Meanwhile, there is still widespread exposure of children to leaded paint in many regions, particularly, developing countries. A survey of 10 countries in Asia, Africa, South America and eastern Europe found much leaded paint on sale, some with lead levels ranging from 4 000 to nearly 40 000 parts per million (ppm), compared to the US recommended limit of 90 ppm (UNEP/WHO, 2010). Moreover, China has reported many serious childhood lead poisoning incidents in recent years.

3.3 Lead in petrol 1922–1925: the early warnings of hazards to the public

3.3.1 Origins of lead in petrol

Until 1925, the principal source of toxic lead for the public was household paint. This changed dramatically when General Motors, in second place behind Ford Motors in car sales, sought to compete with its new higher performance Cadillac. The new GM engine had a severe engine 'knock' that arose from the premature ignition of the petrol, meaning that GM needed to find an anti-knock additive for the petrol. Their chief chemist, Thomas Midgely, who later invented the CFC chemicals that created the hole in the ozone layer, (see EEA, 2001, Ch. 7 on halocarbons), found an old German patent for tetraethyl lead (TEL) and discovered that it could be used in petrol to control the engine knock.

Alternatives to petroleum-based fuel, such as ethanol, were available. They were likely to be much less profitable, however, especially given the family and financial links between GM, the chemical company, DuPont, and Standard Oil. Pierre Dupont was chair of the GM Board, his brother Irene ran DuPont, both had close links with Standard Oil, and in 1924 the three companies created the Ethyl Corporation of America to produce TEL.

It was made clear at the outset that the word 'lead' was not to be used in the company name or sales literature: the little known term, 'ethyl' was used instead so as not to alarm the public.

This was an early example of the censoring of sensitive words from the discussion of hazards, a practice repeated in the other *Late lessons from early warnings* case studies, for example asbestos (EEA, 2001). For example, the word 'cancer' in the early studies of asbestos workers was initially replaced by the less well known terms, 'tumour' or 'malignancy', at the request of asbestos manufacturers.

3.3.2 Early warnings of risk and 'authoritative assertions' of safety

During World War I, TEL was evaluated for possible use as a battlefield weapon. Mansfield Clark, a professor of chemistry familiar with this work, warned the US Public Health Service (PHS) in 1922 about the 'serious menace to the public health' that would arise from the use of TEL in petrol because 'on busy thoroughfares it is highly probable that the lead oxide dust will remain in the lower stratum.' (Mansfield Clark, 1922)

The Surgeon General of the US Public Health Service, Huge Cummings, responded some months later by writing to Pierre Dupont, Chair of the Board of GM, asking if the public health effects of TEL had been taken into account, 'since lead poisoning in human beings is of the cumulative type resulting frequently from the daily intake of minute quantities.' (Needleman, 1997)

Thomas Midgely replied by saying that GM had given the question 'very serious consideration ... although no actual experimental data has been taken'. However, they were confident that 'the average street will probably be so free from lead that it will be impossible to detect it or its absorption.' (Midgely, 1922)

Midgely's response has parallels in other *Late lessons from early warnings* case studies, including those addressing asbestos, CFCs and BSE in Volume 1 (EEA, 2001). In response to early warnings about public health hazards, interested parties often make 'authoritative assertions' about the absence of risk despite having little or no data to support their claims. 'No evidence of harm' is thereby mischaracterised as 'evidence of no harm. This approach to early warnings of potential harm is still common ([3]).

In order to provide some evidence to back up their assertions of safety, GM paid the US government's Bureau of Mines to conduct some animal experiments, but within tight reporting constraints imposed by the Ethyl Corporation. These conditions included the replacement of the word 'lead' by 'ethyl', even in internal correspondence, and the submission of draft reports to the Ethyl Corporation for their 'comments, criticism and approval' before publication. The chief chemist in the Bureau of Mines 'raised his concerns about this censorship but was assured by his director that … it would not be so bad if the word lead were omitted as this term is apt to prejudice somewhat against its use' (Needleman, 1997).

([3]) For example, there are no studies in children of the potential head cancer hazard of using mobile phones: the early suspicions of risk have come from studies in adults only. Yet it is widely asserted that there are no risks to children from the use of mobile phones. In 2007, 2009 and 2011 the EEA issued 'early warnings' about the potential hazard of head cancers from mobile phones, particularly in younger people. See Chapter 21 on mobile phones.

Such contractual gagging had already been condemned as unprofessional by Yandell Henderson, Professor of Physiology at Yale, who had turned down an invitation by GM to study TEL two years earlier. He was now asked by the Bureau of Mines to join their investigation but he declined, saying that it was 'extremely unfortunate' that the work was being funded by GM as there was an 'urgent need for an absolutely unbiased investigation'. He was prepared to investigate the hazards but only 'on the assumption that so terrible a poison as TEL should not be generally introduced until absolute proof was available that no danger to the public would be involved'. Soon after, his long standing contract with the Bureau of Mines was terminated, as well as his contract with Standard Oil: an early example of the harassment of 'early warning' scientists which is repeated in this and other chapters.

Henderson was later to testify against the use of TEL in petrol at its 'one day trial' in 1925 (discussed below).

By 1925 industrial production of TEL had been under way for nearly two years but within months it had caused the dramatic deaths of a dozen or so workers and mental illness in many others (Box 3.5).

The news media ran dramatic headlines about the TEL deaths: 'Mad gas claims third victim' and 'Bar Ethyl gas as fifth victim dies' appeared above pictures of workers being taken away in straitjackets.

New York State then banned the sale of leaded petrol. This put pressure on the PHS and the TEL industry to somehow demonstrate that though **workers** may be at risk, partly because of their 'carelessness', or because they 'worked too hard', as the factory management claimed, the **public** would not be at risk from TEL in their car fuel.

Standard Oil had already confidently asserted that no 'perils existed in the use of this gas in automobiles', even though no evidence had been gathered to support that view.

The day after the fifth employee at their TEL plant died, Standard Oil's assertions regarding the safety of TEL received support from the Bureau of Mines, which published a report showing that animal studies indicated no risks to the public from TEL.

On 1 November 1924, *The New York Times* (1924) ran the headline: 'No peril to public after long experiments with motor exhausts'.

However, the Bureau of Mines report was heavily criticised. It was labelled as 'inadequate' by Cecil Drinker, editor of the Journal of Industrial Hygiene, David Edsall, Dean of Harvard Medical School, and others, including the Surgeon General (Drinker, 1925). They considered that the number of animals used was too small and the duration of exposure was too short to draw reliable conclusions about safety. These are still features of some current toxicology that can result in underestimation of hazards (see Chapter 26 on science for precautionay decision-making).

Some public health specialists supported the Bureau of Mines and the Ethyl Corporation, but again with confident assertions rather than robust evidence.

For example, Dr Emery Hayhurst of the Ohio Department of Health provided an unsigned

Box 3.5 TEL workers die in the 'house of butterflies'

On Thursday 26 October 1924, Ernest Oelgert, a TEL worker at Standard Oil's Bayway labs in New Jersey, began hallucinating and then became extremely paranoid, running round the plant saying that 'three were coming at me'. By Saturday he had to be forcibly constrained and taken to the nearest mental hospital where he died the next day.

Over the next five days, four other TEL workers from the plant died and another 35 showed severe neurological symptoms of lead poisoning. At the other two TEL workplaces, the DuPont plant at Deepwater, New Jersey, and GM's research lab in Dayton, Ohio, at least six other workers had died.

Despite their declared difficulties in getting the facts out of the companies and the hospitals, *The New York Times* journalists uncovered more than 300 cases of lead poisoning at the Deepwater plant. Workers called that TEL plant 'the house of butterflies' as they frequently had hallucinations about insects during their bouts of lead poisoning.

editorial in the American Journal of Public Health, stating that 'observational evidence' and other reports from around the country have 'corroborated the statement of complete safety so far as the public health has been concerned' (Ethyl Gasoline, 1925). Few people knew that, at that time, he was also a paid consultant to the Ethyl Corporation and advisor to the Bureau of Mines (Hayhurst, 1924).

These 'authoritative assurances' failed to quell public and scientific concern. The Surgeon General responded to requests for action from public health experts, who felt that both the public's health and the probity of the PHS were at risk from the TEL issue. He organised a high level conference of all the key actors, stating that leaded petrol 'is a public health question of extreme seriousness … if this product is actually causing slow poisoning and serious effects of a cumulative nature' (New York World, 1925).

The conference took place in Washington on 24 May 1925.

3.4 'Progress' or precaution?

3.4.1 The 'one day trial' of the 'gift of God'

Every major stakeholder was represented at the meeting. Industry opened the debate by making four main points: leaded petrol was essential to the industrial progress of America; all innovation entails risks; the deaths and disabilities caused by TEL in the manufacturing plants were due to the carelessness of the men in not taking precautions; and there was no risk to the public from the different exposure conditions in the streets, compared to the factories.

No 'innovation' other than TEL was discussed at the meeting, despite the declared intention of the Surgeon General to spend two or three days discussing alternatives to TEL. The toxicologist Robert Kehoe spoke first for industry, citing lack of evidence of risks to the public; he was followed by eight other industry representatives who took up the morning session.

The public health representatives used the afternoon to try to shift the burden of proof back to their opponents, arguing that industry needed to show that TEL was safe for the public, rather than public health scientists needing to show that it was dangerous.

Dr Yandell Henderson, Professor of Physiology at Yale, told the conference that lead was as serious a public health menace as infectious diseases. He foresaw that 'conditions will grow worse so gradually, and the development of lead poisoning will come on so insidiously ... that leaded petrol will be in nearly universal use … before the public and the government awakens to the situation' (USPHS, 1925). His claims proved to be prescient.

Dr David Edsall, Dean of Harvard Medical School, also dismissed the view of industry that 'nobody has shown any symptoms of lead poisoning'. He went on to say that: 'I cannot escape feeling that a hazard is perfectly clearly shown … here today, and that it appears to be a hazard of public moment, and that the only way it could be said it is a safe thing to continue with this hazard would be after very careful and prolonged and devoted study.' This did not happen until the 1970s.

Edsall was followed by Dr Touart, who had treated many of the workers. He too emphasised the central issue of the burden and strength of evidence: 'It seems to me that ... this ethyl gas is under suspicion and therefore should be withheld from public consumption until it is conclusively shown that it is not poisonous.'

Haven Emerson, Professor of Public Health at Columbia University, observed that industry's use of deaths as an indicator of hazard was unsound: information about functional and mental disabilities of those that did not die would also be needed.

However, industry was supported by some of the other public health scientists at the meeting. They observed that, while there was solid and direct evidence of industrial benefits from TEL, evidence on health risks to the public was not available. This asymmetry between short-term economic benefits and long-term health hazards is another continuing problem.

Dr Hayhurst of the Ohio Department of Health said that 27 months of public use of leaded petrol 'should have sufficed to bring out some mishaps and poisonings suspected to have been caused by TEL'. It had not, so he was prepared to declare that leaded petrol was safe.

His position was based on two weak assumptions: that existing statistics, collected for other purposes, provided reliable evidence of safety from a new technology; and that a short, two-year-period after first exposure would be enough to uncover any new hazards. These assumptions are still common in debates on current health hazards.

Some public health experts who supported industry at the meeting had earlier expressed their concerns about the health risks, but only in private. Hayhurst, for example, despite being a consultant for the Ethyl Corporation, had written to the PHS a week before the May meeting expressing the concerns that he shared with some of the PHS scientists, such as Dr Thompson, who had declared that 'lead has no business in the human body ... everyone agrees lead is an undesirable hazard and the only way to control it is to stop its use by the general public'.

However, Hayhurst continued his letter by noting that his scientific judgement was influenced by political and economic factors. 'Personally, I can quite agree with Dr Thompson's wholesome point of view but, still, I am afraid human progress cannot go on under such restrictions … if we are to survive among the nations. Dr Thompson's arguments might also be applied to the thousand and one other poisons and hazards which characterise our modern civilisation' (Hayhurst, 1925).

The country's foremost authority on lead, Alice Hamilton, told the May meeting that there was no way to know how to regulate leaded petrol so that it would be safe. 'You may control conditions within a factory ... but how can you control the whole country?' She later spelled out the dangers further, noting that even under the strictest factory conditions the use of lead resulted in poisoning, sooner or later (Hamilton, 1925).

The meeting seemed to be going the way of precaution and public health until Frank Howard, first President of the Ethyl Corporation, concluded the industry view: 'You have only **one** problem', he told the health scientists, 'is this a public health hazard?' Industry, he said, had other problems such as ensuring that automobiles and oil played a key role in the industrial progress of the nation. 'Our continued development of motor fuels is essential in our civilisation'. The development of TEL after a decade of research was an 'apparent gift of God'. What is our duty under these circumstances, he asked, 'should we say no: we will not use a material (that is) a certain means of saving petrol? Because some animals die and some do not die in some experiments, shall we give this thing up entirely?'

In a couple of rhetorical sentences he put the burden of proof back onto the public health scientists to prove that TEL was dangerous. He had also put them on the defensive by making them appear to be reactionaries who were retarding human progress and technological innovation on the unproven grounds that there could be public hazards.

The meeting ended after less than seven hours. The Ethyl Corporation announced that there would be a temporary ban on leaded petrol sales until a 'blue ribbon committee' of top-level scientists set up by the PHS after the meeting had studied the issue.

After the meeting Alice Hamilton thought that the direct involvement of the top scientists and decision-makers from industry and government would produce the right results, especially if there was 'a blaze of publicity turned on their deliberations'.

3.4.2 Blue ribbon committee findings

This perceived victory of objective science over short-term economic and political interests was short lived. The scientific review committee was under great time pressure to produce its report, so a very limited, seven month, study of 252 garage and filling station attendants, chauffeurs and factory workers was conducted. The committee concluded that 'at present there are no good grounds for prohibiting the use of ethyl gasoline [petrol] ... provided that its distribution and use are controlled by proper regulations'. A recommendation from committee member Winslow to continue the search for alternatives was omitted from the final committee report.

The report included clear caveats, however, stating that:

> 'Owing to the incompleteness of the data, it is not possible to say definitely whether exposure to lead dust increases in garages when tetraethyl lead is used. It is very desirable that these investigations be continued ... It remains possible that if the use of leaded petrol becomes widespread, conditions may arise very different from those studied by us which would render its use more of a hazard than would appear to be the case from this investigation. Longer exposure may show that even such slight storage of lead as was observed in these studies may lead eventually in susceptible individuals to recognizable lead poisoning or chronic degenerative disease of obvious character ... The committee feels this investigation must not be allowed to lapse.'

Panel 3.1 A road not taken: the alcohol alternative to lead in 1925

Bill Kovarik

The US Geological Service (USGS) and the US navy performed over 2 000 tests on alcohol and petrol engines in 1907 and 1908 and concluded that: 'In regard to general cleanliness, such as absence of smoke and disagreeable odors, alcohol has many advantages over gasoline or kerosene as a fuel. The exhaust from an alcohol engine is never clouded with a black or grayish smoke.'

USGS continued the comparative tests and later noted that alcohol was 'a more ideal fuel than gasoline' with better efficiency despite the high cost'. Others were also experimenting (see Box 1.6).

GM was also interested in long-term security of fuel supplies, as is apparent in an unpublished du Pont study drafted by a member of the firm's legal staff. According to the study (Wescott, 1936):

> '…An important special motive for this research [into ethyl alcohol] was General Motors' desire to fortify itself against the exhaustion or prohibitive cost of the gasoline supply, which was then believed to be impending in about twenty-five years; the thought being that the high compression motors, which should be that time have been brought into general use if knocking could be overcome, could more advantageously be switched to [ethyl] alcohol.'

The DuPont conclusion is supported by internal memos sent by Midgley. Alcohol was the 'most direct route ... for converting energy from its source, the sun, into a material that is suitable for a fuel…' he said in one internal memo.

To promote alcohol-blended fuels among automotive and chemical engineers in October 1921, Midgley drove a high compression ratio car from Dayton to an October 1921 Society of Automotive Engineers (SAE) meeting in Indianapolis using a 30 % alcohol blend in petrol. 'Alcohol has tremendous advantages and minor disadvantages,' Midgley told fellow SAE members in a discussion. Advantages included 'clean burning and freedom from any carbon deposit... [and] tremendously high compression under which alcohol will operate without knocking... Because of the possible high compression, the available horsepower is much greater with alcohol than with gasoline.'

'From our cellulose waste products on the farm such as straw, corn-stalks, corn cobs and all similar sorts of material we throw away, we can get, by present known methods, enough alcohol to run our automotive equipment in the United States,' he said. The catch was that it would cost two dollars per gallon. However, other alternatives looked even more problematic — oil shale would not work and benzene from coal would only bring in about 20 % of the total fuel need (Midgley, 1921).

Despite their enthusiastic support for alcohol as a 'fuel of the future', Midgley and his boss, Charles Kettering, categorically denied the existence of alternatives to TEL once they had begun to invest in TEL production facilities:

> 'So far as science knows at the present time, tetraethyl lead is the only material available which can bring about these [antiknock] results, which are of vital importance to the continued economic use by the general public of all automotive equipment, and unless a grave and inescapable hazard exists in the manufacture of tetraethyl lead, its abandonment cannot be justified' (*The New York Times*, 7 April 1925).

Information about alternatives could have emerged with more social and scientific force at this critical moment in the history of TEL ([4]). For example, it was widely thought that the May 1925 conference would last several days in order to discuss alternatives to TEL: the Surgeon General had declared his intention to do so at the opening of the May conference.

A report published but not released by the US Department of Commerce a few days before the May conference showed that alternative antiknock additives (mostly ethyl alcohol blends in petrol) were being

([4]) 'Ethyl leaded gasoline crashed through the modest defenses of the American public health system of the 1920s not only through brute force of industry's political influence over government but also due to the disorganized information resources available to public health advocates', particularly regarding the potential for alternatives to TEL (Kovarik, 2003).

Panel 3.1 A road not taken: the alcohol alternative to lead in 1925 (cont.)

used routinely in two dozen other industrial nations. And anyone familiar with the Midgley papers and statements of 1921 and 1922 would see that by 1925 he was contradicting his own published research.

Information about alternatives did not emerge from the 'one day trial' of TEL in 1925, however, except in a few statements by public health scientists and hints in the media. No record of any dissent exists, even though the industry was now flatly contradicting its own previous research and statements on the alcohol alternative.

In 1933 the US Defence Agency and US navy conducted tests on alternative fuels and found that Ethyl leaded petrol and 20 % ethyl alcohol blends in petrol were almost exactly equivalent in terms of brake horsepower and useful compression ratios. This report was never published.

Other potential substitutes for tetraethyl lead known to Kettering and the US automotive industry were based on the I.G. Farben/BASF Fischer-Tropsche and Bergius processes for making synthetic fuels from coal. This was seen as such serious competition to TEL that Standard Oil entered into a 'full marriage' agreement with Farben in which Standard agreed to stay out of the world chemical business and Farben agreed to stay out of the world fuel business — no matter how World War II progressed (Davis, 2007).

The wide variety of alternatives and substitutes known in the 1920s and 1930s were forgotten by the 1960s. Histories of the oil industry omitted any mention of alternatives.

In 1974, when Thomas Reed of MIT began his ground-breaking investigation of alcohol fuel as an alternative to petrol in the wake of the Arab oil embargo, he was unaware of any other similar work before him. It was as if, having found in TEL the one solution to the engine knock problem, no other solution — and no other history — was necessary.

Defeating the alcohol competition to leaded petrol

By the mid-1930s, Ethyl leaded petrol succeeded beyond all expectations. Public health crusaders who found this troubling still spoke out in political forums but competitors were not allowed to criticise leaded petrol in the commercial marketplace. In a restraining order forbidding such criticism, the Federal Trade Commission told competitors to stop criticising Ethyl petrol since it 'is entirely safe to the health of [motorists] and to the public in general when used as a motor fuel, and is not a narcotic in its effect, a poisonous dope, or dangerous to the life or health of a customer, purchaser, user or the general public.' (US FTC 1936)

During the 1930s, the few attempts to promote alcohol petrol were met by fierce and unfair competition from the Ethyl company, which led to an anti-trust case against Ethyl Corporation in 1937. By then Ethyl leaded petrol was used in 70 % or more of American petrol (90 % according to Ethyl's advertising) and in all but one major brand — Sunoco. Dealers who cut prices or who used alcohol or benzene in other fuels were not allowed to wholesale Ethyl's lead additive.

'It seems clear that the Ethyl Gasoline Corporation has exercised its dominant control over the use of Ethyl fluid substantially to restrain competition by regulating the ability of jobbers to buy and sell petrol treated with ethyl fluid and by requiring jobbers and dealers to maintain certain prices and marketing policies', a 1937 Department of Justice memo said. Ethyl lost the suit at the Federal District Court level in 1938 and at the Supreme Court in 1940. The company was ordered to make the product available to any customer who met minimum technical criteria.

Many scientists, businessmen and farmers believed that making fuel from corn and cornstalks would help put people back to work and ease the severe problems of the Depression. This movement for alcohol fuels became part of a broader campaign for industrial uses for farm crops to help fight the Depression. The 'farm chemurgy' movement, as it was called, with alcohol fuel as a controversial centrepiece, had grown into an unprecedented mixture of agronomy, chemistry and prairie populism. Many felt that the time had come to compete directly with the oil industry. 'Try a tankfull — you'll be thankful,' the Agrol brochures said. The blend was sold to initial enthusiasm at 2 000 service stations. Although Agrol sold for the same price as its 'main competitor', leaded petrol, it cost wholesalers and retailers an extra penny to handle it and this cut into their profit. By 1939, the Agrol plant had closed (Hale, 1934; Kovarik, 2003 and 2005).

Box 3.6 Early London buses experiment with alcohol fuels

In 1919 the London General Omnibus Co. also compared petrol with blends of ethyl alcohol and benzene. Mileage was about the same, with petrol slightly ahead. 'In all other respects the [alcohol] fuel compared favourably with petrol, and exhibited the characteristics of other alcohol mixtures in respect of flexibility, absence of knocking and cleanliness' (although it would later emerge that benzene is a dangerous carcinogen.)

The bus experiment also showed that a large-scale switch from petroleum was technically feasible and needed in any case to increase security of fuel Contentsies. 'We are fast squandering the oil that has been stored in the fuel beds, and it seems so far as our present knowledge takes us that it is to the fuels experimented with that we must turn for our salvation,' concluded the omnibus company engineer.

The Committee recognised the limitations of its small, interim and retrospective study and strongly urged the PHS to obtain funds from Congress for long-term prospective studies that could follow the history of leaded petrol and its consequences that were 'not now foreseen'. However, the PHS never undertook such research. For the next 40 years all studies of TEL were conducted and funded by the Ethyl Corporation and GM (Markowitz and Rosner, 2002).

Shortly after the Surgeon General's committee had declared that TEL was safe for general use, in 1926, the Public Health Service recommended that the allowable concentration of TEL be set at 3 cc per gallon. Ethyl quickly agreed to comply, relieving the government of any pressure to introduce the regulations on lead in petrol that had been called for by the expert committee.

For the next 35 years lead toxicity as a public health issue virtually disappeared from sight, while at the peak of TEL production some 250 000 tonnes of lead were released into the air in the United States every year.

3.5 Lead contamination is 'normal and safe'

After the Surgeon General's report of 1926 had given the go ahead to industry, Robert Kehoe, the toxicologist from the University of Cincinnati, who had claimed the safety of TEL at the 1925 meeting, was cultivated by the TEL industry as the dominant authority on lead. C. F. Kettering established a laboratory in Cincinnati with an initial gift of USD 130 000 from Ethyl, E. I. DuPont and General Motors. He had initially asked Kehoe to study the worker deaths at the Ethyl plant in Dayton and now he asked him to direct the Kettering laboratory.

Kehoe later also became a corporate officer at GM and a consultant to DuPont.

Data on the health effects of TEL were sparse, and the only source of funding for research came from industry sources. The strong recommendation from the Surgeon General's 1926 report that there should be publicly funded research on TEL was not implemented.

Kehoe's early studies compared lead concentrations in workers in direct contact with TEL with men in the same plant but who had other jobs. He designated this second group as 'unexposed' controls. When he found lead in the excreta of his so-called unexposed group, he concluded that as lead was naturally present in all the workers it could not be very harmful to them. The mere presence of lead in workers, he argued, could not be an indicator of poisoning.

This view had been vigorously attacked by David Edsall, Yandell Henderson and others at the Surgeon General's 1925 meeting. They had argued that, as potentially all workers in the Dayton plant were exposed to TEL fumes, any comparison of workers within the plant would be of little value as exposed controls would mask the full effects of lead.

Kehoe eventually came to see the merit in his critics' assertions: clearly he had chosen the wrong control group. To answer his critics he searched for an unexposed group in a remote farming village outside Mexico City, far removed from industry or urban pollution. There he sampled food, utensils and the excreta of the residents, which he found also contained lead.

This observation of 'natural' lead levels in Mexican farmers became the nucleus of Kehoe's position

throughout his career. From this observation he concluded that lead in petrol presented no danger to the public, making the same mistake in argumentation that he had made with the Dayton workers. He assumed that general lead contamination was 'normal' and therefore 'natural' and harmless at those 'low' levels. It was not until the geologist Clair Patterson questioned this view some 30 years later that this argumentation was successfully challenged: 'normal' lead exposures in the 20th century were far from 'natural' (Patterson, 1965).

The Second World War years saw the economics and politics of TEL plumbing new depths. The Ethyl Corporation and Standard Oil had continued to develop their business links with Hitler's Germany which they had begun in the 1930s when Ethyl formed the German company Ethyl Gemeinschaft and Standard Oil linked up with the largest German company, I.G. Farben, one of the main corporate supporters of Hitler. This enabled them to provide the German war machine with the technical ability to improve the fuel efficiency of their tanks, lorries and planes by using leaded petrol (Box 3.7).

Industry control of both the economic and public agenda seemed complete by the 1950s but a new perspective was emerging from well outside the TEL community, which would soon seriously challenge industry's virtual dominance of this intellectual terrain.

Is 'normal' lead contamination really 'harmless'?

In 1965, Kehoe's monopoly on lead data was threatened by a geochemist from outside the public health debates. Clair Patterson was a research associate in geology at the California Institute of Technology. His measurements of the isotopic ratios of certain minerals convinced him that the long-held consensus of geologists that the age of the Earth was 3 billion years old was wildly wrong. Patterson's studies placed the age of the earth at 4.5 billion years, a serious challenge to the orthodox scientific view.

His findings were fiercely rejected by believers in the conventional paradigm but they were eventually confirmed, his sceptics refuted, and the geology textbooks revised.

Patterson uncovered the errors in the conventional geological view by employing extraordinary measures to avoid contamination while collecting and analysing his specimens. As a result his measurements were much more accurate than those of earlier workers.

Many scientists would have treated the contamination of his reagents as a technical annoyance to be overcome and then forgotten. To Patterson it was not a nuisance but a clear indication of lead contamination from human activities, which needed to be further investigated. From the depths of the Pacific Ocean he brought tuna to the surface with extreme care to avoid contamination. He studied pre-iron age mummies that had been buried in sandy soil and he sampled cores from the Greenland ice pack. By slicing the ice cores he was able to date the specimen precisely and show the time course of lead in the atmosphere.

Patterson and his colleagues showed that technological activity had raised modern human body lead burdens to levels that were some 600 times higher than that of our pre-industrial ancestors.

In 1965, in response to an invitation by the editor of the *Archives of Environmental Health*, he submitted a long article entitled 'Contaminated and natural lead

Box 3.7 TEL and 'treason' in Germany

In March 1942, Thurman Arnold, a US Assistant Attorney General, told a Senate Committee investigating war profiteering that without the leaded petrol from Ethyl, the Nazis could not have flown their planes or fuelled their land vehicles so efficiently. The Chairman of the Committee, Harry Truman, called the alliance between some American companies and I.G. Farben 'treason'.

A German memo found after the war supported his view: 'It need not be especially mentioned that without TEL the present methods of warfare would be impossible. The fact that since the beginning of the war we could produce TEL is entirely due to the circumstances that shortly before the war the Americans had provided us with the production plans complete with their know how. It was moreover the first time that the Americans had decided to give a licence on this process to a foreign country ... and this only on our urgent request to Standard Oil to fulfil our wish' (Davis, 2007).

environments of man'. Kehoe was asked to review the manuscript and to decide whether it should be published. Kehoe argued for the paper's publication so that Patterson could be offered up for demolition. 'I should let the man, with his obvious faults, speak in such a way as to display these faults.'

He went on: 'The inferences as to the natural human body burden of lead are, I think, remarkably naïve. It is an example of how wrong one can be in his biological postulates and conclusions, when he steps into this field, of which he is woefully ignorant, and so lacking in any concept of the depth of his ignorance that he is not even cautious in drawing sweeping conclusions. This bespeaks the brash young man, or perhaps the not so young [Patterson was 43 at the time] passionate supporter of a cause. In either case, hardly the mark of the critical investigator. It must be faced and demolished, and therefore, I welcome its 'public appearance'.' (Kehoe, 1965).

Patterson's *Archives of Environmental Health* paper fundamentally altered the vocabulary of the debate over the health effects of lead. He recognised that because a certain level of lead was commonplace it did not mean it was without harm. He argued that the term 'normal' should be replaced by 'typical'. 'Natural' should be reserved for those concentrations of lead that existed in the body or environment before contamination by human activities.

It also showed that the so-called 'unexposed' subjects in Kehoe's studies of the Dayton plant workers, or his Mexican farmers, were contaminated by lead, and this lack of a truly unexposed part of the study population would dilute or hide risks of exposure. This dilution of risks by background contamination is now a much more common problem for public health, given the widespread exposures of most people to low levels of chemicals and radiations.

The *Archives of Environmental Health* paper released a fusillade of angry responses from orthodox toxicologists. Their fury focused on Patterson for his hubris in stepping outside his field to talk about people instead of rocks, but they also attacked the editor of the *Archives* journal. This is another example of 'shooting the messenger' which pervades this and most other 'Late Lessons' stories, from John Snow and cholera in 1864 (EEA, 2001) to those current scientists who publish warnings of hazards about climate change, genetically modified organisms and electromagnetic fields.

The controversy over Patterson's paper crystallised the opposing views held by him and Kehoe. Those who adhered to Kehoe believed that lead poisoning occurred only at high doses with obvious signs of severe illness. Patterson clearly spelled out the other position: elevated levels of lead found in all humans were associated with sometimes silent disturbances in body chemistry. Perhaps, Patterson argued, everyone was poisoned to some extent.

For the TEL industry, however, much more than professional reputation were at stake. A group from Ethyl Corporation visited Patterson and tried, in his words, to 'buy me out through research support that would yield results favourable to their cause.' He refused to cooperate (Patterson, 1992).

Following the meeting with Ethyl, his longstanding contract with the Public Health Service was not renewed, and his substantial contract with the American Petroleum Institute was terminated. Members of the Board of Trustees at California Institute of Technology visited the chairman of his department asking that he be fired. Patterson responded with a lecture in which he predicted that future scientists would show that Ethyl's activities were poisoning both the environment and people, and that their operations would eventually be shut down.

Publicly vilified and professionally threatened, Patterson would eventually be recognised by the scientific establishment for his extraordinary contributions to science. He would win the Goldschmidt Medal, the equivalent of the Nobel Prize in geochemistry, be elected to the National Academy of Sciences, and have both a mountain peak in Antarctica and a large asteroid named after him. He also provided the main character for a Saul Bellow novel (Box 3.8).

3.6 1966: US Congress asks awkward questions

In 1966, Senator Edward Muskie, Chairman of the Senate Subcommittee on Air and Water Pollution, presided over hearings on the future Clean Air Act of 1970. He gave considerable attention to the status of lead in the air and in petrol. The Surgeon General, William Stewart, one of the first to testify, gave testimony that revealed the government's concern, perhaps for the first time, about the effects of lead at low doses, particularly in children and pregnant women:

> 'Existing evidence suggests that certain groups in the population may be particularly susceptible to lead injury. Children and pregnant women constitute two of the most

Box 3.8 Saul Bellow and 'zones of incomprehension' in scientists

In *The Dean's December*, Saul Bellow described Professor Sam Beech, a character easily recognisable as Clair Patterson, his friend. 'These scientists were diapered babies when they went public with a cause. But Beech somehow inspired respect … He had authoritatively dated the age of the earth, had analysed the rocks brought back from the moon.'

Bellow describes Beech's theories about the relationship between lead and social disorder and the chilly reception they received from the orthodoxy. 'Here science, which itself was designed for deeper realisation, experienced a singular failure. The genius of these evils was their ability to create zones of incomprehension. It was because they were so fully apparent that you couldn't see them' (Bellow, 1982).

> important of such groups. Some studies have suggested an association between lead exposure and the occurrence of mental retardation among children' (Needleman, 2000).

Once again Kehoe was the industry's principal witness. Two years earlier he had said that enough was known about TEL toxicity to allow the amount of TEL to be increased without risk, noting: 'that no other hygienic problem in the field of air pollution has been investigated so intensively, over such a prolonged period of time, and with such positive results'. When Muskie pointed out that the Public Health Service and others disagreed with Kehoe and that many felt that there were unanswered questions and a need for more research, Kehoe responded:

> 'I would simply say that in developing information on this subject, I have had a greater responsibility than any other persons in this country. The evidence at the present time is better than it has been at any time that this is not a present hazard' (Needleman, 1998).

However, Muskie pressed on: 'would it be desirable if a substitute for lead in petrol could be found?' Kehoe replied: 'There is no evidence that this (TEL) has introduced a danger in the field of public health … I may say the work of the Kettering Laboratory … has established that ... lead is an inevitable element in the surface of the earth, in its vegetation, in its animal life, and that there is no way in which man has ever been able to escape the absorption of lead while living on this planet'.

One week later Clair Patterson testified. He began by attacking the belief that natural lead cycling and human activity contributed about the same amount of lead to the environment. About 10 thousand tonnes of lead were naturally recycled each year, he said, while millions of tonnes were emitted due to industrial and transport emissions. Large numbers of people are sickened, he believed, as a result of this unnatural load, and the brain is the most significant target. Patterson attacked the PHS for relying on industry data:

> 'It is not just a mistake for public health agencies to cooperate and collaborate with industries in investigating and deciding whether public health is endangered; it is a direct abrogation and violation of the duties and responsibilities of those public health organisations. In the past, these bodies have acted as though their own activities and those of the lead industries in health matters were science, and they could be considered objectively in that sense. Whether the best interests of public health have been served by having public health agencies work jointly with representatives of the lead alkyl industries in evaluating the hazards of lead alkyl to public health is a question to be asked and answered.'

Industry had traditionally measured the prevalence of lead toxicity by counting deaths, or at least severe damage to the brain. Muskie raised the question of a larger pool of unrecognised toxic illness, an issue that had been first raised at the one day trial of leaded petrol in 1925 (Needleman, 2000): 'Is it conceivable that there is something different in the deleterious effects on health from low-level exposure than from more concentrated exposure leading to classical lead poisoning?'

Patterson replied: 'when you expose an organism to a toxic substance it responds in a continuum, to continuously changing levels of exposure to this toxic substance. There is no abrupt change between a response and no response. Classical poisoning is just one extreme of a whole continuum of responses of an organism, human organism, to this toxic metal.'

Muskie's inquiry marked the government's shift away from complacency about the hazards of lead. His Senate hearings established a new premise: that lead poisoning was not only a disease of workers; it could be an insidious, silent danger to the public. The notion that lead poisoning was an all-or-nothing phenomenon was discredited and replaced by degrees of disease spanning across a biological continuum of 'effects' to 'adverse effects'. The issue still dominates current discussions about chemicals, radiation and other public health hazards, where early 'effects' are often dismissed as having no biological or ecological significance.

3.7 Lead in petrol poisons catalytic converters — so it's got to go

In 1962 GM sold Ethyl and in 1970 GM announced that it would begin installing catalytic converters in its new models in order to comply with the Clean Air Act of 1970. As a result, GM stated, it would be necessary to phase out lead in petrol as it was poisonous for the platinum in the catalytic converter. Apparently, poisoning a technology was more important than poisoning people.

To Ethyl's management this was a betrayal and they resolved to fight the growing environmental movement in the United States. They argued that it was fully justified to speak out for this additive, which had saved billions of dollars for the American economy and helped make the modern automobile possible. To combat lead regulation, it formed a defence team and called it, with unconscious irony, the 'Ethyl Air Conservation Group'. The Group was staffed with Ethyl officials and members of the Hunton and Williams law firm. Lawrence Blanchard, a partner in Hunton and Williams and board member of Ethyl, headed the group.

EPA medical officers continued to push for a separate health standard, fearing that if a substitute for platinum were discovered sometime in the future, lead would return to fuel. In 1973, aware that 200 000 tonnes of lead were emitted from the exhausts of American cars each year, the EPA promulgated a regulation phasing down lead content in all petrol. Its target was to reduce lead in petrol to 0.5 g/gal within five years (Schoenbrod, 1980).

The TEL industry responded by skilfully exploiting the growing national anxiety about fuel supplies caused by the spike in the price of oil, which had reached unprecedented levels by 1973. The EPA estimated that the oil penalty from phasing out lead was 30 000 barrels per day. Industry's calculations were different: on 2 December 1973 a full page advertisement appeared in *The New York Times* showing an oil barrel bearing an American flag pouring oil down a manhole. Its headline proclaimed that removing lead from petrol would have the effect of dumping one million barrels of oil a day.

On 6 December 1973, however, the EPA released the final regulations requiring a phased reduction of lead in petrol to protect health. Ethyl Corporation and DuPont sued in court, arguing that removing lead would cost an enormous amount of money and crude oil resources; that no one had been poisoned by lead in air; and that any effects in humans reported at low doses of lead were not **adverse** health effects. The court agreed with industry, setting aside the regulations as 'arbitrary and capricious'.

On appeal, the earlier judgement was overturned and the EPA regulations upheld. The court stated that 'the regulatory action under this precautionary statute [the Clean Air Act] should precede, and hopefully prevent, the perceived harm.' Furthermore, 'in making his policy judgment by assessing risks the Administrator is not required to limit his consideration to the danger presented by lead additives 'in and of themselves'. He may consider the cumulative impact of lead additives with other sources of human exposure to lead' (Ethyl Corp. v Environmental Protection Agency, 1976).

Ethyl, PPG Industries, DuPont, NALCO Chemical and the National Petroleum Refiners Association then appealed to the Supreme Court, where they lost.

3.8 Public funding to study lead poisoning in children

In 1970, the US Surgeon General had called for early identification of children with 'undue' lead exposure. His statement avoided the loaded term 'poisoning' but indicated that this was probably more lead than a child should have. For the first time since 1925 significant research funds were allocated from Federal sources to study the health impacts of lead on children. The industrial monopoly on scientific data was drawing to an end.

Professor Herb Needleman was one of the public health scientists who used the recently released public funds to research the low-dose effects of lead on children's IQ. His seminal paper on the subject (Needleman et al., 1979) showed that the higher the lead content, the greater the negative impact on IQ. His work shifted another paradigm by focusing not on the **flow** of blood through the body but on the

Box 3.9 Lead in petrol: 'it's all about economics...'

Late one night after a long day's work on the issue of lead in petrol, Herb Needleman and others from the EPA expert committee had dinner at the home of an EPA staffer. After dinner and a liberal amount of red wine, Needleman asked Jacobs from DuPont why, with its wealth of excellent research chemists, it had not developed a safer petrol additive to replace TEL. In Needleman's words:

'Jacobs, who had matched my intake, told me that their economists had modelled the future sales of leaded gasoline and projected that the consumption of gasoline would soon level off, and perhaps decline. Given such a projection, the company would not invest USD 100 million in research and development funds. I learned a valuable lesson that night: the entire debate about scientific studies, about the health risks for children, was merely a shadow play. The real decision had been made by DuPont's economists. Their plan was clear: don't budge on TEL and seek medical and environmental arguments to support the choice' (Needleman, 2000).

stocks of lead in the bones. His innovation was to analyse 'milk' teeth from more than 2 000 infants and to correlate their lead content with their later development in terms of intelligence and behaviour.

He observed that the average IQ of this group of children fell by 5 points, a shift that was dismissed by industry as 'small' and insignificant. This view ignored the effect on very large groups of children who were at both ends of the normal distribution of IQ, i.e. those either severely handicapped or exceptionally gifted, whose numbers would be doubled and halved respectively (Bellinger and Bellinger, 2006) ([5]).

Industry responded to this dramatic observation with unprecedented opposition, resorting eventually to a character assassination of Needleman.

Needleman later followed up the 1943 Byers discovery of the **chronic** anti-social behaviour of children who had 'recovered' from **acute** lead poisoning, confirming the association between childhood lead poisoning and anti-social adolescent behaviour (Needleman, 1996). Studies have further confirmed the link between lead and anti-social behaviour (WHO, 2010).

3.9 1977–1995: the phase down of lead in petrol

The EPA published its *Air quality criteria for lead* in December 1977, which stated that lead in air and in dust was a significant source of human exposure to lead, and that brain damage could occur in individuals with no acute symptoms of lead poisoning. The Air Office of EPA used the new criteria document to determine a standard for lead concentrations in air.

With the new standard in place and the gradual retirement of old cars that ran on leaded fuel, air lead levels began to fall. In 1977 air concentrations in Philadelphia ranged between 1.3 and 1.6 μg/m^3, whereas by 1980 the concentrations were between 0.3 and 0.4 μg/m^3 (Needleman, 2000). Similar trends were observed in most major cities.

Between 1976 and 1980, the amount of lead consumed in petrol production dropped by 50 % and the blood lead level of the average American dropped by 37 %. Furthermore, in its second volume of the *Air quality criteria for lead* the EPA concluded that, contrary to the claims of the industry, the relationship between petrol production and air lead levels was causal. It noted that between 1975 and 1984 the lead consumed in petrol had decreased 73 %, while the corresponding composite maximum quarterly average of ambient air lead had decreased by 71 % (USEPA, 1986).

In the 1970s the toxic threshold for lead in blood was defined as 60 μg/dl. The reduction of blood lead levels gradually allowed comparisons with children whose background blood lead levels were 1μg/dl or less. As a result, effects of lead on children's IQ have been found at levels below 10 μg/dl, with most of the cognitive impairment seeming to occur at blood lead levels as low as 5 μg/dl (Lanphear et al., 2000).

([5]) Chapter 23 on costs of inaction provides an illustration of this effect in Figure 23.1.

Box 3.10 Lead levels in blood decline

The phasing-out of leaded petrol between 1976 and 1995 was associated with a more than 90 % reduction in the mean blood lead concentration (Annest et al., 1983; CDC, 1997; Jones et al., 2009). The percentage of children in the United States aged between one and five with blood lead levels greater than or equal to 10 µg/dl declined from 77.8 % in the late 1970s to 4.4 % in the early 1990s, and the average lead level of a child in the United States declined to 1.9 µg/dl between 1999 and 2002 (CDC, 2005). At the same time, lead was eliminated from solder used in food cans and new residential paint products (President's Task Force, 2000). An estimated gain of 5–6 points in mean population IQ score was associated with the decline in mean blood lead concentrations, and this gain in IQ has been calculated to yield an annual economic benefit of between USD 100 billion and USD 300 billion in each birth cohort on the US (Grosse et al., 2002).

Similar reports of success in reducing the harm from lead in children level were achieved in Europe and elsewhere as they began to phase out lead in petrol.

In a number of rapidly industrialising countries, too, including China, El Salvador, India, Mexico and Thailand, declines in blood lead levels have followed the removal of lead from petrol (OECD, 1999; Mathee et al., 2006; He et al., 2009). Worldwide, unleaded petrol now accounts for an estimated 99 % of total sales.

Source: WHO, 2010.

Box 3.11 Continuous reductions in the 'safe' level of lead 1960–2010

In the 1960s, an elevated paediatric lead level was defined by the United States Department of Health and Human Services Centers for Disease Control and Prevention (CDC) as a concentration in whole blood of 60 µg/dl.

In the 1970s, the level was reduced to 40 µg/dl, and then to 30 µg/dl. In the 1980s, it was reduced to 25 µg/dl. Most recently, in the early 1990s, the CDC reduced the blood lead level of concern to 10 µg/dl, the level that remains in place today (Surkan et al., 2007).

An international pooled analysis of data from seven cohorts showed an increase in blood lead level from less than 1 µg/dl to 10 µg/dl was associated with a six IQ point decrement, which is considerably greater than the decrement associated with an increase in blood lead level from 10 µg/dl to 20 µg/dl. (Lanphear et al., 2005).

In 2004, 16 % of all children worldwide were estimated to have levels above 10 µg/dl (WHO, 2010).

In 2010 the European Food Standards Agency withdrew its support for a provisional tolerable weekly intake guideline value on the grounds that it was inadequate to protect against IQ loss (EFSA, 2010).

3.10 The pros and cons of leaded petrol

Leaded petrol was finally completely phased out in the US in 1995, seventy years since the 'one day trial' in 1925.

The benefit of taking lead out of petrol exceeded the predictions of even the most convinced lead advocates. Lead levels in children's and adults' blood continued to drop in direct relationship to the reduction in lead in petrol. The average American child's blood lead level in 1976 was 13.7 µg/dl. In 1991 it was 3.2 µg/dl and in 2000 it was 2.0 µg/dl (WHO, 2010).

The health and other costs of lead damaged workers, child bearing women and children to the taxpayer, the Health service and to the economy have been huge and have persisted for decades after the leaded petrol phase out, as contamination persists in soils and dusts (Mielke, 2010). This damage to health has also had large economic consequences as outlined in Box 23.1 in Chapter 23.

Panel 3.2 EU policymaking on lead in petrol — a brief summary

Nigel Haigh ([6])

EU policymaking on leaded petrol emerged mainly from the activities of the UK and Germany. In 1971, the UK government received advice from its Chief Medical Officer that air lead levels should not be allowed to increase above current levels. The government responded by deciding on a phased three-stage reduction in petrol's lead content, from 0.84 to 0.4 g/l to be achieved in 1976. This phase down was then delayed and the deadline postponed until required by the subsequent EC directive. In the same year the German government decided to reduce lead levels but chose a faster programme, which was implemented as planned: 0.4 g/l in 1972 and 0.15 g/l in 1976.

In both countries this in initial action arose in response to scientific advice, without much public pressure. The more leisurely approach of the UK government was possibly linked to the fact that the largest European plant then manufacturing lead additives for petrol was in the United Kingdom.

In 1971 the UK was not yet a member of the EC and it was Germany's unilateral decision that resulted in the EC Commission establishing two committees in 1971 to study the health and technical aspects of lead pollution from motor vehicles. The memorandum concluded that although there was no immediate danger to public health, it was desirable to prevent an increased lead pollution in air. Increasing car use and cross-border sales of petrol by oil refiners therefore warranted EC-wide limits on lead in petrol.

On 10 November 1975, at the European Parliament, the rapporteur of the Environment Committee said that the proposed second stage reduction of lead to 0.15 g/l for regular grade had met with insurmountable opposition in the Committee because it would have required industry to make substantial investments and increased petrol consumption. Since these objections could not be refuted, the Committee preferred to require the Commission to postpone the introduction of the second stage. The Committee did, however, approve the first stage limit of 0.4 g/l.

All subsequent discussion in the Council — where decisions then had to be taken unanimously — was coloured by the existing German limit of 0.15 g/l. Directive 78/611 therefore had to allow Member States to introduce national limits of 0.15 g/l but its main provision was an upper limit of 0.4 g/l.

This example shows how in favourable circumstances a determined Member State can lead its peers despite considerable opposition and scientific uncertainty. In doing so, Germany ensured that higher environmental standards were achieved more quickly than if the Member States had proceeded at their own pace.

In the United Kingdom in 1981, following the report of a scientific committee on lead and health, chaired by Professor Lowther (Lowther, 1980), and of a government working party on lead in petrol (WOPLIP) (UK Department of Transport, 1979), the government decided to require petrol's lead content to be limited to 0.15 g/l, the lowest level that could be required under the Directive. It did not propose lead-free petrol. This recommendation followed a major battle within government: the health and environment ministries were defeated on the second point by transport, energy and the treasury.

Then there was a dramatic change in policy. In April 1983 the Royal Commission on Environmental Pollution (1983) recommended that the government initiate negotiations with the European Commission and other Member States to secure removal of the lower limit of lead in petrol in Directive 78/611 so that at the earliest practicable date all new cars should be required to run on lead-free petrol. The Government immediately accepted this recommendation.

Between these two decisions in the UK (1981 and 1983) there was an extraordinary public campaign. A new organisation called CLEAR (campaign for lead-free air), supported by a millionaire, provided very effective political lobbying and also publicity for the scientific information. It is possible that the Royal Commission only decided to look at the issue of lead because of the campaign, although that is not the view of its Chairman (Richard Southwood). What can be said with some certainty is that the government only endorsed the Commission's conclusions so quickly (within half an hour of publication) because of the campaign and because of an imminent general election.

([6]) This panel is based on extracts from Haigh (1998).

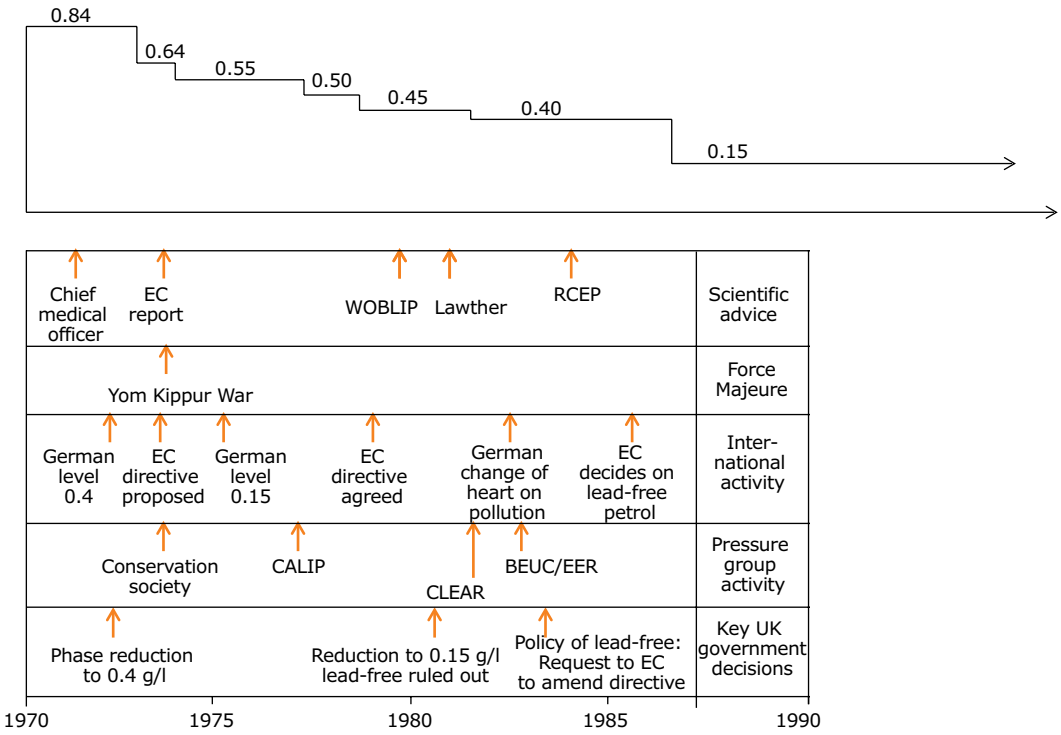
Panel 3.2 EU policymaking on lead in petrol — a brief summary (cont.)

When the first approaches were made to the European Commission in April 1983 the reaction was negative but the coincidence that changed the debate was the concern in Germany about forest die-back, partly caused by air pollution. Germany realised that to achieve its objective of significant NO_x reductions from cars, catalytic converters would be required. Since lead poisons catalytic converters, it would have to be removed. Germany, together with the Netherlands and Denmark, then supported the UK initiative and Directive 85/210 was adopted.

The catalysts for action in the United Kingdom and Germany were similar, but public conscience was excited by two quite different issues: public health and death of forests. It is pure chance that they came together at the same time and if either had been missing it is quite possible that the directive would not have been agreed, or not agreed so quickly. If we are tempted to speculate further, what would have happened if someone had invented a lead tolerant catalytic converter?

Science plays a unique and essential role in informing the public and influencing and guiding public opinion which is a major determinant of policy. But science itself does not always reach the public at a specific point in time when a specific decision is called for. Since we cannot yet claim that there is a European public, but only a collection of national and regional publics, the way the policy debate develops under the pressure of public opinion, more or less informed by science, is very likely to differ between countries. European policymaking is very much about reconciling these differences.

Figure 3.1 Key events which help to explain reduction in lead levels in petrol in Germany, the United Kingdom and the EU



Source: Reprinted with permission from Haigh, 1998.

Panel 3.3 Lead in petrol: a reflection on the German experience

Hans von Storch et al. ([7])

Environmental matters in the early 1970s featured strongly in German politics (Peters, 1980), and Germany was the first European country to impose restrictions on the lead content in petrol. From 1972, German production and importation of petrol with more than 0.4 g Pb/l was prohibited (down from the usual 0.6 g Pb/l), and from 1976 the stricter limit of 0.15 g Pb/1 was imposed. A preliminary analysis of newspaper coverage found that the health dangers of leaded petrol entered the German press in the 1960s. Comparable British articles at that time focused on urban smog.

Unleaded petrol (0.013 g Pb/1) was introduced in Germany in October 1984. Prohibiting the sale of leaded petrol in Germany was not an option because the European Union did not then allow such trade restrictions among its members. Instead, Germany introduced tax incentives for unleaded petrol in 1984, and in 1985 its availability at all German gas stations became mandatory. Enhanced tax incentives in 1986 made German unleaded petrol cheaper than the leaded variety, and its market share increased steadily.

In 1985, the EU mandated that by October 1989 super unleaded petrol had to be available for sale in all member states, alongside the leaded variety (Council Directive 85/210/EEC). In addition, member states were asked to adopt a 0.15 g Pb/1 limit voluntarily. Unleaded petrol was defined as containing no more than 0.013 g Pb/1. In 1987, Directive 87/416/EEC emphasised the importance of the availability of unleaded petrol for sale in every country. All Member States were then allowed to prohibit national production and sales of leaded 92-octane petrol because of damage to public health and the environment.

According to Löfgren and Hammar (2000), by 1995, unleaded petrol had conquered over 80 % of the market in Germany, Sweden, Finland, Denmark, the Netherlands and Austria, but less than 30 % in France, Greece and Portugal. Higher leaded petrol prices and the widespread adoption of cars using leadaverse catalysts were the two most important factors in reducing the market share of leaded petrol. Löfgren and Hammar also note the importance of effectively informing the public that unleaded petrol can safely be used with non-catalyst cars.

Road lead emissions totalled an estimated 31 000 metric tonnes in 1955 in Europe and this nearly quadrupled to 119 000 in 1975 with increasing car use. While road transport and petrol consumption continued to rise, subsequent petrol lead content regulations nearly halved road lead emissions to 62 000 tonnes in 1985. As unleaded petrol conquered increasingly higher market shares, road lead emissions dropped further to 42 000 tonnes in 1990 and to 19 500 in 1995.

Overall, favourable terms of competition were experienced by producers of cars with high technical standards, who had already gathered experience with catalyst systems on the US market (Hagner, 2000).

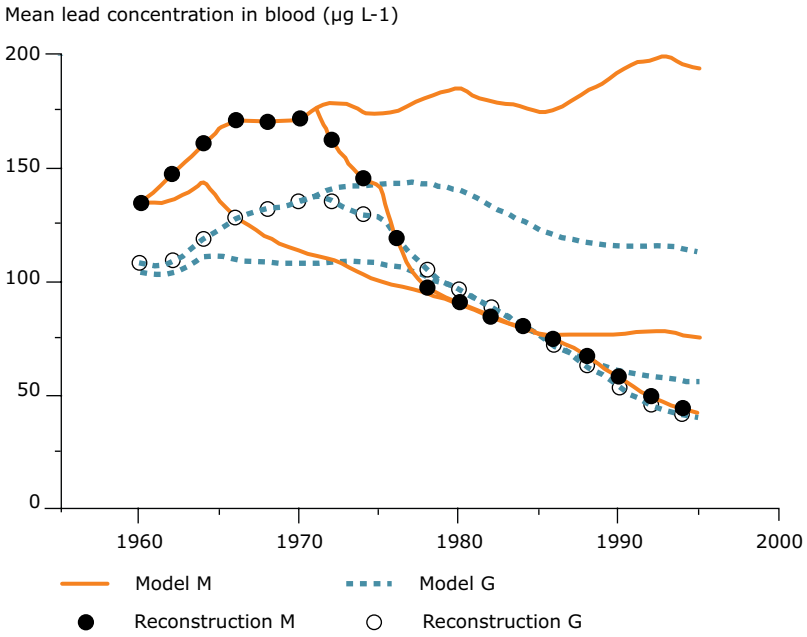
Blood levels in Germany with and without the reduction of lead in petrol
In the 1970s, lead in blood (PbB) values were reaching a level that health officials considered potentially harmful for foetuses and small children. To estimate how PbB levels may have developed if regulations of the use of lead in petrol had been implemented differently a model based on lead emissions was applied. In the case of no or delayed regulations, the model estimates that PbB levels well beyond the critical level would have emerged. Thus, the regulation instituted in Germany since the 1970s has reduced health hazards significantly.

The macroeconomic costs of the regulation seem to have been insignificant in spite of concerns that they would be substantial (Hagner, 2000). In fact, the case of leaded petrol demonstrated the limited utility of purportedly objective cost-benefit analyses, as the costs claimed at the time of the regulations turned out to be significantly biased, due to the vested interests that supported the analyses.

([7]) Adapted from von Storch et al. (2003) with permission from authors.

Panel 3.3 Lead in petrol: a reflection on the German experience (cont.)

Figure 3.2 Scenarios for mean PbB (µg L-1), as derived by the Münster model (M, orange, continuous) and for the Germany model (G, blue, dashed)



Note: Scenario 1 presents an evolution without regulation (i.e. continuing use of 0.6 g/l lead in petrol in Germany, upper curves).

In scenario 2 no unleaded petrol has been introduced in Germany in 1985 (middle curves).

In scenario 3, the regulation was instituted in Germany already in 1961 (lower curves). The reconstructed lead levels in blood are also given as open (Germany model) and full circles (Münster model).

Source: Helmholtz-Zentrum Geestacht Centre for Material and Coastal Research

The conclusion of a successful regulation in terms of limiting risks for human health should not downplay the consequences of the introduction of tetraethyl lead as an anti-knock additive in petrol, in particular since alternatives were known and available already in the 1920s and 1930s (Kitmann, 2000). Heavy metals such as lead pose a large-scale and long-term environmental problem as reduced emissions have limited influence on accumulations in the soil, which will remain for centuries. The strategy of protecting the environment from persistent substances must be based on continuous assessment and precautionary principles (Johansson et al., 2001).

Panel 3.4 The UK experience — expert risk assessments and public campaigns

Erik Millstone

In the United Kingdom, a committee examined the possible dangers of TEL use and submitted their report to the Minister of Health in 1930 (Departmental Committee on Ethyl Petrol, 1930). The committee received advice from several experts, including Dr Kehoe and US Surgeon General Cummings.

Cummings had moved from initial concern to the enthusiastic promotion of TEL writing dozens of letters touting Ethyl leaded petrol to public health leaders around the world. The fact that Cummings reported to Treasury Secretary Andrew Mellon, whose Gulf Oil Co. had exclusive contracts to distribute Ethyl petrol in the south-eastern US, may have had something to do with his enthusiasm.

The committee concluded that 'the widespread use of Ethyl petrol as a motor fuel for motor vehicles would not, in our opinion, increase the proportion of particulate lead in the atmosphere of our streets to such an extent as to constitute a risk even to the health of that part of the population which is most exposed — namely, police officers on traffic control duty and drivers of motor and other vehicles'.

Given the assurances from this report, TEL readily came into use in the UK and the rest of Europe.

By the late 1970s there was evidence of high levels of lead exposure in Britain and strengthening evidence of the toxicity of lead, even at low levels of exposure. The UK government responded by establishing a committee of enquiry. The Lawther report (as it came to be known) reported in 1980 that: 'We have not been able to come to clear conclusions concerning the effects of small amounts of lead on the intelligence, behaviour and performance of children' (Lawther, 1980). That statement was highly controversial. It was subsequently repudiated by several members of the committee for having been overly timid and was criticised by other lead experts (Rutter, 1983; Bryce-Smith and Stephens, 1980). Despite downplaying the dangers of lead in petrol, Lawther nevertheless advised the government and industry to reduce emissions of lead into the atmosphere progressively, without explaining why that advice was provided.

The government subsequently tried to represent the report as if it had proved that children's blood lead levels were entirely harmless. And British Petroleum and Associated Octel, which produced leaded petrol, continued to downplay the toxicity of TEL and atmospheric lead pollution, and the British government resisted efforts to reduce the lead concentration in petrol.

In general, scientists adopted a very cautious approach. For example, a report under the auspices of the Medical Research Council concluded that: 'While the observed statistical associations detailed in this review are consistent with the hypothesis that low-level lead exposure has a small negative effect on the performance of children in ability and attainment tests, the limitations of epidemiological studies on drawing causal inferences are such that it is not possible to conclude that exposure to lead at current urban levels is definitely harmful' (MRC Advisory Group on Lead, 1988).

That approach was marginally modified after the Royal Commission on Environmental Pollution pointed out in 1983 that: 'We are not aware of any other toxin which is so widely distributed in human and animal populations and which is also so universally present at levels that exceed even one tenth of that at which clinical signs and symptoms occur' (RCEP, 1983).

The Lawther committee had recommended that if a child was found to have a blood lead level (or PbB) above 35 µg/dl then steps should be taken to ascertain the source of exposure, and to reduce them (Lawther, 1980). By then, however, evidence of adverse effects below that level was available implying a maximum blood lead target significantly below 35 µg/dL (Chishold, 1976; Needleman, 1979). The Lawther report also neglected to recommend the establishment of a screening programme to identify children with elevated blood lead levels. The committee did, however, recommend that 'There should be a programme for the detection of lead in paint coatings accessible to children in areas where a high incidence of old lead paint surfaces may be suspected, such as old inner city residential areas.' That recommendation was sensible but 30 years later has not yet been properly implemented.

Panel 3.4 The UK experience — expert risk assessments and public campaigns (cont.)

When in 1980, the Lawther Committee recommended that, where a child was found to have a PbB level above 35 µg/dL, an investigation should be conducted to identify and reduce their sources of exposure, it was merely reiterating a policy to which the British government and all other EEC Member States had already agreed three years previously. In 1981 the Department of Health went marginally further when it advised that any child with a PbB over 30 µg/dL should be followed up (Quinn and Sherlock, 1990).

In 1982 the UK government shifted its position and set a maximum figure or 'action level' for lead in the blood (PbB) at 25 µg/dL. When it did so, that decision was made by reference to the results of a blood lead survey rather than toxicological considerations. Surveillance work had indicated that the vast majority of the population then had PbB levels below 25 µg/dL, and therefore endorsing that figure as an 'action level' necessitated no further remedial action. This exemplifies the British government's practice of not setting lead targets until they had already been met.

Throughout the 1980s evidence that lead exerted adverse neurotoxic effects on children at ever lower levels of exposure continued to emerge, especially in the US, Greece and Australia. In the UK an influential pressure group, CLEAR, pressed the government to ensure that the use of lead as a petrol additive was ended. The response of the British authorities to those pressures was the classic tactic of establishing yet another investigative committee, this time under the auspices of the Medical Research Council (MRC). The question posed by the UK government to the MRC panel was: 'does the evidence on childhood neurotoxicity **prove** that levels of lead in British children are doing them obvious harm?' Implicitly, it set a particularly high evidential bar: indicative evidence short of proof would be insufficient. It did not ask: in which physiological system(s), and at which lowest level of exposure, are adverse effects detectable? If it had asked a question of that sort, a rather different answer would have been obtained. The government proposed only to act in the face of compelling evidence rather than, for example, the balance of probabilities.

Eventually, the MRC committee produced two reports. The first one sat resolutely on the fence; it just listed several of the important studies, emphasised their methodological limitations and suggested that if lead was having an adverse neurological effect on British children, the effect was a small one (MRC, 1984).

By 1988, several further studies had emerged, and the second report (MRC, 1988) focused on those recent studies. The committee emphasised many of the methodological limitations of the studies but acknowledged that in the intervening four years the evidence had strengthened. It accepted that 'low level lead exposure has a small negative effect on the performance of children in ability and attainment tests', and so concluded that 'it would be prudent to continue to reduce the environmental lead to which children are exposed.' That final remark was an acknowledgement that the levels of lead to which British children were then being exposed were unacceptably high, although it was couched in language designed not to provoke public anxiety.

In 1987 the United Kingdom eventually started to facilitate the increasing use of unleaded petrol after a preferential tax rate on unleaded fuel was introduced. That policy was adopted to facilitate the use of catalytic converters in motor vehicle exhaust systems rather than in response to evidence of lead's neurotoxicity. Curiously, official efforts to monitor childhood blood lead levels in British children then came to an end, so detailed evidence indicating the beneficial effects of phasing out leaded petrol in the UK have been only fragmentarily documented. It remains difficult, moreover, to estimate the proportion of children in the United Kingdom with elevated blood lead levels.

When the preferential tax change was introduced in 1987, the UK was one of the last industrialised countries to embrace unleaded petrol. It has been difficult to establish the extent to which the slow pace of change could be attributed to the fact that one of the world's main producers of lead tetra-ethyl (Associated Octel) was located in the UK. Nonetheless, it is noteworthy that in the summer of 2010 two former senior executives of Octel were convicted of having bribed government officials in Indonesia and Iraq to continue allowing the use of tetra ethyl lead as a fuel additive in those countries (Leigh et al., 2010).

Of course, leaded petrol also brought many benefits. It improved the energy and fuel efficiency of cars and other vehicles, provided thousands of jobs and generated much profit for the lead, oil and car industries of America, Europe and elsewhere. These benefits could, however, have been attained by alternative uses of the economic capital involved. Indeed, a 10-year phase out of leaded petrol at any time since 1925 would have encouraged innovators to develop less hazardous and perhaps more efficient fuel additives and engine designs. Since the early 1900s, such innovations have been widely recognised as a useful defence against high oil prices and insecure oil supplies.

3.11 European reflections on phasing out leaded petrol

Campaigns to take lead out of petrol in other countries went through similar phases and arguments. Panel 3.1 and Panel 3.3 provide European reflections on lead in petrol, focusing on the EU, Germany and the United Kingdom.

In Europe the legacy of leaded petrol and other sources of lead, such as old mines and lead shot, that can contaminate the food chain via soils and water still pose a threat to the neurodevelopmental health of some children in Europe (EFSA, 2010), as well as to wildlife (Mateo et al., 2007; Rodriguez-Estival et al., 2012).

Meanwhile, lead in electronic waste is an emerging hazard for children in poor countries in Asia and Africa, where waste from rich countries is dumped (Box 3.12) .

3.12 Some late but contemporary lessons

The lessons from the story of leaded petrol are divided into two groups: lessons from the science and lessons from the influence of society on the science. In addition there are some lessons concerning some of the main arguments about the epidemiology that are relevant to many current controversies and which are therefore discussed in Chapter 26 on science for precautionary decision-making.

3.12.1 Some general lessons from the science

1. Much of the early evidence on lead poisoning came from the high exposures of fit, adult, usually male workers. Such findings were widely seen as irrelevant to the much lower exposures of the public to lead in petrol. However, the public can be more vulnerable to low doses of poisons because of sub-groups who are more sensitive to toxicants than workers, such as children, infants, foetuses, the elderly, the sick, pregnant women and the immuno-compromised. In addition, the public are often exposed for up to 24 hours a day and from multiple sources of the same poison via several routes e.g. ingestion and skin absorption from food, water, dust and consumer products, as well as via the inhalation of polluted air. Great care must therefore be taken in assuming that evidence from highly exposed occupational groups, or from low exposures to average populations, is not relevant to sensitive public groups.

2. Much reliance was initially placed on evidence from mortality, or from short-term (acute) poisoning. This can be a poor guide to

Box 3.12 Lead in electronic waste: an emerging hazard

With the global proliferation of computers, cellular telephones and other electronic equipment — as well as rapid cycles of replacement and obsolescence of these instruments — an enormous amount of electronic waste is now generated each year worldwide. Much of this waste — or electronic material near the end of its useful life — is shipped to low-income countries where large numbers of workers in both the formal and informal sectors separate lead, mercury and other metals from the waste for recovery and recycling. In the informal sector, much of the work is performed by children. Elevated lead levels in dust and blood have been reported in the communities and the children performing this work (Xia Huo et al., 2007). In 2004, 16 % of all children worldwide were estimated to have levels above 10 µg/dl (WHO, 2010).

In 2010 the European Food Standards Agency withdrew its support for a provisional tolerable weekly intake guideline value on the grounds that it was inadequate to protect against IQ loss (EFSA, 2010).

long-term (chronic) effects on morbidity such as neurological or reproductive damage.

3. Key assumptions that are critical to outcomes of harm or its absence were confidently asserted rather than demonstrated. For example, the initial assumption from the lead industry, in reply to the US Surgeon General's query about possible health hazards from leaded petrol, was to state that there were none, 'although no actual experimental data has been taken'. This was an early example of assuming that 'no evidence of harm' is the same as 'evidence of no harm' when no relevant research is available to support that assumption. This is a still a common mistake in public health.

4. Another key assumption was that the intake of lead into the body was counteracted by excretion, which was sufficient to achieve a harmless physiological balance, whereby no, or only minimal accumulation of lead in the body would take place. This assumption was not supported by actual evidence of the absence of lead accumulation.

5. Early studies of workers and Mexican farmers did not serve as unexposed control groups as they too were contaminated with lead. When 'unexposed' control groups are also contaminated then true risks will be underestimated.

6. The first study of consumer risks from lead in petrol was too small and short term to detect effects other than acute and gross ones and it was not followed up by the publicly funded longterm monitoring that its authors strongly recommended.

7. Experimental studies in animals documented adverse effects of lead from environmentally relevant concentrations but this evidence was frequently ignored or regarded as irrelevant for humans.

8. Extensive scientific debates, sometimes focusing on diversionary details, or based on the potential for exploiting or even manufacturing scientific doubt helped to maintain the impression that the adverse health effects of environmental lead pollution were unproven. It is often more convenient for a hazardous industry to debate the science than to discuss options for reducing hazards.

9. It was assumed that there was a threshold between biological effects and 'adverse' effects. This is still a dominant assumption in conventional toxicology despite the accumulating evidence that biological effects can be critical steps on the way to adverse effects, as Patterson pointed out in the 1960s. There is usually a biological continuum and not a discrete change. This means that action to avoid significant biological 'effects' will often be needed if we are to prevent, as opposed to merely observe, 'adverse effects'.

3.12.2 The influence of society on science

1. For several decades after the introduction of leaded petrol in the 1920s, virtually no independent research was carried out, and the main source of information was industry and industry-sponsored researchers. It took more independent scientists from outside this group, such as Patterson in the 1960s and Needleman in the 1970s to show, for example, that 'typical' body burdens of lead arising from human activities were not 'normal', as industry claimed, but were hundreds of times higher than before the industrial revolution, and were therefore likely to be harmful, especially to the brains of children.

2. There is a need for sufficient incentives and funds for independent long-term prospective monitoring of potential health hazards when new technologies are introduced.

3. The established and specific technical and economic benefits from leaded petrol, which largely accrued to particular and powerful minorities, were contrasted to the unproven, more general and future health threats to the public. This was an unequal contest, which even influenced many public health specialists, who allowed their appreciation of 'the gift from God', as the car industry described leaded petrol, to override their scientific concerns about health effects.

4. Public health is well served when scientists who discover hazards, especially when funded by the public, play an active role in disseminating both their results and their implications for precautionary or preventive action. Alice Hamilton, Yandell Henderson, Craig Patterson and Herbert Needleman played this role in the US leaded petrol story.

5. Each wave of 'early warning' scientists in the leaded patrol saga, from Yandall Henderson in the 1920s, to Byers in the 1940s, Patterson in the

1960s and Needleman in the 1980s, had either their funding withdrawn, their jobs threatened or their characters assassinated. They share such experiences with other 'early warning' scientists. Such scientists need more support from society via recognition for their work, help with their defence and legal protection against discrimination. This issue is picked up in Chapter 24 on protecting early warners and late victims.

6. The concrete record of decision-making by industries, scientists and governments need to be made publicly available if history is to stand a reasonable chance of being understood and providing relevant lessons for the future.

Table 3.1 Key dates

Year	Event
2nd century BC	First published record of occupational lead poisoning by Nicander.
1695	The count of Württemberg bans lead addition to wine based on Eberhard Gockel's study of lead poisoning in the city of Ulm.
1892	First report of poisoning cases in children from old lead paint.
1920	Leaded paint is banned in Australia and later in Europe.
1921	The octane-boosting property of tetraethyl (TEL) lead is discovered.
1921–1923	Ethanol-based alternative additives are considered by Du Pont and GM but rejected as less profitable than TEL, which goes into production.
1923–1924	Deaths of TEL workers lead to its temporary suspension.
1925	The 'one day trial' of TEL leads to its approval by an expert committee but only under careful monitoring and regulations, which do not take place.
1930–1960s	Kehoe and the TEL industry dominate the research field for next 50–60 years asserting that widespread human lead exposures are 'natural' and therefore safe — and that only acute, clinical effects are serious.
1943	Byers and Lord report chronic brain damage and anti-social behaviour in lead-poisoned children
1965	Patterson reports that current lead exposures are 100 times higher than natural levels and dismisses Kehoes' argument that 'normal' is 'natural'.
1966	Senator Muskie and US Congress start asking questions about leaded petrol and Patterson asserts the likelihood of no safe threshold with a continuum between effects and adverse effects.
1970	US Clean Air Act comes into force. GM announces the phase out of leaded petrol as it poisons the catalytic converters needed to secure the Act's targets for NO_X ,SO_2 and other air pollutants.
1971	UK and Germany begin to reduce permitted levels of lead in petrol.
1973	The US EPA introduces regulations to reduce lead in petrol but is opposed in the courts by industry.
1976	The EPA wins the court case on appeal.
1977	The EPA recognises the existence of subclinical lead poisoning due to environmental lead exposure.
1979	Needleman and colleagues report dose-related mental deficits in children with background lead exposures.
1983	A European Commission study with lead isotopes in northern Italy demonstrates that petrol additives cause substantial human exposures.
1984	Germany introduces low-lead petrol and other countries follow.
1985	A European Commission directive requires Member States to make unleaded petrol available and lowers the limits of lead permissible in petrol.
1995–2000	Virtually all western Europe only uses lead-free petrol.
2012	Nearly all countries worldwide have phased out leaded petrol. Legacy lead persists in water and soils threatening the neurodevelopmental health of some children.

This usually only occurs many years after the relevant events and then only via legal cases for compensation.

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4 Too much to swallow: PCE contamination of mains water

David Ozonoff

PCE (perchlorethylene, also known as 'perc' or tetrachloroethylene), was used in the production of plastic linings for drinking water distribution pipes in the late 1960s and 1970s. This new and relatively untested type of distribution pipe was used in over 700 miles of New England's water distribution systems. Not until 1976 was it discovered that PCE had been leaching into the water from the pipe lining, causing widespread contamination of water supplies that still today require continuous remediation.

Before the pipes were put into production there was a substantial amount of scientific information available about the potential hazards of PCE. This did not include current concerns about PCE's carcinogenicity, teratogenicity and other health consequences of relatively low-level exposure upper most among today's concerns, but many early warnings suggested the need for caution in introducing PCE-based mains pipe linings.

PCE had been used to treat hookworm and data on side effects were in the literature, while later a variety of occupational users were studied, including aircraft workers, small companies in countries where biological monitoring was required, and dry-cleaning firms. Several environmental studies were also conducted to see if drinking water contaminated with PCE or its close relative, TCE (trichloroethylene), was associated with cancer. Results were mixed and the chemical industry consistently denied that PCE was a human carcinogen.

This case study explores the early (pre 1970) history researching the toxicity of the chemical. It also focuses on the failure of one manufacturer, Johns-Manville Corporation, to recognise the warning signals about using a suspected toxic substance. It examines why a new product was deployed without thought to the public health consequences and why evidence of the potential hazard was ignored.

The science has not been hidden. It has been ineffective in guiding and catalysing action. Whether the problem is a failed duty of care or a lack of clarity about what evidence will trigger action, the contemporary argument over how to interpret the scientific evidence is irresolvable within science itself. There are no overarching criteria from the philosophy of science that can dictate a solution.

This chapter also includes two supplementary texts. A panel that analyses the differences between the conclusions of risk assessments based on the same data, focusing in particular on assessments of PCE and TCE. A further panel describes the opportunities to switch to wet-cleaning technologies to reduce the current use of PCE in dry cleaning.

Institutions, large and small, make decisions every day where a conscious application of foresight could prevent a later hazard. Yet such foresight — based on existing information — is often absent.

The present chapter illustrates this with a case study on the use of a now ubiquitous chlorinated ethylene, PCE (perchlorethylene, also known as 'perc' or tetrachloroethylene), to produce plastic linings for drinking water distribution pipes in the late 1960s and early 1970s. Those years represented a strategic and historical turning point in awareness of the importance of environmental carcinogens and teratogens (substances causing embryo malformations).

Some public water supplies are still today contaminated with PCE and require continuous remediation. The use of PCE to apply plastic lining to water pipes occurred when there was already considerable scientific information about the potential hazards it posed. Admittedly, this understanding did not include current concerns about PCE's carcinogenicity, teratogenicity, and other health consequences of exposure to relatively low levels of PCE via various exposure routes, including water mains, whose public health implications remain unresolved. Nevertheless, certain clear early warnings suggested the need for caution in introducing PCE-lined drinking water pipe linings. And the lessons from this early period remain applicable to the situation today.

4.1 PCE linings in water mains

A new and relatively untested type of distribution pipe, installed in the years 1969–1979, is now known to have caused widespread PCE contamination of water supplies in the US state of Massachusetts (Demond, 1982; MDEE, 1982; Larsen et al., 1983).

Efforts to develop and market the new pipe began in the early 1960s when Providence, Rhode Island, Water Supply Board officials sought to replace cast iron mains in low-flow areas that were troubled with colour and taste problems. The Johns-Manville Corporation, a manufacturer of asbestos cement water mains, experimented with clear plastic linings of various kinds. To apply the lining, the plastic was dissolved in PCE and the resulting slurry used to paint the inside of the pipe. The first trial of plastic-lined pipes in 1966 produced water with a slight chemical taste and odour, whose origin was not revealed by routine water quality tests like pH, alkalinity and hardness. In early 1968 Johns-Manville delivered a pipe with the new type of clear lining to the Providence Water Supply Board for testing. It was immediately apparent that air trapped in the pipe took on a chemical odour of slight to moderate intensity, described as similar to chloroform and strongly resembling a commercial dry-cleaning fluid used at a local cleaning plant. Conventional water tests revealed no taste or odour, although the air in the pipe still had a chloroform-like smell.

Further testing showed that under static conditions the lining material continued to contribute a very slight odour even after substantial volumes of water had run through the pipe. Consequently a Johns-Manville representative visited the Providence Water Supply Board, accompanied by two representatives of the company, and they were shown first hand that the water retained a slight odour of chloroform. At a subsequent visit to inspect water samples at a 277-foot pipe with an eight-inch diameter that had been installed the previous month, neither the company representatives nor the water supply chemist detected a similar odour. Explaining the discrepancy, company representatives argued that the pipe with the odour had been kept covered in brown paper and therefore not 'cured' completely.

There is no indication that the taste and odour incident prompted Johns-Manville to investigate the curing process to evaluate whether PCE remained in the liner and potentially contaminated drinking water. Nor is there any record that tests other than routine water quality measures, which did not indicate the nature or amount of organic contaminants, were ever done on samples from the newly developed lined pipe. Not until 1976, when over 700 miles of this pipe had been installed in New England water distribution systems, was it accidentally discovered that PCE had been leaching from the pipe lining into the water.

4.2 Foreseeable harm?

The use of PCE in water mains is a classic case of deploying a new product without considering the public health consequences. In the ensuing battle over who should pay for the damage, Johns-Manville Corporation argued that it did not and could not have known that PCE was a chemical of public health concern, whose presence in drinking water was certainly inappropriate and probably harmful. Much work after 1970 has revealed potential adverse effects from environmental and occupational exposure to PCE, including various cancers, birth defects and autoimmune disease. But could this have been foreseen? If

it was unforeseeable, what factors made it so? Alternatively, if it was foreseeable, what factors prevented adequate foresight?

4.2.1 An insight from the early history of PCE

Before examining these questions, the early history of chlorinated hydrocarbons provides at least one lesson involving PCE. Michael Faraday, now best known for his work on electricity but also a great chemist (Williams, 1965) created hexachloroethane, C_2Cl_6, the first chlorinated hydrocarbon to be synthesised. Heating the mixture produced another gas, perchloroethylene, C_2Cl_4 (PCE).

Faraday was attracted to chlorine chemistry because of a philosophical dispute between his mentor, Sir Humphrey Davy, and Antoine Lavoisier, centred on reconciling the mechanical character of Newtonian mechanics with the notion of free will. Davy and Faraday were Kantians and deeply religious, and the philosophical stakes were extremely high. This resulted in intense disputes with other founders of modern chemistry, including Jöns Jacob Berzelius and John Dalton (Sharlin, 1966).

For the purposes of the present study, the key point to note from this early period in PCE's history is the way that non-scientific concerns can distort scientific disputes. Ideology can make it impossible for protagonists to reverse a course of action or alter a position. But other interests, such as money, market share and reputation, can have similar effects.

PCE's infancy was thus characterised by dispute and doubt. Of course, disputes and doubts are normal in science, particularly when the consequences matter. But this has two corollaries. The first is that a scientific finding may become the subject of dispute and doubt (whether real or manufactured to prevent action) because the outcome matters to someone with the means to challenge the finding and delay action. Conversely, the second corollary is that, if nobody cares or nobody with means cares, there will be little pressure to challenge a scientific finding or explore an issue in greater detail. Results of potentially great significance in other contexts may fail to influence the public health landscape.

4.3 PCE and the chlorinated ethylenes

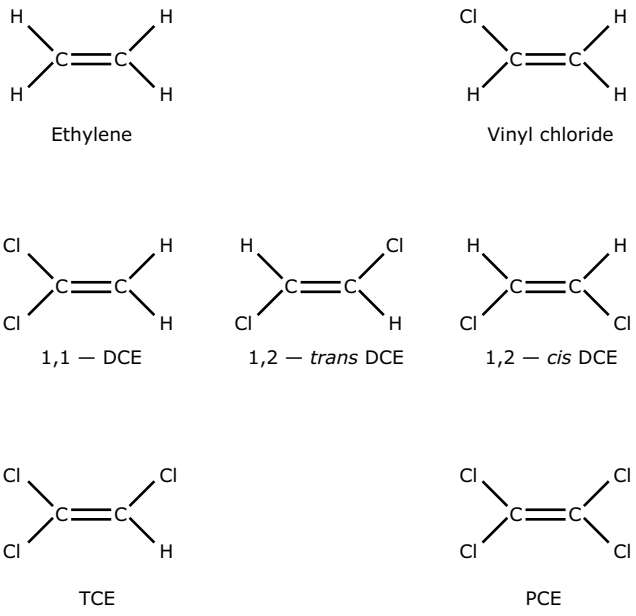
PCE is one of a closely related group of chemicals called chlorinated ethylenes. All the chlorinated ethylenes are built on a common chemical backbone, which consists of two carbon atoms connected by a double-bond. This leaves room or 'slots' for four more atoms, two on each carbon atom. When all slots are occupied by hydrogen atoms, we have the parent hydrocarbon, ethylene. As shown in Figure 4.1, successively replacing each hydrogen atom with a chlorine atom generates vinyl chloride (a known human carcinogen), dichloroethylene (DCE), trichloroethylene (TCE) and tetrachloroethylene (PCE).

All of these chemicals are used by the chemical industry as 'feedstocks' (i.e. the basic ingredients) for plastics or other chemicals. Several are commonly used as solvents for degreasing (i.e. cleaning) metal parts or in the dry-cleaning industry.

The chlorinated ethylenes trichloroethylene (TCE) and perchloroethylene (PCE) were among the highest production volume chlorinated solvents in the twentieth century, used for everything from dry cleaning, metal degreasing and printing to medical applications such as anaesthetics (TCE) or to kill parasitic worms (PCE). These medical and pharmaceutical uses date back almost a century. The familiarity and benefits of these substances should have alerted us to the fact that exposure to these chemicals has biological effects that could also be harmful.

Using PCE to apply plastic resin to the interior of water mains is thus just one of many applications.

Figure 4.1 Chemical structure of chlorinated ethylenes



But the use of PCE in close connection with drinking water occurred at a time when problems could have been foreseen. The early warnings are outlined briefly below.

4.4 Discovery of PCE's toxic effects

Despite PCE's current importance, for more than a hundred years after its discovery by Faraday it saw no significant commercial use. There was little literature about PCE or knowledge of its toxic effects until the 1920s when it was proposed as a treatment for hookworm — parasites of the small intestine that cause severe anaemia. In the nineteenth and early twentieth centuries, hookworm disease affected the health and vitality of millions of rural poor in the United States and elsewhere, stunting children's growth and robbing communities of productivity. Resulting economic losses were substantial (Rosenau, 1935). In the first decade of the twentieth century the Rockefeller Foundation undertook a massive campaign against hookworm disease in the southern regions of the United States using the relatively toxic medicine, thymol. Because thymol had frequent side effects, there was a continuing search for a better agent. One of the first shown to be effective was carbon tetrachloride (CCl_4), but this was less than ideal, leading to the trial of other similar compounds, including PCE.

The introduction of PCE as an anthelmintic (anti-parasite medication) by Hall and Shillinger in 1925 began a process of toxicological evaluation of PCE that has continued to the present day. As new uses for PCE were found in 1934 (dry cleaning) and 1939 (degreasing metals), further studies were undertaken to investigate the effects of PCE on those exposed to the chemical in these new applications.

This pre-carcinogen literature can conveniently be divided into two phases: in the first, from 1925 until approximately 1940, the main interest was in assessing the side effects of a medicine taken by mouth for hookworm disease. In the second phase, from 1940 to 1970 up to the point where PCE-lined pipes were installed, the effects of inhaling PCE from use as a dry-cleaning fluid or degreasing agent were the principal focus of concern.

4.4.1 Phase I: 1925–1940 (PCE use in treating hookworm disease)

When Hall and Shillinger introduced PCE as a treatment for hookworm disease in 1925 they first tested the substance on dogs: 'The question as to the safety of the drug is naturally one of major importance …' (Hall and Shillinger, 1925). Three of the 55 dogs tested died, even though they had received what were believed to be therapeutic doses. None of the dogs that died received the largest doses and as a result Hall and Shillinger became the first of many to comment on potentially significant differences in individual susceptibility.

To test PCE's effects on humans, one of the researchers took a 1 cc (one fifth of a teaspoon) capsule of PCE after breakfast. That night he experienced prompt and complete relaxation of the muscles with slight cerebral discomfort. He had an unusual dream involving levitation, which he believed was due to the effects of the drug.

The dog experiments, self-medication and PCE's chemical structure suggested to Hall and Shillinger that the drug's safety was comparable to carbon tetrachloride (useful in addressing hookworm disease but with known toxicity to the liver), causing lesions similar to those of chloroform. They recommended that PCE be tested under hospital conditions to ascertain its possible value in treating hookworm patients, with due attention to contraindications such as acute or chronic alcoholism, liver disease, infections or other debilitating diseases.

From this modest beginning the use of PCE for hookworm disease gradually increased. Additional studies suggested that PCE, even in relatively small quantities, could have harmful effects on animals and people. But because of its effectiveness as an anthelmintic, PCE's popularity continued to grow and was the subject of several articles (Manson, 1934; AMA Council on Pharmacy and Chemistry, 1936; Wright et al., 1937; Fernando et al., 1939). Thus, while PCE became a commonly used drug, it was not a completely safe one and untoward side effects continued to be reported. These included a paper by Sandground (1941) on two cases of unconsciousness following a normal therapeutic dose. He concluded that:

> 'While for want of a better drug [these cases] should not discourage the use of tetrachlorethylene [PCE], they illustrate the truth of a remark which the late Dr Maurice Hall made to me, to the effect that one cannot assume that any anthelmintic is entirely safe for human use until there are reliable reports on at least a million treatments without any untoward effects.'

The number of other severe side effects from using PCE as a drug is difficult to estimate, although the

question was being considered at the time that the PCE-lined pipes were installed (Bwibo, 1969).

Throughout its use over several decades, PCE tended to produce serious detrimental effects on a small percentage of those treated. As with the earlier dog experiments, the effects were not necessarily related to the dosage. The toxicological picture that emerges from this early literature is evidence of pathologic changes in animals at therapeutic doses, together with reported side-effects in humans, some of which were extremely serious or fatal at doses as small as half a teaspoon (2–3 cc). PCE's potentially lethal side-effects were tolerated because hookworm disease was a major public health problem. There remained uncertainties about the degree of absorption of the drug in humans and the individual variation in susceptibility to its effects. But there was a balance to be struck in terms of achieving public health goals — a balance not found in newer uses.

4.4.2 Phase II: 1940–1970 (PCE in degreasing operations and other industrial uses)

The initial information on PCE's adverse effects came from its therapeutic uses and was sufficient to arouse concern. Subsequent modes of PCE exposure were primarily by inhalation and skin absorption rather than ingestion. Investigators soon began to look more closely at inhalation in particular and for the next three decades much of the study of PCE toxicology involved exposure of human volunteers and animals to PCE via the air. Chronic exposure now joined acute effects as a concern. It is significant that the discipline of epidemiology — the systematic evaluation of the incidence, distribution and possible control of diseases and other factors relating to health — was still primitive and did not enter into most decisions.

In a general review of dangerous gases and vapours, Zernik (1933) noted that Lamson et al. (1929) had produced an optimistic assessment of PCE's risks but contrasted a report by Beyer and Gerbis (1932) of stomach and liver disease ending in death after chronic inhalation of a solution containing PCE as the main ingredient. The extent to which other ingredients might have been responsible for this fatal case was not clear but the potential hazard of PCE exposure appeared evident to the authors.

Dr Alice Hamilton, an industrial health pioneer, was among the first to focus on the new uses of PCE. Writing in *The New England Journal of Medicine* in 1936, Hamilton cautioned that data on PCE's effects on animals might be difficult to apply to human exposures. Humans tended to have more liver damage and less kidney damage than animals exposed to the same substances, she observed. Hamilton also emphasised the differences between acute clinical poisonings and chronic industrial exposures, citing lead and benzene as striking examples of the greater damage that can be caused by low, chronic exposures compared to large, acute ones.

In the discussion that followed her paper, a Massachusetts physician bemoaned the fact that manufacturers were marketing products under trade names, with little information for physicians about the effects of the chemicals. On this point, Hamilton (1936) had observed that:

> 'This, in my opinion, is a problem for the general practitioner since the use of these solvents in industry is increasing by leaps and bounds each day. I have seen many individuals, both male and female, who in my opinion were suffering from conditions brought about by prolonged exposure or exposure under definite circumstances to some of these solvents.'

The importance of low-level chronic exposures was emphasised again in a general review of the pathology of exposure to new volatile solvents, published the following year (St George, 1937). St George noted that slow, chronic intoxications were difficult to recognise and he suggested that chemicals could be broken down into other compounds or retained in the body. Outlining the available information on the toxicity of PCE, he described it as a 'relatively new solvent' and listed its symptoms on inhalation as nausea, giddiness and vomiting with mucous membrane irritation, headache and drowsiness. Echoing the Massachusetts physician, St George (1937) made a special point about warnings:

> 'The danger of these solvents should be explained to every worker and they should be instructed in the preventive measures that have been instituted. When these products are marketed for household use under trade names, etc., detailed instructions should be stated on each container, and it is especially important to state that the product must only be employed in a room with at least one window wide open.'

One of the first to turn his attention directly to PCE as an industrial poison was Carpenter (1937).

He exposed albino rats and human volunteers to PCE vapours at a variety of concentrations. In the rat experiments no pathology was evident at 70 parts per million (ppm) over a 10-week period, but at the next highest level, 230 ppm, there was evidence of congestion, light granular swelling of the kidneys and minimal changes in the liver. Carpenter also exposed himself and his colleagues to PCE concentrations of 500, 1 000, 2 000 and 5 000 ppm. All of them could smell PCE at 50 ppm in air and this odour threshold was reported by many subsequent studies, citing Carpenter. After some hours of exposure, subjects noticed increased salivation, irritation of the eyes, and tightness in the frontal sinuses. One became slightly nauseated at an exposure of 500 ppm for two hours, while higher levels caused more marked effects of central nervous system depression and mucous membrane irritation. At the highest levels, exposure could only be endured for a few minutes. Carpenter concluded that a safe concentration for continuous daily exposure probably lay somewhere between 100 ppm and 500 ppm, but he stated a more precise statement would require additional human experience with exposures within this range.

In the 1940s, despite much discussion about the hazards of chlorinated solvent use, little original work was done, perhaps because of the war effort and the pressures of industrial production. However, several general reviews (e.g. Lehmann and Flury, 1943; Sappington, 1943) recounted information regarding the use of PCE as a drug and the findings of Carpenter (1937) and Barrett et al. (1939).

Morse and Goldberg (1943) affirmed that:

> 'Nevertheless, both solvents are regarded as toxic. There is only one published medical research with which we are familiar [Carpenter] … This investigation by no means clarified the toxicity of perchlorethylene. It stated that 50 ppm produced a definite odour and concluded that a concentration between 100 to 500 ppm is considered safe for daily exposures not in excess of 40 hours per week. This range of 100 to 500 ppm is in need of extensive study'.

They concluded that complaints of headache, nausea and dizziness were common among degreaser operators even when concentrations were well within the generally accepted toxic limit.

Many writers were alarmed by the lack of hard data and the misperception that PCE was non-toxic based on its therapeutic use. For example, in his 1949 textbook on industrial toxicology Fairhall noted that PCE should not be regarded as harmless; indeed, that under certain conditions it was even more toxic than carbon tetrachloride, which was recognised as a serious industrial hazard. Like other authors before him Fairhall called attention to the phenomenon of varying individual susceptibility.

In 1952 a major manufacturer of PCE for degreasing use, the Dow Chemical Company, began to publish reports on the chemical's toxicity. Rowe et al. (1952) assessed the toxicity of PCE vapour to laboratory animals and its effects on human volunteers, with attention primarily focusing on acute effects. Based on this analysis, Rowe et al. argued that exposure should be limited to an average of 100 ppm and should not exceed 200 ppm. They identified irritation of the eyes and central nervous system depression as the prime toxic effects, and considered serious organic injury to be unlikely.

The following year, however, Coler and Rosmiller (1953) reported the effects of PCE exposure and toxicity at a small pump-manufacturing company where parts covered with grease were cleaned with a solvent that consisted of 99 % PCE. A physician who examined a 35-year-old worker with severe stomach bleeding found that he also suffered from severe cirrhosis of the liver and ruptured oesophageal varicose veins. Two of the patient's co-workers complained of malaise, dizziness, light-headedness, headache and irritation of the nose. All three had been exposed to PCE. Worksite exposure measurements showed levels of 200–400 ppm. Subsequent interviews with other workers revealed similar complaints, including tiredness, and feelings of intoxication and hangovers. A few workers reported passing out after exposure but said that they recovered quickly. One worker reported that his eyes 'did not coordinate'. Staggering, stomach aches and slowed ability to think and remember were among the many complaints. Three of seven workers tested had abnormal liver function. The authors concluded that the liver toxicity of PCE should be investigated more thoroughly rather than disregarded. Thus, contemporary clinical observations contradicted the Dow studies.

Coler and Rossmiller's concern was echoed by Lob (1957) in an article entitled, 'The dangers of perchlorethylene'. Lob noted that a toxic industrial chemical is often considered harmless until experience shows the opposite. He then reviewed the animal literature on PCE, remarking that experience was meagre and that the conditions in which investigations had been conducted were

quite varied, meaning that definitive conclusions could not be drawn. He also cited the example of TCE as evidence that the results from animal experimentation could not always be transferred easily to humans.

Lob reviewed clinical experience with PCE, pointing out that it was also scant but identifying ten additional cases of PCE poisoning. One was a fatal case, two more were cases of severe chronic poisoning with damage to the autonomic nervous system, and seven cases were less serious, involving symptoms of fatigue, dizziness, vertigo, headache, nausea and vomiting, anorexia, insomnia, irritability and light cough. The latter symptoms disappeared when the workers were removed from exposure.

Meanwhile, experimental toxicology continued to address PCE (Friberg et al., 1953) but new techniques in animal experimentation were beginning to show inconsistent effects. An investigation attempting to rank chlorinated hydrocarbons according to their liver-damaging potential (Plaa et al., 1958) revealed no correlation between the dose that caused liver damage and the lethal dose in acute exposure experiments.

These concerns spurred further activity in the 1960s on the part of the manufacturer, Dow Chemical Company. In a series of reports, researchers from Dow studied the absorption and excretion of PCE in the body (Stewart et al., 1961a and 1961b; Irish, 1962; Rowe et al., 1963; Stewart et al., 1963; Stewart and Dodd, 1964; Stewart et al., 1965; Stewart and Erley, 1965; Gehring, 1968; Stewart, 1969). Using gas chromatography with infrared spectroscopy or electron capture detection, these researchers discovered that excretion of PCE from the body took an extended time, suggesting that PCE accumulated with chronic exposure. The Dow researchers noted that acute exposure to PCE might, in fact, be a chronic exposure from the body's standpoint because of the slow excretion rate. In studying an accidental over-exposure, they discovered that liver function tests may not become abnormal until two to three weeks after exposure.

The Dow researchers also noted that the mistaken perception that PCE was relatively non-toxic encouraged careless use, which could result in poisoning (Irish, 1962). The Dow reports culminated in a human exposure experiment (Stewart et al., 1970), which found an unexpected prevalence of light-headedness and abnormal neurological results (based on a modified Romberg test) at the lowest exposure levels. The Dow authors could not interpret this unanticipated finding.

Finally, Smyth and his colleagues (1969) added a new and disturbing dimension when they investigated the toxicity of 27 industrial chemicals given to rats in all possible pairs. Using death as the endpoint, they found that most combinations showed no tendency to produce lethal effects in excess of what would be expected from the additive effects of each component separately. Of the nine combinations that did deviate significantly from this pattern, four of them contained PCE, making it the chemical most often associated with causing a net effect greater than the sum of the effects of its separate components. This strongly suggested that PCE could have a potentiating effect on the toxicity of other chemicals (and vice versa).

4.4.3 The view from 1970

The 1960s closed with continued reports of poisoning from PCE at the workplace, usually involving central nervous system depression and concomitant liver damage. There was uncertainty as to the threshold at which such damage first occurred, with some writers considering PCE to be more dangerous than conventionally believed. During that decade there were significant advances in the measurement of PCE and one of its leading manufacturers, Dow Chemical, performed in-house research that was published in the open scientific literature. It was known that individual susceptibility to the effects of PCE varied widely and that the chemical was excreted very slowly from the body, often concentrating there and resulting in a chronic, low-level internal exposure. The suspicion was also raised that PCE could act together with other chemicals to produce a synergistic effect of unknown magnitude.

4.5 Implications for PCE use in water supply infrastructure

What did all the evidence imply for water suppliers contemplating using a product containing PCE?

Leaving aside the acute and chronic effects, there was a potential aesthetic concern. In 1968 the United States Public Health Service Drinking Water Standards stipulated that 'drinking water should contain no impurity which would cause offence to the sense of sight, taste, or smell'. This was done to prevent consumers from seeking alternative but less safe sources of water. Public health experts might have worried that the new pipes could cause a health problem on that basis alone, as a chemical odour was an initial concern.

A review of the medical literature would have added to their unease. It showed that there was considerable individual variation in responses to the chemical, both in the therapeutic environment and in the workplace. Some variation was thought to be inherent and some due to wide variation in the health, diets and exposures of the general population. All these factors were known to affect the potential toxicity. The fact that extremely serious and sometimes fatal side effects were tolerated in mass treatment of a population for a serious disease such as hookworm would probably have been of little relevance to water managers who had no interest in purveying an anthelmintic drug through the water mains.

Experimental work and occupational experience had already shown PCE to be excreted from the body very slowly. Like a bathtub in which the amount flowing from the tap is greater than that draining out, it was plausible that PCE could accumulate from constant daily exposure until it reached the point where it caused toxic effects in some consumers. Using data from Stewart et al. (1965) an elimination rate constant of approximately 25 % (through the lungs) per day can be estimated. Regardless of the level of exposure, after about two weeks (four to five half-lives of 2.5 days each) the level of PCE in the body would have built up to the point where the amount eliminated from the body would be roughly equal to the amount ingested. The final level of PCE would depend on the amount ingested each day.

The maximum level of PCE in water is 100–150 ppm, as determined by its solubility. No measurements of PCE appear to have been made at the time the pipes were installed but assuming a worst case concentration of 125 ppm and the ingestion of 2 litres of water per day implies a constant body burden of approximately 1 gram of PCE. That is close to the dose used to treat hookworm, which had caused serious side effects in some people. For lower exposure, there could plausibly be concern about an 'internal' exposure to levels which would be about four times the daily ingested dose. Concern about such chronic exposures runs through the literature on chlorinated hydrocarbon solvents from Hamilton's 1936 paper onwards.

Public health experts might have been troubled by the emerging literature on the inconsistencies between the animal and human data, as well as inconsistencies in the animal data itself. They might also have been concerned about the possibility that exposures to other chemicals might heighten the toxicity of PCE synergistically.

Public health experts would have been unlikely to view the presence of any PCE in their water favourably unless it was unavoidable. This is not merely a statement based on hindsight. Public health and water managers of that era had been concerned for some time with contamination of groundwater from surface disposal of hazardous wastes like PCE, and the unusual mode of contamination in this case was irrelevant. The environmental historian Craig Colten (1991) has shown that by the early 1950s, 'governmental agencies, professional organisations and industry-trade associations, drawing on three decades of experience, all publicly recognised the hazards posed by the surface disposal of liquid wastes... By the 1940s, it had become apparent that simply protecting a well was insufficient. Public-health officials began to take stronger action to alter industrial waste-disposal practices and thereby prevent the introduction of contaminants into the ground.'

Other historians of waste disposal have come to the same conclusion: the propensity of wastes, including chlorinated solvents, to contaminate groundwater was generally understood in the 1940s–1960s and measures were advocated to prevent it. Put another way, it was understood that contamination of drinking water with chlorinated solvents was a threat to the quality of the water (Amter and Ross, 2001). The fact that in this case the solvent entered the water from the pipe lining rather than land disposal was irrelevant.

4.5.1 Why did Johns-Manville fail to foresee the potential harm?

Johns-Manville Corporation (the pipe manufacturer) may only have recognised the potential harm of PCE with the benefit of 'hindsight'. But the question remains as to why the risks were not recognised earlier.

In the best interpretation, it could be argued that Johns-Manville was never aware of the problem of PCE contamination. Yet, while it is possible that no one in this large industrial concern bothered to think about or investigate the medical literature on PCE, it is quite clear they could have done so. At that point they would have had several options, including redesigning the product, alerting water managers to the potential for contamination from an insufficiently 'cured' product, or continuing to act as if it was not a problem. The company did not even consider or worry about the possibility of insufficient curing, and once the problem was detected, it denied that there

were any health hazards — a necessary position if it were to avoid paying damages for a faulty product.

What is the lesson here? Although there is abundant evidence that Johns-Manville wilfully disregarded and concealed scientific evidence with respect to its principal asbestos products (Ozonoff, 1988), there is no such evidence in relation to PCE. Assuming that knowledge was not hidden, the proposition that Johns-Manville was merely indifferent to these dangers is a plausible explanation for its action; there are many similar examples involving other companies in this period.

The lack of epidemiological evidence would not have been a reason to delay action. Epidemiology was in its infancy and the requirement that even well accepted findings be reconfirmed with epidemiological studies was not yet the norm. The available evidence mainly circulated in the restricted arena of medical specialist literature and the ignorance of most treating physicians and workers about what materials they were being exposed to further served to keep the problem of solvent toxicity off the agenda. This also prevented workers, their unions and their advocates from entering into the conversation about solvent toxicity. If occupational exposures were not on the table, water contamination was also unlikely to be well recognised in this period.

1970 also marked a turning point in the US from minimal federal engagement in workplace and

Panel 4.1 Differences between risk assessments drawn from the same basic data

Christina Rudén

Trichloroethylene, TCE, a relative of PCE, is widely used as a raw material for chemical synthesis, as a solvent for cleaning metal parts and in dry cleaning. A review of 29 TCE carcinogenicity risk assessments conducted between 1973 and 1997 (Rudén, 2002) explored how differences in the selection, interpretation and weighting of primary data affected their differing conclusions.

Classification of TCE risk in risk assessment reports 1973 and 1997

Conclusions of risk assessments: carcinogenicity, epidemiology, human cancer risk				
	No evidence indicating carcinogenicity: *human risk not plausible*	Plausible evidence of carcinogenicity in animals: *human risk not plausible (animal data not considered relevant for humans)*	Plausible evidence of carcinogenicity in animals: *plausible human risk (based on animal data)*	Plausible evidence of carcinogenicity in animals and in epidemiology: *plausible human risk (based on a combination of animal and epidemiological data)*
Total number of assessments 1973–1997	6	10	9	4
Assessments conducted 1995–1996	1	1	1	3

Note: 'Plausible epidemiological evidence' means that people exposed to TCE have greater prevalence of cancer compared to unexposed people.
'Plausible evidence for carcinogenicity in animals' means that animals exposed to TCE in laboratory experiments have an increased incidence of cancer compared to unexposed animals.

Eight of the 10 evaluations that identified a risk for animals but not for humans were conducted by international organisations or industry. Contrastingly, eight of the nine assessments that concluded a human risk based on animal evidence were conducted by government or academic authors. Rudén (2002) observed that this may reflect more risk-averse assessment policies applied by government agencies and academia, and a tendency for industry to apply less precautionary criteria. These wide variations in conclusions continued even within a narrower period, such as 1995–1996, when the evaluating bodies were working from the same available body of knowledge.

Similarly, as shown in the table below, different risk assessors have reached varying conclusions about PCE.

Panel 4.1 Differences between risk assessments drawn from the same basic data (cont.)

Conclusions on the carcinogenicity of PCE

	ECETOC (1999)	IARC (1995b)	ACGIH (1993)	MAK (1992)
Conclusions on PCE carcinogenicity	Plausible evidence of carcinogenicity in animals: *human risk not plausible*	Plausible evidence of carcinogenicity in animals and in epidemiology: *plausible human risk (based on a combination of animal and epidemiological data)*	Plausible evidence of carcinogenicity in animals: *human risk not plausible (animal data not considered relevant for humans)*	Plausible evidence of carcinogenicity in animals: *plausible human risk (based on animal data)*

One important reason why risk assessors differ in their conclusions concerning the size and even the nature of risk is that scientific knowledge increases over time. As risk assessments are updated to include new data the conclusions may change. This is a time-dependent and natural part of the scientific and regulatory process. However, risk assessors may also select different sets of data to support their risk assessments and may interpret key studies in different ways.

An example of this is the interpretation of PCE epidemiology (Rudén, 2006). PCE epidemiology was considered positive in the risk assessment performed by IARC in 1995 and negative in the ECETOC assessment from 1999. The IARC conclusion on epidemiology is based on findings of elevated relative risk of non-Hodgkin's lymphoma (NHL) in three epidemiological studies: Blair et al. (1990), Spirtas et al. (1991) and Anttila et al. (1995). Contrastingly, ECETOC acknowledged the increased incidence of non-Hodgkin's lymphoma in Spirtas et al. (1991) but assigned little weight to the data since the study was initiated because of a priori concerns about lymphatic cancers. ECETOC described the excess of non-Hodgkin's lymphoma in the Anttila study as not statistically significant. Regarding the Blair study ECETOC stated that it did 'not provide results for NHL as a cause of death'. Furthermore, ECETOC concluded that there was 'no excess of deaths due to lymphosarcoma or reticulosarcoma in the Ruder study (1994) and no excess of deaths due to other lymphatic or hematopoietic cancers'. ECETOC concluded that 'available epidemiological studies were either negative or were not sufficient to provide evidence of a relationship between exposure to [tetra] and cancer in humans'. The varying interpretations in the ECETOC and IARC studies are set out in the table below, which is adapted from Rudén (2006).

Interpretation of four epidemiological studies regarding non-Hodgkin's lymphoma by ECETOC (1999) and IARC (1995b)

	ECETOC 1999	IARC 1995
Anttila et al., 1995	Negative (*)	Positive
Ruder et al., 1994	Negative	Data on non-Hodgkin's lymphoma not reported
Spirtas et al., 1991	Positive (**)	Positive
Blair et al., 1990	Negative	Positive

(*) ECETOC described this study as positive on p. 143 ('Anttila et al. reported an excess of NHL...'), and as negative on p.136 ('Increased risks...but none was significant').

(**) Not considered a key study by ECETOC since it was initiated due to a priori concerns about lymphatic cancers.

Various case studies in the first volume of *Late lessons from early warnings* (EEA, 2001) emphasise that such differences are not uncommon in risk assessments. Indeed, as EEA (2008) indicate, this variance in interpretations is attracting increasing attention from regulators and policymakers.

Evidently, evaluators must communicate better about the approach they use to evaluate the strength of evidence and scientific uncertainties. Different evaluators must also employ clear and consistent terminology. This will help minimise the concerns that arise among risk managers and stakeholders when different experts derive different conclusions from the 'same' body of scientific knowledge, or when conclusions and uncertainties are communicated using unclear or inconsistent terminology.

environmental concerns to a prominent role. With the new attention after 1970 came new concerns about contaminating water.

The scientific information on PCE never figured in the water mains product design. It was ignored or invisible. This suggests that the principal reason that Johns-Manville did not care enough to examine thoroughly the risks of using PCE was that nobody made them care. Industrial firms are not people but they nevertheless have interests and intentions, which are rarely related to public health and environmental concerns. The job of a company is to make money for its owners. For Johns-Manville, PCE water mains represented a means of generating profits, with the actual nature of the product having secondary importance. In order for public health concerns to be brought to the forefront, additional mechanisms are needed, most notably criminal and civil liability, both of which rely on state enforcement of legal rules. Other mechanisms are possible, such as moral pressure and voluntary industry standards, but they must all pass the acid test: are they sufficient to make the company care?

Photo: © istockphoto/Steve Jacobs

Once a problem has risen to the level where it can no longer be ignored (and the ability to ignore a problem depends on contextual factors such as the state of knowledge, power relations, economic considerations and political arrangements), much will depend upon a company's assessment of what is at stake. High stakes mean the deployment of considerable resources — resources more at the disposal of large corporations. In such circumstances, uncertainty favours the side of inaction.

4.6 The view from 2012

The period before 1970 had revealed the outline of acute reactions to PCE, and established concern about chronic and delayed effects. Not long after the Massachusetts pipes were installed, an entirely new dimension of PCE toxicology became apparent, concerning carcinogenicity, teratogenicity and other health effects.

In the early 1970s it was discovered that the first member of the chlorinated ethylene series, vinyl chloride monomer, was a human carcinogen (see Chapter 8 on vinyl chloride). This immediately raised the question as to whether other high-volume chlorinated ethylenes, primarily trichloroethylene (TCE) and PCE, might also be carcinogens. By this time PCE was widely used in the dry-cleaning industry, exposing workers and patrons of dry cleaners, and often producing groundwater contamination from improper disposal of spent solvent from the numerous small firms using it.

Because of this heightened suspicion, both TCE and PCE were tested in animal bioassays for carcinogenicity beginning in the mid-1970s (for PCE see NCI, 1977; Mennear et al., 1986). Both were found to be animal carcinogens, although by this time the methodology and validity of animal bioassays had become a matter of dispute and no finding went unchallenged. Attempts at epidemiological verification of PCE's carcinogenicity were difficult because of the long latency for cancer, lack of exposure information and low statistical power of most studies.

A variety of occupational groups were studied, including aircraft workers, small companies in countries where biological monitoring was required, and dry-cleaning firms. Several environmental studies were also conducted to see if TCE/PCE-contaminated drinking water was associated with cancer. Results were mixed and

Panel 4.2 Wet-cleaning technology eliminates PCE use in dry cleaning

Joy Onasch

Massachusetts has designated PCE as a higher hazard substance under the Toxics Use Reduction Act but further policy measures could help phase out the solvent, including by encouraging a shift away from dry cleaning to wet-cleaning technologies. This shift could be further supported by a more comprehensive assistance programme helping convert facilities to professional wet cleaning. As outlined below, the electricity and gas savings involved mean that partnerships with utility companies could help create a programme with additional depth.

Able to dissolve most organic materials, PCE is the most widely used dry-cleaning solvent in the US. The US Environmental Protection Agency estimates that some 85 % of cleaners use PCE as their primary solvent. PCE is also a major contributor to contamination at dry-cleaning facilities, mainly due to past unsafe handling practices. PCE is reported to be the chemical most widely found in groundwater contamination at Superfund sites (TURI, 2007), dry cleaning being one of the main sources.

The concept of wet cleaning in the professional garment care industry has existed for several decades. However, it is only in the last 10 years or so that technology has advanced such that 100 % of garments can be cleaned using the wet-cleaning system. In 1997, Keoleian et al. recommended in the *Journal of Cleaner Production* that larger cleaners could consider operating mixed mode facilities using both dry-cleaning and wet-cleaning equipment.

Today over 150 dedicated wet cleaners operate in California, a state where PCE is being phased out through regulations. California Air Resources Board amendments will over time phase out the use of PCE dry-cleaning machines and related equipment by 1 January 2023. Still, the shift to wet cleaning from solvent-based cleaning has been slow, especially where regulations phasing out solvent use do not exist. Sinsheimer et al. concluded in the *Journal of the Air and Waste Management Association* in 2007 that cleaners they studied in California that switched to professional wet cleaning were able to maintain their level of service and customer base while lowering operating costs. They also found that the cleaners were able to transition to professional wet cleaning without great difficulty and were highly satisfied with the new technology (Sinsheimer et al., 2007).

Onasch (2011) studied a dry cleaning shop in Bellingham, Massachusetts, showing that by becoming a dedicated wet cleaner electricity and natural gas use were reduced by as much as 20 % and even water use was reduced. For this facility, equipment costs were reduced by USD 500 over 12 months, performance costs (claims) were reduced by USD 1 000 over 12 months, operational costs (mainly due to costs of detergents) increased by USD 1 069 over 12 months and costs associated with resource use (calculated using normalised rates) were reduced by USD 2 318 over 12 months. Together, savings totalled USD 2 749 over the 12 months of the study. To replace its solvent machine, the facility spent approximately USD 12 000 (in actual costs, but not factoring in discounts and grant monies received). This implies that the firm would have realised a return on the investment in just under 4.5 years.

Photo: © istockphoto/Frances Twitty

With appropriate training and practice the personnel at this facility were able to master difficult garments and even boasted that wet cleaning resulted in 'whiter' whites and brighter colours than had been possible via dry cleaning.

Time spent cleaning garments was difficult to quantify but with proper training and practice total cleaning time could be reduced due to less pre-spotting, the ability to simultaneously wash and dry in separate machines (unlike the all-in-one traditional dry-cleaning machines) and mastery of the finishing equipment. Indirect benefits of improved air quality, reduced liability, elimination of regulatory oversight, and environmentally friendly niche marketing should all also factor into the analysis of the professional wet-cleaning system.

the chemical industry consistently denied that PCE was a human carcinogen. In each of the individual studies it was possible to find limitations or alternative explanations for positive results (and for negative ones). With each new iteration, new arguments were spun out, sometimes involving epidemiology, later involving sophisticated toxicological arguments as to why PCE could be a carcinogen in rodents but not a carcinogen in humans. In this setting it is not surprising that scientists could look at exactly the same set of data and come to opposing conclusions.

Christina Rudén's panel on inconsistencies between risk assessments of TCE and PCE drawn from the same basic data (Panel 4.1) explores these issues in more detail. Taken as a whole, however, the literature shows a clear and consistent progression towards increasing concern about the carcinogenic effects of PCE. According to Karstadt (1998):

> 'Trichloroethylene and tetrachloroethylene have been reviewed by IARC panels several times: three times (volumes 20, supplement 7, and volume 63) for tetrachloroethylene, four times (volumes 11, 20, supplement 7, and volume 63) for trichloroethylene. Until the consensus meeting that resulted in volume 63 (published 1995) animal evidence for the two chemicals was evaluated as limited and human evidence as inadequate; both evaluations were raised in volume 63, to sufficient in animals and limited in humans. The IARC reviews of those two chemicals clearly show the gradual accretion of human evidence over the years as well as the development of definitive animal data.'

Throughout this period PCE has been on the radar screen of the occupational health and environmental scientific communities, unlike the period before 1970. As a result, fairly strict community drinking water standards have been established, although occupational standards have lagged behind. This inconsistency may partly result from the combination of a weak labour movement and some highly publicised environmental cases involving childhood cancer (e.g. Lagakos et al., 1986).

The problem is no longer invisibility and neglect, but intense scrutiny. The chemical industry has been active and aggressive in countering new information through the strategy of artificially and purposefully creating doubt and uncertainty in the minds of decision-makers. With this chemical now on the cusp of being declared a confirmed human carcinogen in some major national markets, the industry is essentially buying extra time (and creating continuing exposure and disease) by this strategy. Thus 40 years after the hard lesson of the water mains in Massachusetts, a sound precautionary strategy for continued exposure to PCE has still not been initiated.

The means used to avoid or promote action today are different from those of 1970, employing many sophisticated means to create doubt and increase uncertainty about the true value of a regulatory action. The 1970 context was simpler. Evidence was available and not acted on for reasons not complicated by complex regulations, the potential of lawsuits or the activities of environmental or activist organisations. Information about effects and exposure was restricted or non-existent and available primarily to scientists. The industry felt no special need to consult it (although they had contributed to it) and apparently did not. It was of no interest to them.

During both periods the lesson of this small but revealing case study seems clear. Mechanisms are needed to force the production, sharing and publication of information about exposure and effects; normative and legal requirements concerning the duty of care of employers and manufacturers are also required. Alternatives are available, as Joy Onasch's description of wet-cleaning technologies (Panel 4.2) illustrates.

Today, continued argument over how to interpret the scientific evidence is irresolvable within science itself because the same evidence can be interpreted differently and there are no overarching criteria from the philosophy of science that can force a solution.

Whether the problem is a failed duty of care or a lack of clarity about what evidence will trigger action, the history of PCE will continue in the future as it has in the past. The science has not been hidden. It has been ineffective in guiding and catalysing action.

Table 4.1 Early warnings and actions

1860	PCE synthesised
1920s–1960s	PCE used in the treatment of hookworm
1925	First toxicological evaluation of PCE
1925–1940	Clinical and toxicological evaluation of therapeutic use identified a variety of problems and recognised that the responses of different subjects varied
1940–1970	New uses prompt consideration of inhalation dangers; chronic effects studied (central nervous system depression) and new analytical methods brought into play (gas chromatography)
1970–present	Discovery that vinyl chloride is a carcinogen prompts controversy and large literature with competing accounts of PCE's carcinogenicity Environmental and occupational standards were promulgated, generating controversy couched in scientific terms. PCE figures in lawsuits
Today	PCE is regulated in the environmental and occupational environments but controversy continues over where to set standards and whether PCE has caused harm in many legal cases

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5 Minamata disease: a challenge for democracy and justice

Takashi Yorifuji, Toshihide Tsuda and Masazumi Harada ([1])

Minamata disease, which can induce lethal or severely debilitating mental and physical effects, was caused by methylmercury-contaminated effluent released into Minamata Bay by Chisso, Japan's largest chemical manufacturer. It resulted in widespread suffering among those who unknowingly ate the contaminated fish. This chapter documents the story in three phases.

The disease first came to prominence in the 1950s. It was officially identified in 1956 and attributed to factory effluent but the government took no action to stop contamination or prohibit fish consumption. Chisso knew it was discharging methylmercury and could have known that it was the likely active factor but it chose not to collaborate and actively hindered research. The government concurred, prioritising industrial growth over public health. In 1968 Chisso stopped using the process that caused methylmercury pollution and the Japanese government then conceded that methylmercury was the etiologic agent of Minamata disease.

The second part of the story addresses the discovery that methylmercury is transferred across the placenta to affect the development of unborn children, resulting in serious mental and physical problems in later life. Experts missed this at first because of a medical consensus that such transfer across the placenta was impossible.

The third phase focuses on the battle for compensation. Initially, Chisso gave token 'sympathy money' under very limited criteria. In 1971 the Japanese government adopted a more generous approach but after claims and costs soared a more restrictive definition was introduced in 1977, justified by controversial 'expert opinions'. Legal victories for the victims subsequently made the government's position untenable and a political solution was reached in 1995–1996. In 2003, the 'expert opinions' were shown to be flawed and the Supreme Court declared the definition invalid in 2004.

In September 2011 there were 2 273 officially recognised patients. Still, the continuing failure to investigate which areas and communities were affected means that the financial settlement's geographic and temporal scope is still not properly determined. Alongside deep-seated issues with respect to transparency in decision-making and information sharing, this indicates that Japan still faces a fundamental democratic deficit in its handling of manmade disasters.

This chapter is followed by three short updates on the effects of mercury poisoning since Minamata; on attempts to contain it, including the 2009 global agreement to phase mercury out of economic activity; and on the need for better information about contaminant exposures to enable policymakers to make informed choices that balance the benefits of fish consumption against the assumed adverse effects of low-level methylmercury exposures.

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5.1 Introduction

The Minamata disease story is one of blinkered awareness by industry and government, of inaction, refusal to take evidence seriously, insistence on high levels of proof before addressing the problem, and delay, delay, delay.

In 1972 scientists, politicians and the public were shocked by the presence of two Minamata disease patients on the platform at the first global environmental conference, held in Stockholm — the United Nations Conference on the Human Environment (Harada, 2004). They were halting and unsteady, they struggled to speak. They had been poisoned by mercury in their environment.

It took a further thirty-eight years for the first session of an Intergovernmental Negotiating Committee, also held in Stockholm, in June 2010, to start developing a global legally binding instrument on mercury pollution prevention, following the elaboration of a legally binding instrument on mercury at the United Nations Environment Programme (UNEP) Governing Council in February 2009.

At the Intergovernmental Negotiating Committee's opening session, the representative of Japan reported that his government wished to host the conference at which the global mercury agreement would be agreed (UNEP, 2010). He proposed that it be called the 'Minamata Convention', indicating the international community's resolve to ensure that the human health and environmental disaster caused by methylmercury in the Bay of Minamata would never be repeated (UNEP, 2010). He also reported that the Japanese government would contribute all it had learnt about reducing the risk of mercury (METI, 2010).

Despite the Japanese government's apparent determination, many problems remain unresolved in Japan. Key aspects of the disaster are unknown, such as the number of Minamata disease sufferers and exposed residents, and the area and duration

Photo: In 1972 United Nations Conference on the Human Environment in Stockholm focused on the Minamata disease. (From the left) Dr Noboru Ogino, Mr Tsuginori Hamamoto, Dr Masazumi Harada, Ms Fujie Sakamoto (Shinobu's mother), Ms Shinobu Sakamoto, unknown person, and Dr Soubei Togo. Mr Hamamoto and Ms Shinobu Sakamoto are Minamata disease patients.

of exposure. There is not even a consensus on the definition of Minamata disease (Ekino et al., 2007), making it hard to count the number of Minamata disease patients and determine who qualifies for compensation. Indeed, the diagnostic criteria that the Government has consistently used to certify Minamata Disease were judged medically invalid by the Japanese Society of Psychiatry and Neurology (JSPN) in 1998 (JSPN, 1998) and declared invalid by the Supreme Court in 2004 (McCurry, 2006). Nevertheless, the government has not changed the criteria.

The criteria currently being used to diagnose Minamata disease are too strict, meaning that even patients with the related neurological symptoms lack government accreditation. And without government recognition of a Minamata disease diagnosis, a patient will not be properly compensated. Consequently, in September 2011 although 2 273 individuals were officially recognised as Minamata Disease patients (Minamata Disease Museum, 2010), several tens of thousands have neurological symptoms characteristic of methylmercury poisoning but remain formally unrecognised as Minamata disease patients (McCurry, 2006; Watts, 2001; Sankei Shinbun, 2011; Yorifuji et al., 2013).

Given this continuing conflict and suffering, Masazumi Harada ([2]), has observed that when the government of Japan expressed a desire to share its experience and expertise, and to name the new global convention on mercury phase-out after Minamata, it should not merely report its technical success in controlling mercury pollution. It should also 'report to the world that there still remain unsolved problems in Minamata. Not only cases of success but also cases of failure can be valuable lessons for the world' (Kumamoto Nichinichi Shinbun, 2010b).

In this chapter, the history of Minamata disease is presented chronologically, broadly separating the discussion into three parts: the period before 1968; specific issues associated with congenital Minamata disease; and the period after 1968. The chapter concludes with the lessons that can be drawn from the history of Minamata disease.

5.2 Minamata disease in the period up to 1968

5.2.1 Early warnings and signs of Minamata disease: from wildlife to children

'Don't think of labourers as humans; treat them as cattle and horses'

This quote is widely attributed to the Chisso factory founder Shitagau Noguchi, suggestive of past attitudes towards workers, residents and the environment in Minamata (Miyazawa, 1996).

Minamata is the south-western part of Kumamoto Prefecture in Japan, facing Shiranui Sea (Map 5.1), 1 000 km from Tokyo. In 1908, the Nihon Carbide factory was established in Minamata. Later that year it merged with Sogi Electric to form Nihon Chisso Hiryo Kabushiki Gaisha (Japan Nitrogenous Fertilisers). The firm initially used carbide to produce ammonia for fertilisers but, having purchased a German patent for producing ammonia without carbide in 1921, it began using carbide and acetylene (derived from carbide) to manufacture a wider range of organic synthetic compounds.

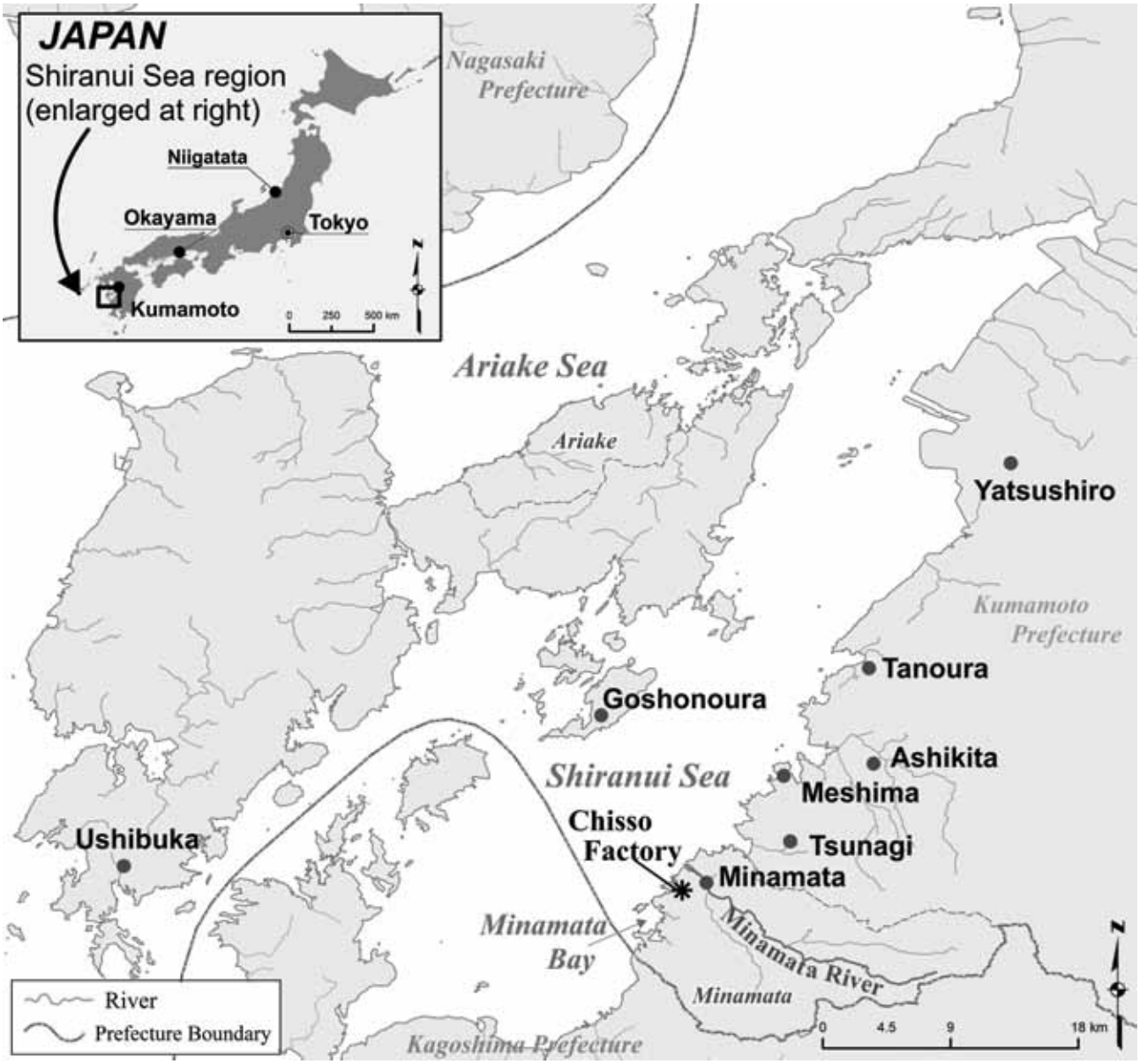
One such compound was acetaldehyde. The factory began producing it in 1932 from acetylene gas, using mercury as a catalyst. The process was developed by Hikoshichi Hashimoto, who later became factory manager and served as Minamata's mayor ([3]).

It is now understood that the effluent from the acetaldehyde production contained methylmercury and this caused Minamata disease. In fact, Vogt and Nieuwland had already shown in 1921 that organic mercury was synthesised in producing acetaldehyde (Ishihara, 2002). In the 1930s, Zangger (1930) and Koelsch (1937) reported on intoxication due to occupational exposure to organic mercury or methylmercury (short-chain organic mercury) (Ishihara, 2002). A researcher at Chisso factory demonstrated in 1951 that organic mercury is synthesised in the production of acetaldehyde (Arima, 1979) but it is not clear whether the Chisso factory was aware of the toxic effects at that time.

([2]) Masazumi Harada, co-author of the present chapter, started researching Minamata disease in 1961 and went to Stockholm with the Minamata patients in 1972.

([3]) He seems to have played a similar role as that of Peter Stockmann, the mayor in Ibsen's play 'An enemy of the people', where he opposed taking action on the public health doctor's report on pollution of the town's spa baths and in favour of suppressing the report. The Chisso doctor Hosokawa, whose report on Minamata disease in the Chisso factory cats was also suppressed, drew some comfort from reading 'An enemy of the people.'

Map 5.1 Map of Shiranui Sea region



Source: Dr. Saori Kashima, Department of Public Health and Health Policy, Hiroshima University Graduate School of Biomedical Sciences, Hiroshima, Japan.

The factory's knowledge of the Zangger study (1930) was considered at the Minamata Disease Trial in 1987 (Hashimoto, 2000) but the findings were inconclusive.

The Chisso factory's acetaldehyde production initially peaked at 9 159 tonnes in 1940, a level not matched after the war until 1955. By 1960, however, it had quintupled to 45 200 tonnes (Figure 5.1), making up 40 % of Japan's total output (Arima, 1979). In 1951, to increase production of acetaldehyde, the factory changed the oxidiser of acetaldehyde production from manganese to iron (Miyazawa, 1996). This production change and related technical improvement are considered to have increased methylmercury waste from the factory (Miyazawa, 1996). Nishimura and Okamoto (2001) estimate a more than eight-fold increase from 1951 to 1959.

In 1952, the factory succeeded in producing octanol from acetaldehyde (Miyazawa, 1996). Japan had previously relied on imports of octanol, an important ingredient in plastics. As a result, the factory increased production of acetaldehyde and by 1959, the factory accounted for 85 % of Japan's octanol output (Hashimoto, 2000). As a consequence the methylmercury waste from the factory also increased.

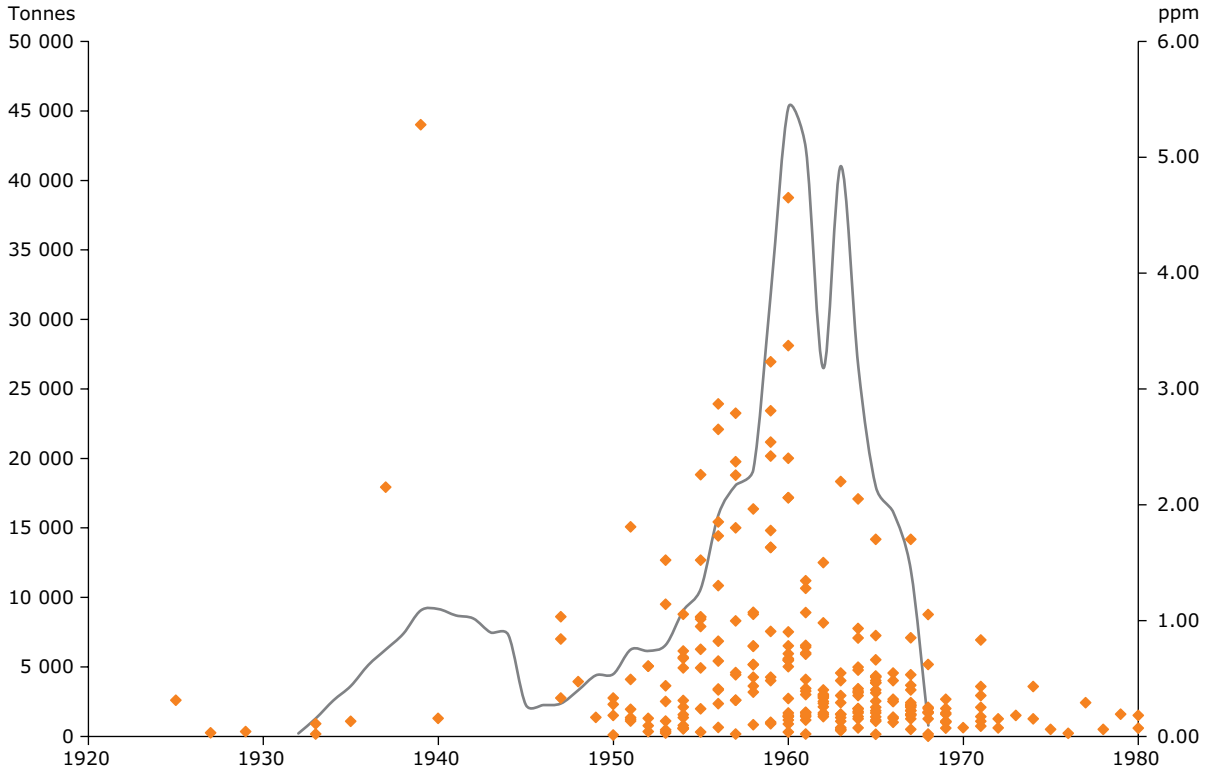
The economic significance of this production was considerable. Japan had recorded a trade deficit since the end of the Second World War (Ministry of Finance, 2011) and plastic products were key Japanese exports at that time helping to reduce its deficit. As the most advanced chemical company during those decades, the Chisso factory clearly had an important economic role.

Minamata city grew with the factory, 'reaching a population of 20 000 in 1921, 30 000 in 1941, 40 000 in 1948, and a peak of 50 000 in 1956' (George, 2001). The factory was a main employer in the city: at least 3 811 of Minamata's 19 819 workers were employed at the factory in 1960 (Ui, 1968). In addition, the factory not only paid half of the local taxes in Minamata but also provided public facilities, such as a factory hospital (Ui, 1968). Hikoshichi Hashimoto, who developed the method to produce acetaldehyde, went on to serve four terms as Minamata's mayor (1950–1958 and 1962–1970) after managing the factory during the Second World War (George, 2001). In these circumstances, Minamata was known as Chisso's 'castle town' (after the capital cities of the feudal lords who controlled much of the lives of its citizens) (Harada, 2004).

The first hints of what was to become Minamata disease may be apparent in reports of the factory's impact on the local fishery (Harada, 2004). Around 1925–1926, the company began to receive requests for compensation from the fishing cooperative. On the condition that no further complaints would ever be lodged, Chisso paid a small amount of 'sympathy money'. The issue of fishery damage arose again in 1943 due to carbide residue from acetylene production and another compensation contract was concluded. And after the war the issue of fishery damage resurfaced in 1949 but compensation negotiations reached no conclusion and the issues faded.

The fishermen knew that it had become more difficult to catch fish; that barnacles did not attach themselves to boats moored near the factory waste outfall; and that fish could not live in water from the outfall. But, the factory would not listen to them, replying that these facts were 'not scientific, not supported by data' (Harada, 2004), although the fishing cooperative

Figure 5.1 Acetaldehyde production at the Chisso factory (line) and methylmercury concentrations in the umbilical cords of residents around the Shiranui Sea (dots)



Source: Reprinted from Science of the Total Environment, vol. 408, 272–276, Yorifuji, T., Kashima, S., Tsuda, T. and Harada, M., 'What has methylmercury in umbilical cords told us? — Minamata disease', Copyright (2009), with permission from Elsevier.

collected and showed detailed data of the fishery damage (described below). In addition, neither the company nor the government assisted in identifying an appropriate scientific protocol for researching the fishermen's significant concerns.

From around 1950, strange phenomena started occurring around Minamata Bay (Harada, 2005). Fishermen witnessed huge numbers of fish rising to the surface and swimming around as though they were crazy. Sea birds that had become unable to fly were seen crouching on the shores of the bay. Oysters and cockles were washed up onto the beach rotting with their shells open, emitting a horrible stench. During this period, according to the data collected by the fishing cooperative, total fish catch of 459 225 kg on average in the period 1950–1953 dropped to 172 305 kg in 1955 and 95 599 kg in 1956 (Harada, 2004).

In 1952, fishermen requested Kumamoto Prefecture to address the situation. The Fisheries Division at Kumamoto Prefecture asked the factory about the discharge treatment and the factory submitted documentation, which reported that mercury was used in the process of producing acetic acid (a substance produced after acetaldehyde) (Chisso factory, 1996). Reiji Miyoshi at the Fisheries Division inspected the factory five months later and reported that the discharge should be analysed (Miyazawa, 1996). However, Kumamoto Prefecture did not conduct a further survey of the fishery damage or the discharge and the fishery damage continued. Moreover, neither Kumamoto Prefecture nor any other group (including the research group at Kumamoto University) ever used the factory documentation indicating mercury use to identify the etiologic agent for Minamata disease or its production mechanism.

Around 1953, local cats, which ate great quantities of fish, began exhibiting strange behaviour: drooling and staggering about, undergoing convulsions or running in circles as though they were mad, or leaping up into the air and charging forward (Harada, 2004). Eventually, fishermen had no more cats. In August, 1954, a local newspaper reported that fishermen in a village (Modo) were annoyed by the increase in mice due to the annihilation of cats (Kumamoto Nichinichi Shinbun, 1954). These strange occurrences were an omen of what would happen next to humans. Watching the 'dancing cats', people began to feel uneasy. Indeed, a few patients with neurological symptoms of unknown origin were detected during this period and a subsequent study revealed that the first patient was traced back to 1942 (Nishigaki and Harada, 1975).

Cats eating great quantities of fish from the polluted Minamata Bay went mad and died after strange dancing and convulsions.

Photo: © istockphoto/Taner Yildirim

On 21 April 1956, a paediatrician at Chisso Hospital, Kaneki Noda, examined a girl aged five years and 11 months. The girl had difficulty in walking and speaking; she appeared to be in a drunken state, unsteady on her feet and slurring her words. She was hospitalised two days later. On the same day, her sister, aged two years and 11 months, developed the same symptoms and she was hospitalised on 29 April. Subsequently, Dr Noda learned of other patients with similar symptoms in the neighbourhood. He officially notified the Minamata Public Health Centre on 1 May 1956 (Harada, 1995 and 2004; Miyazawa, 1996).

Hasuo Ito, the Director of the Public Health Centre, interviewed the children's mother in detail about the disease. He then made a report to the Health Department at Kumamoto Prefecture (Ito, 1996). A newspaper in Kyushu Area, the south-western area of Japan, reported the disease on the 8 May (Miyazawa, 1996). On 28 May, the Minamata Doctors Association, the Public Health Centre, Chisso Hospital, the municipal hospital, and the city government established the Minamata Strange Disease Countermeasures Committee

(Harada, 2004). Subsequently, doctors including Dr Noda and Hajime Hosokawa, the Director of Chisso Hospital, identified numerous new cases. According to the report of Dr Hosokawa, 30 cases including 11 deaths were identified by 29 August (Hosokawa, 1996).

The first official patients lived in a secluded spot at the end of a tiny inlet off Minamata Bay, where five or six families huddled together on the narrow strand. They were so close to the sea that they could have cast a fishing line from the windows at high tide. They were people who lived as one with nature. Because the outbreak of the disease was spontaneous and occurred among neighbours, the doctors at the factory and officials at the Public Health Centre suspected that they were dealing with a contagious disease and moved the patients to an isolation ward. Officials from the Public Health Centre went to the patients' homes and made a show of spraying them with disinfectant.

Transferring the patients to an isolation ward may have indicated an intention on the part of doctors and the city — out of good will or for political reasons — to mitigate the residents' anxiety and to exempt the patients from medical expenses. The patients hated it, however, and it fostered discrimination against them. They were shunned by other community members and experienced years of discrimination (Harada, 2004).

This was the beginning of Minamata disease.

5.2.2 The cause: fish and shellfish contaminated by factory discharge (1956–1957)

In response to the request of the Minamata Strange Disease Countermeasures Committee, Kumamoto University School of Medicine established a research group including various medical departments on 24 August 1956 (MDRG, 1966). In the epidemiological section, Shoji Kitamura and his group conducted both descriptive and analytic epidemiological studies (Kitamura et al., 1957). In the descriptive study, the time sequence of cases was evaluated on a spot map, which indicated that the disease was not contagious. The analytical study revealed a relationship between the family occupation (fishing) and the disease, and a dose-response relationship between eating fish caught in Minamata Bay and the disease. Prof. Kitamura concluded that the disease could be induced by continuous exposure to a common factor, which seemed to be contaminated fish in Minamata Bay.

On 3 November 1956, the Research Group on Minamata Disease reported that the disease was not contagious but rather a food poisoning incident resulting from intake of fish contaminated by a heavy metal in Minamata Bay. It also reported that the factory's effluent was considered the cause of contamination (Kumamoto University, 1956). Furthermore, in the second debrief session on 26 February 1957, the Research Group recommended prohibiting fishing or applying the Food Sanitation Act (Miyazawa, 1996). The Act could be used to take actions against food poisoning, such as prohibiting the sale or distribution of food. An individual disobeying such a prohibition could face criminal punishment.

In November 1956, the Scientific Research Team of the Ministry of Health and Welfare of Japan (MHWJ) started an epidemiological investigation in Minamata (Matsuda et al., 1996). In March 1957, they demonstrated a relationship between the family occupation (fishing) and the disease, consistent with the Kumamoto University Research Group's epidemiological study. Moreover, they showed that families living closer to Minamata harbour, where factory effluent was discharged, were affected more than families living further away. For example, all seven families in the Tsukinoura area included at least one patient, while 33 % (7/24) of families included a patient in the Yudo area. Noting that sea water and mud in Minamata Bay was strongly affected by the factory effluent, the Research Team inferred that fish caught in Minamata Bay were contaminated by the effluent. They concluded that the disease could be induced by contaminated fish in Minamata Bay and that the factory and its effluent should be fully investigated to elucidate the disease's mechanism.

In response to these findings, the local government of Kumamoto Prefecture considered applying the Food Sanitation Act in March 1957 (Kumamoto Prefecture, 1996b) because Shizuoka Prefecture had used the Act to address an episode of shellfish food poisoning in 1950 (Shizuoka Prefecture, 1996). The local government had the authority to decide whether to apply the Act but asked for an opinion from the national government on 16 August (Kumamoto Prefecture, 1996a). On 11 September 1957, Masayoshi Yamaguchi, the Chief of the Public Health Bureau of MHWJ replied to the local government as follows (bold added) (MHWJ, 1996a):

I. 'We recommend that you should continue your policy of warning against the ingestion of fish and shellfish caught in a specified area of Minamata Bay because it may lead to the

occurrence of the unknown disease of the central nervous system.'

II. 'There was no clear evidence that **all** fish and **all** shellfish are poisoned in the specified area in Minamata Bay. Therefore, we have decided that it is impossible to apply Provision 4-2 of the Food Sanitation Act to all the fish and shellfish to be caught in that area.'

Japan's Food Sanitation Act provides that a local government's public health centre must investigate food poisoning outbreaks in detail and take measures in response. When a cause (e.g. an institution or food) is identified, the exposed area and residents must be investigated and the sale or distribution of the cause prohibited. In Minamata, despite the risk outlined in paragraph I of the reply, consumption of contaminated fish was not prohibited based on the reasoning in paragraph II. Although the Minamata Public Health Centre, like the Minamata Strange Disease Countermeasures Committee, identified severely affected patients from the start of its work, it did not further investigate the area and the exposed residents epidemiologically. Residents continued to eat contaminated fish without effective information.

In 1990, the government of Japan asserted that another reason it did not apply the Food Sanitation Act in 1957 was that the etiological agent (methylmercury) had not been identified in 1957 (Environment Agency et al., 1999). While the etiologic agent may not have been clearly identified in 1957, however, the cause/transmission (ingesting fish caught in Minamata Bay) was identified in 1956. Indeed, fish in Minamata Bay were recognised as food causing Minamata disease even in records of food poisoning published by MHWJ in 1956 (Department of Environmental Sanitation, 1957).

It is perhaps surprising that the governments of Shizuoka and Kumamoto Prefectures responded differently to their respective food poisoning episodes, although each had the same strength of evidence that shellfish or fish were contaminated with an unknown etiologic agent. Shizuoka Prefecture decided itself to apply the Food Sanitation Act, while Kumamoto Prefecture asked MHWJ and finally did not apply the Act. Miyazawa (1996) has argued that Kumamoto Prefecture's response reflected the Prefecture's concern about the compensation claims that Chisso factory would have faced if the Act had been invoked.

The early epidemiological studies identified the causes of the health impacts but concentrated solely on severely affected patients and did not investigate the health status of residents in affected areas, as required by the Act. This caused serious problems later. Since the government undertook no effective countermeasure, subsequent research sought to discover the etiologic agent or its mechanism of production in university laboratory settings rather than using epidemiological studies to find moderate cases or investigate health in local settings. During this period, local residents were almost unaware of the finding that the fish and shellfish were contaminated. Although some residents probably knew of the contamination from newspapers and their own experiences, poor fishermen in particular could not stop fishing, as this was their only means of survival.

Whereas affected fishermen lacked political power locally and nationally, Chisso factory was supported by the local government and Ministry of International Trade and Industry of Japan (MITIJ) at that time. Subsequent events clearly indicate that Chisso factory had considerable influence in Japanese industry and society. The Chief of the Department of Environmental Health who recommended not invoking the act in his reply to local government in 1957 had taken measures beyond the law to address a polio outbreak in the 1950s, importing vaccine from Russia. When a lawyer later asked him why he had avoided prohibiting fish consumption in the Minamata disease outbreak in accordance with the Food Sanitation Act despite taking measures beyond the law in the polio outbreak, he replied 'Chisso never existed behind the polio outbreak'.

In the late-1950s, the officers of MITIJ sent weekly demands to the Water Quality Maintenance Section of the Economic Planning Agency of Japan (EPAJ) that wastewater bans should never be implemented. The MITIJ officers urged their counterparts to 'stick it out' and 'offer opposition to the ban', stressing that 'Japanese economic growth would never be realised if such a big industry, Chisso, were stopped. Never stop it!' (Hashimoto, 2000).

5.2.3 Organic mercury theory (1958–1959)

With neither the factory not the Government taking appropriate measures to control the outbreak, exposure continued and spread. Following a research meeting on 15 February 1958, Masayoshi Yamaguchi, Chief of the Public Health Bureau of MHWJ reported to other ministries and local governments on 7 July 1958 that: 'Minamata disease was caused by intake of contaminated fish and shellfish. The discharge from Minamata factory

(Chisso factory) affected Minamata Bay. The same chemical toxicant (which the discharge of which affected the bay) was considered to poison the fish and shellfish' (MHWJ, 1996b).

A local newspaper reported the news, describing it as the first MHWJ statement to mention the factory as a cause (Kumamoto Nichinichi Shinbun, 1958). Yamaguchi, who made the statement, explained later in court that MHWJ had reported to Kumamoto Prefecture because it expected the Prefecture to take control measures based on the Food Sanitation Act (Miyazawa, 1996). However, the Act was not invoked.

Following the MHWJ statement the factory took steps to dilute the discharge containing methylmercury. In September 1958 it changed the drainage route of acetaldehyde production from Minamata Bay to Minamata River (Harada, 1995 and 2004; Miyazawa, 1996), where some effluents (such as phosphoric acid effluent, carbide residue) were already discharged (Nishimura and Okamoto, 2001). Several other factors probably also influenced the factory's decision to act (Miyazawa, 1996): the factory had learned of Kumamoto University's focus on mercury; high mercury concentrations had been detected in shellfish in Minamata Bay; the factory wanted to increase acetaldehyde production; and everyone knew that residents continued to eat fish.

Hajime Hosokawa, Director of Chisso hospital, objected to the plan. He also noted that 'if patients were detected in the area around the Minamata River, it would prove that the discharge was the cause' (Miyazawa, 1996). However, the plan was executed — without the knowledge of local residents. Exposure subsequently spread not only in Minamata Bay but along the entire coast of Shiranui Sea. Fish and cats began to die in other villages (Harada, 1995). And from 1959 onwards, patients with similar neurological symptoms were identified among the residents of other villages around the Shiranui Sea (Kumamoto Nichinichi Shinbun, 1959; Ninomiya et al., 1995; Yorifuji et al., 2008).

Meanwhile, researchers at Kumamoto University's School of Medicine continued their efforts to find the etiologic agent of Minamata Disease and its biological mechanism of action. This was not easy because the Research Group knew nothing about the interior of Chisso factory (Harada, 2005): what was produced, how it was produced, what substances were used and which processes. At that time the Research Group received no assistance from the engineers at Chisso factory or even from the organic chemistry sector of Kumamoto University's School of Engineering.

The Research Group identified various possible etiologic agents — manganese, thallium and selenium — but when fed to cats these substances did not produce effects comparable to organic mercury (Takeuchi et al., 1960). Although mercury was the first etiologic agent considered, Shoji Kitamura of the Research Group has recollected with regret that 'Mercury was taken off the list on the assumption that such an expensive material would never be thrown away in the sea' (Harada, 2004).

Douglas McAlpine, a British neurologist, visited Minamata on 13 and 14 March 1958. He examined 15 Minamata disease patients and made a very valuable observation, noting that symptoms such as constriction of the visual field, impaired hearing and ataxia closely resembled those of methylmercury poisoning reported by Hunter et al. (1940).

McAlpine reported his observations in the journal Lancet in September 1958 (McAlpine and Araki, 1958). In his paper, he pointed out that the disease was caused by eating fish caught in Minamata Bay as well as the toxic action of a chemical compound contained in the effluent from Chisso factory (McAlpine and Araki, 1958). Moreover, he listed methylmercury as one of the metals which could induce Minamata disease. This was the first time that methylmercury was identified as a potential etiologic agent. McAlpine's observations were important but before he could report them to a Japanese Society of Neurology Conference he was stopped by a professor of Kumamoto University on the grounds that too many theories would be confusing (Harada, 2004).

Meanwhile, another researcher, Tadao Takeuchi, also suspected that the etiological agent was organic mercury since he also saw similarities to so-called Hunter-Russell syndrome (Hunter et al., 1940; Hunter and Russell, 1954). Takeuchi et al. (1960) extracted significant levels of mercury (not organic mercury) from patients' organs at autopsy and also succeeded in inducing similar neurological symptoms in cats by feeding them organic mercury.

Shoji Kitamura and his Research Group likewise extracted large quantities of mercury from mud and shellfish in Minamata Bay (Kitamura et al., 1960b), and noted that concentrations decreased as the distance from the factory increased. They extracted mercury from experimentally affected cats at autopsy and ascertained that mercury levels

increased in shellfish bred in the bay, demonstrating that mercury was accumulating internally (Kitamura et al., 1960b). On 22 July 1959, researchers finally concluded that the etiological agent was mercury based on the clinical characteristics and animal experiments (Kumamoto Nichinichi Shinbun, 1959; Kumamoto University, 1996).

During this period, researchers at Kumamoto University School of Medicine suspected that the mercury concentrations were a byproduct of vinyl chloride production. This is because when they had asked the factory in 1957, the factory had only mentioned vinyl chloride among organic synthetic compounds that the factory produced, and mercuric chloride was actually used as a catalyst in the production process (Miyazawa, 1996). In addition, they noticed that vinyl chloride output growth paralleled the increase in patients (Takeuchi et al., 1960). Although focusing on the vinyl chloride process, the Kumamoto University Research Group was unable to show how inorganic mercury in the waste from producing vinyl chloride changed to organic mercury.

Leonard Kurland of the National Institute of Health (NIH) in the US visited Minamata in September 1958 and examined patients. In a subsequent article, he supported the Kumamoto University's conclusion that the etiologic agent was organic mercury in *World Neurology* and also focused on vinyl chloride production (Kurland et al., 1960). However, a local newspaper, the 'Minamata Times', published by Masao Shino, a Minamata citizen, already noted on 10 December 1959 that mercuric salt was used as a catalyst in producing acetaldehyde and suspected the relationship between the acetaldehyde production and the disease (Minamata Times, 1996). This information must have been leaked from workers inside the factory.

On 7 October 1959, Hajime Hosokawa, Director of Chisso Hospital, succeeded in inducing Minamata disease in a cat, labelled number 400, which had been given waste water from acetaldehyde production daily for 78 days (Harada, 2004). This important finding, which was not made public, clearly shows that the waste from acetaldehyde production actually contained organic mercury. If the Kumamoto University Research Group had known of this finding it could have made great process. Instead, when Dr Hosokawa reported the cat number 400 result to the factory, the findings were kept secret and the factory prohibited further studies (Miyazawa, 1996). When allowed to restart experiments in 1960, Hosokawa found that cats given waste water from acetaldehyde production also manifested disease. However, he resigned from the factory in April 1962, without being able to make the results public.

Later in 1962, Jun Ui, a postgraduate engineering student, and Shisei Kuwabara, a photographer, visited a doctor at the Chisso factory (Mishima, 1992) and found a note concerning the results of the experiments on cats. Kuhabara photographed this evidence when the doctor was out of the room. They subsequently showed the photograph to Dr Hosokawa who acknowledged its authenticity. Ui later related these facts along with other details about Minamata disease in the monthly magazine Goka and the information played an important role in the first Minamata disease lawsuit (Tomita, 1965). Despite suffering from lung cancer, Dr Hosokawa testified in the first Minamata disease lawsuit in 1970 from his hospital bed, making two key points (Mishima, 1992): first, cat number 400 had definitely demonstrated symptoms of Minamata disease; second, his recommendation that the factory waste should not be shifted from Minamata Bay to the mouth of the Minamata River had been ignored. He died later that year.

Wastewater containing methylmercury from Chisso factory was led directly into Minamata Bay.

Photo: By Eugene Smith © Aileen M. Smith

Based on the Kumamoto University Research Group's July 1959 report, organic mercury was recognised as the etiological agent by the Minamata Food Poisoning Committee organised by MHWJ on 12 November 1959 (MFPC, 1996). However, there was no mention of the source of the contamination, Chisso factory. Indeed, before the Committee announced that organic mercury was an etiologic agent, the section chief of the MHWJ Environmental Sanitation Department told the Committee's representative not to conclude that the factory was a cause because it was not 'scientifically' proved (Miyazawa, 1996). And after the Committee had reported its opinion to the Minister of Health and Welfare, it was suddenly dissolved. No official reason was ever given.

An inter-ministerial meeting was held on the day before the Minamata Food Poisoning Committee's announcement. There, an MITIJ representative told researchers and other officers that: 'No similar patients have been observed around chemical factories with the same system as Chisso. If the operation by Chisso were causal, we would find such patients around those factories. Furthermore, the mercury used in the Chisso factory as a catalyst is inorganic. The causative agent that you have identified is organic mercury. No means by which inorganic mercury could be converted to organic mercury has been identified. We cannot accept the explanation that waste water from Chisso contains the etiologic agent of Minamata disease' (Hashimoto, 2000).

In September 1959, Chisso factory likewise refuted the organic mercury theory based on the absence of similar disease at other factories; difficulties explaining the abrupt increase in patients since 1954 and uncertainty regarding the organic chemical reaction mechanism (Minamata factory, 1996). This was despite the fact that a factory researcher had already demonstrated that organic mercury was synthesised in the production of acetaldehyde in 1951 (Arima, 1979).

The factory also claimed that it was difficult to trust the Kumamoto University Research Group because it had considered other theories (manganese, thallium or selenium) before identifying organic mercury (Minamata factory, 1996). In line with Chisso's counterargument, Raisaku Kiyoura, a professor at Tokyo Institute of Technology, claimed that mercury concentrations in Minamata Bay were not higher than those in other areas (Harada, 2004). Furthermore, Takeji Ohshima, the Executive Director of the Japanese Association of Chemical Industries, suggested that the cause might be explosives dumped into Minamata Bay by the Japanese military (Harada, 2004).

The debate suggests that Chisso factory intentionally, although inconsistently, used reductionist argumentation to postpone action. On one hand, despite the abundance of evidence that had already existed since 1956, Chisso factory contended that the only way to prove causality between its production processes and the organic mercury concentrations was to demonstrate, via a reductionist approach, the chemical mechanism linking the two. On the other, it criticised the researchers at Kumamoto University for applying a reductionist approach by considering other possible metals first. In addition, the consistency argument (relating to the absence of similar disease in other areas and abrupt increases in patient numbers) was also intentionally used to postpone action.

Recent analysis provides the following explanations for the absence of similar disease near comparable factories. First, the factor's output of acetaldehyde was the highest in Japan at that time, accounting for one third or a quarter of national production (Hashimoto, 2000). Second, methylmercury by-product per unit of acetaldehyde production was higher than at other factories due to technical improvements to increase acetaldehyde production (Hashimoto, 2000; Miyazawa, 1996). Third, the factory's proximity to the sea meant that the chloride ion concentration of industrial water was high, which changed the methylmercury byproduct to volatile methylmercuric chloride (Hashimoto, 2000; Nishimura and Okamoto, 2001). It was then discharged when the acetaldehyde was purified by distillation.

Organic mercury represented the most credible explanation but was resisted by Chisso, the chemical industry and the MITIJ. The MITIJ therefore ordered Chisso to return the drainage outfall of acetaldehyde production to Minamata Bay (from the Minamata River) and to install wastewater treatment equipment within the year (Harada, 2004). The factory therefore established a purifying system for the contaminated water in December 1959 (Arima, 1979; Harada, 2004).

Most residents believed that the discharge of the etiological agent would soon cease. However, the system installed, as should have been known by Chisso at the time of installation, was completely ineffective at removing methylmercury (Irukayama, 1969). It was installed only to give the appearance of action by the company and researchers at Kumamoto University were deceived by being given a fake sample from Chisso factory (Miyazawa, 1996). Unsurprisingly, mercury concentration in fish and

shellfish in Minamata Bay failed to decline after the system was installed (Irukayama, 1969). To make matters worse, the effluents also continued to be discharged into Shiranui Sea (Irukayama, 1969). As a result, residents not only in Minamata Bay but also in the other villages around Shiranui Sea continued to be exposed.

5.2.4 Detecting the organic mercury production process and social recognition of Minamata disease (1960–1963)

Although researchers were now satisfied that organic mercury was the etiologic agent of Minamata disease, no steps were taken to control the poisoning. Researchers concentrated on identifying organic mercury in organisms or finding the mechanism by which it was produced. On 14 February 1960, Makio Uchida, a professor at Kumamoto University, extracted organic mercury in a shellfish in Minamata Bay (Harada, 2004; Uchida et al., 1960). Subsequently, researchers at Kumamoto University made further important findings: confirming that short-chain organic mercury was toxic, extracting methylmercury sulfide from shellfish, and inducing Minamata disease in cats and mice using the substance (Harada, 2004; Sebe et al., 1961; Uchida et al., 1960).

In February 1960, the Minamata Disease General Investigation Committee was established to replace the dissolved MHWJ committee and research Minamata disease (MDGIC, 1996). Many of the discussions in the Committee centred on possible objections to the organic mercury theory and served only to obscure the theory (George, 2001). Its last meeting was held in March 1961. Finally, in March 1962, Fisheries Agency abandoned research regarding Minamata disease (Arima, 1979). After that, no research activities were conducted by government agencies until 1968.

In April 1960, the Minamata Disease Research Council, known as the 'Tamiya Committee', was established (Miyazawa, 1996). Its chair was Takeo Tamiya, President of the Japanese Medical Association, and all members were from universities in Tokyo. Primarily sponsored by the Chisso factory, the Tamiya Committee attempted to obscure the organic mercury theory. The Committee wished to involve Kumamoto University but Kansuke Sera, Dean of Kumamoto University School of Medicine, refused the request (George, 2001), which was a remarkable and noteworthy act.

Researchers on the supposedly 'authoritative' Tamiya Committee disputed Kumamoto University's organic mercury theory by arguing that other factors were responsible (Harada, 2004). On 13 April 1960, Raisaku Kiyoura published a newspaper article promoting his theory that a group of organic chemicals called amines were responsible ([4]). He claimed that amines, not mercury, were detected in shellfish that caused Minamata disease in cats. Any detailed examination would have demonstrated the dubious medical validity of that counter-theory but the mass media were enthusiastic (Harada, 2004).

The next year, Kikuji Tokita, a professor of Toho University, proposed that eating rotten fish was the cause and the etiologic agent was again suggested to be amines. However, people in Minamata, despite their poverty, were able to eat as much fresh fish as they wanted. Anyone who visited Minamata and observed the life of its people would understand immediately that his theory was wrong. In his paper, the name of Chisso factory, Takeji Ohshima (who had suggested that dumped munitions were responsible) and Raisaku Kiyoura were listed in the acknowledgments. George (2001) notes the emphasis placed on the 'line of attack-that scientists from the "centre" could be trusted over those from "hick" universities on the periphery'. Importantly, all researchers recognised that fish were a cause.

During this period, researchers at the Department of Internal Medicine at Kumamoto University School of Medicine conducted a large investigation to locate unidentified Minamata disease sufferers and determine whether Minamata disease occurred in a chronic form and, if so, what its diagnostic features were (Tokuomi et al., 1962). They targeted 1 831 residents in affected areas, of whom 1 152 (62.9 %) participated, and used a questionnaire to identify participants who needed further physical examination. The study identified 131 participants with neurological signs similar to Minamata disease (Kumamoto Nichinichi Shinbun, 1962), although only 24 of these had severe symptoms. Finally, the Screening Council for Minamata Disease Patients (described below) recognised two of cases as having Minamata disease (Miyazawa, 1996 and 2007).

Although this investigation could be seen as an important step towards fully describing Minamata disease (e.g. the nature, threshold, frequency and severity of symptoms; the scale of poisoning; and the prognosis) in practice the investigation could not go far beyond the boundaries of earlier

([4]) An amine is any derivative of ammonia in which one or more hydrogen atoms are replaced by alkyl or aryl groups.

epidemiological studies. This is probably because researchers at Kumamoto University, keen to protect the organic mercury theory from a steady flow of criticism at that time, focused on the typical and severe cases of organic mercury (Hunter-Russell syndrome) (Miyazawa, 2007), even though this was contrary to the primary object of their investigation. They did not use non-exposed areas as controls to compare prevalence and they did not follow up with the 131 participants identified as having similar symptoms to Minamata disease. Finally, when publishing their findings in March 1962 (Tokuomi et al., 1962), the researchers gave the impression that Minamata disease was no longer a problem, observing that 'Minamata disease seems to have terminated at last.'

Meanwhile, in 1960 the Kumamoto Prefecture Institute for Health Research investigated the mercury concentration in hair samples from 1 645 healthy fishermen from around Shiranui Sea (Doi and Matsushima, 1996; Matsushima and Mizoguchi, 1996). It was the first large survey using hair samples. The distribution of a high concentration (0–920 ppm) of mercury among the hair samples indicated that the contamination had spread throughout entire Shiranui Sea. The mercury content in Minamata was the highest (a median of 30 ppm) but the mercury content in Goshonoura (median 21.5 ppm) on the other side of the Shiranui Sea was also about 10 times higher than that of residents in the non-exposed city of Kumamoto (median 2.1 ppm) (Doi and Matsushima, 1996; Matsushima and Mizoguchi, 1996; Ninomiya et al., 2005). Among 199 residents examined in Minamata, 61 residents (30.7 %) had hair mercury concentration greater than 50 ppm, while even in Goshonoura 153 residents (13.2 %) among 1 160 examined had those levels of mercury.

Two other investigations were conducted up to 1962 (Doi et al., 1996). Although the investigators claimed that further follow-up studies were needed because the contamination source was not removed and the mercury concentration in hair samples was high, Kumamoto Prefecture decided to stop the investigation in 1962 (Miyazawa, 1996). Furthermore, the health status of the fishermen who provided hair samples was never followed up and the fishermen were never informed of the mercury concentration results.

After Masachika Kutsuna replaced Kansuke Sera as Dean in April 1961, Kumamoto University School of Medicine adopted a conciliatory attitude to Chisso factory (Miyazawa, 1996). It joined the Tamiya Committee and began to receive research funding from Chisso factory and the Tamiya Committee. Indeed, when Kumamoto University published a volume of their research reports in 1966, Chisso factory was listed in the acknowledgments (MDRG, 1966). From that time, Minamata disease became a sensitive problem in Kumamoto University. When a local news paper reported that Prof. Irukayama extracted methylmercury chloride from the sludge of the factory (Kumamoto Nichinichi Shinbun, 1963), Dean Kutsuna reprimanded him and called Chisso factory to apologise for the news (Miyazawa, 1996). Later on, an instruction was handed down in the School of Medicine: 'you can do experimental research about Minamata disease but do not conduct clinical research.' It was said that clinical research 'is not research but rather work conducted by social activist or Prefecture Government' (Harada, 2004) because if researchers included human beings, they naturally became involved in various social problems surrounding Minamata disease.

Finally in 1962, Katsuro Irukayama, a professor at Kumamoto University School of Medicine succeeded in extracting methylmercury chloride from the sludge of the acetaldehyde production process in the factory (Irukayama et al., 1962). Although it was not disclosed, Chisso factory laboratory also extracted methylmercury chloride from the sludge (Miyazawa, 1996). This showed that methylmercury was a by-product of acetaldehyde production and present in discharges from the factory. However, the Food Sanitation Act was not applied as a result of these findings, nor was the factory regulated in any other manner.

Important scientific findings continued. In addition to the success extracting methylmercury chloride from the sludge of the factory, in 1962 an unusual occurrence of cerebral palsy infants was diagnosed as resulting from methylmercury intoxication during fetal life (Harada, 2004). However, the public's attention began to shift away from Minamata Disease. Chisso factory paid 'mimaikin' ('sympathy money') to patients in 1959 meaning that many, including researchers, believed that the issue was settled. Furthermore, from 1962 to 1963, there was a big dispute at Chisso over workers' pay (Harada, 2004). The issue of Minamata disease began to be forgotten except among sufferers and their families.

5.2.5 Niigata Minamata disease and proof of the causal relationship (1964–1968)

Although the source of contamination, the causal food, the etiologic agent and the process creating the methylmercury had all been identied, the government

did not regulate fish consumption or factory waste at Chisso. In January 1965, similar methylmercury food poisoning occurred in Niigata, causing 'Niigata Minamata disease' (Niigata Prefecture, 2007; Saito, 2009). The factory responsible (Showa Denko) operated in the same way as Chisso in Minamata, with methylmercury being discharged during acetaldehyde production. Although the damage was less than Minamata, over 1 500 individuals (Niigata Prefecture, 2007) were needlessly affected. Once more, cats started dancing and dying from madness in Niigata as a harbinger to the human consequences that were to follow (Harada, 2004).

From the beginning, MITIJ and Chisso had disputed that the factory was the cause of Minamata disease. A compelling argument, in their eyes, had been the observation that 'No similar patients have been observed around other production plants with the same system as Chisso. If the operation by Chisso was causal, we would find such patients around these other factories' (Hashimoto, 2000). At that time, Chisso was by far the largest producer of acetaldehyde, and Showa Denko was the second most important (Harada, 2004). The appearance of Minamata disease in the vicinity of Showa Denko was a powerful refutation of their argument.

A legal case relating to Niigata Minamata disease went on trial in 1967 and on 26 September 1968 the government of Japan finally agreed that there was the causal relationship between wastewater from Chisso (and Showa Denko) and Minamata disease (MHWJ, 1996c). By then, however, this admission was immaterial as acetaldehyde was no longer necessary and production had stopped by May 1968 (Arima, 1979). Twelve years had passed since the institution and food contaminant had been identified. In total, 488 tonnes of mercury were discharged into the sea from 1932 to 1968 (Miyazawa, 1996).

5.3 Congenital Minamata disease: intrauterine methylmercury poisoning

Minamata disease can be considered a typical example of industrial pollution (Ui, 1968) for several reasons. First is the manner of the outbreak. Minamata disease is a form of food poisoning (and indeed carried through the food chain) as a result of environmental pollution. Second, it is a classic example of how decisions supposedly based on factual judgements were influenced by political, financial, legal and even psychological factors (such as hierarchies within society, within and between scientific disciplines and between different wings of government, and supposed 'loss of face' in admitting error). Corruption also played a role.

However there is another reason why it will long be remembered: the discovery of congenital Minamata disease. Before congenital Minamata disease was proven, it was believed that the womb protected the foetus from poisons. This was the first clear-cut case of chemical poisoning transmitted through the placenta to the foetus. A paragraph from Harada (2005) conveys the normal attitudes towards congenital Minamata disease at that time (1961):

> When conducting a survey in the area of frequent outbreak of Minamata disease, I came upon two brothers on a veranda. Their symptoms were exactly the same; so I assumed that they must both have Minamata disease. However, their mother said, 'The 9 year-old contracted Minamata disease when he was 3 years and 6 months, but the 5 year-old has cerebral palsy.' 'Why?' I asked, to which she responded, 'The younger one has never eaten fish; he was born this way, so it's not Minamata disease.' I was convinced right away. This is because we used to believe at that time that the placenta would not let poisons pass though. Then the mother added, 'That's what doctors say. Both my husband and this older child got Minamata disease. My husband died in 1954. I ate the same fish. At the time the younger boy was inside of me. I think the reason I have few symptoms of the disease is because this child absorbed all the mercury that I ate.' At the time I thought this was just the fancy of an amateur who knew nothing about medical science. But time proved that she was correct. Her words were prophetic in speaking of the suffering of the foetus because after that time we had many experiences of congenital cases.

Many infants born after 1955 showed symptoms resembling those of cerebral palsy in the affected areas (Kitamura et al., 1959 and 1960a). Shoji Kitamura mentioned in 1959, 'It is possible that the substance causing the poisoning was transferred to the infants through the placenta or mother's milk, producing symptoms similar to those of Minamata disease' (Kitamura et al., 1959). Careful clinical and epidemiological studies were conducted (Harada, 1978). All the patients displayed similar symptoms (Harada, 2005) including mental retardation, disturbed coordination, deformities of limbs, poor reflexes, poor nutrition, and impaired growth. Most were hyperactive, suffered from muscular spasms and uncontrollable slow writhing, had squints,

One of the symptoms of Minamata disease is deformed limbs.

Photo: By Eugene Smith © Aileen M. Smith

produced excess saliva resulting in drooling, and were subject to sudden mood changes.

Epidemiologically, the patients were coincident with Minamata disease both in timing and location (Harada, 1964). Their mothers consumed a large amount of fish and exhibited mild symptoms of Minamata disease. Furthermore, 13 infants (6.9 %) among 188 infants born during the period 1955–1958 suffered from severe cerebral-palsy-like symptoms in the three most heavily contaminated areas (Harada, 1964). Since the overall incidence of cerebral palsy in Japan was 0.2–0.6 % at that time, this clearly showed that this incidence of cerebral-palsy-like infants (congenital Minamata disease patients) was very high (Harada, 1964).

Despite these clinical and epidemiological features, it took a long time for congenital Minamata disease to be accepted as a fact. Mothers of children seeking assistance with medical costs were told that they would only be helped once some children had died, had been autopsied, and the nature of the illness had been confirmed (Harada, 2004). Finally, two autopsies of infants confirmed methylmercury intoxication during foetal life. Then, in December 1962, 17 patients were officially diagnosed with congenital Minamata disease (Miyazawa, 1996). Later research revealed that the disease existed in a broader region, and 66 cases including 13 deaths were identified by Harada (2005 and 2007). However, no other epidemiological studies to investigate the existence of congenital Minamata disease have ever been conducted.

One reason why it took five to eight years to confirm congenital Minamata disease is that researchers had never previously seen a case of poisoning through the placenta (Harada, 2005). In addition, researchers who became convinced that the disease was being transferred from mother to foetus were told (for example by the Screening Council for Minamata Disease Patients and city officials) that they had no proof (Harada, 2005). Because organic mercury was only recognised as the etiologic agent in 1959, mercury levels in hair or umbilical cord blood were not previously measured at birth. However, in 1968 Masazumi Harada realised that the Japanese tradition of preserving the umbilical cord might make it possible to measure methylmercury concentrations in preserved umbilical cords as an indicator of foetal exposure. He collected umbilical cords among the residents around Shiranui Sea and was able to demonstrate a correlation between acetaldehyde production in Chisso factory and the concentration of methylmercury in umbilical cords (Figure 5.1) (Nishigaki and Harada, 1975; Yorifuji et al., 2009a). This supported the hypothesis that methylmercury affected foetuses in the uterus via the placenta.

A continuing problem relating to intrauterine exposure to methylmercury is the effects of low to moderate exposure (Harada and Tajiri, 2009), i.e. exposure that is below the level that produces the full effects but is nevertheless debilitating. While symptoms of congenital Minamata disease can be similar to cerebral palsy, some individuals exposed to a high umbilical cord mercury level did not show exactly these symptoms — and were therefore disregarded — despite showing other mental disabilities, behavioural anomalies or other cerebral dysfunctions. They were missed because of the failure to implement proactive epidemiological investigation targeting residents exposed to methylmercury via the uterus.

It is well established that methylmercury concentrations in congenital Minamata disease and Minamata disease patients are higher than in healthy individuals. But we now know that methylmercury concentrations in other mentally retarded groups are also higher than in healthy people (Harada et al., 1999). Further investigation of mental retardation cases revealed clumsiness in finger movement and other light motor dysfunctions. The on-going developments regarding the effects of low to moderate exposure among residents underline the continuing failure to investigate the consequences of Minamata thoroughly. Further follow-up

studies are needed targeting congenital Minamata disease patients and more moderate exposure to methylmercury in the uterus. Nothing can reverse the history of exposure but much could and should be done to mitigate and learn from its effects.

5.4 Chaos implementing the Minamata disease accreditation system (1968 to present)

After the Japanese government accepted the causal relationship between Chisso factory and Minamata disease in 1968, attention shifted to the 'accreditation' of the disease in individual patients, in order to determine compensation claims. The payment of compensation can be grouped into four phases. First, Chisso paid 'sympathy money' without accepting responsibility. Second, 1971 witnessed an early application of the precautionary principle, when accreditation criteria were relaxed and applications for compensation soared. Third, the government introduced far harsher accreditation criteria in 1977. Fourth, a period of 'political settlements' took place from 1995/96 until the present, with the government and Chisso factory attempting to settle the conflict by paying lump sums (not as compensation) without changing the strict criteria or recognising affected individuals as official patients.

All of this was done without formally defining Minamata disease and legal cases still continue because the geographic and temporal boundaries for claimants still lack an agreed evidential basis.

5.4.1 Accreditation system

As of 2012, the Minamata disease accreditation system remains based on Japan's Pollution-Related Health Damage Compensation Act. This involves passive assessment based on applications by patients to become accredited (Minamata Disease Museum, 2007; Ministry of Environment, 2006), rather than the active surveillance system based on the Food Sanitation Act, described earlier.

The Judgment Committee for Minamata Disease Accreditation (an advisory body to the Governor of the Prefecture) determines whether 'the applicant is a Minamata disease patient' based on the results of a medical examination (Minamata Disease Museum, 2007; Ministry of Environment, 2006). Committee meetings are held in the cities of Kumamoto and Kagoshima, nearly 70 km from Minamata, and committee members do not directly examine the applicants, regardless of their proximity. The Committee consists largely of neurologists, with a few pathologists, ophthalmologists (eye disorder experts) or otolaryngologists (ear and throat experts). Having considered a case, the Committee makes an assessment by unanimous decision and submits it to the Governor of the Prefecture. If the judgment is positive then the Governor accredits the applicant as an officially recognised Minamata disease patient. Compensation is not available without accreditation, which can take a long time. For example one patient accreditation took 25 years (Miyazawa, 1996), imposing a significant burden on the applicant.

The Environmental Agency of Japan (EAJ), a predecessor of the Ministry of Environment of Japan, determined the official position that patients with a 'probability of 50 % or more' of having the disease are to be accredited as Minamata disease patients (Ministry of Environment, 2006). As such, a quantitative approach is supposed to be applied. In practice, however, the Committee for Accreditation uses a qualitative diagnostic method, based on whether the symptoms match those documented for the 'Hunter-Russell' syndrome.

As described below, the criteria for accreditation have been revised several times since their introduction in 1959 (Yorifuji et al., in press), with profound implications for those affected by Minamata disease.

5.4.2 History of the accreditation system

Prior to 1969, the initial disease accreditation system, the 'Screening Council for Minamata Disease Patients', was used to identify patients who deserved low 'mimaikin' ('sympathy money') payments from Chisso factory (Harada, 2004; Minamata Disease Museum, 2007). This was not considered compensation, nor was it done based on any law because Chisso factory insisted that it was not proven that it was the cause of Minamata disease (Miyazawa, 2007).

The settlements, in effect decided by Chisso factory, were very small. A death resulted in a lump sum payment of JPY 300 000 (about EUR 2 900 today) while affected adults received JPY 100 000 (about EUR 960) annually and children JPY 30 000 (about EUR 290) annually (Minamata Disease Museum, 2007). The contract provided that 'the patients relinquish their claim to further compensation even if it is decided in the future that Minamata disease is caused by Chisso's effluents' (Harada, 2004). In its judgement at the First Minamata Disease Lawsuit in 1973, the court nullified these agreements as a

breach of the common good (Minamata Disease Museum, 2007).

By 1969, eighty-nine Minamata disease patients, excluding those with congenital Minamata disease, had been accredited through this system (Minamata Disease Museum, 2007). At that time, patients suffered not only from the disease itself but also faced discrimination from Minamata citizens in part because accredited patients could obtain compensation money. This climate in Minamata deterred residents from seeking accreditation. Instead, some sought to hide their neurological symptoms (Miyazawa, 2007).

In the 1960s, large-scale incidences of health effects from environmental pollution were identified elsewhere in Japan, for example, methylmercury poisoning in Niigata (Niigata Prefecture, 2007), air pollution in urban areas (Yoshida et al., 1966), cadmium poisoning in Toyama (Osawa et al., 2001), and arsenic poisoning in Miyazaki (Tsuchiya, 1977). This lead to a change in the public mood. The Japanese government was forced to take active measures to prevent further cases, and make better provision for patient support and compensation. In 1969, the Act on Special Measures for Pollution-Related Health Damage Relief (later changed to the Pollution-Related Health Damage Compensation Act) was created. It came into effect the following year (Minamata Disease Museum, 2007). Subsequently, the EAJ was established in July 1971.

As a result of the Act, the Screening Council for Minamata Disease Patients was replaced by the Judgment Committee for Minamata Disease Accreditation (hereafter, 'Committee for Accreditation') at the end of 1969 and this continues to be the responsible body (Minamata Disease Museum, 2007).

On 7 August, 1971, the 'Administrative Vice Director of the EAJ Notice' was published, marking the first real policy change since 1956 (JSPN, 1997). This Notice specified that if it appeared 'clear that a patient had been affected by the consumption of fish and shellfish containing organic mercury, the cause of [his/her neurological signs (characteristic of methylmercury poisoning)] should be presumed to be Minamata disease, even if other causes were conceivable' (George, 2001). The approach reflected the usual thinking with respect to food poisoning and was not dissimilar to the precautionary principle concept, as developed in Europe in the following decade. The Notice listed neurological signs such as constriction of the visual field, ataxia (loss of bodily coordination), hearing loss and paresthesia (a disabling tingling sensation, 'pins and needles', on both sides of the body) and did not require combinations of these neurological signs for Minamata disease to be confirmed.

On 20 March 1973, the Kumamoto District Court ordered Chisso factory to pay compensation to Minamata disease patients engaged in a lawsuit against the company (Minamata Disease Museum, 2007). The patients then signed a compensation agreement with Chisso (Minamata Disease Museum, 2007). This resulted in dramatic increase of the number of accreditation applications.

Meanwhile, in 1971, the Department of Neuropsychiatry at Kumamoto University School of Medicine undertook the first and largest cross-sectional population-based investigation to evaluate the prevalence of neurological signs of Minamata disease among local residents (Tatetsu et al., 1972). Leonard Kurland had first suggested this study to the Japanese Society of Neurology but the proposal was rejected and the Department of Internal Medicine therefore did not cooperate in the study.

In the study, three areas were selected for investigation in Kumamoto Prefecture: Minamata (a high-exposure area), Goshonoura (a medium-exposure area) and Ariake (a low-exposure, reference area). The findings demonstrated the severe effects of methylmercury on residents in Minamata and even in Goshonoura. It provoked debate about the 'Third Minamata disease' (following those experienced in Minamata and Niigata) since even in the reference area there were residents with neurological signs of Minamata disease (Miyazawa, 1996), although the prevalence was not so high.

The analysis was highly plausible because the Ariake and Minamata areas are connected by sea (Map 5.1) and fishermen often went to the Shiranui Sea to catch fish. Unfortunately, the findings were made public before the investigation was complete and created a sensation. People stopped buying fish or shellfish caught in Ariake area, causing Ariake's fishermen to protest against the Prefecture and Kumamoto University. A doctor at Kyushu University diagnosed those with neurological symptoms in Ariake as not having the disease, which caused distrust of Kumamoto University researchers. These pressures meant that the research was terminated after only two thirds of the programme had been completed.

Recent publications in international journals (Yorifuji et al., 2008, 2009b, 2010, 2011 and in press) have

shown, however, that even the incomplete findings of the Kumamoto University investigation were valuable and should have been more fully utilised. They fill out the details of Minamata disease: the kinds of symptoms, their frequency and thresholds and the types of residents affected. Unfortunately, this information has never been used for diagnosis or compensation from the 1970s to the present.

The third change in EAJ policy came in 1977 when, following the sensational news of the 'Third Minamata disease', and also a dramatic increase of accreditation applications, the 'precautionary' approach of the 1971 EAJ Notice, based on the notion of food poisoning, was reversed. A new and more rigid set of accreditation criteria for Minamata disease the '1977 criteria' were established (Minamata Disease Museum, 2007; Ministry of Environment, 2006; Yorifuji et al., in press) and remain in force today. Subsequently, there was a rise in the number of patients who had methylmercury-related symptoms but were not formally accredited. This is because the 1977 Criteria once more require a combination of neurological signs (Minamata Disease Medical Research Group, 1995, JSPN, 1997). They also provide that in addition to taking into account a person's exposure history, paraesthesia would now be regarded as a necessary but insufficient criterion for accreditation. Unlike the 1971 Criteria, the occurrence of paraesthesia 'alone' would not result in accreditation.

In 1978, it was decided that Kumamoto Prefecture should issue debt to support Chisso factory in paying compensation money (Ministry of Environment, 2006). This meant that the authorities now had a potential conflict of interest between their duty to the patients and their financial situation. It became increasingly apparent that the accreditation system was an important defensive barrier — not only for Chisso but also for the government (Miyazawa, 2007).

The 1977 Criteria became a continuing source of dispute. In August 1985 the Fukuoka High Court decided that the criteria for accreditation should be relaxed again, allowing more people to qualify (Minamata Disease Museum, 2007). In response, in October 1985, the EAJ summoned eight medical specialists to reconsider the 1977 Criteria (Miyazawa, 2007). Their 'expert opinion' stated that the Criteria remained 'valid' and once more asserted that it was not certain that paraesthesia occurred in isolation in Minamata disease and should not, therefore, be used to accredit patients (JSPN, 1997). Only neurologists were present at the meeting, which was both closed and brief (seven hours). The meeting minutes were not published and no medical evidence was given in public to support their conclusion. It seems inconceivable that they would not have been aware of the prominent research of Bakir et al. (1973), which provides evidence that paresthesia can occur in isolation following methylmercury exposure (JSPN, 1999).

By the early 1990s many accreditation applications (including new applicants and those who had reapplied) and lawsuits remained outstanding, in part because the 1977 Criteria were strict. Indeed, of the 944 patients who satisfied the diagnostic criteria and should have been accredited according to the 1977 Criteria, only 205 patients were in fact accredited by 1981 (Miyai, 1997). Even by 1992, only about one third of the qualified applicants had been accredited (316/944) (Miyai, 1999).

The EAJ therefore asked the Japanese Central Council for Environmental Pollution Control, an advisory body to the EAJ Director, to consider the issue in 1991 (Ministry of Environment, 2006). A 14 member Minamata disease working group was set up, comprising nine members with medical backgrounds and five with legal expertise. Based on the working group's advice, the Council stated that its accreditation of Minamata disease was in accordance with the 1985 'expert opinion' and proposed a medical care project to support exposed residents who had signs of the disease but were not accredited as Minamata disease patients.

In 1995–1996, under a condition that there was no liability on government, a reconciliation (the so-called 'first political solution') was reached based on the Central Council's recognition and the medical care project. According to the reconciliation, instead of issuing further Minamata disease accreditation, Chisso would make a lump sum payment to patients with methylmercury-related symptoms living in the exposed areas but these patients must withdraw any legal action or claim against Chisso (McCurry, 2006). In this reconciliation, about 10 000 patients received lump sum payments of JPY 2.6 million (about EUR 25 000 today) as relief money (not compensation) because neither the government nor Chisso admitted liability and they were not formally recognised as 'Minamata disease patients' (Miyazawa, 2007). Accordingly, this situation could be considered as repeating the 'mimaikin' ('sympathy money') payments in 1959. The number of accreditation applicants fell to zero but one legal action continued in Osaka, where some residents born in Minamata had previously moved.

By this time the Japanese Society of Psychiatry and Neurology (JSPN) — an independent academic society consisting mainly of psychiatrists and neurologists — was becoming increasingly involved. In 1998, it examined whether the medical specialists in the EAJ commission in 1975 had used any medical evidence when creating the 1977 Criteria. It concluded that they did not. Moreover, the JSPN judged the 1977 criteria to be medically invalid based on an evaluation of the data gathered in the Kumamoto University study of 1971 (JSPN, 1998). Subsequently, in a 1999 review, JSPN strongly criticised the 1985 'expert opinion', stating that there was no scientific evidence for the 1985 'expert opinion'; that the 'experts' were selected to justify the 1977 Criteria and the position of the EAJ; and that the 'experts' were guilty of pandering to the government's desires (JSPN, 1999).

Throughout the history of Minamata disease, key decisions have been characterised by very little transparency and much secrecy, making it hard to evaluate their reasoning. In 2003, after the first political settlement, JSPN (2003) analysed the minutes of the Central Committee working group's discussions in 1991, which were disclosed under the Access to Government Information Act ([5]). It concluded that the working group members did not have the medical evidence to support the 1977 criteria; that the 1985 'expert opinion' was not a medical assessment but a government opinion; and that the meeting minutes made it evident that the working group's discussion had been conducted with the sole aim of producing an opinion that complied with the EAJ's view. These facts had, until then, been hidden from the public.

In October 2004, the Japanese Supreme Court decided on the case involving Osaka residents, confirming the liability of the national and Kumamoto Prefecture governments for damage caused by methylmercury poisoning in the Minamata area (McCurry, 2006; Minamata Disease Museum, 2007; Nagashima, 2005). Like the Fukuoka High Court in its 1985 decision, the Japanese Supreme Court also ruled that the 1977 criteria should be relaxed (McCurry, 2006; Nagashima, 2005). Remarkably, the EAJ has still not changed its attitude on the criteria. As a result of the Court's ruling, the number of accreditation applicants began to grow again, exceeding 6 000 by 2008 and 8 000 in 2010) (Minamata Disease Museum, 2010).

In 2009, an Act on Special Measures (the so-called 'second political solution') was passed without changing the strict 1977 criteria. It was determined that Chisso should pay lump sums of JPY 2.1 million (about EUR 20 000) to patients who at least have paresthesia and who had lived in defined affected areas for at least one year during a defined period of time (Kumamoto Prefecture, 2010). Similar to the first reconciliation in 1995–1996, the lump sum money is not compensation but relief money because neither the government nor Chisso admits liability and the patients are not formally recognised as 'Minamata disease patients'.

It is expected that most of the applicants involved in litigation will withdraw their actions. Residents who have never applied for compensation but have neurological symptoms are also able to apply for lump sums. However, the outcome is perplexing. While 2 273 patients were officially recognised as Minamata disease patients in the affected prefectures, there are also at least several tens of thousands of exposed patients with neurological signs characteristic of methylmercury poisoning who have not been formally recognised as Minamata disease patients and not properly compensated.

Despite the enactment of the Act on Special Measures, several lawsuits are still under way because the Act defined the affected area and time period without investigating or defining evidential criteria. It is known that exposed residents with neurological signs characteristic of methylmercury poisoning are observed in areas other than those defined in the Act (Kumamoto Nichinichi Shinbun, 2010a). The approach used in the Act has shortcomings. First, it is inappropriate to define 'areas' based on the notion of food poisoning; instead, exposed persons with relevant symptoms should be counted as patients. Furthermore, the problem will persist because individuals who were exposed in the uterus but were not severely enough affected to be recognised as 'congenital' Minamata disease patients are not covered by the Act.

5.4.3 Criminal charges

One criminal case was put forward against Chisso in 1975 although a number of civil trials were raised against the factory. The report by Hunter et al. (1940) was the best known in Japan, although the danger of using organic mercury in the production had been common knowledge long before 7 May 1932, when Chisso began to discharge effluents containing organic mercury

([5]) The Aarhus Convention and 'right to know' laws have made public access to data and decision-making an issue of critical importance.

into Minamata Bay (Iriguchi 2012). However, the accused stressed that toxicity of methylmercury was not well known before 1956 when the first patient was notified by the Minamata Public Health Center. In 1979, the Kumamoto District Court sentenced the ex-president and the ex-factory-head to two years in prison with three years suspension of sentence. The Japanese Supreme Court accepted the court's ruling as final in 1988.

5.5 What are the lessons of the Minamata disease story?

5.5.1 Medical, scientific and public health lessons

Respond to the signals of sentinel wildlife
As a result of the pollution route, at Minamata harm to wildlife was observed before human harm. Fish and cats died strangely before the first patients were observed in Minamata and surrounding areas, and the same pattern occurred at Niigata. Subsequently, those who lived and worked close to nature and who ate the local fish were the first to suffer from pollution. The earliest cases identified lived close enough to the sea that they could fish from their windows. They were people who lived at one with nature.

This suggests that, as a general rule, when wildlife impacts are observed we should ensure that we understand the epidemiology, identify the source of the problem and take action to prevent human suffering. Minamata showed that effective action (preventing the discharge of pollution) was possible even before the first patients were notified. Early actions are justified by our responsibility to protect the environment — but they can also avoid subsequent harm to humans.

Prevention is possible and essential
As Hajime Hosokawa (Director of Chisso hospital) pointed out 'prevention is far more important than relief.' (Harada, 2004). It was already known in 1921 that organic mercury was synthesised in the production of acetaldehyde (Ishihara, 2002; Vogt and Nieuwland, 1921). And a researcher at Chisso factory had demonstrated that organic mercury was synthesised in the production of acetaldehyde in 1951 (Arima, 1979). Furthermore, intoxication due to occupational exposure to organic mercury was reported in the 1930s in Europe (Ishihara, 2002; Koelsch, 1937; Zangger, 1930). While these reports were published in Europe, especially in Germany (where Chisso had strong links since the 1920s), this is no excuse for a diligent company to be unaware of such important risks. Prevention was possible before the hideous consequences were first identified in 1956.

Early epidemiological studies are valuable
Early epidemiological studies, 'good enough' for their purpose can play a key role in preventing and minimising future harm. The Kumamoto University research group's early study in 1956 demonstrated that eating fish caught in Minamata Bay was a cause of harm and this conclusion has never changed. Minamata is a classic example of how spurious demands for more precision with respect to the cause of harm resulted in unnecessary delay and continuing exposure ('analysis by paralysis'). It was three years before the etiologic agent was found and six years before the mechanism by which methylmercury was produced was (re)discovered. As an important principle, this shows that prompt countermeasures should be conducted when the cause is identified and should not be postponed until an etiological agent or the biological mechanism of action is identified.

In-depth epidemiological studies are also valuable
While early epidemiological studies should have been heeded, far more could have been done to reduce harm if there had been more early epidemiological effort focusing on the features of the disease (such as the threshold, frequency and severity of symptoms; the scale of poisoning; and the prognosis). The first systematic epidemiological study of the features of the disease was not conducted until 1971. An investigation by the Department of Internal Medicine in 1960 only focused on the severest cases and did not follow up with the participants. Similarly the Kumamoto Prefecture Institute for Health Research's investigation of mercury concentrations in 1 645 healthy fishermen in 1960 was not able to follow up the participants. Follow-up studies would have revealed the developments of neurological symptoms or the dose-response relationship between exposure and symptoms.

Instead, the initial emphasis was placed on clinical manifestation (Hunter-Russell syndrome) and became bogged down in legal dispute about what was and was not Minamata disease. However, after organic mercury or fish was identified as a cause, causal criteria (i.e. cause and disease) should have been used in subsequent epidemiological studies. They should also have been used from the outset to certify patients and determine entitlement to compensation.

Demands for excessive levels of scientific proof can exacerbate harm
The history of Minamata disease provides many examples of spurious obstacles and inappropriate

burdens of proof, which prevented speedy and effective action. The demand for high levels of scientific proof (i.e. 'clear evidence' or 'beyond the reasonable doubt') was used as spurious cover, allowing Chisso to delay the search for what turned out to be a simple alternative production technology that avoided methylmercury pollution. Epidemiology demonstrated that poisoning was caused by contaminated fish and the factory discharge in 1956. This was unintentionally confirmed when the drainage route was altered in 1958 causing new victims in the new discharge area. There was a tendency for many stakeholders to accept that high evidential burden was required to justify taking preventative action.

Be wary of deliberately manufactured doubt
Regulators (and others) should be attuned to 'manufacturing of doubt' by those with sufficient means and an incentive to maintain the status quo. At various points, alternative explanations arose for the harm, such as metals, dumped explosives or amines in rotten fish and these were exploited to the full by Chisso and its supporters in government.

Of course, a plurality of viewpoints is essential for scientific analysis. Indeed, during the early stages of the disaster various metals were considered as possible causes but these were dropped when the evidence did not stand up to scrutiny. Ironically, this openness to consider alternative explanations was then used by Chisso to criticise the researchers when they concluded that methymercury was the likely cause.

Several characteristics distinguish those manufacturing doubt, often by proxy, from those promoting genuine open debate. Often they demand high levels of proof for results that demand action from the vested interest but accept low levels of proof (or standards of analysis) for their alternative hypothesis, which may be the object of criticism from scientific peers. They also fail to consider the pros and cons of alternative courses of action judged from the perspective of society as a whole and that of the wider environment.

Look beneath the tip of the iceberg
Throughout the history of Minamata disease, researchers have consistently discovered more subtle effects, at lower exposure concentrations. However neurologists, who occupied a dominant position in the process ([6]), became fixated on qualitative diagnostic method and a set of symptoms (Hunter-Russell syndrome), which were used to determine the disease's presence. This insistence restricted greater understanding of the disease in all its manifestations.

The legalistic approach to accreditation and compensation compounded the problems, encouraging constant premature attempts to define formally what Minamata disease is and is not. A number of scientists involved in the compensation process ended up having their reputations damaged by defending rigid criteria that became increasingly indefensible as time progressed.

Congenital Minamata disease
The uterus is part of the environment: to pollute the exterior environment is to pollute the uterus and thereby to pollute future life (Harada, 2005). Contrary to previous assumptions, we now know that the biological barrier of the uterus (and also the blood brain barrier) cannot be assumed to prevent the transfer of substances not found in the natural world or high exposure to substances that are naturally of low concentrations. The former are synthetic chemical compounds created by man. The latter are things we dig up from the earth, concentrate, process and use in great quantities.

On a practical note, the Minamata disaster has demonstrated the utility of umbilical cords for assessing pollution and shows that simple methods of preservation of biological tissue are sufficient to capture the disease's history (Miller, 1976).

5.5.2 Social lessons

A narrow focus on economic growth subverts society's wellbeing
The economic and political power of one factory or stakeholder can dominate public health interests in a context that is strongly oriented to promoting economic growth. In this case, the factory was Chisso, which had a great influence in Japanese industry and society in the late 1950s and 1960s. Economic growth was the top priority in Chisso and in Japanese society more broadly.

It is noteworthy that after years of scientific evidence of harm to humans, it was only when the

([6]) The excessive dominance of one discipline in a multidisciplinary dispute was noted in *Late lessons from early warnings* Volume 1 (EEA, 2001).

production process was no longer needed that the factory changed its processes and the government altered its stance regarding the harm. In Minamata, acetaldehyde production became unnecessary and stopped on 18 May 1968. Only after this date did the Japanese government officially accept the causal relationship between wastewater from Chisso factory and Minamata disease.

Discrimination perpetuates harm
The Minamata story reveals discrimination in various forms. There was discrimination against the fishermen of South Kyushu, who were poor and situated far from Tokyo, the geographical and political centre of Japan. It is notable that when the discharge from paper manufacturing in Tokyo caused fishery damage in 1958, the Tokyo metropolitan government halted the factory's production (Hashimoto, 2000).

Furthermore, when the disease occurred it was initially considered infectious. Patients were shunned and avoided by other community members and experienced years of discrimination. Fear of this actually prevented patients from coming forward. They also experienced discrimination after they obtained compensation money.

Don't 'shoot the messenger' who brings 'inconvenient truths'
After the Minamata Food Poisoning Committee published its organic mercury theory, the Committee was suddenly dissolved without stated reason. With hindsight, it is evident that their conclusions were not welcome to the authorities. Indeed, researchers at Kumamoto University were criticised as being a 'hick' university by the 'centre' after they proposed the organic mercury theory.

Stakeholders can supress science
Science can be absorbed and suppressed by the stakeholders such as industries and public authorities. Hajime Hosokawa, Director of Chisso hospital, demonstrated that giving a cat wastewater from acetaldehyde production induced Minamata disease. These results were suppressed by the factory. Later, Kumamoto University School of Medicine, which had initially analysed organic mercury as a cause of Minamata disease, joined the (pro-industry, later discredited) Tamiya Committee and began to receive research funds from Chisso factory and the Tamiya Committee. From that time, Minamata disease became a sensitive research issue at Kumamoto University.

Similarly, the Japanese Central Council in 1991 (JSPN, 2003) was not neutral and its discussions were directed towards complying with the EAJ's views. This fact was hidden from the public. Furthermore, JSPN also pointed out that biased distribution of public research funding played an important role in e.g. controlling researchers (JSPN, 2000).

Information must be transparent and broadly communicated
It is important to be transparent with information and to communicate it widely so that events are not repeated elsewhere. With better management of information, Niigata Minamata disease could have been avoided altogether.

While transparency and communications have improved in many advanced industrial economies, the translocation of manufacturing capacity elsewhere means that the consequences of product manufacture may no longer be transparent to consumers in advanced economies. Moreover, there are cases where information is not communicated to the public. Indeed, in Minamata, none of the information generated was publicly communicated to residents during the contamination period.

5.5.3 Inter-disciplinary lessons

Value of lay and local knowledge
Lay and local knowledge should not be ignored. The fishermen knew that that fish could not live in water from the outfall from Chisso factory before Minamata disease occurred. Minamata citizens knew that mercuric salt was used to produce acetaldehyde in 1959. Finally, as described in the conversation between Masazumi Harada and the mother of congenital Minamata disease patient, the mother had deduced that neurological signs observed in her son were due to Minamata disease, at a time when this was assumed to be impossible by experts. The value of lay and local knowledge is one of the 'Twelve late lessons' of Volume 1 (EEA, 2001) ([7]).

Interdisciplinary barriers and the absence of open discussion augment harm
In the Minamata case, a lack of open discussion delayed preventive actions, obscured the features

([7]) See also the report from EEA workshop on Lay, local traditional knowledge and citizen science, June 2011 (http://lltk.ew.eea.europa.eu/about/lltk-and-citizen-science-meeting-report.pdf).

of the disease and postponed its resolution. Researchers at Kumamoto University did not know what was produced at the factory, how it was produced, or what substances were used in which processes. The Research Group did not receive assistance from the engineers at Chisso factory, or from the organic chemistry sector of School of Engineering at Kumamoto University. Even within medicine, epidemiology was considered an inferior discipline and neurologists did not apply epidemiological thinking in certifying patients. Among the universities, it was said that scientists from the 'centre' could be trusted over those from 'hick' universities on the periphery.

The Japanese medical community misunderstood or was unfamiliar with the Food Sanitation Act, which must have bolstered the government's position. According to the Food Sanitation Act, doctors who recognise food poisoning must notify the local health centre, which must investigate the problem. No doctors (both clinicians and researchers) notified this outbreak as food poisoning in Kumamoto Prefecture. Instead, they continued to search for the etiologic agents. Had doctors treated and identified this as food poisoning, the government would have had difficulty not applying the Act.

Even the ministry responsible for health policy was unfamiliar with the Act. In 1990, the MHWJ argued that the government did not apply the Act because the etiological agent (methylmercury) had not been identified in 1957. In fact, the Act should have been applied when cause/transmission was identified. The different approach employed in the food poisoning case in Shizuoka in 1950 suggests that not applying the Act in Minamata was a political choice.

Finally, there was little direct discussion between stakeholders. In Japan, even in 2010, policymaking decisions do not involve stakeholders such as patients' organisations. However, EAJ and the exposed patients do share some common perspectives and conclusions regarding Minamata disease. The protracted legal action might have been shortened via direct dialogue between EAJ and the exposed patients. The fact that experts at the university, the health centre and Chisso were not willing to hear and consider the opinions of lay and local people are symptoms of the same problem. Recently, there are some measures toward Minamata's regeneration, such as making Minamata city a model city for the environment, facilitating waste reduction and recycling etc. (Minamata Disease Museum, 2007). In particular, the word 'Moyainaoshi' (the re-establishment of emotional ties or reconciliation) is often used to strengthen interpersonal ties so that citizens can speak up in public about Minamata disease issues. Despite such efforts, there is still little discussion about how to support patients, investigating the exposed patients etc. to solve the real problem of Minamata disease. It can be said that Japan still faces a problem of democracy (George, 2001).

Table 5.1 Early warnings and actions

1908	The Nihon Carbide factory was established in Minamata
1921	Methylmercury synthesised during acetaldehyde production in Germany
1921	The Chisso factory in Minamata Bay bought German patent and began using carbide and acetylene to manufacture a wide range of chemicals
1925–1926	The company began to receive requests for compensation from the fishing cooperative. On the condition that no further complaints would ever be lodged, Chisso paid a small amount of 'sympathy money'
1932	The Chisso factory in Minamata began to produce acetaldehyde from acetylene gas, using mercury as a catalyst
1930–1937	Mercury poisoning in German factories using acetaldehyde
1943	The issue of fishery damage arose again due to carbide residue from acetylene production and another compensation contract was concluded
1949	More fishery damage negotiations failed. Chisso said the catch data were 'not scientific'
1950	Fishermen around Minamata Bay witnessed huge numbers of fish rising to the surface and swimming around as though crazy. Sea birds were unable to fly. Oysters and cockles were washed up onto the beach rotting with their shells open. Barnacles did not attach themselves to boats fishing near factory outlet
1951	Chisso increased production of acetaldehyde and related methylmercury pollution from the factory
1952	Upon request from local fishermen, the Fisheries Division of the Kumamoto Prefecture inspected the factory and Chisso documents about mercury use and discharge. As a result they reported that the discharge should be analysed. Kumamoto Prefecture and Chisso failed to do this and fishery damage continued
1953	Local cats, which ate great quantities of fish, went mad and died after strange dancing and convulsions
1956	1 May: First official notification of strange disease to the Minamata Public Health Centre. 28 May: Minamata Strange Disease Countermeasures Committee was organised by Chisso Hospital, local doctors and Minamata Public Health Centre. 30 cases including 11 deaths were identified. Kumamoto University Research Group reported that the disease was not contagious (as was claimed at first) but rather a food poisoning from eating fish contaminated by a heavy metal in Minamata Bay

Table 5.1 Early warnings and actions (cont.)

1957	Kumamoto University Research Group recommended prohibiting fishing under the Food Sanitation Act. Japanese Ministry of Health and Welfare Research Group from Tokyo confirms local conclusions and recommends full investigation of Chisso effluents. In response to these findings, the local government of Kumamoto Prefecture considered applying the Food Sanitation Act in March 1957, although the Chief of the Public Health Bureau of the Ministry of Health and Welfare of Japan replied to the local government that it is impossible to apply the Food Sanitation Act. Then, the local government abandoned the application
1958	Chisso changed the drainage route of acetaldehyde production from Minamata Bay to Minamata River
1958	UK neurologist Douglas McAlpine examined 15 Minamata disease patients and reported his observations in The Lancet, listing methylmercury as one of the metals which could induce Minamata disease. This was the first time in a scientific paper that methylmercury was identified as possible cause. McAlpine was prevented from presenting his findings to the Japanese Society of Neurology
1959	On 7 October 1959, Chisso Hospital director Hajime Hosokawa fed factory effluent to cats and induced Minamata disease but this was suppressed until a compensation case in 1970
1959	Organic mercury was recognised as the etiological agent by the Minamata Food Poisoning Committee organised by the Ministry of Health and Welfare of Japan on 12 November 1959. However, there was no mention of the source of the contamination, Chisso factory. Indeed, the section chief of the Ministry of Health and Welfare's Environmental Sanitation Department asks for Chisso effluent case to be removed from report as it was not 'scientifically' proven. After the Committee had reported its opinion to the Minister of Health and Welfare, it was suddenly dissolved
1959	In December 1959, Chisso factory established an ineffective purifying system for the contaminated water
1960	Kumamoto Prefecture Institute for Health Research investigated the mercury concentration in hair samples from 1 645 healthy fishermen from around Shiranui Sea. Results indicated that the contamination had spread throughout the entire Shiranui Sea
1962	An unusual occurrence of cerebral palsy infants was officially recognised as congenital Minamata Disease. Professor Katsuro Irukayama succeeded in extracting methylmercury chloride from the sludge of the acetaldehyde production process in the factory but the Fisheries Agency abandoned research on Minamata disease. No research activities were conducted by government agencies until 1968
1965	Methylmercury food poisoning occurred in Niigata, causing 'Niigata Minamata disease'. The factory responsible (Showa Denko) operated in the same way as Chisso in Minamata
1968	In May, Chisso stopped its acetaldehyde production for commercial reasons. In total, 488 tonnes of mercury were discharged into the sea from 1932 to 1968. After that, on 26 September, Japan's government accepts causal link between wastewater from Chisso (and Showa Denko) and Minamata disease
1969–	Government compensation arrangements applied 'chaotically'. Private compensation cases for Minamata victims begin
1971	On 7 August, 1971, the 'Administrative Vice Director of the EAJ Notice' was published, marking the first real policy change since 1956. The Department of Neuropsychiatry at Kumamoto University School of Medicine undertook the first and largest cross-sectional population-based investigation to evaluate the prevalence of neurological signs of Minamata disease among local residents
1972	The United Nations Conference on the Human Environment was held in Stockholm. Two Minamata disease patients attended and created much public awareness
1973	Kumamoto District Court ordered Chisso factory to pay compensation to Minamata disease patients engaged in a lawsuit against the company
1975	From 1968, Masazumi Harada collected umbilical cords (traditionally preserved in Japan) from residents around Shiranui Sea and demonstrated a link between acetaldehyde production in Chisso factory and methylmercury; supporting the hypothesis that methylmercury could affect foetuses
1977	A new and more rigid set of government accreditation criteria for Minamata disease required a combination of neurological signs: the '1977 criteria'. These remain in force today. Subsequently, there was a rise in the number of patients who had methylmercury-related symptoms but were not formally accredited
1978	Kumamoto local government issues debt to help Chisso pay compensation
1995–1996	In the 'first political solution' the government and Chisso factory attempted to settle the conflict by paying lump sums (not as compensation) in 10 000 cases without changing the strict criteria or recognising affected individuals as official patients
2004	The Japanese Supreme Court confirmed the liability of the national and Kumamoto Prefecture governments for damage caused by methylmercury poisoning in the Minamata area. The court also ruled that the 1977 criteria should be relaxed
2009	The Act on Special Measures (the so-called 'second political solution') was passed without changing the strict 1977 criteria. Chisso to pay lump sums to patients, not as compensation but relief money because neither the government nor Chisso admits liability and the patients are not formally recognised as 'Minamata disease patients'
2009–	UNEP initiates a global mercury phase-out and works to develop a global legally binding instrument on mercury, planned for signature in Japan in 2013
2013–	Private law suits still continue

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From Minamata to Global Health Risk

Philippe Grandjean ([8]) ([9])

While the Minamata incident was being elucidated, other methylmercury poisonings occurred elsewhere due to extensive use of mercury fungicides and improper labelling. Treated seed grain was mistakenly used for bread-making, and the most serious poisoning incident happened in Iraq during a famine in 1970-1971 (Bakir et al., 1973). A widely cited report on 93 poisoned Iraqi adults reported that facial paraesthesia was the earliest clinical sign of poisoning and showed a clear dose-dependence (Bakir et al., 1973). However, the study was small in comparison with the officially recorded 6 500 hospitalisations, of whom 459 died (Bakir et al., 1973), and the amount of treated grain used (100 000 tonnes) would suggest that many more may have been poisoned. The first author of the science report, Farhan Bakir, was later recognised as Saddam Hussein's personal physician, then in exile along with at least one other Iraqi co-author (Giles, 2003; Hightower, 2009). As no useful dose-response data were available from Minamata, the Iraqi data were used for many years as the main documentation for risk assessment. Given the history of the poisonings, one can assume that methylmercury toxicity was at least not exaggerated (Grandjean et al., 2010).

Attention turned to neurotoxicity during brain development as a result of an experimental study: rats exposed during early development showed adverse effects that were not apparent at first, but later became obvious as deranged behaviour in the mature animals (Spyker et al., 1972). This report clearly supported the Minamata evidence as well as a Swedish report 20 years earlier that described mental retardation in two children exposed to methylmercury from treated grain (Engleson and Herner, 1952).

There was another surprise when Swedish researchers examined the chemical fate of mercury in a simple aquarium: methylmercury was formed from inorganic mercury compounds in the aquarium sediment. None was formed after prior autoclaving of the sediment, suggesting that microorganisms played a role (Jensen and Jernelov, 1967). Although these processes were of little significance in Minamata, where methylmercury was formed in the acetaldehyde plant (Grandjean et al., 2010), methylation of mercury suddenly became a world-wide problem. Widespread use of methylmercury for seed dressing or as a fungicide in paper mills was already known to cause local pollution of waterways and coastal waters. Now it turned out that any release of mercury could be converted into the dangerous methylmercury molecule. Studies in North America verified that bio-accumulation took place, with the highest concentrations at the top of the food chains (Fimreite, 1974). Although the first studies were contradicted and explained away, methylmercury contamination of fish emerged as a worldwide concern. Many rivers and lakes were already so polluted with mercury that fish advisories against eating sports fish were issued, especially in countries like Canada, Sweden and the US Advisories against eating locally caught fish now affect over 16 million lake acres and 1.3 million river miles in the US (US EPA, 2007).

Mercury must always have been a natural component of life on the planet, but pollution has released large amounts to the biosphere. Mercury analyses of preserved hair, teeth, and feathers from Arctic indicator species show that current levels are about ten times those in pre-industrial times (Dietz et al., 2009).

After the discovery that exposures to lead at levels considered to be 'low' could cause damage to brain development (Needleman et al., 1979), researchers suspected that methylmercury might have similar effects and may not be safe at common levels of exposure. Some of the most highly exposed populations were indigenous groups. In Canada, a study of 234 Cree children showed abnormal tendon reflexes with increased mercury concentrations in maternal hair which reflected exposure during pregnancy (McKeown-Eyssen et al., 1983). Soon after, a larger study from New Zealand showed that increased levels of mercury in mothers' hair during pregnancy were associated with delayed brain development of their children (Kjellström et al., 1986; Kjellström et al., 1989). The results were published after peer review by the Swedish Environmental Protection Agency, but were ignored for formal reasons by other regulatory authorities, allegedly because the reports had not appeared in a peer-reviewed scientific journal.

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Two large prospective studies were then initiated in the mid-1980s. The largest consisted of 1 000 children from the Faroe Islands and concluded that low-level methylmercury exposure during prenatal development was associated with deficits in several brain functions at school age; clear deficits were apparent well below a previously proposed safe level of 10 μg/g for mercury concentration in maternal hair (Grandjean et al., 1997). On the other hand, largely non-positive findings were initially reported in children from a similar study in the Seychelles (Myers et al., 2003), and the apparent disagreement was perceived as a controversy and fuelled a debate on uncertainty (Grandjean, 1999), with resonance in trade journals, internet sites, commercial campaigns, and even an editorial in the Wall Street Journal. Additional longitudinal data later appeared from Japan, Poland and the US in support of the Faroes conclusions (Jedrychowski et al., 2006; Lederman et al., 2008; Murata et al., 2006; Oken et al., 2008). Although less weighty, several cross-sectional studies also supported the existence of low-level exposure neurotoxicity (Grandjean et al., 2005).

The reasons for the apparent lack of mercury effects in the Seychelles could be that beneficial nutrients in fish might obliterate or dampen the mercury toxicity (Clarkson and Strain, 2003). New research from the Seychelles has recently shown that cognitive development in children was associated neither with maternal fish intake nor with methylmercury exposure, when each of them was considered separately. If maternal fish intake and mercury were included in the statistical analysis at the same time, then fish intake was clearly beneficial, while mercury had negative effects (Strain et al., 2008). Also, in the Faroes, the mercury toxicity became more prominent after adjustment for the beneficial effects of fish intake during pregnancy (Budtz-Jorgensen et al., 2007).

Because of the apparent disagreement between the two major studies and the public health implications of mercury, the US White House in 1998 called for an international workshop with 30 invited experts, who were asked to critically examine the scientific evidence. They emphasised a variety of possible uncertainties. The conclusions stated that 'there are inadequate data … to draw meaningful conclusions at this time' (NIEHS, 1998). Despite the possibility that subclinical toxicity could easily be missed and underestimated, the workshop experts were quite optimistic: 'Measurement error can impact significantly on both the estimated levels of effect and the decision on the level of exposure at which an effect is detected because of the potential for misclassification. However, the data presented in the workshop suggest that the precision of measurements of methylmercury in hair or cord blood is very good.' The experts recommended further research.

At the request of the US Congress, a new expert panel was then convened by the National Research Council (NRC, 2000) to determine whether an exposure limit of 0.1 μg/kg bodyweight per day was appropriate, as proposed by the US EPA on the basis of the data from Iraq. The committee supported the US EPA limit, but recommended that it should be based on the data from the Faroes study (which agreed with the overall evidence including New Zealand and Seychelles).

This recommendation would seem justified and appropriate, but may not be sufficiently protective. First, the exposure limit should address the problem that mercury toxicity may be masked by increased intake of essential nutrients from seafood that promote brain development (Budtz-Jorgensen et al., 2007). If this adjustment is not made, mercury would seem less toxic than it really is. Second, all the calculations have assumed that the mercury exposures are precise, but any imprecision in exposure assessments will result in misclassification and a likely underestimate of the real mercury toxicity. If this factor is taken into account, the exposure limit should be decreased by about 50 % (Grandjean and Budtz-Jorgensen, 2007).

Thus, the first likely cases of developmental methylmercury poisoning were already described in 1952 and subsequently reported from Minamata; replication in laboratory animals was published in 1972; and the first prospective population study of prenatal methylmercury toxicity due to contaminated seafood in humans was published in 1986. However, scientific consensus on prenatal vulnerability was hampered by focusing on scientific details rather than public health implications, and international agreement on the need for protection against prenatal exposures was only reached in 2002, i.e. 50 years after the first medical report that methylmercury can damage brain development.

Environmental methylation of mercury in sediment was discovered accidentally, since systematic studies of mercury's environmental fate were not conducted, and initial studies focused on total mercury concentration, not on the methylmercury compound responsible for brain toxicity. Recognition of contamination of food chains and environmental bioaccumulation of methylmercury was therefore also delayed by several decades.

Following the publication of new data on the adverse effects of low-level exposures to methylmercury,

Important early warnings of methylmercury toxicity

1952	First report on developmental methylmercury neurotoxicity in two infants
1960	Mental retardation in Minamata associated with maternal seafood diet
1955–1972	Poisoning epidemics from use of methylmercury-treated seed grain for baking and cooking
1967	Demonstration of mercury methylation in sediments
1972	Experimental study of delayed effects due to developmental neurotoxicity
1978	Exposure limit based on toxicity in adults
1986	First epidemiology report on adverse effects in children related to maternal fish intake during pregnancy in New Zealand
1997	Confirmation from the Faroe Islands on adverse effects in children from methylmercury in maternal seafood intake during pregnancy
1998	White House workshop of 30 scientists identifies uncertainties in evidence
2000	US National Research Council supports exposure limit based on Faroes data
2004	European Food Safety Authority recommends that exposures be minimised

regulatory agencies requested scientific scrutiny. Expert committees emphasised uncertainties and weaknesses in the available data. Less attention was paid to the question of what could have been known, given the research methods and possibilities, and whether developmental neurotoxicity at low doses could be ruled out. The reports also generally ignored that the imprecision of the measurements most likely resulted in an underestimate of the true effects. Instead, more research was recommended. The insistence on solid evidence promoted by polluters and regulatory agencies therefore agreed with a desire among researchers to expand scientific activities in this area. However, the wish to obtain a more complete proof had the untoward effect of delaying corrective action.

In a commentary on the regulatory delays in dealing with methylmercury poisoning in Minamata, Professor Jun Ui wrote (quoted from D'Itri and D'Itri, 1978): 'It might be a coincidence, but a strange, parallel relationship was observed between the actual symptoms of Minamata Disease and the reactions of these formal organizations. A constriction of the visual field was common among all organizations. Ataxia, a loss of coordination between various parts of the body, was often exhibited in contradictions between the measures taken by various parts of the government. There was also a loss of sensation as the appeal of the victims went unheard and there was little effort to grasp the situation as a whole. Many organizations also reacted with spasmic convulsions when they faced the problem. This was followed by mental retardation and forgetfulness.' It seems that memory loss, narrow-mindedness, and lack of coordination also affected the planning and the interpretation of environmental research on methylmercury in a more general sense.

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Mercury Science and Policy since Minamata: Four Insights for Policy

Noelle E. Selin

Introduction

The events at Minamata, as well as other serious instances of high-dose exposure, showed the extremely toxic potential of mercury. Furthermore, beginning in the 1960s, widespread environmental contamination by mercury beyond locally-contaminated areas began to be measured by scientists and addressed by policymakers. Mercury emerged through the late 20th century as a substance known to pose risks at locations far from its release, and at low doses (UNEP, 2002). In the 21st century, policies continue to be developed to address the global spread of mercury, and scientists and policymakers are becoming increasingly aware of the complexities of the links between human activities such as energy production and connections between mercury and other environmental and health issues. The case history of mercury beyond Minamata provides four major and partially overlapping insights into the application of scientific knowledge to political efforts to deal with environmental and human health hazards, for both scientists and policymakers.

These are the need to:

- conduct research into 'blind spots';
- encourage policy-relevant scientific assessments;
- design policies that can be adapted to changing knowledge; and
- acknowledge and manage interactions between different risk issues.

Conduct research into 'blind spots'

A first insight from the mercury case, for the scientific community, is the need to conduct policy-relevant research into 'blind spots,' and be open for that research to challenge the dominant scientific understanding of a problem. (The scientific inertia that can lead to a focus on conventional paradigms is also illustrated in Chapter 26 on science for precautionary decision-making). The conventional wisdom in the 1970s was that mercury was essentially a local problem. The World Health Organization illustrated this view by stating: 'In the global cycle, most of the mercury is derived from natural sources whereas the local cycle is predominantly concerned with man-made release' (WHO and UNEP, 1976). A lawsuit by US swordfish distributors also challenged US Environmental Protection Agency (US EPA) mercury limits for fish, based on the understanding that anthropogenic mercury remained in directly-contaminated areas. The swordfish distributors argued that mercury in fish was naturally-occurring and thus should not be regulated as a contaminated product (US Court of Appeals, 1980). However, there was early evidence that mercury from human activities could be at least as important as natural mercury in remote areas, as reported by the US EPA in 1973: 'Mercury from burning coal is dispersed widely, and may enter the aquatic or terrestrial environment far from the point of discharge. Since mercury discharged in this way is of the same order of magnitude as the total of mercury mined in the world, it appears advisable to try to develop a technology to remove mercury either from the coals or from stack gases' (Klein, 1973). Despite these early warnings, mercury continued to enter the global environment at an increasing rate.

The understanding that mercury was a global problem began to emerge as predominant, at least scientifically, in the 1980s and early 1990s. Scientific research demonstrated clearly that industrial contaminants, including mercury and persistent organic pollutants (POPs), were present at elevated levels in areas far from their sources (Selin, 2010). A review of environmental concentrations of mercury in the Arctic environment in 1997 by the Arctic Monitoring and Assessment Programme (AMAP) noted that circumpolar levels of mercury were increasing in lake and ocean sediments and in the livers and kidneys of marine mammals (AMAP, 1997). While research about the degree of anthropogenic relative to natural contamination was still uncertain, AMAP urged Arctic countries to develop international mechanisms to address mercury contamination. The changed scientific understanding of mercury as a substance that travels long distances and poses risks far from its release points slowly began to shape policies to address mercury internationally.

Scientific understanding of the mercury problem continues to evolve. While international policy is now addressing the widespread spatial scale of mercury as a global problem, scientific research is also illuminating the multiple timescales under which mercury affects humans and the environment (Selin, 2011). Mercury mobilised from fossil sources continues to circulate in the land-atmosphere-ocean system over timescales longer than those considered by policies. It will take an estimated

3 000–10 000 years for mercury so mobilised to return to deep-ocean sediments (Mason and Sheu, 2002; Selin et al., 2008). A corollary to this is that only about one third of mercury currently entering ecosystems comes from direct anthropogenic activity. Another third results from natural sources, and the remainder is legacy mercury, previously emitted from anthropogenic sources, continuing to circulate between the land, ocean and atmosphere. This means that human perturbations to the global mercury cycle are very long-lived, and the Earth system will recover only slowly from historical mercury contamination. On the other hand, some environments may respond very quickly to decreases in mercury input (Harris et al., 2007). One example is the Northeast US, where, coincident with and likely as a result of regional policies to reduce emissions, concentrations of mercury in fish declined from 1999 to 2004 (Hutcheson et al., 2006). Monitoring the continuing impacts of mercury in ecosystems, and potential improvements resulting from policies, will require this evolving scientific understanding of the environmental timescales of mercury to be taken into account.

Encourage policy-relevant scientific assessments

A second insight from the interface with science and policymaking, relevant to both scientists and policymakers, is that scientific information on new risks can influence the policy process through targeted, international scientific assessments. These are widely applied to inform international and global policymaking on environmental issues such as ozone depletion and climate change (Eckley, 2001; Mitchell et al., 2006). In the case of mercury, they provide a mechanism for new scientific understanding to be taken up and addressed. This suggests that scientists should participate actively in international assessment processes.

An example of the influence of scientific assessments on mercury policy occurred in the late 20th century. The process that led to the 1997 AMAP assessment, discussed above, was a critical factor in bringing mercury contamination of remote areas to public attention (Selin and Selin, 2008). Partially influenced by the AMAP work, the Convention on Long-range Transboundary Air Pollution (CLRTAP), a regional agreement among the countries of the United Nations Economic Commission for Europe (including western and eastern European countries, Russia, the United States and Canada), was one of the first international bodies to express interest in addressing mercury. Following their own scientific assessment process (UNECE, 1995), CLRTAP countries negotiated a protocol on heavy metals, which was adopted in 1998 and entered into force in 2003. The protocol requires parties to reduce emissions of three heavy metals (lead and cadmium as well as mercury) below 1990 levels (or, alternately, below the year of their choice between 1985 and 1995), and to apply limit values and best available techniques to control major sources.

Another example of scientific assessments of mercury influencing policy came when, in response to growing global concerns about mercury, a mercury assessment organised by the United Nations Environment Programme (UNEP) concluded that there was 'sufficient evidence of significant global adverse impacts to warrant international action to reduce the risks to human health and/or the environment arising from the release of mercury into the environment' (UNEP, 2002). Despite this strong statement, policy actions following this pronouncement proceeded slowly, as there were strong political interests both in favour of and against a mercury treaty (Selin and Selin, 2006). However, in 2009, partly as a result of a change in the position of the United States (after a change in presidential administration), countries agreed to begin negotiations on a global, legally-binding instrument to address mercury. The process towards a global mercury treaty began in 2009 with the goal of completing negotiations in 2013. This delay shows that even with strong scientific assessments, gaining international consensus, balancing political and stakeholder interests, is a lengthy process, and can be slow to respond to new scientific information and understanding of the problem.

Design policies to adapt to changing knowledge

A third insight, for policymakers, is that policymaking processes and policies should be designed so that specific policies can be revised and adapted to reflect new information and changing scientific understanding. Early policies, focused on local contamination of mercury, did not address its long-range impacts, and new institutional frameworks such as a mercury treaty are thus needed to address mercury as a global problem. As noted above, gaining political agreement for new institutions can delay action for years to decades. As scientific work continues to reveal new information and paradigms change, flexible policies might be able to respond more quickly.

Even today, few policies address the full complexity of mercury in the environment. While there are several forms of mercury emitted from ecosystems

— long-lived forms that transport globally and other forms that cause local impacts — policies generally treat all forms of mercury in the same way. A recent review of the effectiveness of the CLRTAP heavy metals protocol noted that pollution control techniques specified by the protocol primarily address the forms that cause local impacts, raising questions about how effective mercury controls are at addressing the forms that cause global contamination (van der Gon et al., 2005). In addition, there are few links between policies that address emissions and those that address exposure and impacts (Selin, 2011).

Policies for minimising mercury exposure through dietary advice for fish consumers are one area where interventions have been expanded, formalised and revised over time. In 2003, the Joint FAO/WHO Expert Committee on Food Additives (JECFA) revised its provisional tolerable weekly intake (PWTI) of methylmercury from 3.3 μg kg–1 bodyweight per week down to 1.6 μg kg–1 bodyweight per week, specifically to protect against developmental toxicity for childbearing women. Some countries have also set domestic standards. For example, the United Kingdom Food Standards Agency recommends that pregnant women and children under 16 avoid eating shark, marlin and swordfish, and minimise their consumption of tuna to four medium-sized cans or two steaks per week (United Kingdom Food Standards Agency, 2004). In Sweden, pregnant or nursing women are advised to avoid eating fish high in mercury more than two or three times a year (Sweden National Food Agency (Livsmedelsverket), 2011). Some research has shown that the consequence of dietary advice focused on methylmercury has been an overall decrease in fish consumption by pregnant women (Burger and Gochfeld, 2008). There is growing scientific understanding of the benefits of n-3 polyunsaturated fatty acids (n-3 PUFAs), nutrients present in fish and shellfish, on prenatal development (Mahaffey et al., 2011). Some fish, however, such as mackerel or herring, are high in n-3 PUFAs and low in mercury, suggesting that dietary advice could better reflect fish choices to maximise benefit and minimise risk (Mahaffey et al., 2011). However, sensitive populations continue to be exposed to high levels of methylmercury, suggesting the potential for improved risk management (Mahaffey et al., 2009).

Acknowledge and manage interactions between risk issues

As a fourth and final insight, for both scientists and policymakers, the mercury case shows that acknowledging and managing both environmental and societal connections between different risk issues can be critical. From an environmental perspective, in addition to the potential benefits of fish consumption noted above, other pollutants such as PCBs may be present in different kinds of fish, complicating efforts to provide dietary advice (Mahaffey et al., 2011). Climate and other environmental changes can affect the mercury problem by changing environmental pathways of contamination (AMAP, 2011).

Societal issues such as economic development also intersect with the mercury issue. While global emissions of mercury have remained relatively constant since 1990 (Pacyna and Pacyna, 2002; Pacyna et al., 2006; Pacyna et al., 2009), this reflects increases in Asia, resulting from rapid industrialisation and the increasing use of coal, compensating for decreases in North America and Europe. Future Asian economic development, particularly in China, could lead to dramatic increase in mercury emissions from that region (Streets et al., 2009). In addition, increasing gold prices can lead to increased use of mercury in artisanal and small-scale gold mining (Spiegel and Veiga, 2005).

Governance-related connections have additional importance. Actions in the 1980s to reduce air pollution had substantial co-benefits for mercury reductions in Europe and North America, as traditional air pollutant controls can potentially achieve > 90 % emission reductions for mercury (Northeast States for Coordinated Air Use Management, 2010). Information about the long-range transport and low-dose effects of other substances, such as persistent organic pollutants, have also helped to improve the scientific understanding of mercury risks (Selin, 2010). Finding ways to harness and encourage co-benefits, while mitigating shared risks, is a complex and continuing challenge.

Concluding remarks

After decades of science and policy actions, mercury still poses significant challenges to society. A major reason is that conceptions of the mercury problem were initially limited, and scientific and policy understanding has continued to expand and increase in complexity, increasing complexity unfortunately being the rule rather than the exception in addressing environmental risks.

The case of mercury shows that both scientists and policymakers can play an important role in risk management, through the four major insights

summarised above. Scientists should encourage early research into 'blind spots' expanding understanding of environmental complexity. Policymakers should support, and scientists should participate in, targeted and international scientific assessments for policy. Policymakers should also be conscious that scientific information can and will change and design policies accordingly. Finally, both scientists and policymakers would benefit from acknowledging the full complexities and links between environmental risks. Understanding and managing multiple, linked environmental and human stressors is a primary challenge for sustainability.

While it is tempting to assume that our current understanding of the mercury problem represents a comprehensive picture of the real world, history suggests that both our understanding of the problem and our strategies to address it probably continue to have blind spots. A substantial area of uncertainty, for example, is the mechanism by which mercury is converted to methylmercury in the ocean. Additional connections with other risks — both environmental and social — are likely to be identified in the future. Drawing lessons from the mercury case, by encouraging expanded research paradigms, supporting scientific assessments, designing dynamic policies, and exploring and taking advantage of cross-issue connections — would help societies to better address risks and surprises in the future.

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Mercury in fish — the need for better information about contaminant exposures

Argelia Castaño

There is no doubt about adverse effects of mercury in highly exposed populations, but the question is where to put an acceptable level for the general population? The major source of methyl-mercury is fish and particularly large marine fishes like tuna, sharks and swordfish. Fish and marine products are rich in unsaturated fatty acids which reduce the risk of cardiovascular disease and therefore are beneficial for health. Cardio-vascular disease is related to high consumption of red meat and dairy products and low intake of vegetables and fruits. Public health authorities are therefore recommending a Mediterranean diet with a high proportion of fish, marine products, vegetables and fruit as a way to reduce cardiovascular disease burden.

However, the authorities are facing the dilemma of balancing the benefits of fish consumption with the assumed adverse effects of low level methyl-mercury exposures. Should the policymakers advise against fish consumption because of contaminants or are the negative effects of the contaminant burden still minor compared with the positive effects of a healthier diet? The issue is even more serious for indigenous populations, for example in the Arctic region, which traditionally have a diet based on marine species (seals, whales) which today have high levels of contaminants. Should we recommend these populations to change their diet to a Western life style diet with the accompanying new health problems like obesity and diabetes? The contaminants are there — we have to accept this although we should try to reduce the exposure by all means — but we have to be pragmatic in establishing the safe levels and not exaggerate the risks in the light of the obvious benefits.

Security and confidence are the driving forces for decision-making. For mercury we have a good knowledge base from experimental and epidemiological studies connecting body burdens and adverse effects. What is critical to assess is the exposure. How much mercury are we exposed to in our daily lives and from where is it coming?

The decision makers need robust information before they can decide on mitigation strategies. The European Commission within the frame of Environment & Health action plan 2004-2010, has funded a project to standardise protocols for human biomonitoring in Europe ([10]). The protocols and methodologies that were developed are now being tested in a pilot study co-funded by 17 EU Member States with contribution from the EU LIFE+ programme ([11]). This study, which will be reported by the end of 2012, will provide an insight into mercury levels in children and their mothers in Europe, measured for the first time under strictly standardised and harmonised conditions.

It will then be possible to map human mercury exposure at a European level with real and comparable numbers, even though the sample cannot be considered representative at national levels. For individual Member States this mapping provides an important benchmark which could assist in national mitigation strategies. Information of this kind is essential both for developing a European position for international negotiations concerning the implementation of the Global Mercury Treaty currently being progressed by UNEP and for helping national authorities and consumers to make better-informed choices about healthy diets.

([10]) http://www.eu-hbm.info/cophes.
([11]) http://www.eu-hbm.info/democophes.

6 Beryllium's 'public relations problem'

David Michaels ([1]) and Celeste Monforton ([2])

Scores of workers employed in nuclear weapons production have been diagnosed with chronic beryllium disease (CBD), a progressive and irreversible inflammatory lung disease. This chapter presents a history of knowledge and public policy about preventing beryllium-related disease, focusing primarily on the United States beryllium industry's role in shaping US regulatory policy.

Over several decades increasingly compelling evidence accumulated that CBD was associated with beryllium exposure at levels below the existing regulatory standard. The beryllium industry had a strong financial incentive to challenge the data and decided to be proactive in shaping interpretation of scientific literature on beryllium's health effects. It hired public relations and 'product defence' consulting firms to refute evidence that the standard was inadequate. When the scientific evidence became so great that it was no longer credible to deny that workers developed CBD at permitted exposure levels, the beryllium industry responded with a new rationale to delay promulgation of a new, more protective exposure limit.

This case study underscores the importance of considering the hazards from toxic materials throughout the entire product life cycle. While primary producers of beryllium products may be able to control exposures in their own facilities, it is unlikely that many secondary users and recyclers have the expertise, resources and knowledge necessary to prevent beryllium disease in exposed workers and residents in nearby communities.

The primary lessons of this chapter are widely applicable to many environmental health controversies. In particular, it illustrates the practice of 'manufacturing uncertainty' — a strategy used by some polluters and manufacturers of hazardous products to prevent or delay regulation or victim compensation.

This chapter is followed by an analysis of the rationale for corporate behaviour in the regulation of beryllium. It is argued that the availability of occasional and limited opportunities for companies to change course without suffering onerous consequences would encourage them to rethink their position and create an obligation on shareholders to take the responsible course. Although this may be perceived as letting them 'get away with it', the end result may be better public policy and corporate responsibility.

([1]) Although Dr David Michaels currently serves as the Assistant Secretary for the Occupational Safety and Health Administration (OSHA), US Department of Labor, this article was written while he served on the faculty of The George Washington University. It reflects the personal views of the authors, and does not purport to reflect the official views or positions of OSHA or the Department of Labor.

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6.1 Introduction

In a dramatic announcement on a national television news magazine in April 2000, Bill Richardson, the United States Secretary of Energy, acknowledged that his department had collaborated with the beryllium industry to defeat a 1975 attempt by the Occupational Safety and Health Administration (OSHA) to reduce workers' exposure to beryllium. The collaboration had been documented in a powerful newspaper exposé (Roe, 1999). 'Priority one was production of our nuclear weapons', Richardson stated, '[the] last priority was the safety and health of the workers that build these weapons' (ABC, 2000).

The Secretary of Energy's declaration was remarkable; rarely do the most senior officials in government admit deception that resulted in death and disability of its own citizens. Yet, for those in the public health community, Richardson's candid announcement was long overdue. Scores of workers employed in nuclear weapons production have been diagnosed with Chronic Beryllium Disease (CBD), a progressive and irreversible inflammatory lung disease. In the decades leading up to the announcement, increasingly compelling evidence accumulated that CBD was associated with exposure at levels below the standard in place at the time. In response to this evidence, the beryllium industry waged a concerted campaign to delay a safer standard. The industry hired public relations and 'product defence' consulting firms to refute evidence that the old standard was inadequate. Eventually, when the scientific evidence became so great that it was no longer credible to deny that workers developed CBD at levels permitted by an out-dated standard, the beryllium industry responded with a new rationale to delay promulgation of a new, more protective exposure limit.

In the television interview, Secretary Richardson described how the Department of Energy (DOE) had changed course, and was now lowering the level that triggered protection for beryllium-exposed workers in the US nuclear weapons complex from 2.0 $\mu g/m^3$ to 0.2 $\mu g/m^3$ (micrograms of beryllium per cubic meter of air). The Department's new Chronic Beryllium Disease Prevention Program was designed to provide further protection for workers from a substance so hazardous that no safe level of exposure has ever been established.

The DOE standard covers only workers employed in the nuclear weapons complex. Although OSHA has acknowledged the inadequacy of its present workplace beryllium exposure limit, it has not updated its standard, which covers workers in the private sector. Researchers at the National Institute for Occupational Safety and Health (NIOSH) have estimated that there are between 28 000 and 107 000 private-sector workers potentially exposed to beryllium in the US; only 1 500 of these are employed in primary producers of beryllium products (Henneberger et al., 2004).

This case study presents a history of the knowledge and public policy about preventing beryllium-related disease, focusing primarily on the US beryllium industry's role in shaping US regulatory policy. A similar investigation has been performed in the United Kingdom (Watterson, 2005). Although the present study primarily discusses events in the United States, it is worth noting that Brush Wellman, the leading US manufacturer of beryllium products, has operated factories in Europe and that Brush Wellman's actions influenced beryllium safety and health policy throughout the world.

The present study is based on a review of documents and on the personal knowledge of one of the authors (David Michaels), who, as Assistant Secretary of Energy for Environment, Safety and Health, directed the DOE efforts to issue a stronger beryllium standard and develop a programme to provide compensation payments to workers with CBD. Some of the documents cited were obtained from government files and others were provided by attorneys who obtained them via litigation.

6.2 Early warnings and the first beryllium workplace exposure standard

The first significant industrial use of beryllium occurred in the 1930s, in production of fluorescent lamp tubes. Soon after the metal was first introduced, dozens of workers employed at fluorescent lamp factories in Massachusetts developed a form of chemical pneumonitis now known as Acute Beryllium Disease (ABD) (Hardy, 1950). It quickly became apparent that workers could not safely work with beryllium without respiratory protection.

Beryllium's importance grew dramatically with the Manhattan Project, the secret initiative to construct atomic weapons, and the subsequent expansion of the nuclear weapons industry, fuelled by the Cold War. This lightweight metal is a vital component in nuclear weapons. Beryllium slows down the neutrons released when an uranium atom is split in an atomic chain reaction; this facilitates the splitting

of more atoms, thereby increasing a weapon's power, or 'yield'. In the early years of US nuclear weapons production many cases of beryllium disease occurred among workers employed at privately operated beryllium production plants and among residents living near these facilities.

To its credit, the DOE's predecessor, the Atomic Energy Commission, acted quickly. Coming soon after the success of the Manhattan Project, the AEC had a group of very capable scientists who had virtually invented the field of radiation protection (Hacker, 1987). The AEC focused its attention on beryllium, funding numerous studies at laboratories and universities throughout the country. Most importantly, AEC environmental health specialists developed a beryllium exposure limit.

In many ways, the AEC had no choice but to tackle the problem directly. Since the weapons complex was now the nation's primary consumer of beryllium products, the AEC tacitly assumed responsibility for researching the health perils that the valuable metal posed. In a 1947 report, *Public Relations Problems in Connection with Occupational Diseases in the Beryllium Industry*, the AEC openly acknowledged problems of both 'obvious moral responsibility' and public relations, the latter exacerbated by the fact that, unlike remote research and bomb-making facilities, some beryllium-processing factories were located in more populous areas. The 1947 report states bluntly,

> 'There is no doubt at all that the amount of publicity and public indignation about beryllium poisoning could reach proportions met with in the cases of silicosis or radium poisoning.' It also notes that the industry was already reporting problems recruiting workers 'because of local prejudice … engendered by actual and rumored experience with beryllium poisoning' (Tumbelson, 1947).

The origin of the AEC beryllium exposure limit is discussed in the autobiography of Merril Eisenbud, an AEC industrial hygienist who went on to be the Environmental Protection Administrator of New York City. Eisenbud describes how he and Willard Machle, a physician who was a consultant to the firm building the Brookhaven Laboratory in Long Island, New York, decided on the number while in the back seat of a taxi on their way to a meeting at the laboratory in 1948. In his autobiography, Dr Eisenbud reports that he and Dr Machle selected 2 $\mu g/m^3$ for workplace exposures and 0.01 $\mu g/m^3$ for community exposures 'in the absence of an epidemiological basis for establishing a standard' (Eisenbud, 1991). Instead, the scientists used what Herbert Stokinger of the US Public Health Service later described as a 'crude analogy' to protect health (Stokinger, 1966).

The AEC 'tentatively' adopted these exposure limits in 1949 and then reviewed them annually for seven years before permanently accepting them (Stokinger, 1966). The agency applied this exposure limit in its own facilities and incorporated adherence to the exposure limit into its contracts with manufacturers that supplied it beryllium products. OSHA later adopted the 2 $\mu g/m^3$ limit when it first issued workplace exposure standards in 1971. While the story of Eisenbud's 'taxicab standard' has been often retold, a recent reviewer of the historical data has suggested that the workplace exposure limit was actually selected on the basis of feasibility not health protection (Egilman et al., 2003).

The 2 $\mu g/m^3$ exposure limit was a great step forward. It was very stringent for its time, and its acceptance was probably aided by two factors. The first was that it addressed a severe problem; the human cost of acute beryllium disease was so great that the accompanying 'public relations problems' threatened the AEC's mission. Second, nuclear weapons production was well funded — essentially a 'cost-plus' operation in which the participating companies were assured a healthy profit. For the most part, the weapons plants were run by private employers, with the US government reimbursing their costs, plus an additional percentage awarded as profit. The largest US manufacturer of beryllium products was Brush Wellman, now known as Materion; Brush (as it was often called) was both a vendor to the US government and a contractor, operating a beryllium products production facility for the AEC in Ohio from 1950 to 1956.

The 2 $\mu g/m^3$ exposure limit was an immediate success; ABD virtually disappeared and there appeared to be a reduction in new cases of CBD as well. But it was not long before questions arose about the level of beryllium exposure necessary to cause CBD.

6.3 The science and its use

6.3.1 Evidence of CBD at exposures below the 2 $\mu g/m^3$ standard

With funding from the AEC, Dr Harriet Hardy established the Beryllium Case Registry (BCR) at the Massachusetts General Hospital in 1952. ABD and

CBD case reports were sent to the BCR, to track the disease and to aggregate a sufficient number of cases to conduct epidemiologic analyses (Hardy, 1955; Hall, et al., 1959; Hardy, 1962). As of 1972, the BCR had recorded at least 20 CBD cases among workers who started employment after 1949, the year the AEC exposure limit was adopted (NIOSH, 1972). By 1975, that number had risen to at least 36 (OSHA, 1975), suggesting the disease might be occurring in workers whose exposure was below the 2 μg/m^3 exposure limit. Moreover, CBD had been diagnosed in persons with no workplace exposure to the metal, including individuals who simply laundered the clothes of workers, drove a milk delivery truck with a route near a beryllium plant, or tended cemetery graves near a beryllium factory (NIOSH, 1972).

Although the acute illness was typically seen among workers exposed to very high levels of soluble forms of beryllium, the distribution of the chronic form of beryllium disease did not follow the usual exposure-response model seen for most toxic substances. Instead, CBD was found among workers and community residents without substantial exposure histories. As early as 1951, Sterner and Eisenbud reported that exposure levels were not correlated with CBD severity, and hypothesised an immunological susceptibility (Sterner and Eisenbud, 1951).

Scores of workers exposed to beryllium from manufacturing nuclear weapons developed Cronic Beryllium Disease.

Photo: © istockphoto/Oleksiy Mark

In 1966, *Beryllium: Its Industrial Hygiene Aspects*, was published under the direction of the American Industrial Hygiene Association for the AEC. Dr Stokinger, the editor of the text, asserted that:

> 'Numerous cases of the chronic disease have occurred from exposures to seemingly **trivial** concentrations of a beryllium compound that at higher levels produced no effect; no dose-response relationship appears to hold' (Stokinger, 1966) (emphasis added).

It was becoming increasingly clear that a simple, linear dose-response relationship (risk increasing in direct proportion to dose) did not apply to this metal, and that it might not be possible to identify a threshold below which no CBD cases would occur.

In these early years, the community cases were evidently viewed as anomalous, or the result of episodes of high exposure. CBD incidence among workers did appear to drop dramatically with the reduced exposure associated with the standard, leading to speculation at the time that the 2 μg/m^3 exposure limit might be overly conservative (Breslin and Harris, 1959; Stokinger, 1966). There thus appeared to be a conundrum: how could there be community cases and occasional case reports of workers with very low exposures, while the standard appeared to be effective in systematic studies of beryllium production workers? With hindsight, we can speculate that the explanation is that CBD is an immune-mediated disease with considerable inter-individual variability in susceptibility, and a dose-response relationship which is probably driven by 'peak' exposures — possibly of very short duration — which standard methods of exposure assessment do not detect.

Throughout the 1970s and 1980s, CBD case reports involving workers whose exposures were below 2 μg/m^3 continued to emerge. In 1974, for example, representatives of NGK, a Japanese beryllium producer that also operated a manufacturing facility in the US, travelled to the US to meet with local beryllium industry executives. The Japanese delegation brought a report of five CBD cases that had occurred among workers exposed below the 2 μg/m^3 standard (Kohara, 1974; Shima, 1974). Similar cases occurred at US plants, including four cases among workers at a single scrap metal reclamation facility who were consistently exposed to beryllium below 2 μg/m^3 (Cullen et al., 1987).

Today, it is understood that CBD is initiated by an immune system response to beryllium exposure; the

associated adverse health effects begin well before the disease has pulmonary manifestations that allow diagnosis with a chest x-ray or pulmonary function test (Newman et al., 1996). The first published reports of CBD diagnosed using blood lymphocyte proliferation tests (BeLPT) appeared in 1983 (MMWR, 1983). By the end of the decade the diagnostic techniques had progressed significantly, allowing clinicians to more easily identify individuals with beryllium sensitisation (BeS), an immunologic condition that is a precursor to CBD (Kreiss et al., 1989; Mroz et al., 1991).

Using the BeLPT as a screening tool, researchers have found CBD prevalence rates ranging from 0.1 to 4.4 % among beryllium-exposed workers in the nuclear weapons, ceramics, primary beryllium manufacturing, metal machining, and copper-beryllium alloy industries, with Be(S) prevalence in these groups from 0.9 to 9.9 %. In most of these surveys, workers identified through the BeLPT as beryllium sensitised were given clinical evaluations to determine whether they had CBD. Depending upon the workplace, the CBD rate among workers with BeS ranged from 9 to 100 % (Kreiss et al., 1993a; Kreiss et al., 1993b; Kriess et al., 1996; Stange et al., 1996; Kreiss et al., 1997; Deubner et al., 2001; Henneberger et al., 2001; Newman et al., 2001; Stange et al., 2001; Sackett et al., 2004; Welch et al., 2004; Rosenman et al., 2005; Schuler et al., 2005; Schuler et al., 2008).

These studies diagnosed CBD or BeS among workers, including clerical workers and security guards, who had only experienced bystander exposure to beryllium. Clinical follow-up studies have found that individuals with BeS progress to CBD at a rate of 6 % to 8 % per year, but it is not known if all individuals with BeS will eventually progress to CBD (Newman et al., 2005).

6.3.2 *Evidence of beryllium's capacity to cause cancer*

In addition to its non-malignant effects on the lungs, beryllium has been shown to be a lung carcinogen. By the 1970s, significant toxicological evidence had accumulated on beryllium's carcinogenic effects, leading an NIOSH official to assert in 1977 that 'probably no compounds known to man give so consistent a carcinogenic response in so many animal species as do the compounds of beryllium' (NIOSH, 1977). This indictment of the potential risk of beryllium exposure compelled OSHA to propose a new occupational exposure limit for beryllium of 1 $\mu g/m^3$, measured as an eight-hour time-weighted average. NIOSH then recommended lowering the permissible exposure limit further, to 0.5 $\mu g/m^3$ (NIOSH, 1977).

Brush Wellman assembled a team of toxicologists, statisticians and physicians to challenge the new regulatory initiative (Michaels, 2008). The stakes were high for Brush: 'If beryllium is determined to be a carcinogen and so labelled and so regulated it would only be a matter of time until its usage would shrink to a point where it would no longer be a viable industry' (Brush Wellman, 1977). Ultimately, intense lobbying by the industry and the US Departments of Defense and Energy and the election of President Ronald Reagan prevented OSHA from finalising a new workplace exposure limit (Roe, 1999). Nonetheless, NIOSH continued to conduct epidemiological studies of cancer risk among beryllium-exposed workers (Steenland and Ward, 1991; Ward et al., 1992). The results of these studies, along with the extensive animal evidence, led the International Agency for Research on Cancer to list beryllium and beryllium compounds as Group 1 agents (i.e. carcinogenic to humans) in 1994 (IARC, 1994) and to reaffirm the designation in 2009 (Straif et al., 2009). Similarly, the US National Toxicology Program designated beryllium in 2002 as a 'known human carcinogen' (NTP, 2002).

6.3.3 *The beryllium industry's public relations efforts*

The increasing evidence of adverse health effects associated with beryllium exposure continued to create a problem for the industry. If government agencies formally designated beryllium as a substance for which there is no safe exposure level or as a carcinogen, the economic consequences for the industry could be significant. The industry's customers would be more likely to look for substitutes for the light-weight metal (Brush Wellman, 1977; Hanes, 1992b).

Beryllium producers decided to be proactive in shaping the interpretation of scientific literature on beryllium's health effects. Aspects of the programme were detailed in a 1987 internal Brush Wellman memo, with the subject line 'Proposed program for filling need for new and accurate beryllium health and safety literature'. The memo by Martin B. Powers, a retired Brush Wellman executive who was a consultant to the company, and Dr Otto P. Preuss, Corporate Medical Director, warned:

> '… the literature on Be published in the last twenty years has been very damaging. The

> literature is constantly being cited, either to our doctors at medical meetings in rebuttal of the Brush experience, or by potential customers as the cause of their unwillingness to use our products. Federal Government regulatory agencies, such as OSHA and EPA [the US Environmental Protection Agency], publish much of this material and then in the absence of good data, cite these erroneous documents to support regulatory activities.'
>
> 'What is needed to combat this situation is a complete, accurate and well written textbook on Be health and safety. It will have to be financed by Brush (or Brush and NGK?) and the bulk of the work done by Marty Powers and Otto Preuss. To be fully acceptable and credible, however, it will have to be published under the auspices of some not-for-profit organization such as a university or medical group. … In addition to the book, we should have a number of medical papers published in prestigious medical books' (Powers and Preuss, 1987).

Beryllium: Biomedical and Environmental Aspects was published in 1991; two of its editors were Martin Powers and Otto Preuss, along with a respected academic physician (Rossman et al., 1991).

In the face of increasing evidence about the toxic effects of their products, the beryllium industry also turned for assistance to the public relations (PR) firm Hill & Knowlton (Hill & Knowlton, 1986). This firm has gained much notoriety for its now well-known efforts in manufacturing and promoting scientific uncertainty for the tobacco industry (Brandt, 2007; Glantz et al., 1996). In the proposal it sent to Brush describing how it could help, Hill & Knowlton echoed the AEC 'public relations problem' memo of 1947:

> 'Beryllium undoubtedly continues to have a public relations problem. We still see it cited in the media, as well as in our conversations with people who should know better, as a gravely toxic metal that is problematic for workers … We would like to work with Brush Wellman to help change these common erroneous attitudes. We envision a public relations program designed to educate various audiences … to dispel myths and misinformation about the metal' (Marder, 1989a).

Hill & Knowlton proposed to prepare 'an authoritative white paper on beryllium … [which] would serve as the most definitive document available on beryllium.' The PR firm also suggested projects to engage outside scientists in independent reviews of Brush Wellman materials, 'to nurture relations with the Environmental Protection Agency' and 'to challenge all unfair or erroneous treatment in the media to set the record straight' (Marder, 1989a).

Appended to the letter was a document in which Hill & Knowlton boasted of their experience assisting other corporations who faced regulatory difficulties stemming from their production of hazardous products, including asbestos, vinyl chloride, fluorocarbons and dioxin. There was no mention, however, of the firm's work for the cigarette manufacturers. Matthew Swetonic, the staff member proposed to direct the PR effort, had been a key player in Hill & Knowlton's efforts on behalf of a cigarette manufacturer to convince the public that non-smoker exposure to environmental tobacco smoke was harmless (Swetonic, 1987) and to 'create a favorable public climate' to assist in defeating lawsuits filed by smokers with lung cancer (RJR Nabisco, no date). In addition, Swetonic had previously performed public relations work for Johns-Manville, the asbestos producer, and had been the first full-time executive secretary of the Asbestos Information Association (Asbestos Textile Institute, 1973).

Once hired, Hill & Knowlton sought to reassure Brush's customers of the safety of beryllium. The firm drafted a series of letters for Brush to send to their beryllium ceramic customers, downplaying beryllium's hazardous properties (Marder, 1989b; Davis, 1989a; Davis, 1989b).

6.3.4 Manufacturing uncertainty about beryllium and disease

By the late 1980s, the continued incidence of new CBD cases raised concerns among health and safety professionals who previously believed the 2 $\mu g/m^3$ 'taxicab standard' was adequate to protect workers from CBD. Dr Eisenbud, who had become a consultant to Brush Wellman, notified the company in 1989 that 'he did not feel that he could defend the 2 microgram standard any longer' (Rozek, 1989).

The rising number of CBD cases also contributed to an increase in litigation. Brush management recognised that a change in the OSHA standard could be used in legal suits brought by sick workers. 'Maintaining the existing [OSHA]

standard is fundamental to successfully defending against any product liability litigation', a Brush official asserted in 1989 (Rozek, 1989). This effort was an integral part of Brush's Health, Safety and Environment Strategic Plan in 1991:

> 'Employ legal means to defeat unreasonably restrictive occupational and emission standards and to challenge rulemaking and other regulatory activities that seek to impose unreasonable or unwarranted changes. Resist an attempt to make the existing occupational exposure standard of 2 micrograms/cubic meter, as measured and calculated by Brush, more restrictive. The standard is safe, it is one of the most stringent standards, and it is fundamental to our product liability defense' (Rozek, 1991).

In contrast, the evidence of the standard's inadequacy was clear to the DOE. In 1991, the nuclear weapons agency began the process of lowering the exposure limit to reduce workers' risk of developing CBD. The change was opposed by the beryllium industry, whose position is summarised in this excerpt from a 1992 Brush Wellman letter:

> 'We regret that DOE apparently still intends to abandon the existing standard of over 40 years standing with no evidence, either that the existing standard is unsafe or that the new proposed standard affords any greater degree or [sic] safety. The NIOSH recommendation of 1977, which fortunately no one ever adopted, of 0.5 micrograms, introduced an element of confusion that can only be compounded by DOE's proposed introduction of a third number. A proliferation of numbers as 'standards' can only weaken the acceptance, and therefore, the efficacy of the individual protection afforded. Confusion is never in the best interests of the worker' (Hanes, 1992a).

Progress on a more protective rule was also impeded by opposition from within the DOE. The offices responsible for manufacturing nuclear weapons argued that money spent protecting workers would mean less money for producing arms. The debate continued for several years, leaving the proposed rule in limbo.

Despite the institutional obstacles, US government safety officials continued to advocate a new, more protective standard. The DOE health and safety office sponsored a series of public forums to gather information on beryllium's health effects. At one session, Brush Wellman's Director of Environmental Health and Safety asserted (according to minutes of the meeting): 'Brush Wellman is unaware of any scientific evidence that the standard is not protective. However, we do recognize that there have been sporadic reports of disease at less than 2 $\mu g/m^3$. Brush Wellman has studied each of these reports and found them to be scientifically unsound' (DOE, 1997).

This was the industry's primary argument; subsequent studies have demonstrated that the underlying logic to the argument was flawed. At the time, however, it was not difficult to go back into the work history of anyone with CBD and speculate that, at some point, the airborne beryllium level may have exceeded the standard. Even if no evidence for overexposure was found, it was assumed that exposure over the standard had occurred because the worker had developed CBD. Brush did this, and then reasoned that the 2 $\mu g/m^3$ must be fully protective since everyone who had CBD must have at some point been exposed to levels above the standard.

Although flawed, this tautological construct served as the basis for Brush's defence of the 2 $\mu g/m^3$ exposure limit. Talking points prepared for Brush executives advised:

> 'you may be asked in some fashion whether or not the 2 $\mu g/m^3$ standard is still considered by the company to be reliable. Your answer should be as follows:
>
> 1. Experience over several decades has, in our view, demonstrated that levels of airborne beryllium within the OSHA threshold limit value afford a safe workplace.
>
> 2. In most cases involving our employees, we can point to circumstances of exposure (usually accidental), higher than the standard allows. In some cases, we have been unable (for lack of clear history) to identify such circumstances. However, in these cases we also cannot say that there was *not* excessive exposure' (emphasis in original) (Pallum, 1991).

This position, however, could not be maintained indefinitely. As the DOE provided medical screening to more workers, the number of CBD and BeS cases continued to grow, reaching several hundred by the middle of the decade (DOE, 1998). Moreover, the growing literature reporting cases of CBD associated with low levels of exposure undermined the claim

that the old standard was safe (Wambach and Tuggle, 2000). Scores of beryllium-exposed workers who had developed CBD filed civil suits against Brush, alleging that the firm failed to disclose information about the material's toxicity. Continued denial of the relationship between low-level exposure and CBD was unlikely to be a successful strategy to oppose either the claims raised by sick workers or the attempts by the DOE and OSHA to strengthen their beryllium exposure standards. Instead, Brush Wellman asserted that not enough was known to prevent CBD from occurring. If true, the industry might avoid liability in CBD litigation.

In 1998, Brush Wellman and NIOSH embarked on a collaborative research initiative, conducting medical surveillance of beryllium-exposed workers and examining the beryllium-CBD relationship. The research partnership has been productive, delivering findings that have substantially contributed to the literature on beryllium disease (NIOSH, 2002).

In December 1998, the DOE officially proposed a rule to protect workers from CBD, including an action level of 0.5 μg/m^3, or 25 % of the OSHA standard, and asked for public comment on the proposal (DOE, 1998). Brush Wellman no longer asserted that the old standard was effective in preventing CBD but instead took the position that not enough was known to prevent CBD from occurring. During a public hearing in February 1999, a Brush representative offered this new rationale for the DOE to delay issuing a new standard. He testified that 'important research is underway which may provide a scientific basis for a revision to the occupational standard for beryllium,' pointing to studies on particle size, particle number and particle surface area (Kolanz, 1999).

For assistance in promoting this new strategy, Brush turned to Exponent, Inc., a US firm that provides scientific and technical support to polluters and manufacturers of dangerous products (Exponent, Inc., 2006). Exponent, Inc. is a leading practitioner of 'product defence', a specialisation that aims to help corporations reduce their regulatory burden and defeat liability claims that arise in the civil justice system (Michaels, 2008). With Exponent's assistance, in September 1999 Brush Wellman convened a conference, co-sponsored by the American Conference of Governmental Industrial Hygienists, to bring 'leading scientists together to present and discuss the current information and new research on the hazards posed by beryllium' (Paustenbach et al., 2001).

At the time of the conference, the DOE was a few months away from issuing its final ruling, and OSHA had recently signalled its intention to revise its outdated 2 μg/m^3 standard (OSHA, 1998). The paper summarising the proceedings, entitled 'Identifying an Appropriate Occupational Exposure Limit (OEL) for Beryllium: Data Gaps and Current Research Initiatives' voiced the same position that DOE officials had heard earlier in the year. Specifically, that more research was needed on the effects on CBD risk of particle size, exposure to beryllium compounds and skin exposure. Although it is not uncommon for a scientific paper to call for additional research, this paper went further, advocating postponement of any changes in the workplace beryllium exposure standard: 'At this time,' the paper concludes, 'it is difficult to identify a single new TLV (threshold limit value) for all forms of beryllium that will protect nearly all workers. It is likely that within three or four years, a series of TLVs might need to be considered… In short, the beryllium OEL could easily be among the most complex yet established' (Paustenbach et al., 2001).

In December 1999, the DOE completed its work, mandating that protection from beryllium exposure in DOE facilities be triggered at 0.2 μg/m^3 rather than the 0.5 μg/m^3 level the agency had proposed some months earlier (DOE, 1999). In its ruling, DOE relied on a common industrial hygiene measure of exposure: full-shift concentration by weight of airborne beryllium.

The government's responsibility is to protect public health using the best available evidence. More research was, and is, needed, but since the relationship of CBD to beryllium particle size, number of particles and surface area was, and remains, poorly understood, the officials responsible for protecting the health of beryllium-exposed workers determined that new policy should not be delayed until this research was completed.

6.3.5 New evidence but no new OSHA standard

Once the DOE prepared to issue its new standard, OSHA, the lead US agency for worker safety and health, recognised an opportunity to update its own beryllium standard. In written comments to the DOE, OSHA's Assistant Secretary acknowledged the inadequacy of the current OSHA standard, writing:

> 'we now believe that our 2 μg/m^3 PEL does not adequately protect beryllium-exposed

> workers from developing chronic beryllium disease, and there are adequate exposure and health effects data to support [the DOE's] rulemaking.'

The letter continues by citing existing data:

> 'Cases of chronic beryllium disease have occurred in machinists where 90 % of the personal exposure samples found levels of beryllium to be below the detection limit of 0.01 μg/m^3 … Viewed from OSHA's regulatory perspective, these DOE study results document risk of sensitization to beryllium of 35–40 per 1 000 workers and risk of chronic beryllium disease to machinists of 94 per 1 000' (Jeffress, 1998).

Despite a commitment to issue a new standard by September 2001 (OSHA, 2000), OSHA did not propose a rule to protect beryllium-exposed workers. When President George W. Bush's Administration took office in 2001, OSHA formally dropped its commitment to strengthen the beryllium standard, asserting it needed more information before deciding how to proceed (OSHA, 2002).

Scientific knowledge on the risks associated with low-level beryllium exposure continues to accumulate, silencing those who had previously defended the adequacy of the current standard. In the few years since DOE issued its standard, US researchers, including several affiliated with Brush Wellman, have published several epidemiologic studies that provide additional evidence that OSHA's standard does not fully prevent CBD (Henneberger et al., 2001; Kelleher, et al., 2001; Schuler et al., 2005; Stange et al., 2001; Rosenman et al., 2005; Madl et al., 2007). Finally, in 2006, a literature review and editorial supported by Brush Wellman acknowledged that the current OSHA standard 'provides insufficient protection for beryllium-exposed workers' (Borak, 2006).

Beryllium exposure continues to be a public health concern at 'downstream' facilities, which use beryllium products but are not involved in primary production, in recycling facilities, and in communities adjacent to beryllium-processing facilities. In 1999, the diagnosis of a sentinel CBD case in a metals recycling plant in Quebec, Canada resulted in the identification of 31 additional cases at three metals plants (Robin, 2005). It also prompted a survey that identified 2 789 workplaces where beryllium was used in that province, including 63 golf club manufacturers and 15 bicycle manufacturers (Tremblay, 2005). There have also been eight new cases of community-acquired CBD recognised between 1999 and 2002 in the US (Maier et al., 2008)

Given the wealth of new research, is it now possible to identify a safe level of beryllium exposure? Unfortunately, it is not. There are many complex questions to answer, and there are relatively few workplaces in which these questions can be easily studied. A committee of the US National Research Council recently concluded that 'it is not possible to estimate a chronic inhalation-exposure level that is likely to prevent BeS and CBD' (National Research Council, 2008). This scepticism is shared throughout the scientific community; in the opinion of three NIOSH scientists, the evidence gathered to date suggests that 'attempts to define a safe air concentration of beryllium for all workers are not likely to be successful' (Kreiss et al., 2007).

This uncertainty does not, however, justify deferring implementation of programmes to reduce exposure. There is ample evidence that interventions designed to reduce beryllium exposure to the lowest achievable levels have successfully decreased BeS and CBD incidence (National Research Council, 2008). Furthermore, in 2009 the American Conference of Governmental Industrial Hygienists issued a Threshold Limit Value recommendation of 0.05 μg/m^3, which is well below both the current OSHA and DOE standards (ACGIH, 2009).

Since at present there is no compelling evidence for a safe level of beryllium exposure, it would be prudent public health policy for manufacturers to substitute a less toxic material for beryllium whenever possible. However, in those products and processes in which there is no adequate substitute for beryllium, such as the production of nuclear weapons, exposure should be reduced to the lowest level technically feasible.

6.4 Lessons for policymakers

The primary lessons of this case study are widely applicable across many environmental health controversies.

The first is that **the absence of evidence is not evidence of absence**. In the decades following the reduction in beryllium exposures in the early 1950s, relatively few new CBD cases were diagnosed. This is likely attributable both to improved working conditions and the limitations of the

diagnostic methods available at the time. With the development of the BeLPT, many new cases were diagnosed, no doubt including cases that would not have been previously recognised as CBD.

There were indications before the advent of the BeLPT, however, that the 2.0 μg/m^3 standard was not fully protective. As CBD and BeS were diagnosed in an increasing number of workers with low exposures, this conclusion became more difficult to avoid.

As this evidence accumulated, the beryllium industry had a strong financial incentive to challenge the data, and to oppose regulatory action that would result in a lower exposure limit. It appears this incentive shaped the interpretation given to scientific evidence by scientists employed by the beryllium industry.

This, then, is the second lesson of the case study: **interpretation of scientific data by those with financial incentives for misinterpretation must be discounted**. Scientists employed by the beryllium industry defended the 'taxicab standard' long after it was correctly recognised as inadequate by independent scientists. In particular, work by scientists employed by firms specialising in product defence and litigation support must be seen for what it is: advocacy, rather than science.

This study illustrates the practice of '**manufacturing uncertainty**' — the strategy used by some polluters and manufacturers of hazardous products to prevent or delay regulation or victim compensation (Michaels and Monforton, 2005; Michaels, 2008). The public health paradigm requires that the best available evidence be used to protect the public. By the early 1990s, the accumulated evidence was sufficient for public health officials to justify a more protective workplace beryllium exposure limit. In response, the industry manufactured and magnified uncertainty, producing a series of arguments about why the old standard should not be changed. Extensive research has subsequently confirmed the inadequacy of the OSHA standard; a more protective standard will help prevent CBD and save lives.

Finally, the findings of this case study underscore the importance of **considering the hazards associated with a toxic material throughout the entire life cycle of the product**. While primary producers of beryllium products may be able to control exposures in their own facilities, it is unlikely that many secondary users and recyclers have the expertise, resources and knowledge to prevent beryllium disease in exposed workers and residents in nearby communities. As a result, it would be prudent public health policy to end industrial use of beryllium, except in circumstances where substitution is impossible.

Table 6.1 Early warnings and actions

1930s	First industrial uses of beryllium and first reported cases of beryllium disease
1949	AEC adopted the 2.0 μg/m^3 exposure limit for weapons workers
1952	Establishment of Beryllium Case Registry
1971	OSHA adopted the 2.0 μg/m^3 exposure limit
1975	OSHA proposed a 1.0 μg/m^3 exposure limit but this was never approved
1980s	BeLPT used to diagnose cases of CBD
1989	DOE proposed a 0.5 μg/m^3 exposure limit for DOE weapons and clean-up workers
1999	DOE issued a 0.2 μg/m^3 exposure limit for DOE weapons and clean-up workers
2009	ACGIH recommended a 0.05 μg/m^3 exposure limit
2012	OSHA has yet to propose new workplace beryllium standard

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Corporate behaviour in the regulation of beryllium: could there have been a different outcome if the company had room to turn around?

Tee L. Guidotti ([3])

The response of commercial organisations to uncertainty with respect to environmental and occupational risks continues to challenge regulators and parties interested in a regulatory intervention in the face of corporate resistance.

Viewed from within the organisation, corporate objectives and protection align with other seemingly valid reasons to oppose change and create a stronger argument from within than may be perceived from the outside. One suspects that most corporate leaders involved in situations like this live in a world of cognitive dissonance and denial rather than cupidity. Few people, other than sociopaths, tolerate the belief that they cause harm and suffering. Rather, most people with strong personalities tend to deny their role in a bad situation and the consequences of their actions, and to believe the denial. Reinforced by group-think, rationalisation, corporate culture, and a technical staff able and willing to provide justification for the denial, such behaviour becomes normative. The challenge is not to condemn the behaviour — that is easy. It is to understand it in order to control it. (Prevention is probably not possible given human nature.)

Beryllium: a case study

Michaels and Monforton (2008 and present volume) have published a comprehensive history of the occupational exposure standard for beryllium in the US and its failure to adequately protect workers. Their work is a valuable contribution to our understanding of the beryllium issue, about which there have been a number of serious misconceptions (Guidotti, 2008).

The only significant manufacturer and supplier of beryllium metal in the US, Brush Wellman, used various arguments to rationalise opposition to the proposed beryllium standard, first asserting that 2 $\mu g/m^3$ was adequate, then playing on uncertainty, challenging the data on which the proposals were grounded, first for beryllium disease and later for carcinogenicity. In this they were initially abetted by the US Department of Energy (DOE), which initially resisted an evidence-based precautionary protective standard, presumably to protect the nuclear industry. There were many allegations of scientific malfeasance and inappropriate political influence. Notwithstanding the fact that both DOE and the American Conference of Governmental Industrial Hygienists, a major voluntary body recommending exposure guidelines, have proposed lower occupational exposure limits, the federal regulator, the Occupational Safety and Health Administration, has still not proposed a new 'permissible exposure limit' for beryllium after at least 35 years of deliberation.

Brush Wellman was, and still is, a highly profitable company that had, and still has, a near monopoly on the product. At the time it had little other business, although it is now more diversified. The company stands accused by Michaels and Monforton of cupidity and arrogance in resisting a protective federal standard in the face of steadily accumulating evidence for the toxicity and carcinogenicity of the metal. Doubtless, the company has a different narrative, but this panel is not about the company's culpability. Seen another way, the story of Brush Wellman, and other companies, is a case study in organisational behaviour and response. However, it may also be read slightly differently to be about pathway dependence and how the initial worldview of a highly organised institution may commit it to a line that ultimately proves disgraceful for itself and tragic for the victims of occupational hazard.

The doctrine of 'shareholder value' and resistance to changing course

Michaels and Monforton assume throughout that the reluctance of Brush to accept new findings regarding Be risk was motivated by the desire to maintain corporate revenues. To set the stage, it is important to realise that, in the US, there appears to be no recognised legal responsibility of corporations other than to shareholders and to obey the law. The concepts of corporate responsibility and of corporate beneficence have been litigated many times and decisions have consistently upheld the interests of shareholders above all other stakeholders (Pérez Carolli, 2007). The most famous example of this is a 1919 Michigan Supreme Court decision that blocked Ford Motor Company from reducing the price of Model T automobiles as a public benefit (and

([3]) This text is an adaptation of a critical review prepared for the European Environmental Agency, Copenhagen, as part of *Late lessons from early warnings*.

to create a larger consumer class) at the expense of paying dividends to shareholders. Some legal scholars have argued, persuasively, that this ruling has been misunderstood and its significance has been exaggerated (Stout, 2008). However, there have been many other decisions that have had the collective impact of emphasising that although a corporation may act in a beneficent manner, it is not entitled to do so at the expense of shareholder interests, at least not without their permission.

From the legal point of view, and at least from a lay reading of the legal situation, which is at least what corporate officers would have understood in the 1950s and 1960s, corporations appear to be obliged to optimise value, profits, and shareholder interest, not community or social benefits except insofar as they advance the interests of the corporation and therefore the interests of the shareholders who own it. This reality can be lamented and argued, but it is deeply grounded in American jurisprudence and business culture.

The point to be made before further discussion is not that this concept is, or can be, abusive and antisocial — that it can be is obvious. It is that it was believed and that, notwithstanding waves of management interest in 'corporate responsibility' (most notably in the 1960s), this belief has been assumed in corporate culture and was part of a management philosophy of maximising 'shareholder value' for the last thirty years. Under US law, a corporation cannot be faulted for maximising profits, as long as they are within the law, just as an individual cannot be faulted for trying to minimise the taxes he or she pays, as long as the taxpayer is within the law. Whether Brush Wellman violated the law is outside the scope of this panel and is not directly addressed by Michaels and Monforton (2008).

Likewise, there is also the influence in business circles of the parallel and highly influential argument of Milton Friedman and the Chicago School of economists that the purpose of business is to increase wealth and that social benefit is a question of how that wealth is invested, a decision that the owners of the wealth should make, not the corporation (Friedman, 1970). One answer to Friedman would be that corporations are given a franchise to perform socially useful functions, providing goods and services in exchange for making profit, but this is not the forum to argue this point.

One obvious legal solution is for the interest of stakeholders to be revisited. If the corporation faces catastrophic sanctions if it admits it was wrong, then the interest of the shareholders in a corporation should be for it to capitulate. However, in the real world, fines are too low, sanctions are too weak, and legal actions too likely to settle for the anticipated consequences to force changes in corporate behaviour. The executives of a bad corporation are usually better off seeing the issue through to the end and then, if the consequences are dire, changing management, taking golden parachutes, and leaving the task of refurbishing the image of the company to the next executive team.

Another legal solution should be possible, however. If a corporation has the option of ending a course of action that would lead to consequences so serious that shareholders' interests would be compromised, they would then have a fiduciary and legal responsibility to their shareholders to retreat from an untenable position and accept the need to change course. Opportunities coming at key times in the narrative to change direction without onerous consequences could have made it possible for corporate leaders to drop their resistance to the proposed standard without admitting they were wrong. Creating such opportunities might make it possible for the leaders of such companies to change course on a pragmatic basis on the grounds that they are minimising loss to shareholders and reducing potential punitive damages that the company would have to pay.

Whether this policy would motivate corporate leaders on a destructive track to change course on their own initiative is uncertain, although it is likely that it would if the consequences are high. These are not stupid people, after all. What is certain is that legislation, regulatory policy, or a judicial opinion to this effect would create grounds for shareholders to take legal action against the officers of a corporation and put enormous pressure on them to change their position when it became untenable. Another advantage of such a policy is that it is consistent with conservative business values of responsibility to shareholders and maintaining shareholder value, and therefore hard to argue against.

National security and rationalisation

People tend to believe what is aligned with their own interest and do not recognise these beliefs as rationalisation. It is quite likely that corporate leaders of the day saw reasons other than corporate protection that aligned with their financial interests of profit maximisation. The sequence of events takes on new significance when seen from the perspective of the times.

Initially, the trade-off as seen from the ramparts of the military-industrial complex involved a risk/risk calculation in which the perceived security consequences would have been catastrophic and the potential for harm to workers seemed remote and uncertain. Issues of workers' rights to know, the sustainability of the industry without occupational health controls, and the uncertainty of risk from Be were undoubtedly secondary to security issues **as they were understood at the time**. In hindsight, this was highly unfortunate but at the time it was not unreasonable, given that the world was in a bipolar 'Cold War' between two nuclear powers, the Soviet Union and the US, together with its nuclear-armed allies France and the United Kingdom. Later, the rationale for opposing revision of the standard seems to have been based on a calculus of risk/benefit, in which the perceived risks of inadequate military defence with nuclear weapons was replaced by the perceived benefit to society of Be alloys.

In the context of an industry central to national security, it is not clear that the issue could have played out in any other way, unless there was some means of making a gradual transition to a more protective standard or resolving the uncertainties over the standard test for Be sensitivity (which in combination with a positive chest film or CT scan or biopsy results makes the diagnosis of beryllium disease) at an earlier stage. The 2 μg/m^3 standard is widely recognised as not adequately protective and was shown to be so at the time. However, once it was established, it took on a life of its own and became 'sticky' — that is, difficult to dislodge — until the evidence became overwhelming. This may have been, in part, because the leap to 0.5 μg/m^3 was or appeared to be too great technically and raised fears that the defence industry would be disrupted, leaving the country unacceptably vulnerable. However, reluctance to accept that a change was needed appears to have been driven mostly by uncertainties over the blood test (BeLPT), which was still in development and was perceived as unproven, a perception helped along by its alignment with financial interests.

Toward the end, it is clear that the emerging motivation for delay was perceived risk to the company. Here again there is another, unstated side to the story. It is clear that much of the opposition was self-serving but the company could legitimately have been seen at the time to be what is now called in 'homeland security' terminology a 'critical industry', providing an essential service or product. This dynamic would have, again, conflated the company's interests with the national interest (along the lines of 'what's good for us is good for the nation') and provided a rationale for maintaining the status quo on the grounds (specious but persuasive) that the company needed to stay in business and profitable to meet a national need.

Acceptable risk and accountability in risk assessment

It became apparent as the issue dragged on that no standard was fully protective, because of the stochastic (probabilistic, rather than deterministic) nature of the immune response. When this is true, as it is of many allergens, of fine particulate air pollution, and of lead exposure in children, the problem becomes one of determining 'acceptable risk' based on social criteria. Modern societies usually choose one in a million risk of a serious outcome or death as the acceptable risk, although in practice risks on the order of one in a thousand are the norm in occupational health. In this case, the company management was trying to make this determination alone, without collective input, because they (corporately) believed that they understood the problem best. However, they did not, and they were working in a social vacuum, focused on the company's priorities and beliefs. In a democracy, the question of 'who gets to decide' is answered formally by 'the representative of the people', that is, the government, and informally by who has possession of the data.

In the event, the initial standard of 2 μg/m^3 obviously worked well to reduce pressure to lower the standard. (It has since been reduced, first to 0.5 μg/m^3 in 1998 and then to 0.2 in 1999 but only as an internal standard within the Department of Energy, not through adoption by OSHA.) Although the story (told by Merril Eisenbud, who was involved in its formulation) that the initial 2 μg/m^3 was worked out in a taxicab on the way to the decisive meeting and was revised upward at the last minute, suggests an overly casual approach, in the absence of scientific evidence for a threshold or a 'no-observed adverse effects level' a reasonable consensus based on informed opinion is not a bad substitute for data. It certainly worked to eliminate acute Be disease, which was initially the concern. A standards-setting committee consisting of informed experts is not unlike a Delphi group, making sequential estimates based on feedback from the scientific literature and from their peers. It resembles (imperfectly) the estimation of an a priori probability in Bayesian statistics. Insisting on the inadequacy of a standard which was lacking more rigorous science, when evidence did not exist, is like

applying the legal and political standards of today to ancient history. It is also difficult to find experts with practical experience outside the industry or with no interest in the outcome of deliberations, making conflict of interest a given and a matter of degree.

Michaels and Monforton make the blanket statement that 'The interpretation of scientific data by those with financial incentives must be discounted.' However, financial incentives attach to almost everyone who has a professional interest in a particular topic, including those who receive support, to be critical of a position and offer expensive tests. Thus, the essential problems, beyond disclosure, are not the financial incentives but the degree of influence exerted on the investigator, the completeness of reporting, and the validity of the information. The validity question can be further unpacked into issues of honesty and integrity, data quality, methodological issues, bias, handling of uncertainty, correct scientific interpretation of complicated evidence, and whether selection or misclassification bias is introduced due to business or other activities that attach to the position of the party involved. (For example, workers at a particular plant in the Be industry may be different from other workers or workers in other plants, such that a study sponsored by the company may have a bias. But the same may also be true of a study performed by an academic researcher.) Professional and personal incentives, which may be as powerful as financial incentives, attach to everyone involved because once a position is taken publicly it is human nature to be emotionally invested in defending it.

To their credit, Michaels and Monforton use the term 'discounted' rather than 'ignored', but in practice few who advocate tighter regulation may make the distinction. In fact, exclusion of corporately-sponsored research and the 'grey literature' risks losing an immense body of valuable information. Society is already denied significant benefit by obstacles to accessing proprietary information. Current practices within the insurance industry, for example, together with rules against collusion and price-fixing, militate against sharing information that would be highly useful in establishing the health risk of various groups, such as workers covered by workers' compensation (Guidotti, 2000).

Seen in this light, and assuming that accountability is not possible in the adversarial setting of business interests, the issue reduces to one of transparency. Can the data be audited and the analysis reconstructed? Who will ensure the integrity of the auditors? In this regard the experience of the Health Effects Institute (HEI) is pertinent. HEI routinely commissions a reanalysis of data from the most significant studies it supports on air pollution health effects, a process that to date has confirmed the original findings in every case but is considered essential to acceptance of the findings by industry (in this case, the automobile manufacturing industry). This model is not so easily to apply to corporately sponsored research, however, because there is no external mechanism for guaranteeing quality assurance and no contractual obligation to cooperate with an audit or means of ensuring transparency.

Another model that may be applicable is the current drive to require drug companies to register clinical trials, so that those that have negative results or that demonstrate harmful effects cannot be buried. Establishing a data repository is a logical step in this process but there would of course be legitimate issues of business knowledge, anti-trust prohibitions, and proprietary information to navigate. How such an arrangement could be enforced when applied to corporately-sponsored research is not clear but a voluntary approach led by responsible companies would place considerable pressure on those that did not participate.

However, these are technical solutions and partial at best. The deeper issue is one of organisational behaviour and commitment to a wrong decision in the face of diminishing room to manoeuvre.

One could have made the point in 1983 that acceptance of the BeLPT, the blood test for immune sensitivity, would have protected the company through demonstration of due diligence, but at the time a consensus on the validity of the assay had not emerged. (As Michaels and Monforton pointed out, it was impeded by the machinations of a cooperative academic. Even today, the BeLPT has to be positive in two tests before a diagnosis is considered to be confirmed.) Michaels and Monforton make a major case for the idea that 'the absence of evidence is not evidence of absence', however in the case of the BeLPT there was abundant evidence but the performance of the test was disputed. Until the test was validated, it was not unreasonable for non-scientists to be sceptical. The deeper question is who determines when a method is valid: scientists, regulators, or corporate interests? Likewise, who determines when data are sufficient and when evidence is actually absent?

Faced with uncertainty and bolstered by intimations that the test may not be definitive, it was actually a logical (and, from their point of view, probably responsible) decision for

the company to delay and to require further information. As time went on, this position may have become untenable scientifically but the stakes were also rising. A late admission that the assay was valid would have been tantamount to admitting that the company had stalled and allowed further cases. In short, the company was pulled along in a situation in which, as uncertainty over the test diminished, the stakes increased, perhaps exponentially, making it increasingly difficult to accept or stop questioning the test and making it paradoxically more attractive to defend their earlier position. Small wonder that, in a classic demonstration of organisational behaviour, the company leadership did not want to admit, and as individuals probably truly did not believe, that they had erred.

Lessons learned

The Brush Wellman experience demonstrates that a significant internal disincentive of companies to accept new findings is fear of liability and reputational damage. Add to this the perceived fiduciary responsibility to shareholders, the shame of admitting that decisions may have harmed workers, and the (probably inflated) costs of installing more stringent controls and it is easy to see how denial and rationalisation would be the mode of behaviour. In the case of Be, these measures were relatively expensive: separation of sensitised workers through Be-free buffer zones and containment and reassignment of sensitised workers.

Seen in that light, and assuming that the Brush Wellman leadership was generally honest in their own terms (on the face of it, a problematical assumption), the company could be viewed as being pulled along by events into an increasingly untenable situation, until their position was completely indefensible. It would be going too far to characterise this as a 'tragedy' for them, in the dramatic sense of a fatal flaw that brings down the protagonist. However, it is apparent that one problem with the narrative is that there was never a moment at which Brush Wellman could change direction without paying what it considered to be an unacceptable penalty. Because of legacy liabilities, the deep investment the company had in believing otherwise, and the slow evolution of the science, the management of the company appears to have been slogging through a tunnel of diminishing dimensions, seeing no exit and no path except what lay ahead. At the beginning, the issue was cost (probably overestimated, as it usually is), loss of market share, and saving face. At the end, it may have been massive financial and legal liability.

Perhaps the key issue is at what point an organisation can change course, when it is allowed to do so, and how it can do so given its internal drivers and culture. The question may need to be recast as how information controlled by the company can be effectively accessed, with protection, so that the leadership has a viable escape route from an impossible situation.

The essential question for reconstructing the company's behavioural and motivational history is, therefore, was there ever a point along the way where it was 'safe' for Brush to change course? Was there an opening that allowed internal forces within the company that might have better understood the issue to break with the management line and to accept the health risks of Be at low levels without what they perceived to be unacceptable consequences (and psychic pain)?

This does happen. Liggett & Myers, the American tobacco company, made a dramatic break with the rest of the industry in 1996 and both settled tobacco-related cases and unilaterally declared that it accepted that smoking is addictive (Borio, 2003). It did so because it saw a window of opportunity to reduce its risk and because it recognised that the industry position had become untenable. (There is no reason to think that they did so because it was right or for the greater good. It was a business decision, pure and simple.)

If one expects corporations, and the attitudes of corporate leadership, to change in response to new information, rather than to fight new information because of fear, denial, or risk of loss, there must be exit or escape opportunities. This may mean unpalatable choices and bright lines where today the picture is murky, such as opportunities to forgive legacy liabilities, legal defences (such as a clear definition of when due diligence has been achieved), and a threshold for sufficient knowledge (a clear standard of when knowledge about risk is sufficient to act, not just first awareness that there may be a problem). Organisations cannot be expected to change their positions unless they are given a 'way out' that may involve forgiving past liability and reducing punitive damages. (This is largely what happened with the DOE contract worker's compensation programme.)

The threat of strong grounds for legal action or board action by dissident shareholders introduces a new counterweight to the equation and is a

bigger stick than it might first appear. It is also not necessary to assume that shareholders would force management to choose the path of conciliation out of self-interest to protect their equity, or that a righteous shareholder rebellion would be provoked by outrage over corporate behaviour. After all, most shareholders are apathetic and unengaged in corporate governance. Rather, management would know that if they did not act appropriately, dissident shareholders or hostile suitors could use their failure to act opportunistically for their own purposes, using the argument that they were destroying shareholder value and should be replaced. Also, large shareholders (such as pension funds) are interested in stability and yield and are likely to avoid investing in companies that fail to take opportunities to reduce their risk exposure.

The lessons from the Be case are unpleasant but clear: if corporations are expected to reverse course, there must be room for them to turn around. Pressure builds resistance and ultimately denial and may be counterproductive at times. Perception and judgment align with interests, and people on different sides of an issue see the problem differently. Correcting the system to facilitate resolution may require trade-offs with unpleasant implications. The opening of opportunities for bad corporations to escape legal or financial consequences is not an attractive solution from the moral perspective but may lead to the greatest good for the greatest number.

Another lesson from the Be case is that once a standard is set, it becomes 'sticky'. It develops a constituency and an infrastructure to support it. Changing a standard has to overcome inertia and the accumulated weight of experience and acceptance. A policy of sequential standard-setting based on scientific evidence is inherently flawed. There will always be new scientific information. It is more reasonable to expect that standards will become more stringent and to accept a realistic policy of continuous improvement, anticipating that standards evolve rather than pretending that each standard is definitive. Standards can be as much impediments as instruments of worker protection. A policy of continuing improvement and progression over time in reducing exposures is the natural alternative approach, although perhaps unattainable in the current political context. The problems with such a policy lie in initiating it and sustaining it in an equitable manner.

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7 Tobacco industry manipulation of research

Lisa A. Bero ([1])

This chapter differs in some ways from the others in Volume 2 of *Late lessons from early warnings*. The history of 'second hand', 'passive' or 'environmental tobacco smoke' (ETS), to which non-smokers are exposed overlaps with the history of active smoking. Those affected include the partners and children of smokers, and the bartenders and other workers who have to work in smoky environments.

The focus in this chapter is on the strategies used by the tobacco industry to deny, downplay, distort and dismiss the growing evidence that, like active smoking, ETS causes lung cancer and other effects in non-smokers. It does not address the history of scientific knowledge about tobacco and how it was used or not used to reduce lung cancer and other harmful effects of tobacco smoke. There is much literature on this ([2]) and a table at the end of the chapter summarises the main dates in the evolution of knowledge in this area.

The chapter concentrates on the 'argumentation' that was used to accept, or reject, the growing scientific evidence of harm. Who generated and financed the science used to refute data on adverse health effects? What were the motivations? What kind of science and information, tools and assumptions were used to refute data on the adverse health of tobacco?

The release of millions of internal tobacco industry documents due to law suits in the US has given insights into the inner workings of the tobacco industry and revealed their previously hidden involvement in manipulating research. However, this insight is not available for most corporate sectors. The chapter discusses the possibilities of 'full disclosure' of funding sources and special interests in research and risk assessment in order to secure independence and prevent bias towards particular viewpoints.

While smoking bans are now being introduced in more and more countries, other industries are drawing inspiration from tobacco company strategies, seeking to maintain doubt about harm in order to keep hazardous products in the marketplace.

The chapter also includes a summary of the tobacco industry's role in shaping risk assessment in the US and Europe to serve its own interests.

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([2]) For example, two contrasting yet complementary histories of cancer in general and smoking in particular are Davies (2007) and Keating (2009).

7.1 Introduction

This chapter describes the strategies that the tobacco industry has used to influence the design, conduct and publication of scientific research on second-hand smoke; and how the tobacco industry used this research in attempts to influence policy. It represents an expansion of an earlier article, 'Tobacco industry manipulation of research' by Bero (2005).

The primary motivation of the tobacco industry has been to generate controversy about the health risks of its products. The industry has used several strategies including:

1. funding and publishing research that supports its position;

2. suppressing and criticising research that does not support its position;

3. changing the standards for scientific research;

4. disseminating interest group data or interpretation of risks via the lay (non-academic) press and directly to policymakers.

The strategies used by the tobacco industry have remained remarkably constant since the early 1950s when the industry focused on refuting data on the harmful effects of active smoking, through to the 1990s, when the industry was more concerned with refuting data on the harmful effects of second-hand smoke. Tobacco industry lawyers and executives, rather than scientists, have controlled the design, conduct and dissemination of this research.

When data on risk appear to be controversial, users of the data should investigate the sources of controversy. This can be done only if interest group involvement in all steps of the risk determination process is transparent and fully disclosed. Since the tobacco industry's efforts to manipulate research are international endeavours and are shared by other corporate interests, individuals around the world should be aware of the strategies that the industry has used to influence data on risk.

Communicating accurate information on risk is essential to risk perception and risk management. Research findings, often from basic science, epidemiology and exposure or engineering research, provide the basis for information on risk. These research findings or 'facts' are, however, subject to interpretation and the social construction of the evidence (Krimsky, 1992). Research evidence has a context. The roles of framing, problem definition and choice of language influence risk communication (Nelkin, 1985). Furthermore, scientific uncertainties allow for a wide range of interpretation of the same data. Since data do not 'speak for themselves' interest groups can play a critical role in generating and communicating the research evidence on risk.

An interest group is an organised group with a specific viewpoint that protects its position (Lowi, 1979). Interest groups are not exclusively business organisations; they can comprise all kinds of organisations that may attempt to influence governments (Walker, 1991; Truman, 1993). Therefore, interest groups can be expected to select and interpret the evidence about a health risk to support their predefined policy position (Jasanoff, 1996). For example, public health interest groups are likely to communicate risks in a way that emphasises harm and, therefore, encourages regulation or mitigation of risk (Wallack et al., 1993). Industry interest groups are likely to communicate risks in a way that minimises harm and reduces the chance that their product is regulated or restricted in any way. Disputes about whether a risk should be regulated or not are sometimes taken to the legal system for resolution (Jasanoff, 1995). Thus, interest groups often have two major goals: to influence policy-making and litigation.

Beginning in the 1970s, the tobacco industry influenced the collection, interpretation and dissemination of data on risks of exposure to second-hand smoke. The analysis below suggests that this was history repeating itself; in the 1950s, the tobacco industry had used similar strategies to manipulate information on the risks of smoking. Moreover, other corporate interest groups appear to use similar tactics (Special Issue, 2005; White et al., 2009).

Many of the strategies available to interest groups — for example sponsoring, publishing and criticising research — are costly. Industry might therefore be expected to dominate examples of such activities because corporate interest groups are more likely to have the resources to launch expensive, coordinated efforts. In contrast, public health groups, which tend to act independently, are less likely to command such resources (Montini and Bero, 2001).

Industry examples may also predominate because some interest group activities have come to light through the documents released during the 'discovery' process in law suits. For example, the asbestos and tobacco industries were required to release large amounts of internal correspondence

when they were sued by groups attempting to show that they were harmed by industry products.

7.2 Scientific community knowledge about the hazards of second-hand smoke exposure

Environmental tobacco smoke, or second-hand smoke, is a complex mixture of thousands of gases and fine particles emitted by burning tobacco products and from smoke exhaled by smokers, as well as smoke that escapes while the smoker inhales and some vapour-phase related compounds that diffuse from tobacco products. During the 1970s and 1980s, data on the harmful effects of exposure to second-hand smoke began to be published in the scientific literature. Seminal epidemiological studies in 1981 demonstrated that second-hand smoke exposure was associated with lung cancer (Hirayama, 1981). United States Surgeon General and National Academy of Sciences reports in 1986 concluded that second-hand smoke was a cause of disease (US DHHS, 1986; NRC, 1986).

A landmark European epidemiological study on lung cancer and second-hand smoke was initiated by the International Agency for Research on Cancer (IARC) in 1988 and published in 1998. The publication reported a 16 % increase in lung cancer risk for non-smoking spouses of smokers and a 17 % increase for non-smokers who were exposed in the workplace (IARC, 1998).

In 1992, the US Environmental Protection Agency (EPA) released a risk assessment classifying ETS as a Group A human carcinogen (US EPA, 1992). The tobacco industry criticised the methodology of the US EPA risk assessment for its study selection and statistical analysis. The industry also criticised the epidemiological design of the studies included in the risk assessment, the ways that these studies controlled for bias and confounding, and measured ETS exposure (Bero and Glantz, 1993). The EPA revised the report in response to valid criticisms and the report was approved by the Scientific Advisory Board. The report was improved but the sheer volume of tobacco industry comments that required consideration probably delayed its release. Although the science was valid, the tobacco industry successfully attacked the US EPA risk assessment in court on procedural grounds (Flue-Cured Tobacco Co-op vs. US EPA, 1998) and the tobacco industry had similar procedural objections to the report of Australia's National Health and Medical Research Council, 'The health effects of passive smoking' (NHMRC, 1997).

In 1997 the California EPA published the final report of a risk assessment entitled 'Health Effects of Exposure to Environmental Tobacco Smoke' (Cal-EPA, 1997). The California risk assessment was more comprehensive than the US EPA's assessment because it examined the association of second-hand smoke exposure, lung cancer and respiratory illness, as well as cardiovascular, developmental, reproductive and childhood respiratory effects. The California EPA risk assessment also addressed criticisms brought by the tobacco industry against the US EPA risk assessment. The California risk assessment was the result of a collaborative effort between the Office of Environmental Health Hazard Assessment (OEHHA) and the Air Resources Board (ARB), two of the six constituent organisations of the California EPA. The Scientific Review Panel that endorsed the report concluded that second-hand smoke is 'a toxic air contaminant' that 'has a major impact on public health' (Cal-EPA, 1997).

In June 2005 the California Scientific Review Panel approved an updated draft report on Identification of Environmental Tobacco Smoke as a Toxic Air Contaminant (Cal-EPA, 2005). The report concluded that second-hand smoke exposure is causally associated with developmental effects (e.g. inhibited foetal growth, sudden infant death syndrome, pre-term delivery), respiratory effects (e.g. asthma, acute and chronic respiratory symptoms in children, middle ear infections in children), carcinogenic effects (e.g. lung cancer, nasal sinus cancer, breast cancer in younger, premenopausal women) and cardiovascular effects (e.g. heart disease mortality, acute and chronic heart disease, morbidity).

The growing evidence documenting the adverse health effects of second-hand smoke was clearly a threat to the tobacco industry as early as the 1970s. Restrictions on smoking could lead to reduced daily consumption of cigarettes and a decline in sales. The tobacco industry responded with its own science to the independently generated data on tobacco-related adverse health effects.

7.3 Tobacco industry strategies to subvert scientific knowledge

Policymaking is facilitated by consensus (Kingdon, 1984; Mazmanian and Sabatier, 1989; Sabatier, 1991). Scientific research, on the other hand, is characterised by uncertainty. The uncertainty that is familiar to scientists poses problems when decision-making occurs in a public forum. Thus, it is often to the benefit of corporate interest groups to generate controversy about evidence of a product's

health risks because such controversy is likely to slow or prevent regulation of that product. Similarly, scientific debate over the data and methods used in risk assessment, for example, can hinder the development of the risk assessment (Stayner, 1999).

The release of previously secret internal tobacco industry documents as a result of the Master Settlement Agreement in 1998 has given the public health community insights into the tobacco industry's motives, strategies, tactics and data (Bero, 2003). These documents show that for decades the industry has been motivated to generate controversy about the health risks of its products. They have also revealed that the industry was concerned about maintaining its credibility as it manipulated research on tobacco (Bero, 2003).

The strategies used by the tobacco industry have remained remarkably constant since the early 1950s. During the 1950s and 1960s, the tobacco industry focused on refuting data on the adverse effects of active smoking. The industry applied the same tools it developed during that period when it subsequently refuted data on the adverse effects of second-hand smoke exposure during the 1970s through the 1990s.

A 1978 report prepared by the Roper Organization for The Tobacco Institute noted that the industry's best strategy for countering public concern about passive smoking was to fund and disseminate scientific research that countered research produced by other sources:

> 'The strategic and long-run antidote to the passive smoking issue is, as we see it, developing and widely publicizing clear-cut, credible, medical evidence that passive smoking is not harmful to the non-smoker's health' (Roper Organization, 1978).

Philip Morris promoted international research related to passive smoking in order to stimulate controversy, as described in the notes of a meeting of the UK [Tobacco] Industry on Environmental Tobacco Smoke, London, 17 February 1988:

> 'In every major international area (USA, Europe, Australia, Far East, South America, Central America and Spain) we are proposing, in key countries, to set up a team of scientists organized by one national coordinating scientist and American lawyers, to review scientific literature or carry out work on ETS **to keep the controversy alive**' (emphasis added) (Boyse, 1988).

The tobacco industry organised teams of scientific consultants all over the world with the main goal of stimulating controversy about the adverse health effects of second-hand smoke (Barnoya and Glantz, 2006; Chapman, 1997; Muggli et al., 2001; Grüning et al., 2006; Assunta et al., 2004).

A variety of studies show that industry sponsorship of research is associated with outcomes that are favourable for the industry (Lexchin et al., 2003; Barnes and Bero, 1998; Barnes and Bero, 1997). One possible explanation for this bias in outcome is that industry-sponsored research is poorly designed or of worse 'methodological quality' than non-industry-sponsored research. However, there is no consistent association between industry sponsorship and methodological quality (Lexchin et al., 2003).

Factors other than study design can affect the outcome of research, including:

- the framing or social construction of the research question;
- the conduct of the study;
- the publication (or not) of the study findings.

The tobacco industry has manipulated these other factors in a variety of ways. First, by using its funding mechanisms to attempt to control the research agenda and types of questions asked about tobacco. Second, the industry's lawyers and executives have been involved in the design and conduct of industry-supported research. Third, the tobacco industry has sponsored publications of its own funded research, and suppressed research not favourable to the industry.

Box 7.1 summarises the range of strategies that the tobacco industry has used for decades to manipulate information on the risks of tobacco. These strategies are described in more detail in the remainder of this section.

7.3.1 Strategy 1: fund research that supports the interest group's position

The first element in the tobacco industry's strategy to influence data on risk has been to sponsor research designed to produce findings that are favourable to the industry.

Funding research can stimulate controversy in multiple ways. First, it can put the research agenda

Box 7.1 Tobacco industry strategies to manipulate data on risk

1. Fund research that supports the interest group position.
2. Hide industry involvement in research.
3. Publish research that supports the interest group position.
4. Suppress research that does not support the interest group position.
5. Criticise research that does not support the interest group position.
6. Change scientific standards.
7. Disseminate interest group data or interpretation of risk in the lay press.
8. Disseminate interest group data or interpretation of risk directly to policymakers.

in the control of the interest group. Second, it can produce data to refute research on risk conducted by others. In addition to stimulating controversy, funding research serves other useful purposes for the tobacco industry. The research can be disseminated directly to policymakers and the lay press. It can provide good public relations for the tobacco industry by establishing it as a philanthropic body that funds scientific research. Similarly, funding research can increase the industry's credibility. One of the criteria that the Philip Morris Worldwide Scientific Affairs Programme considered when deciding whether to fund a research application was whether the research would enhance the credibility of the company (Malone and Bero, 2003).

The US tobacco industry funded research through its trade association, The Tobacco Institute (Bero et al., 1995; Hanauer et al., 1995), internally (e.g. internal company research), externally (e.g. by supporting the research of scientific consultants) and through sponsored research organisations. Tobacco industry lawyers and executives were involved in selecting which research to fund. Most of the research did not undergo any form of independent scientific peer review but was funded on the basis of its potential to protect the interests of the companies.

Lawyer involvement in research

In the mid-1990s, internal tobacco industry documents were circulated by industry whistle-blowers. By 1998, the availability of tobacco industry documents increased exponentially as a result of the settlement of a suit by the State of Minnesota and Blue Cross/Blue Shield against the major tobacco companies. The Master Settlement Agreement between the attorneys general of 46 states and Brown & Williamson/British American Tobacco, Lorillard, Philip Morris, RJ Reynolds, the Council for Tobacco Research and The Tobacco Institute released millions of additional documents to the public. These documents provide an unprecedented look at how tobacco industry lawyers were involved in the design, conduct and dissemination of tobacco industry-sponsored research (Bero, 2003). By involving lawyers in research, the tobacco industry protected their research activities from public discovery and kept their lawyers informed about science relevant to litigation.

The internal tobacco industry documents include descriptions of research that was funded directly by law firms. For example, the law firms of Covington and Burling, and Jacob and Medinger, both of which represent a number of tobacco company clients, funded research on tobacco (Bero et al., 1995). Lawyers selected which projects would be funded. The supported projects included reviews of the scientific literature on topics ranging from addiction to lung retention of particulate matter. The law firms also funded research on factors potential confounding the adverse health effects associated with smoking. For example, projects examined genetic factors associated with lung disease or the influence of stress and low-protein diets on health (Bero et al., 1995). Thus, some of the research funded by law firms served the purpose of deflecting attention away from tobacco as a health hazard and protecting the tobacco companies from litigation.

Other research was funded directly by the tobacco companies but lawyers were involved in selecting and disseminating these projects. For example, tobacco companies funded individuals to serve as consultants to prepare expert testimony for Congressional hearings, attend scientific meetings, review scientific literature or conduct research on the health effects of tobacco or second-hand smoke (Hanauer et al., 1995). At one tobacco company, Brown & Williamson, the legal department controlled the dissemination of internal scientific reports (Hanauer et al., 1995). The lawyers at Brown & Williamson developed methods for screening

scientific reports from their affiliated companies in order to ensure that scientific information related to tobacco and health would be protected from discovery by legal privileges. In a memo dated 17 February 1986, J. K. Wells, the Brown & Williamson corporate counsel, outlined one method for protecting industry produced research data:

> 'The only way BAT [British American Tobacco] can avoid having information useful to plaintiff found at B&W is to obtain good legal counsel and cease producing information in Canada, Germany, Brazil and other places that is helpful to plaintiffs' (Wells and Pepples, 1986).

Although tobacco industry public statements claimed that the tobacco companies were funding objective research to gather facts about the health effects of smoking, lawyer involvement in the research served to control the scientific debate on issues related to smoking and health and protect from discovery scientific documents that were potentially damaging to the industry.

Research organisations

The tobacco industry also formed research funding organisations, which gave the appearance that the research they supported was independent of influence from the industry.

The **Council for Tobacco Research** (CTR) was formed by United States tobacco companies in 1954 as the Tobacco Industry Research Committee (TIRC). The industry stated publicly that it was forming the TIRC to fund independent scientific research to determine whether there was a link between smoking and lung cancer. However, internal documents from Brown & Williamson Tobacco Company have shown that the TIRC was actually formed for public relations purposes, to convince the public that the hazards of smoking had not been proven (Glantz et al., 1996).

Research that is sponsored by federal organisations or large foundations is typically peer reviewed by other researchers before funding is approved. Although the Council for Tobacco Research had a Scientific Advisory Board consisting of well respected researchers, not all of the research funded by the CTR was peer reviewed by this board. Beginning in 1966, tobacco industry lawyers became directly responsible for many of the funding decisions of the CTR. Between 1972 and 1991, the CTR awarded at least USD 14 636 918 in special project funding (Bero et al., 1995). Lawyers were not only involved in selecting projects for funding but also in designing the research and disseminating the results (Bero et al., 1995).

The research funded by CTR, although initially useful for public relations, became increasingly important for the tobacco industry's activities in legislative and legal settings. This evolution is described in a memo dated 4 April 1978 from Ernest Pepples, Brown & Williamson's vice president and general counsel, to J. E. Edens, chairman and CEO of Brown & Williamson Tobacco Company:

> 'Originally, CTR was organized as a public relations effort. … The research of CTR also discharged a legal responsibility. … There is another political need for research. Recently it has been suggested that CTR or industry research should enable us to give quick responses to new developments in the propaganda of the avid anti-smoking groups. … Finally, the industry research effort has included special projects designed to find scientists and medical doctors who might serve as industry witnesses in lawsuits or in a legislative forum' (Pepples, 1978).

The Pepples memo gives insight into why lawyers became increasingly involved in the selection of research projects for CTR.

The **Center for Indoor Air Research** (CIAR) was formed by Philip Morris, R. J. Reynolds Tobacco Company and Lorillard Corporation in 1988 (CIAR, 1988). The founding companies were joined by Svenska Tobaks A.B., a Swedish domestic tobacco company in 1994 (CIAR, 1994). The stated mission of CIAR was 'to create a focal point organisation of the highest caliber to sponsor and foster quality, objective research in indoor air issues **including environmental tobacco smoke**, and to effectively communicate research findings to a broad scientific community' (CIAR, 1989). CIAR's mission statement was modified in 1992 to eliminate the words referrring to environmental tobacco smoke (CIAR, 1992a; CIAR, 1992b). The elimination of research on second-hand smoke from the mission statement was followed by a shift in the research agenda of CIAR to one that would prevent it investigating the health effects of second-hand smoke.

Similar to the CTR, CIAR awarded 'peer-reviewed' projects, which were reviewed by a Science Advisory Board, and 'special-reviewed' projects, which reviewed by its Board of Directors consisting of tobacco company executives (Barnes and Bero, 1996). From 1989 to 1993, CIAR awarded USD 11 209 388 for peer-reviewed projects and USD 4 022 723 for

special-reviewed projects (Barnes and Bero, 1996). Seventy per cent of the peer-reviewed projects funded by CIAR examined indoor air pollutants other than tobacco smoke. Thus, the industry appeared to be financing peer-reviewed projects through CIAR to enhance its credibility, to provide good publicity and to divert attention away from second-hand smoke as an indoor air pollutant.

In contrast to the peer-reviewed projects, almost two-thirds of CIAR's special-reviewed projects were related to second-hand smoke (Barnes and Bero, 1996). In addition, most special-reviewed projects studied exposure rather than health effects. It is therefore possible that the tobacco industry was funding research through CIAR to develop data it could use to support its frequent claim that persons are not exposed to sufficient levels of passive smoke to cause any serious adverse health effects (Tobacco Institute, 1986).

The tobacco industry may have also been funding special-reviewed research through CIAR to develop scientific data that it could use in legislative and legal settings. Six CIAR-funded investigators have testified at government hearings. All of the statements submitted by them supported the tobacco industry position that second-hand smoke exposure is not harmful to health. Data from two of CIAR's special-reviewed projects were presented at hearings held by the United States Occupational Safety and Health Administration (OSHA) regarding its proposed indoor air quality regulation. Data from a third special-reviewed project was presented at a Congressional hearing related to a proposed ban on smoking on commercial aircrafts. One CIAR-funded study was investigated extensively by the United States Congressional Subcommittee on Health and the Environment after it was cited in testimony before numerous government agencies. The CIAR-funded study had concluded that, with good building ventilation, clean air could be maintained with moderate amounts of smoking (Turner et al., 1992) and was used to support testimony that indoor smoking restrictions are not necessary. However, the Congressional Subcommittee found that data for this study had been altered and fabricated. An earlier CIAR-funded study by the same organisation was also severely compromised because The Tobacco Institute selected the sites where passive smoking levels were measured for the study (Barnes and Bero, 1996).

The Center for Indoor Air Research was disbanded as part of the US Master Settlement Agreement in 1998. However, in 2000, Philip Morris re-created an external research programme called the 'Philip Morris External Research Program' (PMERP) with a structure similar to that of CIAR. Like CIAR, PMERP's grant review panel consisted of a cohort of external peer reviewers, a science advisory board, and an internal, anonymous review and approval committee. Three of the six advisory board members had a previous affiliation with CIAR. The majority of the named reviewers also had previous affiliations with the tobacco industry (Hirschhorn et al., 2001).

Research is an international endeavour

The tobacco industry applied the strategy of covertly funding research on an international scale. In Latin America and Asia, tobacco companies, working through the law firm Covington and Burling, developed a network of physician and scientist consultants to prepare and present data to refute claims about the harms of second-hand smoke (Assunta et al., 2004; Barnoya and Glantz, 2002). In Germany, tobacco companies and the German Association of the Cigarette Industry developed a similar team of consultants and funded research through various foundations and research organisations (Grüning et al., 2006). In many cases, the industry employed the next strategy discussed below: hiding its support for the research.

In summary, funding research serves multiple purposes for the tobacco industry. The research that is directly related to tobacco has been used to refute scientific findings suggesting that the product is harmful and sustain controversy about adverse effects. Tobacco industry-supported research has been used to prepare the industry for litigation or legislative challenges. The industry may also have funded research not directly related to tobacco in order to generate good publicity, enhance industry credibility and to distract from tobacco products as a health problem.

7.3.2 Strategy 2: hide industry involvement in research

A defining characteristic of the tobacco industry's response to independent evidence of the harms of second-hand smoke has been attempts to hide its involvement in refuting this evidence. In both of the cases described below, tobacco companies were secretly involved in generating data to suggest that second-hand smoke was not harmful and suppressing data suggesting that it was.

Philip Morris European research programme on second-hand smoke

As early as 1968, executives at Philip Morris began planning a new biological research facility that

would focus on examining the effects, including carcinogenic effects, of second-hand smoke exposure in various animal species. In 1970, Philip Morris purchased a research facility in Germany, Institut für Industrielle und Biologische Forschung GmbH (INBIFO) (Diethhelm et al., 2004). Philip Morris hired Ragnar Rylander, a Swedish university professor, as the coordinator of INBIFO. Rylander communicated INBIFO's research findings to Philip Morris executives in the United States, who would then decide whether to disseminate the research more widely or keep it secret. Research that remained unpublished included studies providing evidence that 'sidestream smoke' (which enters the air from a burning cigarette, cigar or pipe) is more toxic than 'mainstream smoke' (which is inhaled directly) (Diethhelm et al., 2004). Published research included an epidemiological study suggesting an association between lung cancer and green tea, a finding that would be useful to the tobacco industry in distracting from the harms of second-hand smoke (Tewes et al., 1990).

One of the most striking features of the INBIFO programme was that its coordinator, Ragnar Rylander, had long-standing and secret links to the tobacco industry. Thus, he conferred a false sense of credibility to the programme. Professor Rylander's association with the tobacco industry was investigated by an official university committee, the Fact Finding Commission of the University of Geneva. The committee concluded that Rylander was acting as a sponsored agent of the tobacco industry, rather than as an independent researcher when he testified as a scientific expert, organised scientific congresses and directed research at INBIFO (Fact Finding Commission, 2004). An extensive analysis of internal tobacco industry documents found that Rylander took no initiatives 'in the area of [second-hand smoke research] without first consulting extensively with his contacts within the tobacco industry'(Fact Finding Commission, 2004).

Tobacco industry creation and dissemination of a study on second-hand smoke

The tobacco industry's development of the Japanese Spousal Smoking Study provides another example of industry involvement in designing, conducting and disseminating research, and its efforts to hide this involvement.

In 1981, Takeshi Hirayama published an influential study showing an association of second-hand smoke exposure and lung cancer (Hirayama, 1981). The Hirayama study has been voted the most influential paper ever on second-hand smoke (Chapman, 2005) and was the most frequently cited study in regulatory hearings on smoking restrictions (Montini et al., 2002). In these hearings, tobacco industry representatives have argued that the Hirayama study is flawed due to misclassification bias (Bero and Glantz, 1993; Schotland and Bero, 2002). Furthermore, analysis of internal tobacco industry documents by Hong and Bero (2002) has shown how the tobacco industry hid its involvement in creating a study, the Japanese Spousal Smoking Study, to support its arguments about misclassification bias.

The tobacco industry documents reveal that although the Japanese Spousal Smoking Study was undertaken by named Japanese investigators, project management was conducted by Covington and Burling (a tobacco industry law firm), the research was supervised by a tobacco industry scientist and a tobacco industry consultant assisted in reviewing the study design and interpreting the data (Hong and Bero, 2002). The documents show that the tobacco companies that funded the study did not want any of these individuals named as co-authors on any of the resulting scientific publications. Although the tobacco companies considered using the Center for Indoor Air Research (CIAR) as 'a cover' to fund the study, three companies agreed to fund the study directly. Progress reports for the study were prepared on Covington and Burling stationery. When the study was prepared for publication, the tobacco industry consultant was the sole author (Lee, 1995). The publication acknowledged 'financial support from several companies of the tobacco industry' (Lee, 1995). This acknowledgement tells the reader little about who was actually involved in the design, conduct and publication of the study. The hidden roles of the tobacco company lawyers and scientist raise questions about who was accountable for the research (Hong and Bero, 2002).

The analysis of tobacco industry documents (Hong and Bero, 2002) was noticed by Dr E. Yano, one of the Japanese investigators who was originally involved in the Japanese Spousal Smoking study. Dr Yano had been unaware that Dr Lee had published the study. He had retained the original data from the study and has reported that Dr Lee's published analysis excluded data that did not support misclassification bias (Yano, 2005). Dr Yano demonstrated that using the full data from the Japanese Spousal Smoking Study changes the conclusion of Lee's published report. After 10 years, the scientific community was able to obtain data that had been suppressed by the tobacco industry.

7.3.3 *Strategy 3: publish research that supports the interest group position*

Research has little impact unless it can be cited. The tobacco industry has realised that funding research that supports its interests must be followed by the dissemination of such research in scientific literature. The tobacco industry uses several vehicles to publish the findings of its sponsored research, including funding the publication of symposia proceedings, books, journal articles and letters to the editors of medical journals. To suggest that the research it funds meets scientific standards and that there is substantial support for its position, the tobacco industry then cites its industry-funded, non-peer-reviewed publications in scientific and policy arenas.

Symposium proceedings

Scientific meetings or symposia often result in the publication of books or journal articles that summarise the research presented there. The pharmaceutical industry, for example, publishes reports of symposia containing poor quality and unbalanced articles favourable to particular drugs (Bero et al., 1992; Rochon, 1994). The tobacco industry has sponsored numerous symposia on second-hand smoke (Bero et al., 1994) and paid for scientific consultants to organise and attend these meetings (Barnoya and Glantz, 2002, 2006; Muggli et al., 2001).

Between 1965 and 1993, reports on 11 symposia on passive smoking were published. Six were published as special issues of medical journals, while five were published independently as books. None of the symposia was peer reviewed; six were sponsored by the tobacco industry or its affiliates such as the Center for Indoor Air Research, The Tobacco Institute and Fabriques de Tabac Reunies. Two of the six industry-sponsored symposia did not explicitly acknowledge industry sponsorship. The tobacco industry sometimes sponsored conferences through independent organisations so that their sponsorship would be hidden (Bero et al., 1995; Bero et al., 1994).

The symposia on passive smoking were attended by an international group of scientists and held across the world, including Europe, the United States, Canada, Japan and Argentina. One symposium report was published in Spanish. CTR special projects were often used to support scientists to prepare talks for conferences and to send scientists to conferences (Glantz et al., 1996).

On the surface, articles from symposia look like articles from peer-reviewed journals. To test the hypothesis that symposium articles on second-hand smoke differ in content from articles on second-hand smoke appearing in scientific journals, Bero et al. (1994) compared the symposia articles to a random sample of articles on passive smoking from the scientific literature and to two consensus reports on the health effects of passive smoking (US DHHS, 1986; NRC, 1986). Of the symposium articles, 41 % (122/297) were reviews, compared with 10 % (10/100) of journal articles. Symposia articles were significantly more likely than journal articles to agree with the tobacco industry position that tobacco is not harmful (46 % compared to 20 %), less likely to assess the health effects of passive smoking (22 % compared to 49 %), less likely to disclose their source of funding (22 % compared to 60 %), and more likely to be written by tobacco industry-affiliated authors (35 % compared to 6 %). Symposium authors published a lower proportion of peer-reviewed articles than consensus report authors (71 % compared to 81 %) and were more likely to be affiliated with the tobacco industry (50 % compared to 0 %) (Bero et al., 1994).

Symposia proceedings can potentially influence policy because they are often cited as if they are peer-reviewed articles and balanced reviews of the scientific literature, with no disclosure of their industry sponsorship. For example, tobacco industry-sponsored symposia on second-hand smoke have been used to attempt to refute both peer-reviewed journal articles and risk assessments of second-hand smoke (Bero and Glantz, 1993; Schotland and Bero, 2002; Chapman et al., 1990). Symposia articles have also been cited in tobacco industry public relations materials and the press (e.g. Tobacco Institute, 1986); and as the consensus of a gathering 'of leading experts from around the world' who disagree with the published literature on passive smoking (Johnston and Sullum, 1994).

In summary, tobacco industry-sponsored symposia articles on second-hand smoke consist, in large part, of review articles that reach different conclusions about the health effects of passive smoking than peer-reviewed journal articles or consensus reports. Furthermore, symposia are more likely to publish research that discusses issues that distract from tobacco as a health problem. The tobacco industry affiliations of symposia authors suggest that industry control over publication and research funding is likely to influence the presentation of findings.

Quality of tobacco industry-funded symposium publications

When policymakers, judges, lawyers, journalists and scientists are presented with tobacco industry-sponsored symposium articles, they must decide whether to incorporate these publications into

their deliberations. Although the lack of balance and peer review suggests that tobacco industry-sponsored literature may lack scientific rigour, the issue of peer review and study quality is a contentious subject. Methodological quality is determined by the presence or absence of study design characteristics aimed at reducing bias, such as blinding, follow-up, controlling for confounding and controlling for selection bias.

Barnes and Bero (1997) assessed the methodological quality of the research presented at symposia. As articles from pharmaceutical industry sponsored symposia have been found to be of poor methodological quality (Rochon, 1994; Cho and Bero, 1996) it was hypothesised that articles from tobacco industry-sponsored symposia would be poorer in methodological quality than peer-reviewed journal articles. Other characteristics of articles were evaluated that might be associated with quality, such as disclosure of the source of research sponsorship and the study's conclusions, topics and design. Original research articles on the health effects of second-hand smoke published in peer-reviewed journals were compared to those published in non-peer-reviewed symposium proceedings from 1980 to 1994.

The study found that peer-reviewed articles were better quality than symposium articles independent of their source of funding, their conclusions on the health effects of second-hand smoke and the type of study design. Peer-reviewed articles received higher scores than symposium articles for most of the criteria evaluated by the quality assessment instrument.

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Quality of tobacco industry-sponsored review articles

Policymakers and clinicians often rely on review articles to provide accurate and up-to-date overviews of a topic of interest (Montini and Bero, 2001). As already noted, a large proportion of symposium articles are reviews of the health effects of second-hand smoke (Bero et al., 1994) and are frequently cited in response to government requests for information (Bero and Glatz, 1993; Montini et al., 2002; Schotland and Bero, 2002). In view of their importance in guiding policy, it is somewhat disconcerting that published review articles often reach markedly different conclusions about the adverse health effects of second-hand smoke.

Barnes and Bero (1998) conducted a study to evaluate the quality of review articles on the health effects of passive smoking and to determine whether the conclusions of review articles are primarily associated with their quality or with other article characteristics. The a priori hypotheses were that review articles concluding that passive smoking is not harmful would tend to be poor in quality, published in non-peer-reviewed symposium proceedings and written by investigators with tobacco industry affiliations. The topic of the review and the year of publication were also reviewed as potential confounding factors.

In the sample of 106 review articles, the only factor associated with concluding that passive smoking is not harmful was whether the author of the review article was affiliated with the tobacco industry (Barnes and Bero, 1998). As shown in Table 7.1, review articles concluding that passive smoking is not harmful were about 90 times more likely to be funded by the tobacco industry than those concluding that second-hand smoke is harmful. Methodological quality, peer-review status, outcomes studied in the reviews, and year of publication were not associated with the conclusions of the articles. Thus, sponsorship of review articles by the tobacco industry appears to influence the conclusions of these articles, independent of methodological quality.

The tobacco industry has argued that independent reviews of second-hand smoke are flawed because studies with statistically significant results are more likely to be published than studies with statistically non-significant results (Dickersin et al., 1992; Shook, Hardy and Bacon, 1993). The industry argues that publication bias — the tendency to publish work with statistically significant results — prevents the identification of all relevant studies for reviews of the health effects of second-hand smoke (e.g. Armitage, 1993). Bero et al. (2004) conducted a preliminary

Table 7.1 Factors associated with review articles concluding that passive smoking is not harmful to health: multiple logistic regression analysis

Factor	Odds ratio (95 % CI)	P value
Quality score	1.5 (< 0.1–67.5)	0.83
Not peer reviewed v. peer reviewed	1.3 (0.3–5.4)	0.70
Tobacco industry sponsored v. not tobacco industry sponsored	88.4 (16.4–476.5)	< 0.001
Outcomes — lung cancer v. other clinical outcomes	1.6 (0.2–10.3)	0.63
Heart disease v. other clinical outcomes	1.6 (0.2–14.7)	0.67
Year of publication	1.1 (0.9–1.3)	0.45

Source: Barnes and Bero, 1998.

study of publication bias showing that statistically non-significant studies are published: approximately 20 % of the published peer-reviewed articles on passive smoking present statistically non-significant findings.

By interviewing investigators studying second-hand smoke and health effects, Misakian and Bero (1998) determined that studies with statistically non-significant results take about two years longer to be published than those with statistically significant results. For studies conducted in humans, only statistical significance was predictive of time to publication, not study design or sample size. Thus, the tobacco industry's argument that statistically non-significant results are not published is invalid.

Since statistically non-significant results are published but take longer to be published than statistically significant results, reviews of research should attempt to include unpublished data and be periodically updated. Reviews conducted by the Cochrane Collaboration, for example, attempt to identify unpublished studies and include them in reviews if they meet quality standards. Cochrane reviews, which are published online, are also regularly updated (Bero and Rennie, 1995).

7.3.4 Strategy 4: suppress research that does not support the interest group position

Interest groups are eager to fund and publish research that supports their position and hesitant to publicise research that does not. In some cases, tobacco industry lawyers and editors have edited their externally funded scientific research publications; in other cases they have prevented publication of the research (Hong and Bero, 2002; Muggli et al., 2001; Barnoya and Glantz, 2002). Editing has included attempts to obscure evidence on adverse health effects by using the code word 'zephyr' for 'cancer' in internal memos about health effects research (Glantz et al., 1996; BAT, 1956).

Research conducted internally by tobacco companies or through industry-controlled research organisations is likely to be suppressed if it is unfavourable to the industry. For example, the German tobacco industry-supported research organisation, INBIFO, did not publish its research showing that sidestream smoke is more toxic than mainstream smoke (Grüning et al., 2006).

Tobacco companies have also conducted internal research on the use of chemical additives to reduce, mask or otherwise alter the visibility, odour, irritation or emission of second-hand smoke. Some of these studies showed that the additives increased emissions of toxins such as carbon monoxide or the carcinogenic substances, N'-nitrosoniornicotine and benzo(a) pyrene (Conolly et al., 2000). Virtually none of this research has been published in scientific literature, however, and data on additives is not typically available to public health policymakers.

7.3.5 Strategy 5: criticise research that does not support the interest group position

Another strategy that the tobacco industry has used to stimulate controversy about research on risk has been to criticise research that is not favourable to its position. Science is improved by constructive criticism. However, the tobacco industry has misused legitimate means of scientific debate, such as letters to the editor of scientific journals and editorials. The tobacco industry has also used less legitimate methods to criticise research, including attacking the integrity of researchers or obtaining data through lawsuits and reanalysing it using inappropriate techniques (Barnes et al., 1995).

In order to get its views into public commentary on risk assessments (Bero and Glantz, 1993; Schotland and Bero, 2002) or the lay press (Chapman et al., 1990), the tobacco industry has frequently cited letters to the editor as if they were peer-reviewed

journal articles. Letter authors affiliated to the tobacco industry often fail to disclose their affiliation. These findings support the suggestions by a number of journal editors that letter writers should disclose potential conflicts of interest and that journals should peer review letters (Rennie, 1993).

As mentioned above, the tobacco industry has maintained large teams of international scientific consultants (Chapman, 1997; Muggli et al., 2001; Barnoya and Glantz, 2002). A major goal of the tobacco industry's scientific consultancy programme was to refute data about the harmful effects of tobacco. Industry consultants were paid to criticise independent research on tobacco and second-hand smoke via participation in scientific conferences; publications such as conference proceedings, journal articles and books; media appearances; testimony at tobacco litigation trials; forming a scientific society on indoor air; and preparing statements for government committees. The industry consultant programmes were international and were used to discredit research conducted by non-industry scientists around the world (Chapman, 1997; Muggli et al., 2001; Barnoya and Glantz, 2002).

7.3.6 Strategy 6: changing scientific standards

As described above, the tobacco industry has devoted enormous resources to attacking and refuting individual scientific studies. In addition, the industry has attempted to manipulate scientific methods and regulatory procedures for its benefit. The tobacco industry has influenced the debate around 'sound science' (Ong and Glantz, 2001), standards for risk assessment (Hirschhorn and Bialous, 2001), international standards for tobacco and tobacco products (Bialous and Yach, 2001) and laws related to data access and quality (Baba et al., 2005).

The tobacco industry has played a major role in developing ventilation standards for indoor air quality and in establishing international standards for tobacco and tobacco products. The International Organization for Standardization (ISO) develops international standards for tobacco and tobacco products, including the measurement of tar and nicotine yield. The tobacco industry, working through the Cooperation Centre for Scientific Research Relative to Tobacco (CORESTA) gathered scientific evidence for ISO and suggested the standards that were adopted (Bialous and Yach, 2001). These standards incorrectly imply that there are health benefits from low-tar and low-nicotine products (Djordjevic et al., 1995). The tobacco industry has also been involved in developing ventilation standards for over 20 years. The industry influenced the development of ventilation standards by the American Society of Heating, Refrigeration, and Air Conditioning Engineers (ASHRAE) by generating data and presenting it to the committee (Bialous and Glantz, 2002). This resulted in a standard that ignores the health effects of second-hand smoke exposure, concentrating instead on a 'comfort' standard.

In the early 1990s, the tobacco industry launched a public relations campaign about 'sound science' and 'good epidemiological practices' (GEP) and used this rhetoric to criticise government reports, particularly on the harms of environmental tobacco smoke. All scientists agree that research should be rigorously conducted. But the 'sound science' and 'GEP' campaigns were public relations efforts controlled by industry executives and lawyers to promote unreasonably high standards of proof about the harm caused by the industry's products. For example, 'sound science' rhetoric argues that epidemiological studies can never establish evidence of harm because they cannot 'prove' causality. This approach ignores the fact that a comprehensive assessment of risk involves considering all the evidence related to a toxin, not just the epidemiology (Ong and Glantz, 2001).

The tobacco industry also developed a campaign to criticise the technique of risk assessment of low doses of a variety of toxins (Hirschhorn and Bialous, 2001). The tobacco industry worked with the chemical, petroleum, plastics and chlorine industries to develop its criticisms of risk assessment. In fact, the first version of GEP was drafted by the Chemical Manufacturers Association. After about ten years, by the late 1990s, the industry's 'sound science' public relations campaign ended. The tobacco industry then turned to advancing the 'sound science' concept through legislation (Baba et al., 2005).

One major goal of the tobacco industry has been to obtain data from independent studies and reanalyse it using 'sound science' criteria to reach different conclusions. Philip Morris, for example, used a three-step strategy to obtain data:

1. asking the researchers for the data directly;
2. litigation;
3. encouraging the enactment of policies that release data (Baba et al., 2005).

The industry's efforts resulted in 'sound science legislation': laws that influenced access to data and standards for data analysis.

In 1998, the United States Congress enacted a data access law as a rider to the Fiscal Year 1999 Omnibus Appropriations Act (US Congress, 1999). The law, for the first time, made all data produced under federally funded research studies available on request through the Freedom of Information Act (FOIA) (Zacaroli, 1998). Two years after the adoption of the data access provision, another amendment was added to the 2001 Omnibus Appropriations Act. The Data Quality Act (2000) requires the Office of Management and Budget to develop government-wide standards for data quality in the form of guidelines. Individual federal agencies must promulgate their own conforming guidelines based on OMB's model and adopt standards that 'ensure and maximise the quality, objectivity, utility and integrity of information disseminated' by federal agencies (OMB Watch, 2002). The standards to be adopted were created by the industry sponsors, not independent researchers.

While the public had an opportunity to comment on implementing the laws, these amendments were initially passed and adopted without a legislative hearing, committee review or debate (Renner, 2002). The scientific, academic research and public health communities voiced concerns during the public comment period about potential problems with confidentiality of medical information, discouragement of research subjects, misinterpretation of incomplete or prematurely released data sets, delay of research, protection of national security information, and administrative and financial burdens (AAAS, 1999). The research community was also concerned that these measures were supported by industry groups seeking to contest environmental and other regulations (Zacaroli, 1998).

Although the tobacco industry intended to hide its involvement in the data access and quality acts, internal industry documents reveal that these policies were driven by tobacco industry efforts to coordinate corporate interests. Tobacco industry strategies to advance sound science legislation included (Baba et al., 2005):

- demonstrating that the public cares about the issue by sponsoring a poll on issues of data access and rules of epidemiological studies that can be made public;
- leveraging allies and groups that have already taken a stand on the issue;
- using scientists and technical conferences to focus on the issue;
- encouraging a small group of members of Congress to take a stand on the issue;
- encouraging the Administration to take a stand for sound science;
- mobilising allied industries (i.e. fishing, utilities, waterworks) to lobby their local representatives;
- helping to organise coalitions for other epidemiological issues coming up soon (e.g. fishing industry, mercury, methyline chloride);
- educating and mobilising the business community on sound science v. junk science and the federal legislative/regulatory process;
- using states to generate action — conducting briefings in states on epidemiological studies and the need for uniform standards and encouraging the passage of state laws;
- developing broad bipartisan support for 'freedom of information' with regards to the data behind regulations and laws;
- leveraging lobbyists to contact key legislative members;
- briefing the media;
- briefing business coalitions on the need for data access;
- using the Congressional Science Committee to influence Congress.

Together, the data access and data quality acts provide a mechanism for challenging the scientific merit of data outside scientific journals and other channels of scientific review (McGarity, 2004; Kaiser, 1997). As scientists, legal experts and environmentalists have pointed out, however, the data access and data quality riders have the potential to block agencies from using emerging science from non-industry sources and to slow the regulatory process (Kaiser, 2003; Hornstein, 2003; Shapiro, 2004). The laws can be used to prevent future policies and to repeal existing policies that do not meet the data quality standards. The laws could shift the scientific standards of data used for policy purposes to favour standards promulgated by industry. Finally, access to data and quality standards are not applied equitably; they only apply to data generated with government funding, not industry funding.

Panel 7.1 Shaping risk assessment in the US and the EU: the role of the tobacco industry

Katherine Smith, Anna Gilmore and Gary Fooks

The interest of Philip Morris in shaping risk assessment was precipitated by the US EPA risk assessment of environmental tobacco smoke (ETS), which resulted in ETS being categorised as a class A human carcinogen (Hirschhorn and Bialous, 2001). Philip Morris challenged the assessment as part of its broader 'sound science' campaign (Ong and Glantz, 2001). This involved lobbying for laws requiring that:

- epidemiological studies meet a particular set of criteria or standards before they can officially inform policy decisions;
- epidemiological data used in publicly funded studies be made available through freedom of information requests.

Although the tobacco industry's campaign was ultimately unsuccessful in overturning the EPA's classification of ETS, it did manage to place 'a cloud over its validity' until 2002 (Muggli et al., 2004), leading to delays in subsequent introduction of protective legislation. Further, Philip Morris had some success in introducing data access laws and shaping the Data Quality Act (2000) (Baba et al., 2005).

Philip Morris believed that a similar campaign might be even more effective in Europe, where officials had not yet taken up the scientific threat of ETS to the same extent. From the mid-1990s onwards, therefore, it focused its campaign more heavily on Europe. Here, informed by what the Chemical Manufacturers Association had termed 'good epidemiological practice' (GEP), Philip Morris concentrated on lobbying for a mandatory set of criteria or standards that epidemiological studies would have to meet before they could be officially considered by policymakers in Europe (Ong and Glantz, 2001). The Philip Morris standards for 'good epidemiological practice' included a requirement for evidence relating to relative risks of less than 2.0 to be disregarded as too weak to warrant policy intervention.

As of late 2000 Ong and Glantz (2001) concluded that, despite the efforts of Philip Morris, 'no European Union resolution on GEP had been produced'. As far as we are aware, this remains the case.

British American Tobacco (BAT) managers studied the Philip Morris campaigns carefully and from 1995 onwards considered lobbying for a mandatory requirement for 'structured risk assessment' in EU policymaking because they believed it could be used to prevent the introduction of public smoking restrictions (Smith et al., 2010; BAT, 1995 and 1996). By this stage, the industry was well aware of the negative health impacts of second-hand smoke and was simultaneously trying to influence the evidence-base on this issue. BAT managers believed that 'a legislated demand for structured risk assessment', governed by strict 'rules for the assessment of epidemiological and animal data' would 'remove the possibility of introducing public smoking restrictions that are based on risk claims' (BAT, 1995).

Our analysis of BAT's internal documents has not yet established precisely what BAT managers meant when they used the term 'structured risk assessment'. All of the documents with titles indicating that they include detailed information on this issue have been redacted ([3]).

A 1995 BAT document makes it clear that the company's interpretation of 'risk assessment' involved a set of 'rules for the assessment of epidemiologic and animal data', which BAT managers believed would, if applied, make it 'apparent that ETS has not been proven to be a cause of disease in non-smokers' (BAT, 1995).

BAT managers wanted to use risk assessment as a way of limiting officials' discretion. For example, a document discussing the company's efforts to influence risk assessment says: 'The challenge will be to persuade government departments to subordinate policy or judgemental considerations in favour of scientific rigour in risk assessment' (Gretton, undated [circa 1995]).

([3]) See for example BAT (1991 and 1996). The Legacy Tobacco Documents Library website, which hosts these documents, states that the term 'redacted', 'Indicates whether the document contains words or sentences that were erased (redacted) by the tobacco company due to confidentiality issues (i.e. trade secrets, attorney/client privileges) before the document was publicly released' (University of California, 2011).

Panel 7.1 Shaping risk assessment in the US and the EU: the role of the tobacco industry (cont.)

In practice, this constituted a way of undermining the precautionary principle as a basis for policy decisions.

The key innovation of BAT's European campaign was the decision to focus on promoting risk assessment within a framework of 'cost-benefit analysis', a term that BAT used interchangeably with business impact assessment (see Smith et al., 2010). This had the additional effect of embedding economic considerations into the risk assessment process, which would also require interventions to protect the public against particular risks to be justified on the basis of economic costs (BAT, 1996; European Policy Centre, 1997).

BAT initially sought advice on how to shape risk assessment in the EU from the US advisers to Philip Morris, Covington and Burling (Covington and Burling, 1996). They advised BAT that although there was little interest in risk assessment within the European Commission at the time it might be possible to include 'structured risk assessment' in detailed guidance for business impact assessments, which had been flagged as a priority for the European Commission in 1996.

BAT was aware that a campaign for regulatory reform with known links to the tobacco industry was unlikely to succeed (Honour, 1996). It had been advised to work through a 'front group' and to recruit other companies with similar interests, such as other large firms in regulated sectors (MacKenzie-Reid, 1995). Following this advice, BAT approached the European Policy Centre (a prominent Brussels-based think tank with strong links to the Commission) to lobby for regulatory reforms on its behalf (Smith et al., 2010). BAT and the European Policy Centre then jointly set about recruiting other business interests to this campaign (Smith et al., 2010). These companies, which included large corporations from the oil, chemical and pharmaceuticals sectors, established an invitation-only sub-group within the European Policy Centre, known as the Risk Forum (Smith et al., 2010).

These efforts contributed to certain amendments to the Treaty on European Union (EU, 1997), placing a legal duty on the Commission to 'consult widely' and to minimise the potential 'burden' of policy changes on 'economic operators' and others (EU, 1997). BAT interpreted this to mean that business impact assessment and risk assessment were now mandatory within EU policymaking. The company perceived this as 'an important victory' (BAT, undated).

The guidelines for EU officials on how to undertake impact assessment have been revised several times since and now incorporate guidance on undertaking risk assessment (European Commission, 2009).

In 2006–2007, under pressure to open up to civil society organisations and other members of the European Policy Centre (which was under new leadership), the coalition of companies involved in the think tank's Risk Forum left and established a separate organisation called the European Risk Forum. This group describes itself as 'an expert led, not-for-profit think tank' (European Risk Forum, 2008a), despite solely representing corporate interests, virtually all of which are connected to the chemical and tobacco industries. This was confirmed via personal correspondence from the Forum's chair, Dirk Hudig, in February 2010. The European Risk Forum is now actively encouraging the European Commission to adopt a more structured approach to risk assessment and risk management (European Risk Forum, 2008b), although it remains unclear precisely what this involves.

Recent analyses suggest that these corporate efforts have been somewhat successful in redefining policymakers' understandings of and responses to risks, including those that limit use of the precautionary principle in the EU (Löfstedt, 2004) and the United Kingdom (Dodds, 2006). However, as risk assessment continues to be actively debated in Brussels, it is not yet possible to assess the success of the BAT or Philip Morris campaigns.

It is of course legitimate for corporate interests to contribute to discussions on assessing scientific evidence and weighing up risks. However, it is important to ensure that this influence is transparent, is not excessive in comparison to other stakeholders, and does not compromise public welfare.

7.3.7 *Strategy 7: disseminate interest group data or interpretation of risk in the lay press*

While the tobacco industry appears to have recognised the importance of publishing work that supports its position in the scientific literature, the industry also seems aware of the need to get research data directly into the hands of the public and policymakers. How, then, were the public and other stakeholders involved in generating, presenting, understanding, communicating and using science to refute data on the adverse health effects of tobacco?

The important role of the media in communicating risk has been extensively studied (Nelkin, 1985; Raymond, 1985). The tobacco industry has been active in stimulating controversy in lay print media about the health effects of second-hand smoke. In a cross-sectional sample of 180 North American newspaper and 95 magazine articles reporting on second-hand smoke research between 1981 and 1995, Kennedy and Bero (1999) found that 66 % of newspaper articles and 55 % of magazine articles left readers with the impression of continuing controversy about second-hand smoke research. However, the proportion of those articles concluding that the research was controversial remained relatively constant.

Although tobacco industry-sponsored research studies were not widely cited in lay press articles, tobacco industry affiliated individuals were often cited (Kennedy and Bero, 1999; Malone et al., 2001). Among the 180 newspaper articles examined by Kennedy and Bero (1999), 52 % cited tobacco industry officials, whereas 56 % cited government officials and 46 % cited independent scientists. This citation of tobacco industry officials as experts on scientific studies on second-hand smoke could have contributed to the emphasis on controversy.

7.3.8 *Strategy 8: present interest group data or interpretation of risk directly to policymakers*

The last strategy in the tobacco industry's effort to stimulate controversy about data on risk has been to get its funded research directly into the hands of individuals who are likely to influence policy. A series of in-depth case studies have been undertaken, examining the role of research evidence in the development of two risk assessments of second-hand smoke, two state indoor air regulations and two United States federal tobacco regulations (Schotland and Bero, 2002; Roth et al., 2003, Bero et al., 2001; Bryan-Jones and Bero, 2003). Each study addressed the role of the tobacco industry in developing risk assessments and regulations by analysing archival data, including written commentary and hearing transcripts, and interviewing key policymakers.

In the United States, the processes for developing these risk assessments and regulations involves the appropriate government agency reviewing the relevant scientific literature, preparing a draft report, collecting written and oral public commentary, and revising the report based on that public commentary (Jasanoff, 1987 and 1996, Silbergeld, 1993). Public participation in the process is important for shaping the findings of the final risk assessment or regulation, and for public acceptability of the findings (Jasanoff, 1987). Furthermore, public commentary could help prevent the 'capture' of the risk assessment process by interest groups (Wilson, 1989).

Risk assessments of second-hand smoke

As noted earlier in this chapter, the US Environmental Protection Agency (EPA) published a risk assessment of environmental tobacco smoke (ETS) in 1992, which concluded that passive smoking is associated with lung cancer in adults and respiratory disease in children. The risk assessment's development was considerably delayed by the tobacco industry's criticisms of the report (US EPA, 1992). Sixty-four per cent (69/107) of submissions received by the EPA during the public commentary period claimed that the conclusions of the draft were invalid and, of these, 71 % (49/69) were submitted by tobacco industry-affiliated individuals (Bero and Glantz, 1993). The tobacco industry-affiliated reviewers supported their criticisms of the risk assessment by selectively citing non-peer-reviewed literature, especially articles from symposium proceedings (Bero and Glantz, 1993). Thus, tobacco industry-sponsored research that was not published in the peer-reviewed scientific literature was submitted directly to the EPA for review.

Schotland and Bero (2002) examined the development of the California risk assessment, revealing that participation in the public contribution process was not balanced among all interested parties, and was dominated by the tobacco industry. Critics and supporters of the risk assessment used different criteria to evaluate the science, suggesting that they were constructing the evidence to support their predefined positions. Similar to the US EPA risk assessment, the tobacco industry was able to use its funded research to support its arguments against the California risk assessment.

Indoor air regulation
During the 1990s, the Washington and Maryland Occupational Safety and Health Administrations each promulgated regulations restricting smoking in private workplaces. The US Occupational Safety and Health Administration also proposed a workplace smoking restriction but this failed. Internal tobacco industry documents show that one strategy the industry used to defeat the proposed federal regulation was to 'produce data to counter the findings about the adverse health effects of second-hand smoke' (Bryan-Jones and Bero, 2003). Despite the tobacco industry's use of this strategy and others to defeat the Maryland and Washington regulations, the state regulations were passed (Mangurian and Bero, 2000).

The two states' regulatory development processes required a public commentary period. Opposition to the regulation came primarily from the tobacco industry, small businesses, and business organisations and appeared to be coordinated (Bero et al., 2001). Much of the business group opposition was supported by the tobacco industry, although this support was not disclosed in the public commentary (Mangurian and Bero, 2000). Although arguments not related to science were more common than scientific arguments as a whole, arguments about science were used more often by opponents than supporters of the regulations (Bero et al., 2001). As in the other examples cited in this chapter, opponents of regulation, primarily the tobacco industry, cited industry-sponsored symposium proceedings or peer-reviewed journal articles of low methodological quality to support their criticisms of the science on which the regulations were based.

Apparent disagreement among experts during public testimony reinforces uncertainty about the data underpinning risk estimates or regulations. The studies of the Washington and Maryland regulations suggest, however, that the industry-supported experts used different criteria to evaluate the science, different bodies of evidence to support their claims and relied on arguments about specific studies rather than emphasising the body of evidence as a whole. In general, the involvement of tobacco industry lawyers and executives in the design, conduct and dissemination of research has an impact on how controversy can influence public opinion and policy decisions.

Box 7.2 describes how the tobacco industry worked to undermine tobacco control activities at the World Health Organization.

7.4 Lessons learned

The tobacco industry has had a long-standing strategy of funding research and disseminating it through their sponsored, non-peer-reviewed publications. These strategies have remained relatively consistent as the industry has evolved from refuting research on active smoking to refuting research on second-hand smoke. Despite the questionable conduct of much of this research, the tobacco industry has widely disseminated it to lay journalists and policymakers. In addition, the tobacco industry has a record of suppressing and criticising research that is unfavourable to its position. Tobacco industry lawyers and executives, rather than scientists, have been in control of the design, conduct and dissemination of this research, thereby protecting the research from public discovery. Since the tobacco industry's efforts to manipulate research are international endeavours, there is a need for global awareness of the strategies that the industry has used to influence data on risk.

When data on risk appear to be controversial, users of the data should investigate the sources of the controversy. Does the controversy exist only because the findings of interest group-funded research are contrary to data collected by others? Is the controversy supported primarily by evidence published in interest group-supported publications? Is the controversy supported primarily by research publications of low scientific quality? Is the controversy perpetuated in the lay press through citation of interest group-affiliated individuals? Are the data that suggests a controversy presented to policymakers only by the interest group?

Policymakers should apply these questions to all situations in which a company has an interest in creating controversy about the risks of its products. The tobacco industry differs substantially from other industries in the deadly nature of its products when used as directed, and the historical lack of regulation of tobacco products. However, the tobacco industry's methods for influencing the design, conduct and publication of research are similar to those of other corporate interests. For example, studies examining the association of pharmaceutical industry funding and research outcomes suggest that such funding produces studies with outcomes that are favourable to the sponsor (Lexchin et al., 2003; Cho and Bero, 1996; Bekelman et al., 2003). The reasons for this observed association of funding and outcome are not clear (Bero and Rennie, 1996). For example, the funding source does not appear to influence the methodological quality of the published research (Lexchin et al., 2003). Therefore, biased outcomes may

Box 7.2 Tobacco industry strategies to undermine tobacco control activities at the World Health Organization

'Tobacco industry documents reveal that, for many years, tobacco companies have deliberately subverted the efforts of the World Health Organization (WHO) to control tobacco use. The attempted subversion has been elaborate, well financed, sophisticated and usually invisible.

The release of millions of pages of confidential tobacco company documents as a result of lawsuits against the tobacco industry in the United States has exposed the activities of tobacco companies in resisting tobacco control efforts. That tobacco companies resist proposals for tobacco control comes as no surprise. What is now clear is the scale and intensity of their often deceptive strategies and tactics.

The tobacco companies' own documents show that they viewed the WHO, an international public health agency, as one of their foremost enemies. The documents show further that the tobacco companies instigated global strategies to discredit and impede the WHO's ability to carry out its mission. The tobacco companies' campaign against the WHO was rarely directed at the merits of the public health issues raised by tobacco use. Instead, the documents show that tobacco companies sought to divert attention from the public health issues, to reduce budgets for the scientific and policy activities carried out by the WHO, to pit other UN agencies against the WHO, to convince developing countries that the WHO's tobacco control programme was a 'first world' agenda carried out at the expense of the developing world, to distort the results of important scientific studies on tobacco and to discredit the WHO as an institution.

Although these strategies and tactics were frequently devised at the highest levels of tobacco companies, the role of tobacco industry officials in carrying out the strategies was often concealed. In their campaign against the WHO, the documents show that tobacco companies hid behind a variety of ostensibly independent quasi-academic, public policy and business organisations, whose tobacco industry funding was not disclosed. The documents also show that tobacco company strategies to undermine the WHO relied heavily on international and scientific experts with hidden financial ties to the industry. Perhaps most disturbing, the documents show that tobacco companies quietly influenced other UN agencies and representatives of developing countries to resist the WHO's tobacco control initiatives.

That top executives of tobacco companies sat together to design and set in motion elaborate strategies to subvert a public health organisation is unacceptable and must be condemned. The Committee of Experts believes that the tobacco companies' activities slowed and undermined effective tobacco control programmes around the world.

Given the magnitude of the devastation wrought by tobacco use, the Committee of Experts is convinced that, on the basis of the volume of attempted and successful acts of subversion identified in its limited search, it is reasonable to believe that the tobacco companies' subversion of the WHO's tobacco control activities has resulted in significant harm. Although the number of lives damaged or lost as a result of the tobacco companies' subversion of WHO may never be quantified, the importance of condemning the tobacco companies' conduct, and taking appropriate corrective action, is overriding'.

Source: Summary of a report of the WHO Committee of Experts on Tobacco Industry Documents (CETID, 2000).

be the results of how the research questions are asked, how the research is actually conducted and whether the results are published (or not published). Food industry funding for research has also been shown to produce outcomes favourable to the sponsor (Nestle, 2002; Levine et al., 2003).

A report by the Union of Concerned Scientists (2007) has documented how ExxonMobil has used the tactics of the tobacco industry to stimulate controversy about climate science. ExxonMobil has raised doubts about the evidence, hidden involvement behind front groups, sponsored scientific spokespersons to criticise the science and attempted to shift the focus away from existing evidence to the need for 'sound science'.

The public health community must learn more about the internal behaviour of corporations other than the tobacco industry in order to make conclusions about similarities in corporate behaviour. The release of millions of internal tobacco industry documents has given the public health community insights into the inner workings of the tobacco industry and revealed

their previously hidden involvement in manipulating research (Bero, 2003). However, this insight is not available for most corporate sectors.

In some of the few other analyses of internal industry documents, Markowitz and Rosner describe how the chemical, asbestos and lead industries manipulated research about the harms of their products (Markowitz and Rosner, 1991, 2000, 2002). Their analysis reveals that these industries used the same tactics as tobacco companies to create controversy about the health effects of tetraethyl lead, asbestos, polyvinyl chloride and other chemicals. A recent issue of the *International Journal of Occupational and Environmental Health* relies heavily on internal company documents that the authors obtained by serving as expert witnesses in litigation (Special Issue, 2005). It describes how a variety of chemical companies and their trade organisations have used the strategies outlined in this article:

1. funding research that supports the interest group's position;
2. hiding industry involvement in research;
3. publishing research that supports the interest group's position;
4. suppressing research that does not support the interest group's position;
5. criticising research that does not support the interest group's position;
6. changing scientific standards;
7. disseminating interest group data or interpretation of risk in the lay press;
8. disseminating interest group data or interpretation of risk directly to policymakers.

The role of the sponsor in designing, conducting and disseminating research can be evaluated only if interest group involvement in all steps of the risk determination process is fully described. Thus, funding sources for all published research should be fully disclosed. Our analyses show, however, that disclosure of funding sources often provides incomplete information about the involvement of the sponsors in the research process. The tobacco industry has a long history of hiding the involvement of its lawyers and executives in the designing, conducting and disseminating research. If internal tobacco industry documents had not been made available to the public, much of what is known about the industry's manipulation of research would have remained undiscovered.

Disclosures should not be limited to describing the roles of the research funders in all stages of the research process. Personal financial ties between investigators and corporate interests (such as consulting fees, stock ownership, honoraria etc.) should also be fully disclosed. Personal financial ties are increasing (Boyd and Bero, 2000) and are associated with favourable research outcomes for the corporate interest, even if the corporate interest is not funding the research (Lexchin et al., 2003). Experts who criticise research describing the harms of a company's product should also fully disclose their financial ties with the company. These complete and accurate disclosures should be found in scientific publications (including research articles, letters to the editor and editorials), citations in the lay press, and testimony in policy or legal settings.

Full disclosure of a sponsor's role in designing, conducting and publishing a study could also improve the peer-review process. Peer reviewers are typically limited by the information available in the article they are reviewing. The peer review process itself should be conducted by individuals with adequate expertise and be independent of industry sponsors.

The findings presented in this chapter also have implications for how experts should be selected to participate in the risk assessment process. As suggested by others, professional competence, diversity of political views, disciplines, opinions and attitudes are important (von Winterfeldt, 1992). However, consideration should also be given to affiliation or interest group bias and how this will affect risk assessment. Encouraging transparency regarding the roles of interest groups in developing and disseminating data on risk will not prevent their involvement in the process. However, such transparency will make it easier to determine which strategies, if any, an interest group has been using to influence the data.

Detailed and accurate financial disclosures of research funding and financial ties are necessary, but not sufficient, for safeguarding the integrity of the research record. One possible benefit of disclosure is that it might discourage scientists from entering into financial relationships that could detract from the perceived integrity of their research. Another possible benefit is that transparency might improve public trust in research (Cho, 1998). Krimsky

(2003), however, has described disclosure as a 'rationalisation for creating more serious conflicts'. He points out that disclosure is a 'public relations' response to dealing with corporate influence on research and not a way of potentially decreasing the effect of the corporate sponsor on research integrity.

Although greater transparency about industry involvement in research could facilitate evaluation of biases in the design, conduct and reporting that might be introduced by such sponsorship, it will not eliminate the biases. Furthermore, if researchers and institutions are concerned that the public views industry-sponsored research as less credible, regardless of any effect on bias, eliminating financial ties may be the best way to deal with the issue. A number of scholars have argued that there should be a total ban on clinical investigators' financial ties to companies that fund their research (Krimsky, 2003; Dana, 2003). These proposed bans eliminate the need for oversight committees to 'manage' the conflict of interest and protect against even the appearance of conflict.

Photo: © istockphoto/Gremlin

Schafer (2003) supports the 'sequestration thesis', which would eliminate direct corporate sponsorship of research and financial ties of investigators. Sequestration could be achieved by forming an independent research institute, funded by companies, to support research. Shamoo and Resnik (2003) have noted, however, that eliminating financial ties and corporate funding may not be realistic today. Some investigators advocate 'self regulation': voluntary compliance with professional society guidelines, or adaptation of the federal conflict of interest policy to clinical trials funded by private sponsors (Boyd et al., 2003).

Support for banning corporate funding of research is most developed among academic institutions that have policies prohibiting researchers from accepting tobacco industry funding for research. For example, some academic institutions, particularly schools of medicine and public health, have developed bans on tobacco industry funding (Herman, 2002). Examples include Harvard University and the University of Sydney. Some funding agencies (e.g. Legacy Foundation) have developed policies that require such bans as a condition for receiving funding (Shield, 2001).

Bans on tobacco industry support for research are warranted in view of the industry's history of deception about its role in designing, conducting and disseminating industry-supported research. They are further justified by the tobacco industry's motives for funding research, which include distracting attention from tobacco's health risks, gaining credibility and using the research for public relations (Cohen, 2003).

Table 7.2 Key dates relating to knowledge of harm from active and second-hand smoke

1604	King James I of England wrote 'A Counterblaste Against Tobacco' expressing his distaste for tobacco, particularly tobacco smoking. This was one of the earliest anti-tobacco publications
1903–1908	In the United Kingdom, the Boer War Recruits Health Report led, in 1908, to restrictions on the sale of tobacco to children under 16 and empowered police to confiscate cigarettes from children smoking in public places
1931	Argentinian oncologist Angel Roffo (1931) produced skin tumours in rabbits with tobacco tar, building on similar work on tars and skin cancer that began with Percival Pott's UK studies of scrotal cancer and chimney sweeps (1775)
1936	US physician Alton Ochsner (1973) sees nine cases of lung cancer in six months after not seeing one in 20 years. Noting that all the patients had begun smoking during World War I, he suggested that smoking was the cause
1938	US statistician Raymond Pearl (1938) uses insurance records to show increased death rates of smokers
1939	Franz Müller (1939) uses 86 cases of lung cancer compared to controls to show that heavy smokers had 16 times the lung cancer deaths than non-smokers: a 'one in a million chance' finding leading to the conclusion that tobacco was the 'single most important cause of the rise in lung cancer'
1930–1941	Schairer and Schöniger (2001) studied 195 lung cancer cases using two control groups (other cancers and no diseases), showing that only three lung cancer cases had not smoked and that a statistical association between tobacco and lung cancer was 'likely'
1942–1944	Seven dissertations were published on tobacco and health effects at the German National Scientific Institute for Research on Tobacco, Jena (Zimmermann et al., 2001)
1946	Percy Stocks (1947), UK chief medical statistician to the General Register Office, noted a 'startling' six-fold increase in male lung cancer between 1930 and 1944
1947	The UK Medical Research Council (MRC) met to discuss action and was attended by Bradford Hill, Alice Stewart, Ernest Kennaway and others. Several possible causes of lung cancer were discussed: tar from roads, urban air pollution, traffic fumes and smoking. These were all probably 'factors which prepare the soil rather than sow the seed' (Tudor Edwards, 1946; Keeting, 2009)
1948	In an MRC study by Doll and Bradford Hill, preliminary results on 156 interviews with patients showed 'definite association' between lung cancer and smoking, although the lack of a link between inhaling and cancer was 'surprising' (Pollock, 1999). This was to provide the eminent statistician, Sir Ronald Fisher, with his denial of the association between smoking and lung cancer for many years
1950	Five papers were published showing the dangers of smoking. Wynder and Graham (1950) (concerning military veterans in the US), Doll and Bradford Hill (1950) (concerning hospital patients in the United Kingdom) concluded that smoking was 'an important factor' in the 'induction/production' of lung cancer. Of 647 cases in the Doll and Bradford Hill study only 0.3 % were non-smokers: a 'one in a million' chance finding. Heavy smokers had 16 times the lung cancer deaths than non-smokers. But this result was 'largely doubted and generally ignored' by the medical establishment (Keating, 2009)
1953	A UK Government Advisory Committee concluded that the 'association was causal' and 'young people should be warned' (Ministry of Health, 1953a, 1953b and 1954)
1954	Preliminary results were released from the study of Doll and Hill (1954) of 40 000 doctors which was to last 50 years. Data on 39 lung cancer cases out of 769 deaths confirmed their earlier findings and now revealed a dose/response effect and an association with heart disease. In the US, Hammond and Horn's (1954) study of 5 000 deaths showed similar results
1954	Publication of scientific studies documenting tobacco's role in cancer and other fatal illnesses together with subsequent media coverage and declining sales was referred to internally by the tobacco industry as the '1954 emergency'. The industry responded with a public relations campaign led by Hill and Knowlton to 'manufacture doubt' about the link between smoking and lung cancer, without actually denying it
1964	A US Surgeon General report, 'Smoking and Health', based on 29 studies, concluded that 'there is a causal relationship between excessive smoking and lung cancer' (US DHEW, 1964)
1970–1980s	The first studies were published showing that second-hand smoking is associated with lung cancer. A US Surgeon General report in 1986 concluded that the link is causal (US DHHS, 1986)
1993–1998	Tobacco industry subverts the WHO International Agency for Research on Cancer (IARC) study and evaluation of second-hand smoking as a human carcinogen

Source: EEA, based on Keating, 2009 and Ong and Glantz, 2000.

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8 Vinyl chloride: a saga of secrecy

Morando Soffritti, Jennifer Beth Sass, Barry Castleman and David Gee ([1])

This chapter is about how early warnings in the 1950s and 1960s concerning the short-term harm of vinyl chloride (VC) to the skin and bones of workers, and to the livers of laboratory animals, were initially hidden from other workers and regulators. This was despite some early misgivings by company experts whose advice was initially ignored by their employers. This pattern was repeated when the later, more devastating news of a rare liver cancer in workers was revealed by long-term animal studies and by an attentive and concerned company physician.

Unlike many other histories, however, this story features a very prompt response from the global chemical industry to the publication of the liver cancer evidence, a response that included funding cancer testing and later compliance with a large reduction in the permissible exposure limits. The case also provides early evidence of reproductive effects of vinyl chloride monomer (VCM).

Other features of this story presage the later and common responses of the corporate world to heightened public awareness and pressure from non-governmental organisations (NGOs) and trade unions, including greatly exaggerated estimates of the likely costs of complying with tighter pollution controls; a frequent mismatch between the position of the trade association and that of many, more progressive companies within the association; but also some relatively quick corporate responses to public, NGO and regulatory pressure.

The chapter also features two legal aspects, which, though more common in the US, are also valuable for Europeans. First, the potentially positive role that judicial review of regulatory proposals can play in providing a societal judgement about the behaviour of corporations. This can embrace not just moral judgements but also judgements about the state of the science and what society should do with it.

Second, the role that document discovery in legal compensation cases can play in revealing the real and until then secret activities of corporations. Any proposals to promote justice for victims of environmental and health harms via no fault administrative arrangements need to be accompanied by other measures to extract information about corporate behaviour.

The chapter is followed by a panel analysing the value of animal testing for identifying carcinogens.

([1]) Authors would like to thank Professors David Rosner and Gerald Markowitz for providing original copies of original documents. Many of the documents used to prepare this paper are a part of the collection of the Cesare Maltoni Cancer Research Center in Bentivoglio, Italy. The original industry documents cited by Markowitz and Rosner in their book, Deceit and Denial, are available to the public at http://www.deceitanddenial.org.

8.1 A veil of secrecy

In January 1973 the US National Institute of Occupational Safety and Health (NIOSH) issued an official 'request for information' to the public, including the chemical industry, requiring that all information relevant to the hazards of vinyl chloride be submitted to the government. Compliance was mandatory.

The 'request' put the US chemical industry (both users and manufacturers) in a difficult position. Dow Chemical and other US manufacturers had signed a 'secrecy agreement' (see Figure 8.1) in 1972 with European chemical companies (Markowitz and Rosner, 2002, p. 182–183). The signed agreements, which were collected by Imperial Chemical Industries Ltd (ICI), United Kingdom, obliged signatories to hold in confidence new animal testing research from Italy, which would eventually contribute to more protective workplace standards.

The US and European chemical companies met in Washington DC on 14 November 1972 at the headquarters of the US Manufacturing Chemists Association (MCA), the trade association of industrial chemical manufacturers.

The scientific findings revealed at the meeting came from a medieval castle in Bentivoglio, Bologna, Italy, equipped with a modern scientific laboratory, world-class animal testing facilities and top-notch scientific staff. Seated at microscopes, a scientific team, led by Professor Cesare Maltoni, was the first in the world to see evidence of cancer in the liver and kidneys of laboratory animals that had been exposed to inhalation of a daily concentration of vinyl chloride of 250 ppm — half the level allowed in workplace air at the time.

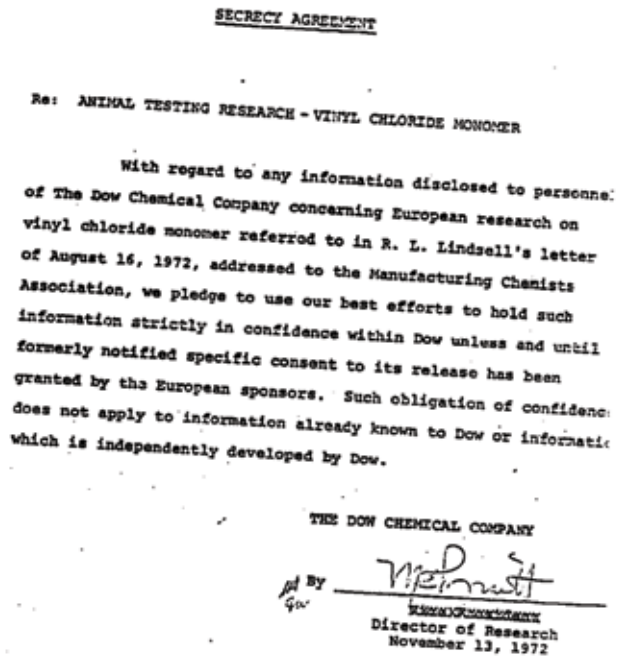
While the companies did not doubt the evidence from these studies, the Secrecy Agreement did not allow them disclose it. Such was the concern about leaks to the public that Mr D. M. Elliott of ICI 'insisted that the work tables be swept clear of paper for note taking before he would discuss anything regarding the European group's efforts. Such was done' (Markowitz and Rosner, 2002, p. 183).

In fact, Professor Maltoni's work was not the first indication that industry standards were inadequate and risked grievous harm to workers. The MCA had set an upper workplace limit for vinyl chloride concentration of 500 parts per million (ppm) in 1954. And despite a growing body of evidence that it was unsafe, this limit remained unchanged for two decades.

Internal corporate documents reveal that in the 1950s the industry already had animal testing data showing the workplace limit to be excessive. By 1961 company toxicologists were internally recommending a limit no higher than 50 ppm. Only in 1974 did the newly established Occupational Safety and Health Administration (OSHA) issue a new standard of 1 ppm. In the interim, workers were exposed to vinyl chloride concentrations that caused excruciatingly painful bone disease and cancer.

This chapter provides a summary of the early warnings and late responses to the dangers of vinyl chloride.

Figure 8.1 Image of the Secrecy Agreement



SECRECY AGREEMENT

Re: ANIMAL TESTING RESEARCH - VINYL CHLORIDE MONOMER

With regard to any information disclosed to personne of The Dow Chemical Company concerning European research on vinyl chloride monomer referred to in R. L. Lindsell's letter of August 16, 1972, addressed to the Manufacturing Chemists Association, we pledge to use our best efforts to hold such information strictly in confidence within Dow unless and until formerly notified specific consent to its release has been granted by the European sponsors. Such obligation of confidenc does not apply to information already known to Dow or informati which is independently developed by Dow.

THE DOW CHEMICAL COMPANY

By

Director of Research
November 13, 1972

Source: Markowitz and Rosner, 2002.

8.2 1930–1999: rapid growth in PVC output

Industrial output of VC began in the 1930s, mainly to support manufacture of polyvinyl chloride (PVC) products as diverse as shower curtains, food containers, floor coverings, pipes, packaging and wire coating. Since the Second World War, the largest use of VC has been in producing PVC and copolymer resins (HSDB, 2006).

Vinyl chloride is used primarily (> 95 %) in the manufacture of PVC (IARC, 2008). The main uses of

PVC are now in building and construction: window and door profiles, pipes and ducts, flooring and wall coverings, wiring and cable insulation, and stadium roofing. With the addition of 'plasticiser' chemicals to make it more flexible, it is also widely used in medical applications (tubing, bags, containers and other medical equipment, including the tubing in heart-lung bypass machines, catheter tubing, containers for intravenous solutions, blood storage bags, tubing for dialysis); electrical cable insulation; consumer products (inflatable children's toys, sports bags); vehicles (underbody coatings, sealants and floor modules, cable insulation, door panels and arm rests, weather strips and window sealing profiles); and packaging (bottles, toothpaste tubes, food packaging).

Global VC production (which is approximately equal to PVC production (IPCS, 1999)) grew swiftly from 450 tonnes per year in 1933 to 54 000 tonnes during the Second World War. By 1952 production was 145 000 tonnes and in 1971 it stood at around 7 million tonnes (IARC, 1974). Total annual world production in 1985 was about 17 million tonnes and in 1999 it was 26 million tonnes (IPCS, 1999). Global production and consumption of VC in 2010 was approximately 34 million metric tonnes. Global VC consumption is estimated to have increased by 4.6 % in 2010. Demand is expected to average growth of around 4.7 % per year from 2010 to 2015, and 4.2 % from 2015 to 2020 (SRI Consulting, 2011).

In 2005, production in Asia had outgrown that in both Western Europe and North America.

The Asia-Pacific region now accounts for around 54.8 % of the global installed VC capacity. The capacity and production of VC has grown very rapidly in China in the past decade. The export market of China for VC has also grown very rapidly. The country has emerged as the largest producer and exporter of VC in the world. Europe has the second largest VC capacity in the world and North America stands third. The VC capacity in Europe and North America is expected to be almost stagnant in the coming years (GBI Research, 2010).

An increasing number of workers worldwide are exposed to vinyl chloride during either its production, the manufacture of polyvinyl chloride or polyvinyl chloride processing. Since the late 1970s when the closed-loop polymerization process was introduced, the concentrations to which workers are exposed have decreased substantially in North America and Western Europe. Levels before that time had been higher than 38 ppm (100 mg/m^3) ([2]). In low and medium-resource countries, older technologies have continued to be used and therefore high exposures probably occur. Exposures in polyvinyl chloride processing plants are usually considerably lower than those in vinyl chloride monomer and polyvinyl chloride production; in Western Europe and North America, current exposure levels are generally below 0.4 ppm (1 mg/m^3). Concentrations of vinyl chloride monomer in ambient air are normally below 0.004 ppm (0.01 mg/m^3), but higher concentrations have been measured in the vicinity of vinyl chloride/polyvinyl chloride production plants (IARC, 2008).

Until the mid-1970s, VC gas was also used as a propellant in a wide variety of aerosols including hair spray by Clairol, leading to elevated exposures and eventually cancer in hairdressers (Castleman, 1981; Infante et al., 2009). In 1974 the US Food and Drug Administration (FDA) noted that using such products in small rooms could result in airborne levels far exceeding the workplace limit at the time. The US Environmental Protection Agency (EPA) issued an emergency suspension of its use as a propellant in pesticide sprays in 1974, and the US Consumer Product Safety Commission (CPSC) banned its use in consumer aerosol products in 1978.

In May 1973, citing the 1958 Delaney amendment of the Food and Drug and Cosmetic Act (which prohibited the use of any food additive which was demonstrated to cause cancer in humans or animals), the US FDA suspended approval for using PVC bottles for alcoholic beverages (Food Chem. News, 1973; US FDA, 1973). As a result of PVC food packaging, VC used to be detected in a wide range of foods, including edible oils, vinegars, margarines and bottled water (Page and O'Grady, 1977; Van Lierop, 1979; Benfenati et al., 1991). However, the US government now limits vinyl chloride to no more than 1 ppm in PVC food packaging materials, so it is no longer detected in food (ATSDR, 2006). VC is not known to occur naturally. Unintentional formation of the compound can occur in landfills where VC forms as a degradation product of chlorinated hydrocarbons used as solvents, and may subsequently be emitted as an air pollutant and to groundwater. VC is also found in tobacco smoke (IPCS, 1999).

([2]) 1 ppm = 2.6 mg/m^3.

Vinyl chloride (VC) is a gaseous chemical intermediate (its boiling point is – 14 °C) used in a number of final products. Even after being polymerised into polyvinyl chloride plastics (PVC), residual unreacted monomers in the plastic can still pose dangers. The VC copolymer 'vinyl chloride-vinyl acetate' is primarily used to produce films and resins, while another copolymer, 'vinylidene chloride-vinyl chloride', is used mainly in food packaging and metal coatings in storage tanks.

8.3 1930–1961: early warnings from animals and humans meet industry indifference

8.3.1 Earliest warnings

The short-term (acute) toxicity of VC was tested by inhalation in animals in the 1930s. It induced drowsiness, loss of coordination and loss of consciousness (i.e. it was a narcotic) at doses ranging from 5 000 to 120 000 ppm depending on the species tested (Patty et al., 1930; Peoples and Leake, 1933; Oster et al., 1947). In rats, congestion of internal organs (particularly the lungs, liver and kidneys) and fluid-filled lungs were observed after inhaling VC at high concentrations (Patty et al., 1930, Mastromatteo et al., 1960; Lester et al., 1963; Prodan et al., 1975). In dogs, severe heartbeat irregularities occurred under narcosis (Oster et al., 1947).

In humans, acute VC intoxication induces giddiness, nausea and headaches. At higher concentrations narcotic effects were also observed (Peoples and Leake, 1933). In a case of accidental poisoning in a PVC plant, VC caused almost immediate death of workers following loss of consciousness (Danzinger, 1960). Accidental spraying of VC caused effects ranging from skin rash to second-degree burns (Harris, 1953).

The first evidence of long-term (chronic) toxicity in workers was reported in the late 1940s by Soviet scientists who expressed concerns about hepatitis-like liver inflammation found in 15 workers (out of 48) exposed to VC (Tribukh et al., 1949). Further studies conducted in PVC factories in the USSR showed cases of vascular disease (angioneuropathy) in workers exposed to VC at levels as low as 5–15 ppm (Filatova and Gronsberg, 1957). Following these observations, technological improvements were made and in 1966 VC levels measured at USSR PVC plants dropped from 40 ppm (100 mg/m^3) to 4–15 ppm (10–40 mg/m^3) (Filatova, 1966).

8.3.2 Ignoring evidence from animal studies

In 1954, the US Manufacturing Chemists Association (CMA) established the workplace threshold limit value (TLV) of 500 ppm, and it remained at that level for two decades despite mounting evidence of its inadequacy. Since the US Occupational Safety and Health Administration (OSHA) would not be established for another 17 years (1971), the TLVs were set by the American Conference of Governmental Industrial Hygienists (ACGIH), which was then as it is now a volunteer organisation with no formal ties to the government. Its members include federal, state, and local government officials, as well as academics and industry consultants (Castleman and Ziem, 1988). Before OSHA, TLVs were often based on inadequate health information, and represented what the industry felt was achievable but not necessarily health protective (Markowitz and Rosner, 2002; Castleman and Ziem, 1988).

A turning point in the history of VC should have occurred by 1961 at the latest. In that year researchers from Dow Chemical published the results of a study on animals (rats, guinea pigs, rabbits and dogs) exposed to VC for seven hours per day at levels ranging from 50 to 200 ppm for six months, and at 500 ppm for 4.5 months. Dow reported liver abnormalities in male and female rats exposed to 500 ppm and an increase in liver weight in rats treated at 100 ppm. Liver enlargement and microscopic degenerative changes at 200 ppm were also observed in rabbits (Torkelson et al., 1961).

In fact, the key conclusions were already known at least two years earlier. Writing to Union Carbide Medical Director Thomas Nale in November 1959, Union Carbide consultant Henry Smyth had remarked that based on an 'off-the-record phone call' from Dow toxicologist V. K. Rowe, it was apparent that vinyl chloride was 'more toxic than has been believed'. 'Even 100 ppm produced organ weight changes and gross pathology', he wrote (Smyth, 1959). According to Smyth, Dow was considering whether this would have 'any bearing on the safety of (food) packaging uses' involving vinyl chloride exposure.

Noting that the 500 ppm TLV was based on a single guinea pig inhalation study from the 1930s, Smyth asked that the information reported remain confidential until published by Dow (Smyth, 1959).

In a letter dated May 1959, V. K. Rowe had likewise indicated to W. E. McCormick at US chemicals firm B. F. Goodrich that the current TLV of 500 ppm

would cause 'appreciable injury' to full-time workers and raised particular concerns about the hazards of long-term exposures (Rowe, 1959).

The MCA in effect set the TLV in 1954 at 500 ppm, and it would remain so until it was lowered to 200 ppm in 1971 and finally to 1 ppm in 1974. The first OSHA limits adopted were the 1968 TLVs, so the permissible exposure limit in the US industries remained at 500 ppm until new rulemaking in 1974.

8.3.3 1963–1971: secrecy over evidence of bone disease in workers

Evidence of the risks of bone disease from VC exposure was not limited to animal studies. In 1963, Suciu et al. published the results of clinical observations of 168 workers engaged in PVC production, which described for the first time the role of VC in causing acroosteolysis — an extremely rare bone disease characterised by excruciatingly painful bone reabsorption, skin changes (scleroderma-like lesions) and vascular changes associated with Raynaud's syndrome and hepatomegaly and splenomegaly (Suciu et al., 1963).

At around the same time the Belgian chemical company Solvay observed two cases of acroosteolysis among workers in one of its factories in Belgium and informed other VC/PVC manufacturers. The same pathology was observed among workers in another factory of the same company in Romania. Between 1962 and 1965 several cases of acroosteolysis were observed in other Solvay VC/PVC factories (Maltoni, 1974a). However, no reports were made public, or to the independent scientific community, governments or workers.

In 1964 Dr John Creech, a physician who was doing regular medical checks for the US chemical company B. F. Goodrich, followed up a worker's complaint about painfully tender fingers and found four cases of acroosteolysis in workers that all worked in the same area of the VC/PVC plant. For Creech, this seemed to be obvious evidence of a link to their workplace conditions (Markowitz and Rosner, 2002, p. 173; MMWR, 1974). Goodrich asked Robert Kehoe of the Kettering Laboratory to investigate ([3]). Kehoe concluded that acroosteolysis was an 'entirely new' occupational disease. The medical Director of Goodrich asked a company physician at another Goodrich plant to 'determine as quietly as possible whether similar conditions existed at his plant', adding that 'We do not wish to have this discussed at all and I request you maintain this information in confidence' (Markowitz and Rosner, p. 174; MCA papers, 12 November 1964).

Other chemical companies took the same line. A Monsanto official, following the decision to x-ray exposed workers, said that 'I am sure that Dr Nessel can prepare these people with an adequate story so that no problem will exist' (Markowitz and Rosner, 2002, p. 174, MCA papers, 7 January 1966). The secrecy strategy extended to trying to restrict news of the disease in Europe. On hearing that a doctor from Solvay Chemical was about to publish his finding of workers with the same bone destruction seen in the B. F. Goodrich cases, the corporate vice president of Goodrich attempted to 'discourage or edit' the publication but was ultimately unsuccessful (Markowitz and Rosner, 2002, 174, MCA papers, 7 January 1966).

Although the public, government regulators, and workers were all kept in the dark, the news about acroosteolysis was shared widely among European and American chemical companies who learned at a private meeting of industry medical staff in June 1966 that 1 % of PVC plant workers and 6 % of the workers who cleaned out the vinyl chloride monomer (VCM) vats suffered from acroosteolysis. Goodrich asked companies to 'use discretion in making the problem public' (Markowitz and Rosner, 2002, p. 175, MCA papers, 17 October 1966). The industry was particularly concerned that the media and the public could have concluded that PVC products, especially those used in food packaging, may also be hazardous, which 'would have been very damaging for industry' (Markowitz and Rosner, 2002, p. 175, MCA papers, 24 January 1967).

In 1967 Goodrich researchers prepared a scientific article reporting 31 cases of acroosteolysis among vinyl chloride workers (Markowitz and Rosner, 2002, p. 176. Ref 40). According to later legal testimony from Dr Creech, the first draft of the article that he saw specifically identified VC as the cause of acroosteolysis, but this information was not included in the final version (Markowitz and Rosner, 2002, p. 176, Ref 41).

Two years later, in early 1969, the results from an MCA-funded study of acroosteolysis by the Institute for Industrial Health at the University of Michigan were presented confidentially to the MCA. The report

([3]) Kehoe also played an important role in the story of lead in petrol, described in the Chapter 3 on lead in petrol.

found that acroosteolysis could affect connective tissue and bones beyond the fingers; that the odour of VC could only be detected at 4 000 ppm, not 400 ppm as previously thought, and was therefore an indicator of much more hazardous exposure than had been thought; that it could not be assumed that workers would be safe from disease at the exposure limit of 500 ppm; and that 'sufficient ventilation should be provided to reduce the VC concentration to below 50 ppm' (Markowitz and Rosner, 2002, p. 177, Ref 45). As this recommendation implied that VC was the cause of the disease, the MCA Occupational Health Committee voted seven to three to refuse acceptance of the report as written, and voted unanimously to accept it only when the report stated that 'Inasmuch as the etiologic agent of the disease is unknown, a level of vinyl chloride below 50 ppm should be used as an index of adequate ventilation' (Markowitz and Rosner, 2002, p. 177, Ref 46).

This 50 ppm recommendation in Spring of 1969 came after the same recommendation was made by Dow Chemical toxicologists in 1961 based on their own studies showing pathological changes in the livers of rabbits that they had been studying (Torkelson et al., 1961). Upon the recommendation of Robert Scala (Esso) in 1965 the ACGIH proposed lowering the TLV to 50 ppm based on the 1961 animal data of Dow scientists Torkelson and V.K. Rowe (Torkelson et al., 1961; Castleman and Ziem, 1988) But then, in a meeting with the ACGIH TLV Committee Chairman Stokinger in 1966, 50 member companies said 50 ppm was too low. Thus, the proposed change to the TLV was put off, according to an unpublished report of a discussion held at Mellon Institute on 1–2 February 1966 (Castleman and Ziem, 1988).

The ACGIH did not lower the TLV until 1971, and then only to 200 ppm based on unpublished evidence of liver damage in workers (Castleman and Ziem, 1988). Although Dow claims that the company reduced its workplace exposure limit to 50 ppm in 1961, it is known that this limit was exceeded (Castleman and Ziem, 1988).

These recommendations by corporate toxicologists and doctors went unheeded repeatedly, allowing continued excessive exposure of workers to continue. That is because the toxicologists and company doctors do not run the companies; corporate toxicological policy decisions are made by corporate executives as business decisions. Thousands of plants were melting and shaping PVC resins into credit cards, phonograph records and countless other products. No effort was made to limit the amount of residual VC monomer left in those resins. An official evaluation that worker exposures must be limited to 50 ppm could increase costs for the giant firms that made PVC polymer resins and some of the many plastic product manufacturers. Disclosure and recognition of the toxicity of VC could also endanger sensitive markets for PVC food packaging and medical applications. Then, there were aerosol products in which VC was used as a propellant.

The final report on acroosteolysis from the Michigan researchers was ultimately published in 1971 in the *Archives of Environmental Health*. It made no mention of the earlier view that the exposure limit of 500 ppm was not likely to be protective. It omitted reference to the inadequacy of the odour threshold. It said that the cause of acroosteolysis was unknown. Although it recommended further research, this was in fact unlikely; B.F. Goodrich executives explicitly decided not to accept any proposals for additional research into the causes of acroosteolysis. This enabled Goodrich and the rest of the industry to act as if the cause was 'unknown' (Markowitz and Rosner, 2002, p. 177).

8.3.4 1970–1983: recognising VC as a carcinogen

As reported by Maltoni (1974a), recognition of vinyl chloride's carcinogenicity began in the late-1960s. At that time, Solvay Chemical Company asked Prof. P. L. Viola, the company doctor at its VC/PVC factory in Livorno, Italy, to perform a long-term experiment to study acroosteolysis.

It was 1967 when Prof. Viola of the Regina Elena National Cancer Institute in Rome started the experiment exposing rats to 30 000 ppm VC vapours for four hours a day, five days a week, for 12 months. The results were a surprise. As Prof. Viola reported at the 10th International Cancer Congress held in Houston, Texas in May 1970, the study showed that after a period of 10 months, 70 % of rats treated developed malignant tumours of the skin and lungs (Viola, 1970; 1971). Immediately following the May 1970 communication, Prof. Cesare Maltoni, then Director of the Addari Institute of Oncology in Bologna, Italy, contacted Prof. Viola to discuss the findings.

While Prof. Viola was conducting his research, Prof. Maltoni and his group had launched an extensive programme of medical surveillance on workers of several chemical industries. In 1970 Maltoni started to detect a higher rate of abnormal cells in the saliva samples collected from workers exposed to VC in the Italian plastics industry (Maltoni et al., 1974b).

On the basis of Viola's experimental results and Maltoni's surveillance of VC/PVC workers, it became urgently necessary to conduct a large-scale experimental research project to better evaluate the carcinogenic potential of VC. Since Maltoni's institute specialised in occupational cancer prevention and rodent cancer bioassays, the major Italian VC/PVC producer at the time, Montedison, expressed interest in supporting research on the potential carcinogenic effects of VC. Later, other European PVC producers joined Montedison, namely ICI (the United Kingdom), Solvay (Belgium) and Rhône-Prugil (France), giving rise to the European Cooperative Group for the study of biological effects of VC.

In July 1971, Maltoni began a large project of multiple integrated experiments to study the carcinogenicity of VC in a laboratory at the Castle of Bentivoglio in the province of Bologna, Italy. This was partly funded by The Bologna Hospital Administration of which the Institute of Oncology 'F. Addarii' was a part. The project involved administering VC by different routes of exposure, at different doses/concentrations and for different periods to animals of both sexes, of various species (rat, mouse, hamster), strains and ages. The project lasted ten years and encompassed the use of more than 7 000 animals observed until spontaneous death; more than 200 000 histological slides were examined.

The financial resources required at the time amounted to more than USD 2 million which came mainly from public institutions and also from the chemical industry (Maltoni et al., 1981). The main results of the experiments were as follows:

1. VC was carcinogenic in all tested animals (rats, mice, and hamsters), producing tumours in the mammary gland, lung, zymbal gland (a gland not present in humans), skin, angiosarcomas of the liver, and others (Table 8.1);

2. VC was carcinogenic when administered by inhalation, ingestion, prenatal exposure ([4]) and possibly by intraperitoneal and subcutaneous injection;

3. a correlation existed between concentration, daily dose and length of exposure, and tumour incidence;

4. newborn rats were more susceptible to the carcinogenic effects of VC on the liver;

Table 8.1 Correlation of tumours in rodents to VC exposure

	Rat	Mouse	Hamster
Mammary malignant tumours (mainly carcinomas)	+	+	
Zymbal gland carcinomas	+		
Nephroblastomas	+		
Liver angiosarcomas, angiomas and fibroangiomas	+	+	+
Angiosarcomas, angiomas and fibroangiomas of other sites	+	+	(+)
Hepatomas	+	(+)	
Encephalic neuroblastomas	+		
Forestomach papillomas and acanthomas	+	(+)	+
Lung adenomas	+	+	
Cutaneous epithelial tumours	(+)	(+)	(+)
Melanomas			(+)
Acoustic duct epithelial tumours			+
Lymphomas and leukemias			(+)

Note: + denotes 'clear evidence of carcinogenicity'; (+) denotes 'borderline evidence of carcinogenicity'.

Source: Maltoni et al., 1984.

([4]) Experimental animal studies gave an early indication of foetal toxicity, which is an issue that emerges from several chapters e.g. Chapter 5 on Minamata; Chapter 7 on tobacco and Chapter 10 on BPA in this volume as well as the chapters on DES, radiation and PCBs in vol. 1 (EEA, 2001). This issue is also taken up in Chapter 26 on science for precautionary decision-making.

5. in rats multiple organs were sometimes affected by the carcinogenic effects of VC;

6. later it was shown that VC induced the onset of tumours at concentrations as low as 10 ppm by inhalation and 0.3 mg/kg body weight by ingestion. Although these did not reach statistical significance, they were considered to be biologically relevant (Maltoni et al., 1977).

Maltoni presented his early results to the scientific community at the 2nd International Symposium on Cancer Detection and Prevention, held in Bologna in April 1973. This presentation does not appear to have attracted the attention of government regulators or the general scientific community. Manufacturers aware of Maltoni's findings were still operating under the 'secrecy agreement' and would continue to do so until 1974. In fact, a meeting between NIOSH and the industry representatives from Dow, Ethyl, Union Carbide and the MCA took place on 17 July 1973 but failed to include mention of Maltoni's presentation at the Bologna Conference a few months earlier. Viola's finding of cancers at exposures of 30 000 ppm was mentioned at the NIOSH meeting but not the evidence of cancer at 250 ppm in Maltoni's studies (Markowitz and Rosner, 2002, p. 189, Ref 106). The latter findings were not published until 1974 in the proceeding of the Conference (Maltoni, 1974b).

It was not until 22 January 1974 that B.F. Goodrich alerted the government and the next day issued a public press release announcing it was investigating the deaths of three workers at its VC/PVC plant in Louisville, Kentucky who had died of an otherwise extremely rare cancer called liver angiosarcoma (Markowitz and Rosner, 2002, p. 191, 192). In fact, Dr John Creech, who had identified the rare bone disease acroosteolysis among Goodrich workers ten years earlier had now identified not three but four cases of angiosarcoma deaths from 1968 to 1973; all were among men working in the PVC polymerisation section of the factory (Markowitz and Rosner, 2002, p. 192; MMWR 1974). This time he was sounding an alarm about worker deaths from a cancer so rare that it accounted for just two dozen deaths in the whole country annually — making four deaths among the several hundred plastics workers akin to an epidemic. More damning still, this rare cancer was also showing up in Maltoni's experimental animals at exposures that were half the workplace exposure limit (Creech and Johnson, 1974).

Creech ultimately identified seven cases of liver angiosarcomas in the Goodrich plant between 1964 and 1974, all among 'pot cleaners' who were lowered into polymerisation reactor tanks 10 feet deep, with no more than a six foot opening for fresh air, to chip polymerised residue off the tank insides (Markowitz and Rosner, 2002, p. 192, 193).

8.4 1974: governments swift response

In the US, governmental response was swift. OSHA held a fact-finding hearing on the possible hazards of manufacturing and using VC and PVC in Washington DC on 15 February 1974. Prof. Maltoni was invited to give an oral presentation of his experimental results — the first time that his findings came officially to the attention of the public and government officials. At the end of the hearing, Dr Selikoff of Mount Sinai Medical School in New York stood up and said 'no question, but I rise merely to voice the thanks of the American scientific community for the beautiful piece of work you have done' (Maltoni, 1974c). Shortly thereafter, Creech and the B.F. Goodrich Director of Environmental Health published the medical report of the four deaths from liver angiosarcomas in workers employed in the Louisville plant in 1968, 1971, and two deaths in 1973 (Creech and Johnson, 1974). A footnote by the editor noted that Prof. Maltoni was the first to show the relationship between exposure to VC and angiosarcoma in mammals. Indeed, it is evident that the notification of liver angiosarcoma in workers exposed to VC by B.F. Goodrich to employees, to NIOSH and to the public was influenced by Maltoni's experimental data. The first results of Maltoni's work were published in 1974 (Maltoni, 1974b). Results of the full project were published in 1981 and 1984 (Maltoni et al., 1981 and 1984).

On 5 April 1974 OSHA established that the occupational environment in VC plants should be monitored so that no employee was exposed to VC at a concentration exceeding 50 ppm (127.0 mg/m^3) (Federal Register, 1974). A few months later the OSHA standard was lowered again to a ceiling of 1 ppm, following Maltoni's May 1974 communication at the New York Academy of Sciences that VC was even carcinogenic when administered to rats via inhalation at 50 ppm (Maltoni and Lefemine, 1975). Later, in 1976 Maltoni reported the onset of tumours considered biologically correlated (but not statistically significant) in rats exposed to low dose of VC, namely: liver angiosarcoma and Zymbal gland carcinoma down to 10 ppm by inhalation and 1 mg/kg by ingestion. None of the specifically VC-related tumours were found at doses of 1 ppm (by inhalation) and 0.03 mg/kg by ingestion (Maltoni et al., 1977).

Subsequent VC carcinogenicity bioassays on rodents confirmed the results of Maltoni's project (Keplinger et al., 1975; Lee et al., 1978; Feron and Kroes, 1979). Despite this very strong evidence the US plastics industry lodged an appeal against the OSHA 1 ppm standard. They lost the case in January 1975 and received a scathing condemnation from the judge (see Box 8.1).

Industry responded quickly and easily to the new standard. An analysis in 2000 found that the costs of industry compliance with the 1 ppm standard were only USD 278 million. Industry had earlier estimated that it would cost them up to USD 90 billion and 2 million jobs. As the *New York Times* noted, 'not one of the doomsday predictions (from industry) has proven accurate', noting also that supplies of VC had expanded, prices had not increased and the industry was expanding, not contracting (Rattner, 1975).

This public relations tactic of using an industry trade association to threaten and sue regulators and issue claims no member company would dare make in its own name would become more familiar after 1974 (see Chapter 3 on lead in petrol and the tobacco case studies in Chapter 7).

Industry has generally exaggerated the projected costs of meeting new regulations, see Chapter 23 on understanding and accounting for costs of inaction.

Angiosarcoma of the liver is considered very rare in humans, with only 20–30 cases per year reported in the US (Gehring et al., 1978; ATSDR, 1995). In the years 1975–1978, immediately following Creech and Johnson's first reports of liver angiosarcomas in workers, medical records, pathological material and medical surveillance revealed other liver angiosarcomas in workers exposed to VC, both in the US and in other countries. According to the Liver Angiosarcoma Registry maintained by Imperial Chemical Industries (ICI) in the United Kingdom 103 cases of liver angiosarcoma were reported among workers exposed to VC in various countries in the period 1974–1983 (Stafford, 1983). VC liver cancer deaths have also been reported in Europe and Asia (see Box 8.2 on the IARC Monograph).

Industry responded to these initial cases of liver cancer by commissioning an epidemiological study of the cancer risk in VC-exposed workers. It concluded that 'the overall mortality (of workers in the vinyl industry) was 75 % of what would be expected in a comparable population of US males' and that 'no cause of death showed a statistically significant excess over what would be expected in a comparable US male population' (Tabershaw and Gaffey, 1974; Markowitz and Rosner, 2002, p. 227). However, it did note that, 'cancers of the digestive system (primarily angiosarcomas) respiratory system, brain, and cancers of unknown site, as well as lymphomas, occurred more often than expected in those members of the study population with the greatest estimated exposure' (Tabershaw and Gaffey, 1974; Markowitz and Rosner, 2002, p. 227).The study

Box 8.1 The judicial critique of industry's lack of action on VCM

In January 1975 Justice Tom Clark, retired from the US Supreme Court, heard the appeal against OSHA for the US Court of Appeals for the 2nd Circuit. Noting the industry policy of delay, feigned ignorance and irresponsibility, he rejected all of the basic arguments of the industry and observed that 'strong warning signals … of long before' had been ignored. Despite years of warnings and research since 1949, including the AOS episode, 'nothing was done' (Markowitz and Rosner, 2002, p. 222–223).

The judge also noted that the ultimate facts regarding the proper standard for protecting workers were 'in dispute' and 'on the frontiers of scientific knowledge' but that 'the factual finger' pointed to the need for a low exposure limit, based on the animal evidence. The OSHA standard came into effect on 1 April 1975.

This favourable ruling for workers and the public, however, was followed by a setback in the US Supreme Court decision of 2 July 1980 in the benzene case which forced OSHA to provide quantitative evidence that there would be a 'significant risk of material health impairment'. OSHA lost its case for a 1 ppm standard for benzene. Dissenting Judge Thurgood Marshall noted that this placed 'the burden of medical uncertainty squarely on the shoulders of the American worker' (Landrigan and Nicholson, 1998). The precautionary principle is designed in part to reverse this burden of proof of harm so that risk makers, not risk takers, have to show, at least beyond reasonable doubt, that chemicals and other stressors are acceptably safe for workers, consumers, and the environment.

was criticised by experts at NIOSH for not including some 75 % of workers with the longest exposure (e.g. for over 20 years) where the greatest cancer risk was to be expected. When more of these were found by independent investigator Dr Joseph Wagoner, he calculated that there was a 57 % excess of cancer deaths in the workers (Markowitz and Rosner, 2002, p. 227). Wagoner explained to a Senate Committee that the Tabershaw-Cooper study had diluted the cancer risk by including recently hired workers with only a year or two of exposure. In his study Wagoner only included workers who had been exposed for over 15 years since he knew that 'we were looking for the *latent effects* or the effects of a carcinogen which appear many years after a person was initially employed' (Senate Committee on Commerce, 1974).

Other experts pointed out that comparing workers' death rates with all US males was likely to underestimate the risk as workers were mainly fit whereas all males included the unfit, the unemployed and the disabled. This is called the 'healthy worker effect' which means, in general, that the expected cancer mortality rate for workers with sufficiently long exposure time for cancer latency if there were no occupational cancer risk should be around 75–80 % of the rate expected for all males in the population from which they came (Fox et al., 1982) (see Chapter 26 on science for precautionary decision-making which identifies these and other methodological limitations of much of the health and environmental sciences which try to avoid wrongly labelling an agent as hazardous (a 'false positive') more than trying to avoid wrongly labelling an agent as being safe (a 'false negative')). See also Chapter 2 on the precautionary principle and false alarms.

8.5 1974–present: does VCM cause brain cancer, other cancers and reproductive effects?

Although by the 1970s the industry was no longer able to deny evidence of liver angiosarcoma, Sass et al. (2005) document continued efforts to suppress or play down the evidence of other cancer types, particularly brain cancers.

In an internal memo in 1976, Ethyl Corporation acknowledged risks for liver angiosarcoma, brain, and lung cancers (Sass et al., 2005). A review by the International Agency for Research on Cancer (IARC) in 1979 determined that VC exposure was a known human carcinogen (Group 1) associated with cancers of the liver, brain, lung and haemo-lymphopoietic system, and that there was no exposure level below which an increased risk of cancer would not occur in humans, that is, no threshold or safe level of exposure (IARC, 1979). A second IARC review in 1987 and a third update in 2007 re-confirmed the previous evaluations and updated the scientific references supporting their conclusions (IARC, 1987; 2008). The most recent IARC update additionally noted that animal studies suggest a higher susceptibility to cancer when exposures take place early in life (Grosse et al., 2007; IARC 2008).

A 1991 study of a VC-exposed worker cohort by Wong and co-workers at first reported an, 'excess in cancer of the brain' (Wong et al., 1991). However, at the request of the chemical industry, which had funded this study, two of the authors made a public retraction two years later, saying that, 'We conclude that our finding of an excess of brain cancer among US vinyl chloride workers reported earlier was not likely related to the chemical' (Wong and Whorton, 1993; Sass et al., 2005; Markowitz and Rosner, 2002, p. 229, 230).

In 2010 The Center for Public Integrity's Jim Morris reported on a lawsuit concerning a brain cancer cluster surrounding a chemical plant operated by Rohm and Haas, now a subsidiary of Dow Chemical Co. In their defence, 'Experts for Rohm and Haas argue that the link (with brain cancer) is tenuous at best and concede only that vinyl chloride in high doses can cause a rare liver cancer called angiosarcoma' (Morris, 2010). Morris's report of the proceedings states, however, that the industry-funded study that Rohm and Haas relied on 'failed to include as many as two dozen fatal cases of brain cancer' — which significantly compromised the ability of the study to detect an elevated brain cancer risk (Morris, 2010).

Reports of excessive deaths from liver carcinoma in workers exposed to vinyl chloride have been published since the mid-1970s in the US (Mundt et al., 2000), France (Saurin et al., 1997), Germany (Weihrauch et al., 2000), the European four-country study (the United Kingdom, Sweden, Italy, Norway) (Ward et al., 2001), Taiwan (Wong, 2002); Italy (Pirastu et al., 2003) and Japan (Makita et al., 1997).

Panel 8.1 provides a personal reflection of some events in the United Kingdom following the Goodrich announcement.

Panel 8.1 VCM: a personal perspective of a year in the United Kingdom after the Goodrich announcement of 1974

Charlie Clutterbuck

After the Goodrich announcement about their three workers with liver cancer, some very expensive and comprehensive measures were taken to deal with the VC hazard. In the United Kingdom, the Employment Medical Advisory Service (EMAS), with the help of the Factory Inspectorate and industry initiated many studies (Forman et al., 1985). The PVC manufacturing units were the subject of closest examination. VCM production plants and PVC fabrication processes were also investigated; so too were warehouses storing PVC, transportation services, meat packers using PVC wrappers, drinks contained in PVC bottles, and emissions into the atmosphere.

Later there would be research into the incidence of liver cancer in the vicinity of VCM plants, where some plants were clearly more dangerous than others (Elliot and Kleinschmidt, 1997). Initially monitoring was carried out irregularly, and then accurate to only about 200 ppm. Later this improved to 10, then 1 ppm, then 1 ppb. Within a few years, it was carried out continuously, in such a way that the levels were known to workers immediately. Soon after alarm systems were introduced control engineering concentrated on improved ventilation systems, reducing leakages at valves and finding ways of cleaning the autoclaves where the vinyl chloride is polymerized, using high pressure water systems.

Within the first year, GBP 9 million was spent on re-organising and improving plant design in the United Kingdom. A further GBP 4 million was estimated to have been lost in production. There may have been the same exaggeration of costs beforehand that there was in the US, but it was all less transparent in the United Kingdom. While much of this cost would have been unnecessary if control measures had been built in at the design stage, it must be granted that the industry did undertake expensive control procedures. Why were these extensive measures undertaken? Coal miners and coke oven workers never got that sort of investment, despite their dust diseases and lung cancers.

There are perhaps two main reasons. Angiosarcomas develop so gradually that they are often well established by the time of diagnosis. The combination of aggressive growth, few treatment options, and extreme rarity makes angiosarcoma one of the deadliest cancers. The moral obligation was clear, especially considering the industry's failure to spot it previously. The rarity of the disease also meant that the causal connection with vinyl chloride was undisputed. What if VCM had caused lung cancer? We may not know even today. And it would have been disputed for many years.

The second reason was that the nature of the plastics industry meant that the hazard was controllable. There were six VC fabrication plants, and a similar number of PVC manufacturing plants. The costs of control, though high, were relatively low in such a capital-intensive industry. If the chemical was widely distributed — like VC's close relative, trichloroethylene (trike), which was found in every engineering shop in the country, it would have been much harder to control.

Until the VC cancers, the plastics industry was perceived as 'clean'; a lot cleaner than the mines or the mills around. But just because there was no evidence of harm the lack of evidence did not mean there was no hazard. This worried the toxicologists and epidemiologists who have since been more alert to toxic possibilities.

The reaction of the trade unions was different in the United Kingdom to that in the US. In the US the main union the Oil, Chemical and Atomic Workers Union (OCAW) had already been on strike for improved health and safety so they took up the campaign vigorously. Their role was critical in the setting of the new Threshold Limit Values — the concentrations workers were allowed to be exposed to.

In the US there were transparent court hearings, where the unions went for a 'no detectable level'. The court decided the level should be 1 ppm, with a 15 minute excursion to 15 ppm allowed, and that that was technically feasible. However in the United Kingdom there was a tripartite committee of the TUC, CBI and government which produced a Code of Practice. This is less legally binding, and it recommended working to 25 ppm.

Panel 8.1 VCM: a personal perspective of a year in the United Kingdom after the Goodrich announcement of 1974 (cont.)

Action taken by workers in the United Kingdom was varied. At ICI Runcorn, spasmodic strike action was taken over a period of nine months for 'danger money'. At Vinatex, Chesterfield, concern was centered mainly on the risk of acreosteolysis, as 20 men suffered from this, and in getting compensation for it. This was typical of UK trade unions at that time, where compensation was more important than prevention.

Elsewhere the workers left it to their national unions to deal with. The national TGWU officer told me that 'they were already looking after everything'. This struck me as odd in comparison to the US union reaction. None of the three main UK unions — GMWU, TGWU, and ASTMS then had their own Health and Safety Officers ([5]). The GMWU made the most effort to inform, using the information from the International Chemical Federation. The TUC's Medical Adviser, Dr Robert Murray said: 'What you've got to say to the workers is that the risk is small; that apart from the risks involved when he drives a car and eats too much, and drinks too much, here is another risk which he has got to live with' (*Nature*, 15 February 1974) ([6]).

I contacted the local unions at BP Baglan Bay — and later at ICI Hillhouse. While visiting Baglan Bay, one of the managers said to me 'Actually we are quite pleased about vinyl: it's the only issue that we are in agreement on with the unions'. I knew there must be something wrong with communications, so made sure the unions got all the information coming from the US and the scientific press, both directly and indirectly through programs like TV 'World in Action'. The attitude changed dramatically. The local unions invited me on site. Now I was refused entry by the management. The workers threatened a 24-hour strike — a massive ordeal for a petrochemical plant. But eventually we had to meet outside the plant — and on the TV programme on an 'Open Door' programme. TU reps at ICI Runcorn said that the same thing happened there — that once they were informed by organisations outside their traditional union sources, they could look after their members' interests better.

The petrochemical industry was successful in removing the grosser hazards while keeping the issue confined to the risk of rare cancer. The arguments were not taken up about related chemical — like trichloethylene, nor did the industry accept that other cancers were causally related. The arguments also confined the fears mainly to the fabrication units, less to those handing the finished product PVC. Over the years the consumer lobby has made sure that residual VC in PVC is cleaned out, and there has been replacement of PVC in food wrapping.

Among the lessons learnt for us 'radical' scientists was the role of science in health matters (Clutterbuck, 1986). Good scientific work could be left in academic filing cabinets, having no impact on people's health. We needed to translate that work, without twisting it, to what people would understand. As a result of the VC experience, a group of scientists at the British Society for Social Responsibility in Science set up the magazine *Hazards Bulletin*: it is still alive and well after 35 years but now known simply as 'Hazards'.

([5]) The 1974 Health & Safety Act made provision for the trade unions to appoint their own safety representatives from amongst the employees and provided for their offsite training by the TUs. This led to ASTMS and GMWU appointing their first National H&S Officers in 1977/1978.

([6]) Dr Murray had previously played down the risks from the potent occupational carcinogen BCME three times in 1969, 1971 and 1974 when the trade union safety representative, Andrew Tree, sent him the US studies and his own analysis of lung cancer deaths in some young, non-smoking men in his BCME exposed colleagues. It was to be 1982 before the UK BCME workers at Mr Tree's Welsh plant were told of the risks, some eight years after the US OSHA had labelled BCME as a human carcinogen (Doyal et al., 1983).

In summary, VC exposure has been associated with the following, in addition to angiosarcoma of the liver:

- brain cancer (Byren et al., 1976; CMA, 1998; Monson et al., 1975; Weber et al., 1981; Environmental Health Associates, 1986; Wong et al., 1991; Mundt, 2000; Lewis and Rempala, 2003; IARC, 2008);
- hepatocellular carcinoma (Byren et al., 1976; CMA, 1998; Pirastu et al., 1990, 1998; Simonato et al., 1991; IARC, 2008);
- hemolymphoreticular neoplasias (Simonato et al., 1991; Weber et al., 1981);
- lung cancer (Buffler et al., 1979; Monson et al., 1975);
- liver cirrhosis (Ward et al., 2001);
- birth defects near PVC manufacturing plants (Infante, 1975);
- miscarriages among VC-exposed workers' wives (Infante et al., 1976a, b; NIOSH, 1977; ATSDR, 2006).

In 2008 IARC published an updated Monograph on vinyl chloride and related compounds such as vinyl bromide, confirming previous assessments (IARC, 2008) (see Box 8.2).

8.6 Some late lessons from vinyl chloride

1. The most important things that changed between 1959 (when internal company advice to lower exposure limits was ignored) and 1974, was that four deaths from a rare liver cancer from one company were publicised (unlike other earlier warnings); that this evidence was supported by strong animal evidence; and that public awareness and concern about toxic chemicals in the environment ensured that this evidence led to quick and radical regulatory and company action, at least in the US. The creation of new US government regulatory agencies — OSHA and the EPA — at the start of the 1970s, in a climate of union and environmental activism and media interest, helped to create this strong and prompt public health response.

2. It turned out that a simple engineering solution had been available all along to

Box 8.2 Conclusions of 2008 IARC Monograph on VCM and related compounds

VCM causes angiosarcoma and heptacellular cancer and the evidence is sufficient to categorise it as a known (Class 1) human carcinogen.

For other cancers *'the Working Group did not find strong epidemiological evidence for associations of exposure to vinyl chloride with cancers of the brain or lymphatic and haematopoeitic tissue or melanoma. Although the associations found for these cancers in specific studies may reflect true increases in risk, the findings were inconsistent between studies, no clear exposure–response relationships were found in the European multicentric study and, for several of the sites, the numbers of observed and expected cases were small'* (IARC, 2008).

The report also uses chemical 'analogy' when evaluating the cancer evidence on vinyl bromide, a chemical cousin of VC but for which there is very much less evidence available than for VC. 'Analogy' is one of the nine criteria that epidemiologist Bradford Hill set out to help experts and others to move from merely observing an association between an exposure and a health effect, like cancer, to concluding that the association is causal (Bradford Hill, 1965).

'In making the overall evaluation the (IARC) Working Group took into consideration the fact that all available studies showed a consistently parallel response between vinyl bromide and vinyl chloride … For practical purposes, vinyl bromide should be considered to act similarly to the human carcinogen, vinyl chloride'. IARC concluded that vinyl bromide is 'probably' carcinogenic to humans (Group 2A) (IARC, 2008).

This reasoning is based in part on 'analogy', a basis for helping to infer likely causality when evidence is scarce. Experience has shown that similar chemical structures commonly exhibit similar toxic effects. Acting on this knowledge enables us to best utilise the very limited data base in toxic substances control.

lower worker exposures and environmental emissions dramatically. Steam-stripping PVC in polymerisation reactors reduced levels of residual VC in PVC resins by 99 %, dramatically lowering exposures in polymerisation plants and PVC fabrication plants. OSHA moved to reduce its enforceable Permissible Exposure Limit from the 1968 TLV of 500 ppm to 1 ppm in the workplace air. The EPA followed with emission standards that greatly reduced the 4 % loss of VC to the environment during PVC production. The VC/PVC industry was easily able to comply and keep growing to this day. It was finally a regulatory success story and another example of how clear and challenging regulations can stimulate innovation ([7]) (Ashford and Hall, 2011; 2012).

3. Although it was threatened that a decrease in worker exposure levels to 1 ppm would cause the collapse of the VC/PVC industry, resulting in losses of USD 60 million annually and 2 million jobs (Washington Post, 1974), an important lesson learned was that technological innovation to reduce exposure levels can indeed be accomplished in a short time without catastrophic consequences on production or employment (Sass et al., 2005).

4. Based on information available to major companies using VC in the 1950s, toxic exposures should have been lowered and applications restricted. However, industry resistance to a discretionary increase of production costs, with the possibility of lost markets as well as decreased profits, is rarely if ever overcome merely by corporate conscience (corporate social responsibility is the current term for this concept). To the business executives who decide what will be made and how, the immediate prospects of regulation, liability and market losses to an informed public are much more persuasive and likely to prompt significant change.

5. The story of the carcinogenicity of VC showed without a doubt the validity of long-term bioassays in predicting not only the general carcinogenicity of industrial agents, but even specific target organs and tissues affected. (Maltoni et al., 1984; Soffritti et al., 2002; Huff et al., 2002). See Panel 8.2 on the value of animal tests in identifying carcinogens without waiting for them to appear in humans ([8]).

6. Although the lowering of the worker exposure level from 500 ppm to 1–3 ppm was undoubtedly a great achievement in 1974, these levels did not continue to be lowered despite experimental evidence which demonstrated even then the risks of exposure at concentrations of 50 ppm and less. The approach to setting exposure levels should be a dynamic one, in which levels are constantly lowered throughout time in light of scientific evidence and technological achievements. This is a lesson that is also found in Chapter 3 on lead in petrol, Chapter 5 on mercury and Chapter 6 on beryllium.

7. The epidemiological evaluation of the carcinogenic effects of VC has certainly underestimated the risk of this compound. From the beginning, attempts were made to reduce the quantification of risk to a few dozen cases of liver angiosarcoma, cases which were discovered often thanks to observations made by workers and clinicians. Beyond liver angiosarcomas however, epidemiological data from the 1970s reported an association between VC and lung cancer, hepatocarcinomas etc. Unfortunately, not enough weight was ever given to these studies, and the 1988 review by Richard Doll, which was widely accepted, concluded that for workers exposed to VC there was no evidence of risk of any other type of tumour than angiosarcoma and a modest risk of lung cancer in workers heavily exposed (Doll, 1988). Doll reported an excess of brain cancers which he dismissed as not statistically significant. However, even in the largest and most well-documented epidemiological study of VC exposure, the average age of the cohort was only 54 years (US EPA, 2000). Given that 80 % of cancer diagnoses are in persons over the age of 55 (ACS, 2005), the absence of a longer time horizon means that not only can we not rely exclusively on epidemiological evidence, but to do so would be a failure of public health, ignoring laboratory evidence

([7]) The link between challenging regulations and the stimulus of innovation was described some years ago (Porter, 1995). It has since been investigated more closely and seems to hold up in many but only specific circumstances (Porter, 2011).
([8]) Extensive research efforts are underway to minimise the use of animals whilst retaining, or improving upon, their value in identifying carcinogens.

while we count the bodies until they become statistically significant.

8. Finally, as stated by Cesare Maltoni, 'the history of VC carcinogenicity has brought forth an important lesson: the studies in the field of environmental and occupational carcinogenesis, particularly in industrialized countries, must … represent an important component of the decision-making processes which regulate the developmental trends of society' (Maltoni et al., 1984).

This issue of slow or hostile corporate responses to early warnings is further examined in Chapter 25 'Why did bisiness not react with precaution to early warnings?' Of course there are, and always have been cases of 'progressive business' ([9]).

Table 8.2 Early warnings and actions

1930s–1959	Acute toxicity of VCM demonstrated in animals and workers in USA, Europe and Russia (where limit of 500 ppm ([10]) exposure was established)
1959	Consultant tells Union Carbide that VCM is more toxic than believed and Dow's toxicologist says 500 ppm limit would lead to 'appreciable' harm
1963	Acroosteolysis (AOL) is observed in workers in Belgium and Romania
1964	Dr John Creech followed up a worker's complaint at US chemical company Goodrich about painfully tender fingers and found four cases of AOL clearly linked to workplace exposure to VC
1965	Esso toxicologist recommends to the ACGIH that VC exposure limit should be 50 ppm. ACGIH accepts industry claims that this is too low and costly and the TLV is left at 500 ppm (Castleman and Ziem, 1988)
1966	European and US chemical companies told that 6 % of VC vat workers had AOL. The results were not shared with regulators or workers
1967	Scientific article by Goodrich researchers identifying 31 AOL cases; first draft mentioned VC as the cause but published article did not. Recommended that workplace exposure be reduced to 50 ppm
1968–1970	Prof. Viola demonstrates 70 % of rats with cancer of skin and lungs at high doses of VCM, i.e. 30 000 ppm over 12 months
1970	Prof. Maltoni finds abnormal cells in workers' saliva
1971	Prof. Maltoni begins large-scale, long-term cancer studies in rats, mice and hamsters (from prenatal exposure to natural death) and TLV in US is lowered to 200 ppm based on non-cancerous liver effects in workers
1973	Maltoni released his first results to the scientific community in the context of the 2nd International Symposium on Cancer Detection and Prevention held in Bologna
1974	Four deaths from rare liver disease (angiosarcoma) at PVC plants of Goodrich, USA, reported to the government and in the media. US government orders lowering of exposure limit to 50 ppm and then to 1 ppm after Maltoni's report of liver cancer at 50 ppm in rats
1979	International Agency for Research on Cancer (IARC) confirms VC as Category 1 human carcinogen for liver, brain, lungs and blood-forming system and found no safe exposure level
1982	IARC re-confirms 1979 conclusions

([9]) The Quakers and some others in the early days of the industrial revolution were pioneers in what, for those times, was progressive business. For example, Josiah Wedgewood on noting the passing of the first effective Factories Act to constrain the excesses of capitalism in 1833, wrote to the UK government asking for similar laws to be applied to his pottery industry.

([10]) Based on one small guinea pig study sponsored by the Bureau of Mines in 1930s which was assumed to provide sufficient evidence to protect workers at an exposure limit of 500 ppm (Markowitz and Rosner, 2002, p. 172). This represents an example of the 'unsubstantiated authoritative assertion'. See Chapter 3 on lead in petrol for other examples.

Panel 8.2 Value of animal testing for identifying carcinogens

James Huff

> *Results of laboratory animal tests to predict human cancer is effective in identifying potential human carcinogens before human exposure, permitting measures to be taken to prevent that exposure, a foolproof way to prevent human cancer.*
> David Rall, former Director of National Institute of Environmental Health Sciences (NIEHS) and creator of the National Toxicology Programe (NTP) (Rall, 2000).

Certain chemicals, mixtures of chemicals, exposure circumstances, lifestyles and personal or cultural habits, occupations, viruses, living conditions, and physical agents have been causally associated with cancers in humans (CalEPA, 1986; RoC, 2011 and IARC Monographs ([11])). Most, however, are not considered potentially carcinogenic and the proportion of 'agents' eventually identified to cause cancer is projected to be relatively low, likely less than 10–15 %. However this is still a large overall number considering approx. 100 000 chemicals in commerce, with an ever larger number of formulations and myriad of products containing these chemicals. Examples of human carcinogens in different categories are listed, with those covered in this volume and EEA, 2001 in bold:

1) Defined chemicals — **benzene,** butadiene, formaldehyde, **vinyl** bromide/**chloride**/fluoride;
2) Mixtures of chemicals — agent orange (TCDD), **polychlorinated biphenyls (PCBs);**
3) Pharmaceuticals — **diethylstilbestrol (DES),** estrogens, phenacetin;
4) Cancer chemotherapeutics — azathioprine, busulphan, chlornaphazine, MOPP;
5) Lifestyles — alcoholic beverages, sunning/tanning, **tobacco** products;
6) Industrial exposures — acid mists, coke ovens, iron and steel founding, leather and wood dusts, rubber industry;
7) Manufacturing processes — aluminium, auramine, coke production;
8) Occupations — chimney sweeps, hair dresser/barber, painters, wood workers;
9) Biologic agents — Epstein-Barr virus, hepatitis B and C viruses, human papilloma virus;
10) Metals and compounds — arsenic**, beryllium,** cadmium, chromium, nickel;
11) Physical agents — **asbestos, ionizing**/ultraviolet **radiations**, UV tanning devices.

For larger and more detailed listings see CalEPA, 1986; CMCRC, 2012; Soffritti et al., 2002; IARC, 2012; NTP TRs, 2012; RoC, 2011.

Operational definition of a carcinogen
A chemical, substance, mixture, agent, or exposure circumstance will be designated as a carcinogen by inducing tumours as evidenced by one or more of these experimental observations:

1) Increased incidence of organ/tissue tumour type(s) compared to controls;
2) Occurrence of tumours earlier than in controls (reduced latency);
3) Development of tumour types not seen or rarely occurring in controls;
4) Increased multiplicity of organ/tissue tumours in individual animals;
5) Increased incidence of total primary tumours: malignant, benign, and/or combined;
6) Increased ratio of total malignant to total benign tumours.

In this operational perspective tumours may be benign, malignant or an appropriate combination of both types (Huff et al., 1989). In some cases preneoplastic lesions (hyperplasia, metaplasia) may be combined with tumours for evaluation, especially with evidence of progression.

These categories also fit into the overall schema of mammalian, including human, carcinogens, yet for humans less is known about these individually; in fact typically only items 1 and 3 are used to associate human cancers with exposures to a carcinogen, with 2 being less common.

1) Increased incidence of tumour type(s) in exposed population compared to unexposed controls (**benzene, metals**, **tobacco**);
2) Occurrence of tumours earlier than in controls (BCME, lung cancer in young workers; DES, clear cell vaginal cancers in young girls);

([11]) IARC Monographs on the Evaluation of Carcinogenic Risks to Humans, vol. 1–100, http://monographs.iarc.fr/ published by International Agency for Research on Cancer (IARC).

Panel 8.2 Value of animal testing for identifying carcinogens (cont.)

3) Development of tumour types not typically seen or occurring only rarely in human controls or populations (**asbestos**, **DES, VCM**).

Current methods to identify carcinogenic potential of chemicals
These rely largely on:

1) Short-term *in vitro* and *in vivo* tests;
2) Mid- and long-term *in vivo* bioassays;
3) Epidemiological investigations;
4) Molecular mechanisms or modes-of-action;
5) Structural-activity-effect-relationships;
6) *In vitro* robotic high-throughput screening (in development);
7) Individual or group scientific interdisciplinary expertise.

> *Primary prevention was … implemented on the basis of the capacity of long-term experimentation in animals to predict similar effects in humans, taking into account biological plausibility but independently of the extent of understanding of the underlying mechanisms.*
> Lorenzo Tomatis, who created IARC Monographs and second Director of IARC (Tomatis, 2006).

Thus, scientific, public health and regulatory communities must continue to utilise all available means and strive to develop newer methods and tools to more easily, quickly, cheaply and reliably identify carcinogens in the human milieu. In particular, there is a need to reduce numbers of animals used in testing for carcinogenic activity and in general to encourage their replacement with other, equally effective, non-animal methods.

This effort continues. However, since adequate human studies are typically absent, are costly and time-consuming or of low power or sensitivity, and alternatives to animals have so far proven unsuccessful, the most useful time-proven method for identifying potential human carcinogens continues to be long-term carcinogenesis experiments (Huff, 1999; Rall, 2000; Tomatis, 2006).

Of approx. 120 recognised human carcinogens (IARC lists 107, RoC 54; with duplications), as well as those probably (61 agents, IARC) or reasonably anticipated (186 agents, Report on Carcinogens (RoC)) to be carcinogenic to humans, all that have been tested adequately are likewise carcinogenic in mammalian cancer bioassays (IARC, 2012; RoC, 2011). Many were identified first in animals and only subsequently in humans (Huff, 1993, 1999). This knowledge, together with similarities in mechanisms of carcinogenesis across species, led to the scientific logic and public health strategy that chemicals shown clearly to be carcinogenic in animals should be considered as being likely and anticipated to present cancer risks to humans; e.g. IARC Monographs Preamble 2012 ([12]); RoC ([13]).

The central aim of hazard identification efforts is cancer prevention, largely by reducing or eliminating exposures to chemicals that cause or are suspected of causing cancer and other diseases (Huff, 2011; Tomatis, 2000).

'Primary prevention has the double ethical privilege of intervening for the purpose of avoiding damage to health for the present and future generations' (Tomatis et al., 1997).

Value and validity of animal bioassays for predicting human cancers
Long-term carcinogenesis bioassays using experimental animals are the most predictive method for identifying likely human carcinogens (Tomatis, 1979; Huff, 1999a; Huff and Melnick, 2006). Since the 1960s, bioassays have proven a mainstay for identifying chemical carcinogens, establishing occupational exposure standards and primary cancer prevention (Tomatis and Huff, 2001). Most importantly, long-term bioassays are both predictive (prospective) and confirmatory (retrospective) for human carcinogens (Fung et al., 1993, 1995). The value and validity of long-term chemical carcinogenesis bioassays centre on the following nine facts (Fung et al., 1993; Huff, 2010; Maltoni, 1976, 1976a; Tomatis, 1979, 2000; Tomatis et al., 1989, 1997, 2001) (list modified from Huff, 2010):

([12]) http://monographs.iarc.fr/ENG/Preamble/index.php.
([13]) http://ntp.niehs.nih.gov/?objectid=03C9AF75-E1BF-FF40-DBA9EC0928DF8B15.

Panel 8.2 Value of animal testing for identifying carcinogens (cont.)

1) Rodents and humans are mammals; there are more similarities — physiologically, pharmacologically, biochemically, genomically — than differences; often being quantitative and not qualitative;
2) All known human carcinogens that could be tested experimentally are likewise carcinogenic to animals;
3) Nearly one-third of human carcinogens were first discovered in animal bioassays;
4) One-third would likely be larger but several human carcinogens were discovered in early industrial times (e.g. benzene), predating standard, more frequent bioassays and some human carcinogens are undefined 'exposure circumstances' (e.g. aluminum production, furniture/cabinet making, rubber industry) not readily testable in animals;
5) For those chemicals known as both animal and human carcinogens, there is at least one common cancer-induced tissue/organ site between both mammalian species;
6) Findings from independently conducted bioassays on the same chemicals are consistent, albeit sometimes with additional or different target sites;
7) Bioassays both predict (prospective: 1,3-butadiene; trichloroethylene; TCDD; VCM) or confirm (retrospective: arsenic, benzene) human carcinogenicity;
8) Most chemicals early studied in animals had an a priori suspicion of being carcinogenic, while later randomly selected chemicals identified fewer carcinogens;
9) Less than 10–15 % of all chemicals if evaluated in bioassays would be predicted to be carcinogenic.

No other *in vitro* assay or *in vivo* bioassay or combination of tests, or even epidemiology (Gennaro and Tomatis, 2005; Huff, 2010, 2011; Huff et al., 1991; Rall 1988, 1990, 1994, 2000; Tomatis, 1979, 2000, 2006; Tomatis and Huff, 2001; Tomatis et al., 1989, 1997, 2001), can claim these collective facts and advantages. Of course not all animal (or human) carcinogens are equal, and one must combine the collective experimental findings with experience to best predict human cancer risks from chemicals judged carcinogenic to animals (Fung et al., 1993; Soffritti et al., 1999, 2002).

Despite the predictive success of cancer bioassays using laboratory animals there is vested interest opposition to their use in identifying carcinogens for preventing cancer:

> *Primary prevention of cancer has stumbled from the very beginning because of the interference of powerful economic interests which perceived that any data indicating a possible cancer risk after exposure to industrial chemicals jeopardises their profits, the protection of which being more important than the protection of human health.*
> Tomatis, 2006.

The history of public health is characterised by persistent struggles between short-term economic interests and long-term public, environmental, and occupational health concerns. Intelligent and judicious use of long term animal cancer testing to identify likely human carcinogens has played, and is playing, a critical role in helping public health win the continuing battle on preventing cancers. Meanwhile extensive research efforts are underway to minimise the use of animals whilst retaining, or improving upon, their value in identifying carcinogens.

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9 The pesticide DBCP and male infertility

Eula Bingham and Celeste Monforton

Dibromochloropropane (DBCP) is a pesticide used against nematodes (roundworms or threadworms) that damage pineapples, bananas and other tropical fruits. It was introduced into US agriculture in 1955 and approved for use as a fumigant in 1964. By 1961 laboratory experiments had shown that it made the testicles of rodents shrink and significantly reduced the quantity and quality of sperm. Nonetheless, the compound was widely marketed and became a commercial success.

In 1977, workers at a production plant became worried that they were unable to father children. An emergency study by a US government agency discovered that in many cases the workers were suffering from deficient or absent sperm. While controls were improved at US facilities, the product continued to be marketed and sprayed in Latin America, the Philippines, some African countries, and elsewhere.

By the 1990s, tens of thousands of plantation workers in these countries had allegedly suffered adverse reproductive effects from DBCP use. The story continues today with contentious legal claims for compensation, contamination of drinking water and industry attempts to prevent a Swedish documentary on the issue from being screened.

This chapter looks at the knowledge available about the hazards and the actions taken, or not taken, to avert them. The DBCP story is significant as it is the first clear example of reproductive damage to workers who manufactured and used a synthetic chemical. This is one of many examples supporting the growing concerns about increasing rates of reproductive and developmental disease, and about the endocrine disrupting chemicals that seem to be playing a role in these disorders.

Protecting production workers, users, consumers and the environment from chemicals that may damage reproduction demands closer integration of scientific disciplines, as well as government action. The lessons of DBCP may help in ensuring timely protection from harm, based on precautionary approaches to scientific evidence.

> 'If anyone wants to use a male birth control drug, I think we have identified one, but it is not very pleasant to use.'
>
> — Dr Charles Hine, Shell Contractor, c. 1960, quoted in Goldsmith (1997).

9.1 The discovery 1977: 'our union members are sterile'

In July 1977, one of the authors of this chapter (Eula Bingham, then US Assistant Secretary of Labor for Occupational Safety and Health) was contacted by Tony Mazzocchi, Vice President of the Oil, Chemical, and Atomic Workers International Union (OCAW) in the United States. He wrote:

> 'In a chemical factory in California during a lunch hour, several workers confided to each other that they were worried about not having children. One worker had a child, but had been trying for another for almost two years and two other young workers had no children and were concerned that there was something wrong. Their wives had been examined and now they thought it might be that they themselves had a problem. When the concerns were passed to other workers, the union arranged for the seven of them to have sperm counts performed. The sperm counts were either zero, or so low, that they showed the men sterile and the union was contacting the US National Institute of Occupational Safety and Health (NIOSH) to perform a Health Hazard Evaluation'.

The chemical responsible for causing sterility in the workers at the California chemical plant was 1,2-Dibromo-3-Chloropropane (DBCP). The compound was first produced in the United States in 1955 and used as a soil fumigant to control nematode worms in the soil. DBCP products carried trade names such as Fumazone, Nemagon, Nemaset, and Nematox (US EPA, 1979; OSHA, 1977a and 1977b; Misko et al., 1993; Clark and Snedeker, 2005; NIOSH, 1977) and were primarily used to protect crops, such as pineapple, bananas, sugar cane and other produce, mostly in the tropics. As a soil fumigant, DBCP was applied at a rate of 10–125 kg/ha, either injected directly into the soil or added to irrigation water.

The three main US manufacturers were Dow Chemical Company, Shell Chemical Company and Occidental Chemical Company, but DBCP was also produced in Europe (by International Chemical Company in the United Kingdom) and in Japan. At its peak an estimated 14.7 million kg of DBCP were used annually prior to its suspension in 1977. Most production was used in the US, Latin America, the Philippines and some African countries.

9.2 Early warnings: 1961–1975

The earliest research on DBCP toxicity was carried out by two chemical companies producing the compound for use as a nematocide. By 1958, both Shell and Dow had obtained toxicological data from experiments on rats showing that DBCP was absorbed through the skin and by inhalation and affected the liver, lung, kidney and testes.

Charles Hine, working then under contract for Shell, reported a variety of adverse effects in laboratory animals, depending on the dose of DBCP vapour administered. At an exposure to 5 ppm (5 parts of the chemical in one million parts of air), the testes in male rats shrank, at 10 ppm most of the male rats had testes half the normal size and at 20 ppm all the male rats were sterile. An internal memorandum prepared by Shell noted: 'We understand that Dow Chemical Company have similar data and are very upset by the effects noted on the testes' (Lykken, 1958).

At that time, scientists working for these companies were clearly worried about the results. John Goldsmith, epidemiologist, later wrote: 'I recall a conversation with the late Dr Charles Hine from the University of California at San Francisco about 1960 at a party, when he said, "If anyone wants to use a male birth control drug, I think we have identified one, but it is not very pleasant to use"' (Goldsmith, 1997).

In 1961, the industry toxicologists published their data from experimental studies (NIOSH, 1977), supporting the initial observations (see Box 9.1). These studies revealed that DBCP had two outstanding toxic effects: an antispermatogenic effect in males and damage to kidneys in both sexes of the rat.

9.3 Pesticide registration and inadequate 'hazard control' 1961–1977

The years 1958–1961 were a critical period for decisions on hazard protection and for the use and marketing of DBCP in the United States and globally. Charles Hine, working as an expert

consultant for Dow and Shell, supported a request for the US Food and Drug Administration (USFDA) to register DBCP as an approved pesticide. His report called for workplace concentrations to be less than 1 ppm and impermeable protective clothing to be used if skin contact was likely.

In a series of discussions between the USFDA, Shell and Dow, the regulator noted that at the lowest exposure level studied, 5 ppm, there were adverse effects after repeated exposures and that the current safety precautions therefore appeared inadequate. However, the Shell representative considered the Hine recommendations to be impractical.

By 1961, Torkelson, Hine and colleagues (Torkelson et al., 1961) recommended that occupational exposure to DBCP should be limited by keeping the airborne concentration below 1 ppm, and stressed that suitable analytical methods rather than sensory perception should be depended upon for control. These authors had interviewed men who had been briefly exposed to 1.7 ppm of DBCP and they described a definite, not unpleasant odour (NIOSH, 1978).

In 1961 the US Food and Drug Administration approved and registered DBCP as a pesticide and recommended the exposure limit of 1 ppm. Thereafter the US Department of Agriculture (USDA) was asked to approve the product labelling, which simply stated: 'Do not breathe vapours, use only in a well-ventilated area and avoid prolonged breathing'. As such, the warning label included no reference to testicular damage.

The USDA initially expressed reservations regarding the warnings on the label but Shell argued that at 5 ppm no adverse effects had been reported and that the odour threshold of 1.7 ppm therefore provided an adequate 'warning' of excessive exposure (Thrupp, 1991). USDA accepted these reassurances even though no studies had been performed to indicate that this approach was safe. Virtually no attempts were made to determine if the measures adopted were indeed safe for manufacturing workers or pesticide sprayers. Neither group was subjected to medical surveillance.

In fact, the 'odour threshold' for DBCP exposure was too high to ensure reliable protection against the toxicity reported in the animal studies. DBCP fumes are only a mild irritant and unlikely to be reported as potentially harmful. Workers could therefore be exposed to dangerous amounts of the chemical without being aware of it.

The labelling and workplace exposure precautions were therefore inadequate from the 1950s until 1977, failing to provide accurate information about the potential health effects of DBCP or to ensure safe working conditions, in the light of the animal evidence. The toxicological data available in 1961 on the potential adverse health effects of DBCP was sufficient to have required specific health warnings, personal protective equipment and medical surveillance. None was provided.

Box 9.1 Animal toxicity data for DBCP: 1958–1975

Torkelson et al. (1961) evaluated the effects of exposing rats to DBCP by inhalation for seven hours a day, five days a week for 10 weeks. The lowest concentration, 5 ppm (parts per million), produced an 18.6 % decrease in the mean weight of the testes, which was not statistically significant. Exposure to 10 ppm resulted in a statistically significant decrease (49 %) in the mean weight of the testes and a significant increase in the weight of the kidney (31.7 %).

In another study reported by Torkelson et al. (1961) male and female rats were exposed to 12 ppm DBCP for seven hours a day, five days a week for 10 weeks. Degenerative changes occurred in the tissue where sperm are formed, reducing the number of sperm cells and increasing the proportion of abnormal sperm cells. Significant increases in the weights of the kidneys occurred in both sexes and there were changes in the kidneys of the males. Changes in the livers of both sexes were also noted.

Exposing guinea pigs and rabbits to 12 ppm DBCP vapour inhalation resulted in statistically significant decreases in the mean weights of the testes in both species (Torkelson et al., 1961).

Toxicological studies by European laboratories also reported around 50 % reductions in the weight of testes and in sperm counts and motility (Rakhmatulayve, 1971; Reznik and Sprinchan, 1975). In female rats, the reproductive cycle was disrupted.

9.4 Actions to reduce exposure in DBCP manufacturing: 1977 and 1978

The National Institute for Safety and Health (NIOSH) was created in 1970. Responding to the suspicions of the DBCP manufacturing workers and a request by their trade union, OCAW, for government help, NIOSH (1977) conducted a health hazard evaluation at the Occidental Chemical Company's Lathrop plant. It reported airborne DBCP concentrations of 0.29–0.43 ppm, measured as an eight-hour time-weighted average. Of 13 workers in the production area, nine had no sperm (azoospermia) and another four workers had very reduced sperm counts (oligospermia). The researchers conducting the evaluation for NIOSH found a 'clear increase in the prevalence of oligospermia with increasing exposure' to DBCP (Whorton et al., 1977). These exposure levels were far below those used in the toxicological studies and also below the recommended 'safe' levels for workers of 1 ppm.

With this alarming information, the President of OCAW formally petitioned the US Occupational Safety and Health Administration (OSHA) on 23 August 1977 to take action to limit worker DBCP exposure to 1 part per billion (1 ppb) parts of air and to conduct medical testing to identify cases of sterility and cancer among exposed workers. This call for action was met with a flurry of activity at the federal government level. OSHA issued an Emergency Temporary Standard (ETS) on 9 September 1977 and proposed a permanent standard in November. Public hearings were held in December 1977 and a final standard was published in the Federal Register on 11 March 1978.

The results of the medical examinations of the OCAW workers provided compelling evidence for OSHA action, but the Administration also evaluated all other available information on DBCP as part of the rulemaking process. This included, for example, data from the Dow Chemical facility in Magnolia, Arkansas, where DBCP was manufactured. Air sampling results revealed concentrations of 0.04 ppm to 0.4 ppm of DBCP calculated as an 8-hour time-weighted average. Furthermore, medical tests revealed that 50 % of the 106 workers examined there had either oligospermia or azoospermia.

These data suggested that exposures below 1 ppm were associated with adverse reproductive effects. However, because DBCP is also absorbed through the skin, dermal exposures may have contributed an unknown but potentially significant amount to the workers' total dose of DBCP.

Based on the evidence of the serious adverse reproductive health effects in animals and humans, and its carcinogenicity in animals (see below), OSHA issued a final standard to limit workers' DBCP exposure to 1 ppb (based on an 8-hour time-weighted average), and to 10 ppb over any 15-minute period. OSHA also required employers to provide initial and annual medical examination for DBCP-exposed workers, respiratory protection and training, among other provisions.

The new rules took effect in April 1978 and were not effectively challenged by any interested party. The US National Peach Council did, however, attempt to delay the regulation with a direct plea to OSHA, expressed in a letter to Eula Bingham, co-author of this chapter. The Council argued that:

> 'While involuntary sterility caused by a manufactured chemical may be bad, it is not necessarily so. After all, there are many people who are now paying to have themselves sterilized to assure they will no longer be able to become parents. How many of the workers who have become sterile were of an age that they would have been likely to have children anyway? How many were past the age when they would want to have children? These, too, are important questions.
>
> 'If possible sterility is the main problem, couldn't workers who were old enough that they no longer wanted to have children accept such positions voluntarily? They could know the situation and it wouldn't matter. Or could workers be advised of the situation and some might volunteer for such work posts as an alternative to planned surgery for a vasectomy or tubal ligation, or as a means of getting around religious bans on birth control when they want no more children. We do believe in safety in the work place, Dr Bingham, but there can be good as well as bad sides to a situation' (US National Peach Council, 1977).

This argument found little favour with OSHA.

Meanwhile studies on exposed production workers were conducted in Israel. In a series of publications researchers discovered DBCP-induced sterility in the six workers at a DBCP-production facility that had been exposed for two to ten years (Potashnik et al., 1978). The workers also had an elevated serum concentration for one sex hormone (follicular

stimulating hormone, FSH, which increases with testicular damage) and damage to the testicular tissue responsible for producing sperm cells.

In a related study, 18 of 23 workers (78 %) involved in DBCP production had abnormal sperm counts, including 12 workers with azoospermia. After several years without exposure to DBCP, some of the workers' testicular function improved but the men exposed for more than 120 hours experienced no improvement (Potashnik, 1984). Similarly, 17 years after being exposed to DBCP the extent of recovery from sperm damage was mixed (Potashnik and Porath, 1995).

9.5 DBCP and cancer?

In 1975, as part of a programme to test pesticides for carcinogenicity, the National Cancer Institute reported that DBCP was carcinogenic in rats and mice. Industry representatives criticised the study at an OSHA hearing in 1977 because of the high doses used. Subsequently, a rodent study of both sexes using much lower doses by Dow Chemical at the Hazleton Laboratory in 1977 resulted in carcinomas of the stomach, liver and renal tubules at the highest dose and a statistically non-significant increase in carcinomas at the two lower doses.

Today, animal experiments using high exposure levels are still employed to evaluate the safety of many chemicals. Industry and other interested parties often assert that such experiments are irrelevant to human exposures, which are usually much lower. There are, however, good reasons to doubt these claims. The small number of animals used in experiments (e.g. usually 20 per exposure group) mean that the doses have to be high in order to reveal any possible hazard that thousands of workers (or many more consumers) face at much lower exposure levels. As a result, high doses have been shown, in very many cases, to be reliable predictors of the hazards humans face at much lower doses.

Since 1992, the US Environmental Protection Agency (EPA) has classified DBCP as a 'probable human carcinogen' ([1]). The International Agency for Research on Cancer (IARC) assessed the evidence as sufficient in experimental animals to classify DBCP as a 2B ('possible') carcinogen (IARC, 1999).

9.6 DBCP risks: from manufacturing to pesticide spraying

While OSHA was attempting to protect workers manufacturing DBCP, the US EPA took steps to protect the health of workers using the pesticide. In September 1977, US EPA administrator Douglas M. Costle announced that under the authority granted by the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA) he was suspending distribution of DBCP. Costle noted that he had this special authority 'in situations where the use of that pesticide appears likely to pose an unreasonable risk to man during the period necessary to conduct and complete a more lengthy administrative proceeding.'

The US EPA examined the scientific evidence and, even though early studies of DBCP sprayers in California and Israel had produced mixed results (Glass et al., 1979; Karraazi et al., 1980), determined that the risk of harm was sufficient to take emergency temporary action to protect workers spraying the pesticide. The US EPA prohibition on using DBCP became permanent in November 1979 and applied to all crops, except for pineapples grown in Hawaii. In 1985 the US also prohibited use of DBCP on pineapples.

9.7 DBCP exports from 1969 to the 1980s: spreading sterility?

DBCP was developed for use against nematodes that attack pineapple plants, so it was not surprising that it was also effective on another tropical fruit: bananas. In the mid-1960s, the Standard Fruit Company began testing DBCP on its banana plantations in Central America; by 1969, DBCP was in full-scale use in Costa Rica and Honduras. The pesticide containers were boldly marked with the brand names Fumazon and Nemagon but, like containers in the United States, provided no warnings to workers about the risk of sterility. Moreover, the labels on the pesticides exported were in English. Even if they had been written in Spanish, there is no guarantee that pesticide sprayers could have read them, since many were illiterate.

The US EPA regulatory ban on using DBCP pesticide in the US did not ban Shell and Dow from manufacturing it and the Standard Fruit Company

([1]) http://www.epa.gov/ttn/atw/hlthef/dibromo-.html.

Box 9.2 The Swedish film documentary, the Dole lawsuit and freedom of speech

Maria Albin

'Bananas!', a 2009 documentary by independent Swedish filmmaker Fredrik Gertten, addresses the attempts of 12 banana plantation workers in Nicaragua to sue Dole Food Company (previously named Standard Fruit) for DBCP-induced sterility. The film closely follows the workers and the controversial personal injury Californian lawyer, Juan Dominguez, who took on their claims.

In July 2009 Dole sued Gertten and the film's producer Margarete Jangard, claiming defamation and seeking a permanent injunction against them screening 'Bananas' in public, displaying the film website or giving interviews promoting the film 'in which any portion of the accusations made against Dole in the documentary film Bananas are republished'.

The lawsuit followed other steps by Dole to obstruct the film's release. Dole sought to have the film withdrawn from the Los Angeles film festival where it was due to be shown in June 2009 (it was moved to a 'special case study screening' to avoid possible legal action). Dole also sent a letter to the Swedish ambassador Jonas Hafström in Washington, asking him to take 'appropriate steps to limit its damaging impact, including urging the filmmakers, WG Film AB and Mr Gertten to act responsibly and halt dissemination of this film in the United States of America and Europe.

The media's response to Dole's efforts was robust. Filmmakers launched a petition for free speech during the Los Angeles film festival. The CEO of the German Documentary Film Association wrote a letter demanding that Dole cease its 'attacks on the freedom of information as well as stop your company's inhuman practices in Latin America which the film "Bananas" criticizes.' The International Federation of Journalists likewise condemned the use of the law to evade media scrutiny and public accountability as an unforgiveable violation of free speech.

Gertten and Jangard regarded Dole's lawsuit as a strategic lawsuit against public participation (SLAPP) — a deliberate attempt by a wealthy party to silence its critics by outspending them in launching a legal action. Accordingly, the filmmakers filed an anti-SLAPP motion and a cross-complaint.

Swedish reaction was strong and media coverage was extensive. The film was shown in Sweden's parliament, causing an exchange of letters between the executive vice-president of Dole and the two MPs responsible for the screening, Mats Johansson of the Conservative Party and Luciano Astudillo of the Social Democrats. Their unusually frank letter reflects Swedish public opinion at that stage:

'It seems clear to us that you are misled by your PR-firm on how to influence Swedish opinion, with a poor understanding of our tradition of free speech during more than two hundred years. As the saying goes: all business is local. We strongly recommend a change of bureau and tactics, if you are at all interested in the Swedish market. But first and most we urge you — in the name of free speech — to withdraw your lawsuit against Mr Gertten.'

MPs signed a cross-party petition urging Dole to withdraw their legal action in the name of free speech, and they were joined in these demands by the CEOs of leading food chains. The action was sufficient to make Dole withdraw its legal action in October 2009. It stated that it made its decision in view of the free speech concerns being expressed in Sweden, although it continued to believe in the merits of its case. The filmmakers withdrew their counter-claim but demanded that their legal fees be reimbursed. However, the threat that Dole would reinstitute the action hampered the distribution of the film.

In 2010, a Los Angeles court decided in favour of the filmmakers, stating that the lawsuit had been what is commonly known as a SLAPP, awarding them almost USD 200 000 in fees and costs and enabling Bananas! to be released in the US.

Having made a film about Dole being sued, Gertten has now made a new film about being sued by Dole. 'Big boys gone bananas!' premiered in October 2011 at the International Documentary Film Festival in Amsterdam.

Sources: http://www.bananasthemovie.com/wp-content/uploads/resources/slapp_ruling_nov17_10.pdf; http://www.bananasthemovie.com/wp-content/uploads/resources/bananas_defamation_complaint_july8_09.pdf; http://www.iidh.ed.cr/comunidades/ombudsnet/docs/doctrina/doc_ccpdh_resoluciones/resolucion%20nicaragua%20final.htm; http://www.bananasthemovie.com/wp-content/uploads/resources/letter_dole-hafstrom_june5_09.pdf; http://www.ifj.org/en/articles/ifj-condemns-attempts-by-embattled-food-company-to-censor-free-speech-in-us.

and other growers continued to use it. When Dow informed Standard Fruit that it was halting shipments of DBCP, Standard Fruit threatened Dow with a claim of breach of contract. To settle the matter, Standard Fruit Company agreed to indemnify Dow for any injuries resulting from exposure to DBCP and implement 'applicable work standards in respect of protective clothing, training etc.' as outlined in the OSHA standard.

Shipping records and billing invoices made available through litigation on behalf of DBCP-injured workers reveal that Shell Chemical also sold the pesticide to growers in the Ivory Coast from 1977 to 1980. Another US manufacturer, Amvac Chemical Corporation, sold DBCP in 1979 to companies in the Philippines, Honduras and Nicaragua. DBCP was still used in Central American banana plantations until at least 1985 (New York Times, 2003).

In the Philippines, workers employed by subcontractors of Standard Fruit used DBCP until about 1986. According to reports collected by lawyers, some of these workers became sterile and reported that they had not been informed about the risk of using the chemical and had not been given appropriate personal protective equipment. In Costa Rica too, there was inadequate protection of DPCP sprayers (Thrupp, 1991).

Similarly, medical evaluations of 28 Panamanian banana workers in August 1993 diagnosed 25 with damaged sperm (Navaro, 1993).

9.8 Banana workers bring compensation cases: 1990–2010

In the early 1990s, more than 16 000 banana plantation workers from Central America and the Philippines filed a class action lawsuit in Texas against US fruit and chemical companies, demanding compensation for permanent sterility linked to DBCP. A 1992 settlement in Costa Rica provided USD 20 million for 1 000 workers. In another lawsuit involving 26 000 workers employed in Latin America and elsewhere, the total settlement in 1997 of USD 41 million provided an average compensation of USD 1 500 to each

Photo: © istockphoto/Francisco Orellana

worker. In 2002, a national tribunal in Nicaragua sentenced the American multinational companies to pay USD 489 million in damages and interest to 450 workers affected by Nemagon. In a lawsuit, filed on behalf of 13 Nicaraguan banana plantation workers, Amvac Chemical agreed in April 2007 to a total compensation of USD 300 000 to the now-sterile workers.

These settlements came 20 years after each of these firms knew about the potential reproductive health risks to DBCP pesticide spray workers, which had stopped their use in the US. Nevertheless, the firms marketed and sold DBCP abroad without ensuring that worker health would be adequately protected. Tens of thousands of banana workers still have suits pending in courts in the US and elsewhere but many of the relevant facts are still unclear and contested by the growers.

9.9 Environmental pollution of soils and water by DBCP

DBCP is a persistent and mobile chemical and has been found in the soil, and in ground and surface water in areas where it has been used. Torkelson et al. (1961) noted that 'its relatively low vapour pressure and high density assures a long residence in the soil', depending on the method of application.

Although DBCP has been banned for use in agriculture for more than 20 years it persists in the environment and in water supplies. Underground aquifers in the Sacramento Valley of California are contaminated with DBCP and, depending on the temperature and pH, the chemical can persist for over a century (Peoples et al., 1980; Burlington et al., 1982; California Environmental Protection Agency, 1999). It was the most frequently detected contaminant in California wells in the early 1990s (Bartkowiak et al., 1995).

The 2010 update of the California Well Inventory Database reported DBCP detections in 254 of 1 312 wells sampled. Concentrations of DBCP found ranged from 0.01–1.7 ppb compared to the US EPA and Californian maximum contaminant level of 0.2 ppb. Between 1986 and 2009 DBCP concentrations declined in about half of the wells sampled from 49 % above the maximum concentration level (MCL) of 0.2 ppb to 25 % being above the MCL.

The US-based interest group Environmental Working Group (EWG) analysed 20 million tap water quality tests performed by water utilities between 2004 and 2009 (EWG, 2009). Their investigations identified 191 water systems in 18 states with DBCP levels in drinking water above health guidelines set by federal and state health agencies. Of these, 48 water utilities had DBCP levels above the US EPA's legally enforceable maximum contaminant level of 0.2 ppb. The World Health Organization's guideline value for drinking water quality is 1 ppb (WHO, 2003).

More than 20 years after DBCP was banned, levels continue to exceed health limits in the tap water of over 4 million Californians.

EWG also noted that 'in 38 communities, the levels of DBCP in tap water are above the so-called 'negligible' risk for carcinogens. In 31 communities, the levels ranged from 20–200 times the amount associated with a 'negligible' risk. A particular concern raised was in the case of infants drinking formula prepared with the tap water.'

9.10 Some late lessons

Lessons for science

1. DBCP exposures below the lowest dose tested in animal studies were mistakenly assumed to be safe.

2. While adverse effects on crude testicular morphology and sperm counts were documented, further studies were not carried out to determine the exposure levels that could have provided more subtle indicators of early stage infertility.

3. The early toxicity studies were carried out before modern protocols became available, but continued application of DBCP in developing countries did not lead to the use of updated protocols to assess the toxicity in further detail.

4. Evidence of harm in animals was not seen by many scientists as relevant to humans.

5. Human reproduction may be sensitive to subtle derangements of physiological processes, thereby causing sub-fertility or infertility in the absence of obvious pathology.

6. No attention was paid to the possible effects on sons of exposed women.

7. Routine medical records and health statistics can be of limited use in regard to adverse effects on reproduction.

8. Skin exposure can contribute significant doses of DBCP: air monitoring alone, as with other skin penetrating chemicals, therefore underestimated total doses received.

9. Independent expert assessments e.g. by the US governmental body, NIOSH, were needed to identify harm and to better protect employees.

Communication and use of research evidence

1. The original evidence for DBCP effects on human male sterility came from the lay and local knowledge of the workers and their wives.

2. It was confidentially asserted that DBCP was safe to use without there being any studies of workers or relevant animal studies to confirm this assumption: an example of the '**authoritative assertion but without evidence**' which appears in other chapters.

3. The toxicity information was translated only into very general warnings on labels: no translations were provided for products exported.

4. The animal toxicological findings did not lead to any surveillance studies of men exposed to DBCP at the production plants until after evidence was observed by the workers.

5. No action was taken to avoid the earlier biological 'effects' in animals until they had become 'adverse effects' in people.

6. The application of DBCP was considered essential by growers, including multinational companies, and they considered the toxicity concerns were too small to be significant.

7. The early scientific warnings were not widely reported but confined to specialist scientific journals or internal company communications.

8. Knowledge from the manufacturing risks did not get taken up by the companies responsible for user risks.

9. National standards to control the risks of DBCP were not transferred into international standards to protect workers from globalised exposures to hazardous chemicals.

10. Early warnings about the persistence of DBCP in soils and water did not get acted upon until many years later.

Compensation for victims

1. Much information about the responses of DPCP producers and user companies only emerged via legal procedures in the compensation cases.

2. Compensation cases in the law courts can be difficult, expensive and very time consuming to pursue (see Chapter 24 on protecting early warners and late victims).

9.11 Conclusion

There is now widespread concern about male infertility, and related reproductive problems, such as testicular cancer and developmental defects, in wildlife, workers and consumers (e.g. WHO, in press; EEA, 2012; BCPT, 2008).

The lessons of DBCP are very relevant to these concerns and to the current exposures of many workers and consumers to the endocrine disrupting substances (EDSs) which seem to be playing a role in the reproductive ill health of both humans and wildlife (see also Chapter 13 on ethinyl oestradiol in the aquatic environment and Chapter 10 on BPA).

Protecting production workers, users, consumers, and the environment from chemicals that may damage reproduction needs the closer integration of scientific disciplines, and government actions if the timely protection from harm, using precautionary approaches to the evidence from science, is to be achieved. The lessons of DBCP may help in this.

Table 9.1 Key early warnings about and recognition of DBCP toxicity

1956	Manufacturing of DBCP began
1958	Two independent rodent studies document testicular toxicity
1961	DBCP is registered as an approved pesticide in the US
1961	Animal studies show effects on testes and sperm
1961	Medical examination of workers at a DBCP production plant takes place but testicular function is not examined
1961	Data on persistence and water solubility are published
1969	Use of DBCP at banana plantation in Costa Rica occurs without appropriate warning labels or safety precautions
1975	DBCP is found to be carcinogenic in two species of rodents, both male and female
1977	Episodes of reduced sperm counts occur in US manufacturing workers
1977	US authorities investigate DBCP toxicity, issue new guidelines, enforce new exposure limits and remove approval, except for special pineapple protection in Hawaii
1977–?	DBCP continues to be exported for use outside the US
1990s	Court cases are brought against employers and producers to compensate for adverse health effects in plantation workers in Latin America and the Philippines
1999	State of California decides to regulate DBCP contamination of drinking water
1990s–2010	Compensation cases for DBCP users in South America are won and lost
2007–today	DBCP remains a contaminant of drinking water in 38 cities in California and elsewhere

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10 Bisphenol A: contested science, divergent safety evaluations

Andreas Gies and Ana M. Soto ([1])

Bisphenol A (BPA) is currently one of the world's best-selling chemicals and primarily used to make polycarbonate plastics. It is widely used in common products such as baby bottles, household electronics, medical devices and coatings on food containers. BPA is known to mimic the female hormone oestrogen and has been found to leach from the materials where it is used.

Studies have suggested that even exposure to low doses of BPA may cause endocrine disrupting effects. As with other hormones, it appears that an organism is most sensitive during development but that effects are often not observed until much later in the lifecycle. This means that at the time when the effects become detectable, the chemical exposure has vanished. This makes it extremely difficult to link exposure to effects in humans.

This chapter maps some of the findings in studies of rodents and humans. It also discusses the challenges of evaluating scientific findings in a field where industry-sponsored studies and independent scientific research seem to deviate strongly. The authors offer suggestions for ways to uncouple financial interests from scientific research and testing.

A widely used and dispersed industrial chemical like Bisphenol A is a controversial example of an endocrine disrupting substance that has implications for policymakers. Different approaches to risk assessment for BPA by US and European authorities are presented. It throws light on the ways in which similar evidence is evaluated differently in different risk assessments and presents challenges for applying the precautionary principle.

The intense discussion and scientific work on BPA have slowly contributed to a process of improving test strategies. While traditional toxicology has relied on a monotonic increasing dose-response relationship as evidence that the effect is caused by the test agent, studies on BPA and other endocrine disruptor chemicals (EDCs) have demonstrated the limitations of this approach and adjustments have been made in some cases.

It has also been widely accepted that effects cannot be predicted by simply thinking of BPA as a weak oestrogen and extrapolating from what is observed for more potent endogenous oestrogens. This lesson is particularly evident in the intense pharmaceutical interest in selective oestrogen response modifiers (SERMs).

The chapter is followed by a panel analysing the value of animal testing for identifying carcinogens.

([1]) This paper is based on the scientific opinions of the authors and does not necessarily reflect the opinions or policies of the institutions they are working for.

10.1 The first known endocrine disruptor: early warnings

Bisphenol A (BPA) is one of the industrial chemicals often referred to as 'emerging environmental substances'. This categorisation is in fact somewhat euphemistic. BPA was probably the first synthetic substance known to mimic the natural female sex hormone oestrogen. As early as 1934, Dodds and Lawson (1936, 1938) were searching for synthetic chemicals that could replace expensive natural oestrogen in pharmacological applications. They identified BPA as a weak functional oestrogen, utilising rat test systems that are still in use today. It failed to make a career as a medicine. Later, other substances like Diethylstilbestrol (DES) were discovered by the same team of British scientists (Dodds et al., 1938). The synthetic oestrogen DES was much more potent than BPA and was subsequently used as a pharmaceutical that showed severe side effects (Meyers, 1983).

Not suitable as a pharmaceutical, BPA was marketed as an industrial chemical. In 1957 BPA was polymerised with phosgene, resulting in what is known today as polycarbonate. That started the plastics revolution that has changed the lives of people around the world. At that time everyone thought that plastics, particularly polycarbonate, were significant advances that would improve our lives.

10.2 A growing problem

BPA is currently one of the world's best selling chemicals, with a total annual production of 3.8 million tonnes in 2006 (Association of Plastics Manufacturers, Polycarbonate/BPA group, 2007). In 2005 and 2006, about 1.15 million tonnes were consumed within the European Union (European Commission, 2008). These figures reflect an increase in consumption of 69 % over a seven year period, an annual increase of 7 to 8 %. Most BPA is used to produce plastics, mainly polycarbonate (66 %) and epoxy resins (33 %) (Association of Plastics Manufacturers, Polycarbonate/BPA group 2007). Many other uses have been identified, such as an ingredient in thermal paper. This is why BPA is regularly found in recycled paper (Terasaki et al., 2007; Vinggaard et al. 2000), which is frequently used to produce food containers (Ozaki et al., 2006; Lopez-Espinoza et al., 2007).

It should be noted that the European Risk Assessment Document was not able to identify the purpose of use of more than 7 000 tonnes of the BPA that is consumed annually within the European Union (European Commission, 2008). Commercial BPA contains up to 16 different phenolic impurities that show structural features of oestrogenic chemicals but have never been toxicologically characterised. These 'minor impurities' represent another 10 000 tonnes annually (Terasaki et al., 2004).

Leaching from plastics

Two out of three tonnes of BPA produced are used to manufacture polycarbonates. This clear hard plastic material is increasingly used where transparent and low-weight synthetic materials are wanted; DVDs, modern car roofs and headlight covers, baby bottles and plastic dishes for use in microwave ovens are all made of polycarbonate. These plastic materials can easily be identified by the recycling code 07 in a triangle or the letters PC. Though BPA is a covalently-bound building block of polycarbonates, the monomer is subsequently released over time from the plastic material (Krishnan et al., 1993; Tan and Mustafa, 2003). Leaching of BPA is increased by the age of the material, alkaline conditions and heating. All polycarbonate items are probably a source of BPA. This gives rise to the concern that a growing stock of material has been built up in our homes and in the environment that is a potential continuous source of BPA exposure.

Polycarbonates are probably the main but not the only source of BPA. It also leaches from dental sealants (Joskow et al., 2006), inner coatings of cans and microwave containers (Brotons et al.,1994; Mariscal-Arcas et al., 2009), and in relatively high concentration from medical devices used in intensive care units (Calafat et al., 2009). Thus BPA is found in many matrices including house dust (Butte et al., 2001), indoor air, hand wipes, solid food, liquid food (Wilson et al., 2007) and drinking water (Shao et al., 2008). The European Union Directive 90/128/EEC includes BPA in the list of chemicals with a specific migration limit in food, set at 3 mg/kg (European Commission, 1990). BPA has been found in canned food at concentrations up to 380 μg/kg (Goodson et al., 2002), but only up to 4.5 μg/kg in canned drinks (Cao et al., 2009).

It is not surprising that BPA is one of those ubiquitous chemicals that are a real nightmare for analytical chemists. The substance can leach easily from plastic laboratory equipment and thus contaminate samples that are to be analysed. As with softeners such as phthalates, great care has to be taken to avoid such contamination.

10.3 Identifying the risk was an accident, not the result of a regulatory process

In 1991, a conference taking place in Wingspread Racine, Wisconsin used the phrase 'endocrine disruptor' for the first time (Markey et al., 2002). In 1992 the first scientific paper using this was published by Bason and Colborn (1992). It described indicators of hormonal de-regulation in wildlife and humans and suspected mainly pesticides as the cause of these emerging effects. BPA was added to the list of potential endocrine disruptors one year later. It was by accident that the risks associated with it were re-discovered. In 1993 a team of endocrinologists at Stanford University found an unknown oestrogenic substance that contaminated their assays. Finally they identified BPA leaching from their polycarbonate cell culture dishes when they were autoclaved (Krishnan et al., 1993). It may be surprising that neither any governmental nor any industry programme for risk identification or risk assessment identified BPA as a problematic hormonally-active substance although such programmes had been run in Europe since 1982 with considerable financial and intellectual input from governments and industry. Although several European chemical companies had a history of hormone research over decades, they did not play a role in identifying and assessing environmental chemicals with hormone-disrupting properties. Industry missed a chance to care for their products responsibly.

In 1995 a number of workshops took place in Denmark, the United Kingdom, Germany and the United States to discuss the upcoming issue of hormonally-active environmental chemicals. One year later the book by Colborn, Dumanowski and Myers (1996) 'Our stolen future', with a foreword by former US Vice-President Al Gore, put this issue on the global political agenda. Meanwhile, in the second half of the 1990s, BPA became the most prominent example of an endocrine disruptor in the scientific and public debate.

10.4 Bisphenol beyond Paracelsus

In the past 100 years almost no toxicological textbook failed to quote Philippus Aureolus Theophrastus Bombast von Hohenheim, better known by his nickname Paracelsus:

> 'Alle Ding sind Gift und nichts ist ohn Gift; alein die Dosis macht das ein Ding kein Gift ist' (Paracelsus, 1539)
>
> (All things are poison and nothing is without poison, only the dose permits something not to be poisonous).

Probably all students of toxicology were taught by their professors that sugar and salt and even water can be a poison if the dose is high enough. BPA challenged our belief that high doses produce more serious effects than low ones. Instead, BPA, like natural hormones, frequently produces dose-response curves that are non-linear. In such experiments very low doses or concentrations show a small effect, intermediate doses cause the most serious effects while high concentrations again show no or only moderate effects. These dose-response curves resemble an upside-down 'U' and are therefore called inverted u-shaped dose-response curves (Sonnenschein et al., 1989). Such dose-response curves occur when tumours are induced in transgenic mice (Jenkins et al., 2011), in snail test systems with regard to clutch size (Schulte-Oehlmann et al., 2001), serum estradiol levels in rats (Akingbemi et al., 2004), calcium influx in rat pituitary cells (Watson et al., 2007), effects on pupal weight and sex ratio in the housefly (Izumi et al., 2008), and reproductive performance in female mice (Cabaton et al., 2011) when these animals are exposed to BPA (Figure 10.1).

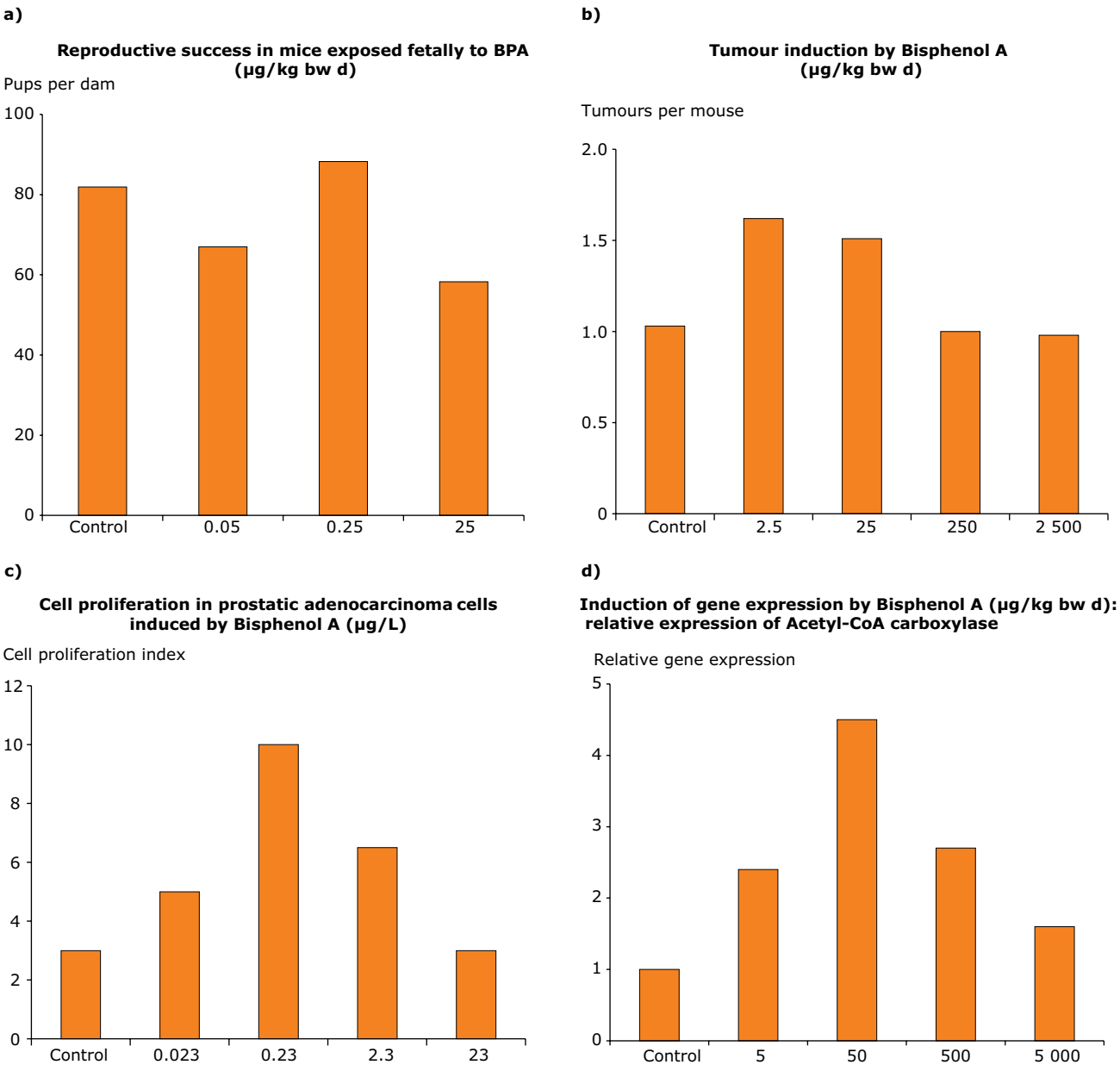
Several mechanisms have been hypothesised to try to explain this phenomenon. The global assessment of state-of-the-science of endocrine disruptors published on behalf of the International Programme for Chemical Safety (IPCS) of the WHO (Damstra et al., 2002) pointed out that no common dose-response mechanism can be expected when endocrine disruptors are under study. These chemicals often mimic naturally-occurring hormones or antagonise them. So they interfere with a naturally-activated system that may be stimulated by low doses and inhibited by over-dosing because receptor-mediated responses saturate (Welshons et al., 2003). Several different mechanisms involving activation of different genes may be involved in the expression of one visible effect. An endocrine-disrupting mechanism resulting in a u-shaped dose response curve may be the result of two or more effects with different dose-response characteristics each, as demonstrated in experiments using cell line models. These non-monotonic effects have been shown experimentally in many *in vivo* and *in vitro* systems (Vandenberg et al, 2012). Although the Endocrine Society, the largest professional organisation of endocrinologists, points out in a recent statement that non-traditional dose-response relations are very common in the action of hormones (Diamanti-Kandarakis et al., 2009), the existence and plausibility

of such effects are still disputed by some scientists and members of regulatory bodies (Sharpe, 2010).

Deviations from monotonic dose-response curves for hormone action are very frequent. Neither do they seem to be rare in toxicology. In 2001, Calabrese and Baldwin analysed 668 dose-response curves that were published in toxicological or eco-toxicological papers in three major journals from 1962–1998: 37 % of the curves were non-monotonic and exhibited a u-shaped form.

This kind of curve is much more than a curiosity. What toxicology did in past centuries was to extrapolate from high doses with frequent and serious effects to low doses where only small effects were expected. A prerequisite for doing this is that the curve is monotonic. The central paradigm of

Figure 10.1 Examples of non-monotonic dose-response curves for BPA



Note: In the test systems shown, small doses show small effects, intermediate doses cause the most pronounced effects while high doses cause no change or even a decrease in effect.

Schematic graphs adopted from the papers, for data and details see the original references.

Source: a) Data from Cabaton et al., 2010; b) Data from Jenkins et al., 2011; c) Data from Wetherill et al., 2002; d) Data from Marmugi et al., 2011

toxicological assessment was: if a high dose of a chemical does not cause harm, then a low dose will not either. Obviously this does not hold true at least for physiological responses to endocrine disruptors. After 500 years it has become clear that Paracelsus's paradigms do not contribute to the protection of human health and environment if they are applied to risk assessments in a naive way.

1997 Colerangle and Roy reported that a low dose of BPA induced a proliferative effect in breast tissue and that BPA was much more potent than expected from its oestrogen-receptor binding profile. Science reacted immediately and since then hundreds of papers on low-dose effects have been published (see Table 10.1). These further demonstrate that the organism is most sensitive during development, that effects are often not observed until later in the lifecycle, and that conventional toxicology testing could be insensitive to BPA if it fails to include in-utero dosing and later life follow-up of appropriate endpoints. The papers also support the observation of non-monotonic dose-response curves for BPA and other hormones, reflecting feedback mechanisms, receptor saturation, and multiple mechanisms of action (Vandenberg et al., 2012). Within the scientific community, there is far-reaching agreement on these concepts and findings. However BPA industry organisations continue to claim that these findings are invalid as 'no study purporting to show low-dose effects has been replicated in a second lab, despite repeated efforts to do so' (Polycarbonate/BPA Global Group, 2012).

10.5 The time makes the poison

The proper development of an organism is an extremely complex process, dependent on external and internal cues and hormonal regulation. Not only the chemical characteristic and the internal dose are important but also the exact timing of the stimulus (Neubert, 1997). For BPA, so far, it has been shown that irreversible developmental effects are caused during the foetal, neonatal or juvenile period in test animals (Palanza et al., 2008) and that the effects observed may be different if the organism is exposed during early or later life-stages (Richter et al., 2007).

Assessing the effects of endocrine disruptors is extraordinary difficult because the time of exposure is not necessarily the time when the effects can be detected. Perinatal exposure to BPA has been shown to affect females: it alters ovarian cyclicity and induces early cessation of oestrus cycles, impairs reproduction, interferes with sexual differentiation of the brain, alters behaviour, alters mammary gland development and induces mammary gland neoplasia (Soto and Sonnenschein, 2010). It has also been shown that BPA can interfere with normal spermatogenesis, reducing sperm numbers later in life in rodents and when the mothers of the pups are dosed during pregnancy and lactation (vom Saal et al., 1998; Okada et al., 2008a). If this also happens in humans, the effects of exposure of the foetus or the newborn may only be seen more than a decade later when the boys reach puberty and sperm becomes available for characterisation. This temporal disconnection between exposure and effect is even larger when the effect observed is breast cancer, because the age of prevalence for this disease is 50–60. For example, prenatal exposure to synthetic oestrogens like DES (Hoover et al., 2011) increase the incidence of breast cancer at 40 years of age or older. At the time when the effects become detectable the chemical exposure has vanished. This makes it extremely difficult to apply epidemiological methods to link exposure to effects in humans. For a realistic risk assessment it is also crucial to characterise the exposure to BPA at the appropriate life stage. Young children have the highest rate of daily ingestion of this chemical (European Commission, 2008) and the internal concentrations of free and toxicologically-active BPA may be much higher than in adults because of their different metabolic capacity (Edginton and Ritter, 2009).

These examples illustrate that dose is only one of the factors that make a poison. Equally important are the time of exposure and the time when effects become visible. For a long time BPA has been erroneously viewed as only a weak oestrogen (Völkel et al., 2005; Goodman et al., 2009). Indeed, *in vitro* studies indicated that BPA competes with estradiol to bind the oestrogen receptors alpha and beta. In these tests relative binding affinities were at least a thousand-fold lower than that of estradiol (Kuiper et al., 1998). Recent results from *in vivo* and *in vitro* studies indicate that BPA can act via a number of different additional cellular target systems, including binding to a non-classical membrane-bound oestrogen receptor (ncmER) (Nadal et al., 2000, 2004; Alonso-Magdalena et al., 2005), an orphan nuclear receptor called oestrogen-related receptor gamma ERR-γ (Okada et al.. 2008b), a seven-transmembrane oestrogen receptor called GPR30 (Thomas and Dong, 2006), and the aryl hydrocarbon receptor (AhR) (Kruger et al., 2008).

In vitro studies also show that BPA can act as an androgen receptor antagonist. BPA can also interact with thyroid hormone receptors (TRs) (Moriyama et al., 2002; Zoeller et al., 2005). These multiple modes of action have recently been reviewed in a number of papers (NTP, 2008; Chapin et al., 2008; Wetherill et al.,

2007). In some of these systems BPA can exhibit equal or even stronger potency than the naturally occurring hormones (Wozniak et al., 2005; Watson et al., 2007).

For a long time influential scientists claimed that low-dose findings were neither credible nor plausible because, from the relative binding strength of oestrogen and bisphenol, considerably lower effects of BPA would have been expected (Greim, 2004). Today we know that their expectations were based on inappropriate assumptions. Recent experiments showing that low-dose effects of BPA are abolished in null mutants of nuclear oestrogen receptors provide irrefutable evidence in this regard (Soriano et al., 2012).

Nowadays there is widespread agreement that BPA is an endocrine-active chemical with multiple modes of action. A recent paper from US Environmental Protection Agency (EPA)'s high throughput testing group, ToxCast, showed that BPA was active in a wide variety of mechanistic assays — one of the most active chemicals tested (Judson et al., 2010) — and a literature review from a US National Toxicology Program (NTP) draft report on obesity provides an excellent review of BPA's multiple modes of action (NIEHS/NTP, 2011).

10.6 Concern or no concern: that is the question

When BPA was polymerised to make polycarbonate, neither the data on non-monotonic dose responses nor the deleterious effects of foetal exposure to DES were known or commonly recognised in science. In addition, since BPA seemed to be a weak oestrogen with activity 1 000–10 000 fold less than estradiol, and since it was assumed that the BPA monomer would not be released from the polycarbonate plastic (Biles et al., 1997), there was no real concern about human exposure and thus toxicity.

The complexity of the exposure assessment, the toxicological profile of BPA, and probably the high economic importance of this substance may have contributed to the fact that risk assessments for this substance differ more markedly than for any other chemical. A number of scientific and regulatory bodies and committees have published risk assessments for BPA. The identified acceptable doses for humans differ by many orders of magnitude.

10.7 BPA reviews and risk assessments

BPA is regulated as a food contaminant and thus falls under the jurisdiction of the Food and Drug Administration (FDA) in the US and the European Food Safety Authority (EFSA) in the EU. Both agencies have provided risk assessments over the past decade, all based on toxicity tests in experimental animals. These regulatory agencies have essentially used Good Laboratory Practice (GLP) guideline studies as the only source of data on the toxicity of BPA (see Box 10.1 for GLP and Good Scientific Practice).

Let's take a look at the GLP guideline studies that have been done to assess BPA toxicity and

Box 10.1 Good Science and Good Laboratory Practice

Science is a self-regulating system. To ensure high quality standards, scientists have developed rules for themselves on how to perform scientific work. These have been laid down by international organisations like WHO (2006) or national scientific societies like DFG (1998) in Germany in comprehensive guidance documents. A peer-review system is the core instrument for safeguarding these rules. As a prerequisite for publication, results and scientific papers are reviewed by peer scientists. In prestigious journals more than three out of four papers are not accepted for publication. This system is a very rigorous form of quality control.

For regulatory purposes, particularly for the testing of chemicals and pharmaceuticals, not all results and procedures need to be published and peer-reviewed. As a reaction to low quality and fraud, a different system of quality control has been established. The system of Good Laboratory Practice (GLP) (OECD, 1998) has been tailor-made for commercial research laboratories, and regulatory agencies worldwide require that this system is applied for tests conducted to fulfil regulatory requirements. GLP regulates how to conduct protocols and report tests. GLP can give technical advice but cannot judge whether a test is appropriate to solve a problem or whether, for example, the relevant outcomes have been studied. GLP does not indicate that good science has been performed or that the scientific results are adequate and sufficient to protect human health and the environment (for comprehensive discussion, see also Myers et al., 2009).

that have been pivotal in the FDA and EFSA risk assessment. There are two multigenerational reproduction studies in rats (Tyl et al., 2002) and one multigenerational mouse study (Tyl et al., 2008) that were regulatory guideline studies done according to GLP. These studies all showed only non-specific toxicity (number of live pups per litter) and they were used to identify a Lowest Observed Adverse Effect Level (LOAEL) of 50 mg/kg body weight per day (bw d) and a No Observed Adverse Effect Level (NOAEL) of 5 mg/kg bw d. At least in the rat study there were significant effects below this level (Heinze and Chahoud, 2003). These effects were regarded as not relevant by the authors. The studies have been criticised because they use traditional toxicological endpoints that cannot detect subtle developmental changes and effects caused by hormones (Myers et al., 2009). Recently a large independent trans-generational study (Ryan et al., 2010) also could not find effects at low doses on behaviour, puberty and fertility of female rats.

On the other hand there are many *in vivo* studies describing developmental effects in rodents at very low doses (Table 10.1). The effects under study were reproductive organ morphology, neurodevelopment and behaviour, male reproductive health, and immunology. At least 46 peer-reviewed published studies report effects at oral doses of 50 μg/kg bw d or less (see Table 10.1) (for review, see Gies, 2007). This dose has been regarded as a safe Acceptable Daily Intake (ADI) in the recent European assessment of the European Food Safety Agency (EFSA, 2010).

Recently a working group of the French health agency ANSES (2011) carefully re-examined all animal studies with low doses of BPA, assessed their quality and compared their results. The panel concluded that animal experiments show effects that could be confirmed on male sperm production, induction of ovarian cysts, endometriosis, and advanced puberty in females. Behavioural effects have been confirmed for maternal behaviour and sexual dimorphic behaviour such as anxiety. Effects on lipogenesis, immune behaviour and breast development were also regarded as confirmed.

An important aspect of dose-response assessment is that it is still not clear what is a no-effect level for BPA's most sensitive end-points. Further research is needed to continue refining methods to reliably assess sensitive endpoints and to conduct the studies with a sophisticated approach to connecting internal free BPA dose with effects. As these studies are pursued, we may find that effects of BPA occur in the low or sub- pg/ml range, the same range as estimates of current human exposure. It is clear that most sensitive endpoints include effects on mammary gland development (Rudel et al., 2011b) and neuro-behavioural endpoints that are not commonly assessed in toxicity studies, even those recently adopted for testing endocrine-active chemicals.

The different assessment documents weight this evidence differently. The main areas of controversy are:

- Do any of the non-GLP peer-reviewed papers that show effects of BPA at low doses contain sufficiently reliable information to be considered in the risk assessment? Putting this question the other way: is the study sponsored by The Society of the Plastics Industry, Inc. (Tyl et al., 2002) and the study of Ryan et al. (2010) so reliable that nearly all other studies can be dismissed?

- Are there any relevant concentrations of free BPA in the body that can cause biological effects or is this substance so readily metabolised that it cannot harm humans?

The assessment of the European Food Safety Agency (EFSA) 2010 and the Risk assessment report of the European Union (European Commission, 2008) state that none of the low dose studies has the quality to provide data for the risk assessment. All these studies have been dismissed. The reasons given were:

- only one or two doses tested;

- low number of animals;

- inadequate statistical processing of the data;

- results not consistent with other studies.

The application of these criteria was used to exclude or ignore significant peer-reviewed scientific results. The fact that they were peerreviewed and published in reputable scientific journals indicates that the members of the scientific community that reviewed all these many papers do not agree with the criteria chosen by EFSA.

10.8 EFSA and EU risk assessments

EFSA identified the study of Tyl et al. (2002) as pivotal. With an assessment factor of 100 applied to the No Observed Adverse Effect Level (NOAEL) an Acceptable Daily Intake (ADI) of 50 μg/kg bw d

was derived. It should be noted that the assessment of the EFSA and other regulatory bodies is based on arbitrarily selected data from this study. The original data from this study showing a significant increase in anogenital distance (AGD) in males but not in females were not taken forward to the risk assessment (Heinze and Chahoud, 2003). Although AGD is not a validated endpoint for regulatory studies, it is an important marker of sexual development in rodents and humans. Changes in AGD show that sexual development has been disturbed (Swan et al., 2005; Longnecker et al., 2007). An increase in AGD is considered a surrogate for virilisation, while a decrease indicates de-masculinisation. In humans, a lower AGD has been shown to be a predictor of poor semen quality in later life (Mendiola et al., 2011). Similar changes of AGD due to low doses of BPA have been found in independent studies in rodents by Gupta (2000) and Somm (2009). In a recent paper, Tyl (2009) the principal author stated that no low-dose effects have been found in this study. This is not in line with the data presented.

EU Risk Assessment Report (RAR)

In contrast to the majority of EU Member States, some Nordic Countries regarded four neuro-behavioural studies as valid for risk assessment (Negishi et al., 2004; Carr et al., 2003; Ryan and Vandenberg, 2006; Adriani et al., 2005). In a footnote to the assessment document they proposed to take these as pivotal studies. The lowest effective concentration in these studies was described by Adriani as 40 µg/kg bw d. With a factor of three for extrapolation from LOAEL to NOAEL and an extrapolation factor of 100 this would result in an ADI of 0.13 µg/kg bw d. This ADI would be lower by a factor of 380 than that of EU RAR.

The National Toxicology Program (NTP) of the United States of America (NTP, 2008). The NTP assessment concluded that BPA was clearly toxic at high doses over 5 mg/kg bw d. In contrast to the EU RAR, NTP does include the results of the low-dose studies in their assessments. Although it states that low-dose effects are difficult to interpret in many cases, NTP concludes that these results should not be dismissed. The low-dose studies provide limited evidence that human health may be affected and there is some evidence that human health may be at risk at current exposure levels. NTP does not indicate a 'pivotal' study but in their risk characterisation they base their estimates on developmental effects reported from mice studies at a dose of 2.4 µg/kg bw d.

NTP did not calculate a Tolerable Daily Intake (TDI) in its assessment. If one applies routine methods to derive an Acceptable Daily Intake (ADI), with a factor of 3 for extrapolation from LOAEL to NOAEL and an extrapolation factor of 100, this would result in an ADI of 0.008 µg/kg bw d. This ADI would be a factor of 6 250 lower than that derived by the EFSA.

Environment Canada and Health Canada (2008). The 2008 Canadian assessment states that 'collectively these (low dose) studies provide evidence that exposure to BPA during gestation and early postnatal life may be affecting neural development and some aspects of behaviour in rodents, the overall weight of evidence was considered limited from the perspective of rigour'. Nevertheless, taking a precautionary approach, the Canadian authorities decided to characterise BPA as a substance that may constitute a risk to humans. So the precautionary risk assessment is based on low-dose neuro-developmental studies. It is not stated which of the studies are taken as decisive. In 2010 the Canadian government listed BPA as a toxic substance.

The Chapel Hill Consensus statement (vom Saal et al., 2007) is not a risk assessment in the classical sense. Thirty-eight scientists, including most of the leading scientists working on BPA, expressed confidence that low doses of BPA disrupt development in many animal models. Their key message is that action is warranted when internal exposure of humans reaches or exceeds the levels that cause serious effects in experimental animals in low dose studies. This consensus statement clearly points to the developing gap between scientific knowledge about BPA and the published opinions of regulatory committees.

The US Food and Drug Administration (FDA, 2008, 2010). In 2008 the FDA issued its risk assessment of BPA which stated that the 'no observable adverse effect' level of 5mg/kg bw d was an adequate margin of safety. The scientific committee of the FDA established a subcommittee in 2008 to review this assessment. The subcommittee harshly criticised the FDA assessment. In particular, it did not agree that the large number of non-GLP studies should be excluded from the safety assessment.

It stated that the weight of the evidence provided scientific support for use of a point of departure substantially (i.e. at least one order of magnitude) lower than the 5 mg/kg bw d level selected in the draft FDA assessment.

In summary the Subcommittee concluded: 'Coupling together the available qualitative and quantitative information (including application of uncertainty factors) provides a sufficient scientific basis to conclude that the Margins of Safety defined by FDA as 'adequate' are, in fact, inadequate.' The Scientific committee of the FDA later adopted this opinion of its subcommittee. Such an explicit statement fundamentally criticising the work of an agency by its scientific advisors is unprecedented.

The report of its scientific advisory committee resulted in the FDA changing its position. On 10 January 2010, the FDA stated that they now 'have some concern about the potential effects of BPA on the brain, behaviour and prostate gland in foetuses, infants and younger children' (FDA, 2010). Thus, for the first time, while it did not change its actual risk assessment of the acceptable daily intake level, it did acknowledge the existence and possible importance of investigator-initiated studies. At that time there were more than 800 investigator-initiated studies published on BPA toxicity.

European Food Safety Authority 2010 BPA Risk Assessment (EFSA, 2010). In 2010 EFSA released an updated risk assessment of BPA. They basically reiterated what they stated in 2006, that BPA was safe to human health and noted that there had been no new compelling non-GLP studies published on BPA. At that time there were more than 800 investigator-initiated studies that were not included in the BPA risk assessment, each one discarded for not meeting specific guidelines.

Thus at that time, the FDA and EFSA still relied exclusively on a handful of GLP multi-generational studies done in contract laboratories that assessed only reproduction, body and organ weights, clinical chemistry and organ histopathology using H&E staining. The same endpoints had been used for the past 50 years: before endocrine disruptors were known, before the developmental basis of disease and gene expression and epigenetics were known, and before low-dose and non-monotonic dose responses were known.

It is remarkable that the FDA and EFSA used guideline studies to indicate that BPA is safe while ignoring over 800 peer-reviewed studies that showed toxicity of BPA at exposure levels below the level of human exposure.

Certainly there are data gaps, but the practice of regulatory agencies of disregarding, or worse, declaring unfit every peer-reviewed study that does not follow the guideline study design cannot be defensible. The scientific literature needs to be assessed on the basis of the strength of the individual studies and the overall strength of the evidence of all the studies in order to show the same or similar effects across doses and times and species.

The German Federal Environment Agency (UBA) (2010). The view of the German Federal Environment Agency (UBA) is that there are sufficient grounds for concern. Numerous studies present, on the whole, a consistent picture, so that, despite uncertainties and gaps in knowledge concerning risk assessment and levels of exposure, there is need for action. The UBA is therefore in favour of precautionary action and restrictions on the use of certain products that contain BPA.

The French Agency for Food, Environmental and Occupational Health and Safety, ANSES (2011). Based on an analysis of all the available scientific literature, an ANSES scientific expert group found 'that there were proven effects in animals (effects on reproduction, effects on the mammary gland, effects on metabolism, the brain and behaviour) and other suspected effects in humans (effects on reproduction, the metabolism of sugars and fats, and cardiovascular diseases). These effects were demonstrated at doses that were significantly lower than the reference doses used for regulatory purposes, especially during certain periods of life characterised by susceptibility to the effects of BPA (pregnancy, pre- and post-natal periods)' (ANSES 2011). This assessment questions parts of EFSA's current assessments.

A joint ANSES and EFSA paper has recently been prepared (EFSA and ANSES 2011). This paper shows that differing assessments persist, partly because they evaluated evidence at different stages of the risk assessment and partly because they use different study quality criteria ([2]).

10.9 Bisphenol A in human bodies

There is little controversy about the external exposure of humans to BPA. The EU Risk Assessment Report

([2]) ANSES and EFSA agree that they have covered different stages of the risk assessment process: ANSES a hazard identification and EFSA a hazard characterisation (2010) and a full risk assessment (2006) from dietary exposure to BPA (2006). This represents one of the reasons for the divergences between their respective work in 2011 and 2010. They recognise that their selection of critical effects is not based on the same study evaluation criteria e.g. routes of exposure (EFSA and ANSES, 2011).

(European Commission, 2008) used two exposure models to estimate human daily intake. One of these was for regional exposure and one for local exposure near a BPA production plant. Total human exposure was calculated by the regional model to be 1.49 µg/kg bw d, and by the local model to be 43 µg/kg bw d. Estimates of daily BPA intake in adults fell within the range 0.008–1.5 µg/kg bw d. Worst-case scenarios for young children estimated up to 11–13 µg/kg bw d. These data, calculated from exposure scenarios, are well in accordance with daily intake figures recalculated from concentrations in urine. Daily intakes estimated from the Centers for Disease Control and Prevention National Health and Nutrition Examination Survey (CDC NHANES) bio-monitoring data range from 0.15–0.22 µg/kg bw d for adults aged 20–60+ years at the 95th percentile (this means that 95 % of the people had concentrations at or below this value) (LaKind and Naiman, 2011). In German children aged 3 to 14, the 95th percentile of the daily intake recalculated from urine concentrations was 0.37 µg/kg bw d and the maximum value among 599 children was 7 µg/kg bw d (Becker et al., 2009). These intakes were similar to those found in children aged 6 to 11 in the US (Calafat et al., 2008). Bottle-fed infants have two times higher urine BPA levels than breast-fed infants (Völkel et al., 2011). Children in neonatal intensive care units have median urinary BPA concentrations about ten times higher than in children aged 6–11 (Calafat et al., 2008; 2009) and 20 participants eating food with limited packaging for three days showed a 66 % reduction in urinary BPA (Rudel et al., 2011a). In studies that report both conjugated and free BPA in urine, > 90 % is conjugated, including in neonates (Calafat et al., 2009). This indicates that there are particularly highly exposed risk groups in vulnerable life phases that have not yet been recognised in current risk assessments. A recent analysis of NHANES data showed that BPA levels did not decline rapidly with fasting time as expected. This suggests significant levels of exposure not related to food, or accumulation in body tissues. The recent finding of transdermal exposure points to additional sources of exposure, and thus to a higher than expected total BPA exposure (Stahlhut et al., 2009)

Major differences exist concerning internal exposure. Only free bisphenol is believed to be biologically active while its conjugated metabolites are probably inactive; however, it should be considered that conjugated metabolites that may be found in the blood can be de-conjugated in peripheral tissues and thus become re-activated. Human bio-monitoring studies from Germany and the US (Schönfelder et al., 2002a; Padnmanabhan et al., 2008) found 4–6 ng/ml free bisphenol in the blood of mothers. These results are almost identical although the studies used totally different techniques. However pharmacokinetic studies (Doerge et al. 2011a), together with data from bio-monitoring studies and model calculations, resulted in estimates of free BPA levels in human blood between 0.1 and 10 pg/ml (Fisher et al., 2011), around three orders of magnitude lower than the above-mentioned directly measured ones.

No free BPA above the detection limit of 2 ng/ml was found in the blood of nine volunteers dosed intentionally with 5 mg/person (Völkel et al., 2002). This study is still the basis of the risk assessment of the EFSA suggesting that no relevant internal concentrations of free BPA can be found in humans. In summary, the EU Risk Assessment report states: 'Considering the evidence as a whole, EFSA concluded that the validity of the reported high blood levels of BPA in unintentionally exposed human subjects is questionable.' Again EFSA ignores consistent results from peer-reviewed scientific work.

New pharmacokinetic studies (Prins et al., 2011; Doerge et al., 2010, 2011; Taylor et al., 2011) show that caveats in this field are legion. Of particular relevance, the Taylor et al study shows that BPA pharmacokinetics is similar in primates and rodents and thus that rodents are suitable models. Moreover routes of exposure, such as dermal exposure (Stahlhut et al., 2009; Liao and Kannan, 2011a, b) and excretion, such as sweat (Genuis et al., 2012), have recently been recognised but have not yet been quantified and thus are additional sources of uncertainty.

Risk assessment is only a protocol used by the regulatory community, not science per se. Uncertainty has to be taken into account and has to be quantified. The plethora of peer-reviewed research showing low-dose effects indicates that applied test protocols and regulatory procedures are not suitable for assessing endocrine disruptors.

A recent review extensively discusses the relevance of measurements of free and conjugated BPA in human blood (Ginsberg and Rice, 2009). Many peripheral organs, including the placenta, show high activity of glucuronidases and sulphatases that are able to cleave conjugated BPA to its free and metabolic active form. Finding the conjugated form in the blood does not predict that the substance is biologically inactive in the tissue. The assumption of EFSA that rapid conjugation protects humans from adverse effects is far from being precautionary.

In contrast the National Toxicology Program (NTP) recognises the possibility that the published values of free BPA may, in some cases, not accurately represent the 'true' concentrations of free BPA in the blood or body fluids of humans or laboratory animals. However, because of the similarity between values reported with different analytical methods, the NTP accepts the published values as sufficiently reliable for use in this evaluation.

10.10 Spheres of influence

In the case of BPA, a large body of scientific literature obviously indicates deleterious effects in rodents at low doses. The effective doses in these studies overlap the doses of current human intake. Most of the European, American and Asian authorities declare BPA to be safe. Industries rely on these risk assessments. Massive pressure from consumers and politicians has forced many companies, for example the major American baby bottle manufacturers and a European aluminium drinking bottle manufacturer, to withdraw their BPA-releasing products from the market. Without doubt, this has had considerable negative effects on the image of the companies, the reputation of their brands and on the earnings of these branches. For many people the question arises whether BPA-producing industries had previously influenced the assessment processes. Such industrial influences on scientists and authorities have been well documented for the risk assessment of tobacco smoke and second-hand smoking in particular (Grüning et al., 2006).

At least one consulting company that had been active for the tobacco industry, the Weinberg Group, has been successfully hired by the BPA industry to influence the European assessment, in particular the classification and labelling (C&L) which is a key instrument for the risk management of chemicals. In its internet presentation the Weinberg Group itself proudly admits:

'In Europe, THE WEINBERG GROUP and its associates have had a five-year long history of working on the polycarbonates/BPA issue… It also includes identification of opponent's likely arguments, and formation of responses to counter these arguments. THE WEINBERG GROUP contributed its academic and regulatory network to the advocacy effort. This approach proved very effective, as ultimately the C&L working group did not follow the recommendation of the Rapporteur Member State to classify BPA as a Category 2 reproductive toxicant, agreeing instead on the more benign Category 3 classification .We have a long-term relationship with this client, and will continue to support this industry as it faces persistent NGO attacks on its products' (The Weinberg Group, 2005).

Classification as a category 2 reproductive toxicant would have required labelling this substance with a skull and bones sign as toxic. Moreover under the new chemical legislation of the European Community, every use of BPA would have required a formal authorisation.

Science is vulnerable. It is based on the independence of scientists and of science itself. In the committee of the European Food Agency AFC — (Panel on additives, flavourings, processing aids and materials in contact with food) nine of the 21 members stated, in the conflict of interest statements they supplied to the agency, that they had worked for at least one company or association under the influence of the industry or for industry itself or had strong links with associations like Greenfacts or ILSI Europe that are dependent on financial support or industries including BPA producers. One member received financial benefits from industry for writing a review (Dekant and Völkel, 2008) on BPA for a scientific journal.

Meanwhile the European Food Safety Authority made considerable efforts to strengthen transparency and scientific independence, as 'the value of its scientific advice is directly linked to the level of trust held in it by the public and therefore seeks to guarantee independence in all aspects of its governance and scientific activities (EFSA, 2012). New rules for independence policy have been launched by EFSA recently.

Without doubt, working for the chemical industry and its organisations or other NGOs is a job like any other. Whether it is wise to give people who are directly or indirectly paid by industry the task of controlling industry may be questioned.

Various scientific papers have investigated whether the outcomes of scientific studies are dependent of the source of funding. In most cases, a significant association has been found (Lesser et al., 2007; Moses et al., 2005; Blumenthal, 2003). An association of funding and outcome can also been detected for studies on BPA (Table 10.2).

Since EFSA reassessed BPA in Europe in 2006 and increased the tolerable daily intake by a factor of five, scientific evidence has accumulated that

shows low dose toxicity and doubts have occurred whether EFSA's decision was unbiased:

- At least ten additional peer-reviewed papers were published showing effects in rodent offspring at oral doses lower than the Tolerable Daily Intake set by the EFSA (see Table 10.1). BPA has been shown to influence body weight and metabolism (Somm, 2009; Rubin et al., 2001) and may be one of the factors contributing to the increasing rates of obesity in humans.
- Numerous other *in vivo* and *in vitro* studies indicate that BPA may not be safe at doses we are currently exposed to.
- Bio-monitoring studies showed that some European and American children are exposed to doses that can produce adverse effects in rodents (for review, see Betts, 2010).
- Vulnerable and highly exposed subgroups, like children in intensive care units, that are not sufficiently covered by current exposure assessments, have been identified (Calafat et al., 2009).
- New sources of BPA have been identified like pacifiers and warm-water tubes (Shelby, 2008).
- Epidemiological studies show that higher exposure of mothers to BPA is associated with increased aggressiveness of daughters when they are two years old (Braun et al., 2009). Like other cross-sectional studies, these associations are not a proof of causation but should be regarded as additional warning signs.
- Free BPA concentrations are associated with oocyte quality (Fujimoto et al., 2011) and embryo quality indicators (Bloom et al., 2011) during human *in vitro* fertilisation.
- BPA levels in the blood of workers are negatively associated with male sexual function (Li et al., 2010).
- Higher BPA exposure is associated with obesity in the general population in the US (Carwile et al., 2011).
- BPA exposure in workers is negatively correlated with the birth weight of their offspring (Miao et al., 2011).
- Gestational BPA exposure affected behavioural and emotional regulation at three years of age, especially among girls (Braun et al., 2011).
- EFSA's assumption that internal doses of free BPA are lower in humans than in rodents at comparable doses is unproven (Gies et al., 2009).
- The European Union has banned baby bottles containing BPA. This ban became effective in 2011 (EU, 2011).

10.11 Lessons to be learned

The 'late lesson' with respect to BPA is the 'same old story' of putting a chemical into widespread use without understanding its health implications, and then trying to resolve public health questions while facing the intense pressure of serious economic consequences. The competing urgency of public health and economic stakes puts the scientific process under enormous pressure. In this perspective the story of BPA resembles those of asbestos, polychlorinated Biphenyls (PCB) and Diethylstilboestrol (DES).

Best science and transparency

In Europe it is timely to dare to start again with the risk assessment of BPA. This assessment must be transparent and conducted by the scientists authoring the papers with high scientific impact in this field. Stakeholder conferences may serve as a forum to make the interests and influence of industry and other NGOs transparent.

Precaution

Until final decisions are made, precautionary measures should be taken to lower human exposures to well below those that cause adverse effects in rodents and behavioural changes in humans in epidemiological studies. This would mean terminating those uses of BPA involving close contact with humans via food or the environment.

Towards more independent science

The new European chemicals legislation REACH (**R**egistration, **E**valuation, **A**uthorisation and Restriction of **Ch**emical substances) relies on the activities of the industry for most risk assessments and toxicity test data. The case of BPA clearly

Table 10.1 Summary of mammalian studies on BPA with effect levels at or below 50 µ/kg bw d, oral administration

Dose (µg/kg bw d)	Organism, age at dosing	Effect	Reference
0.2	Rat, 2-generation study	Anogenital distance in F 1 males, 2 µg/kg in F1 females and 20 µg/kg in F2 females	Ema et al., 2001
0.2	Rat, male adult	Superoxide dismutase, catalase, glutathione reductase and glutathione peroxidase activity in liver ↓, H_2O_2, lipid peroxides ↑	Bindhumol et al., 2003
0.2	Rat, male adult	Prostate size ↑, Testis, epididymis size ↓ H2O2, lipid peroxides ↑	Chitra et al., 2003
0.6	Mouse, pregnancy	Effects on mammary gland development	Ayyanan et al., 2011
1	Rat, 3-generation study	Paired ovary weight in F2 generation ↓, uterine weight in F0 ↓, anogenital distance in female F2 ↓ (Effects were not regarded as relevant by the authors)	Tyl et al., 2002
1.2	Rat, 3-generation study	Litter size ↓, sperm number and motility ↓, post implantation loss ↑	Salian et al., 2009
2	Mouse, pregnancy	Testis and epididymal weights ↑ in offspring	Ashby et al., 1999
2	Mouse, gestation day 11–17, offspring	Aggression ↑, testis weight ↓ in offspring	Kawai et al., 2003
2	Mouse, gestation day 11–17, offspring	Prostate weight ↑, epididymis weight ↓	vom Saal et al., 1998
2	Gerbil, females, 3 weeks after pairing	Changed maternal behaviour	Razzoli et al., 2005
2	Mouse, prenatally, early postnatally	Anxious behaviour ↑ in offspring	Ryan et al., 2006
2	Rat, 3-generation study	Spermatogenesis, sperm quality	Peknicova et al., 2002
2.4	Mouse, gestation day 11–17	Vaginal opening, first oestrus in offspring	Howdeshell et al., 1999
2.4	Rat, male, Postnatal day 21–35	LH, Testosterone and oestrogen levels ↓	Akingbemi et al., 2004
2.5	Mouse, 5 wk	Immune, IFN-gamma and IgG2a ↓	Sawai et al., 2003
2.5	Mouse, pregnancy and lactation	Brain, kidney liver and testes weight ↓, oxidative stress markers ↑ in offspring	Kabuto et al., 2004
2.5	Transgenic mice	Tumour development ↑	Jenkins et al., 2011
5	Mouse, adult male	Testis and seminal vesicle weights ↓	Al-Hiyasat et al., 2002
10	Mouse, gestation day 14–18	Maternal behaviour in offspring	Palanza et al., 2002
10	Mouse, gestation day 14–18	Number and size of dorsolateral prostate ducts in offspring ↑	Timms et al., 2005
10	Mouse, gestation day 11–18	Long-term alteration in neurobehavioral functions in females	Laviola et al., 2005
10	Mouse, gestation day 11–day 8 post partum	Decreased sex differences in behaviour	Gioiosa et al., 2007
10	Rat	Increased prostate hyperplasia	Wu et al., 2011
10	Rat, neonatal	Increased oestrogen-induced prostate intraepithelial neoplasia	Prins et al., 2011
15	Rat, last week of pregnancy	Male behaviour in 6-9 week old offspring altered	Fujimoto et al., 2006
20	Mouse	Chromosomal aberrations, aneuploidy ↑	Hunt et al., 2003
20	Rat, 13 wk	Spermatogenesis ↓	Sakaue et al., 2001
20	Rat, pregnancy	Vaginal morphology in offspring	Schönfelder et al., 2002b
25	Mouse, gestation day 8–23	Structural and histological changes of prostate in offspring	Ramos et al., 2001
25	Mouse, female adult	Number of embryo resorptions ↑, uterine weights ↑	Al-Hiyasat et al., 2004
25	Rat, lactating	DMBA induced carcinogenicity in breast tissue of offspring	Jenkins et al., 2009
25	Mouse, pregnancy	DMBA induced carcinogenicity in breast tissue of offspring	Weber Lozada and Keri, 2011
30	Rats during pregnancy and lactation	Less pronounced sexual behaviour in male offspring, reversed sex differences in brain development	Kubo et al., 2003

Table 10.1 Summary of mammalian studies on BPA with effect levels at or below 50 µ/kg bw d, oral administration (cont)

Dose (µg/kg bw d)	Organism, age at dosing	Effect	Reference
30	Mouse	Immune responses ↑	Yoshino et al., 2003
40	Rat, gestation day 14–postnatal day 6	Sex associated behavioural changes in offspring ↑	Dessí-Fulgheri et al., 2002
40	Rat, pregnancy and lactation	Aggression behaviour in offspring	Farabollini et al., 2002
40	Rat, pregnancy and lactation	Pain sensitivity (hyperalgesia) in offspring	Aloisi et al., 2002
40	Rat, pregnancy and lactation	Changes in spontaneous and amphetamine induced behaviour in offspring	Adriani et al., 2003
40	Rat, pregnancy and lactation	Decrease of playful interactions in offspring	Porrini et al., 2005
40	Rat, pregnancy and lactation	Changes in maternal behaviour in adult females	Della Seta et al., 2005
40	Rat, male PND 23–30	Brain estrogen receptor number altered, testosterone ↓	Ceccarelli et al., 2007
40	Rat, pregnancy and lactation	Spatial recognition memory impaired in offspring, changes in female exploration behaviour	Poimenova et al., 2010
40	Rat, pregnancy and lactation	Impairment of memory, sexual behaviour and locomotor activity in offspring	Goncalves et al., 2010
40	Mouse, day 32–87	Elimination of sex differences in non-reproductive behaviour	Xu et al., 2011
45	Mouse, gestation and weaning	Memory impairment associated with reduction of acetylcholine production in the hippocampus in the male offspring	Miyagawa et al., 2007
45	Mouse, gestation and weaning	↑ Morphine-induced hyperlocomotion and rewarding effect in offspring	Narita et al., 2006
50	Mouse, gestation day 16–18	Anogenital distance and prostate size ↑, epididymal weight ↓ in offspring	Gupta, 2000
50	Rat, gestation and lactation	Deficits in male sexual behaviour in adulthood	Jones et al., 2010
50	Rat, gestation and lactation	Body weight ↑, impaired glucose tolerance, serum insulin ↓	Wei et al., 2011

Note: This table is not comprehensive. Many other studies with other application routes show similar effects. These studies should also not be dismissed for risk assessment purposes as it has been shown that other routes of exposure result in similar internal exposures in the animals.

Source: Taylor et al., 2008, modified from Gies, 2007.

Table 10.2 Outcome of studies on BPA and source of funding

Source of funding	Harm	No harm
Government	94 (90.4)	10 (9.6)
Chemical corporations	0 (0)	11 (100)

Note: Number of studies and percentage in brackets.

Source: Data from Hughes and vom Saal 2005, including studies published until 2004.

shows that the results of industry-sponsored studies and independent scientific studies deviate strongly. Independent science and regulatory toxicology seem to speak different languages. Numerous papers from different laboratories indicate risks at low doses, BPA industry-sponsored studies need doses orders of magnitude higher to produce any effects and if effects are detected they are not taken forward to the risk assessment.

Independent science is interested in finding the effects of a substance and publishing these findings. Independent laboratories usually specialise in a biological system and often have decades of experience in this field. Contracting laboratories have to cover a broad range of endpoints with different chemicals. Thus academic laboratories may be better qualified for testing for subtle changes such as those in early development and behaviour. Also, contract laboratories are per se not economically independent from the producers of a chemical. This has to be considered when weighing the evidence produced by academic research and by contract laboratories.

Independence of scientific advisors to regulatory agencies has been a controversial issue within the scientific community. These problems are obviously not restricted to the case of BPA. A number of measures have been proposed to strengthen scientific independence within the risk assessment process (Holland et al., 2012).

Uncoupling of financial interests and scientific and regulatory research and testing seems to be necessary. Chemical regulation should be based on science and the basis of science is independence. This independence of researchers can be achieved if laboratories are not contracted directly by industry. Research laboratories could be paid by a fund that is financed by the industry, over which industry has no control and which is managed by governments.

The case of BPA shows that results of independent science are of great value and should have an adequate weight within the decision-making process. Without doubt, standard testing by contract laboratories has its value in risk assessment procedures and regulations but their results must not outweigh those from independent academic laboratories. However, there is a need to update the standard testing procedures to incorporate the new knowledge acquired through independent research.

Strengthening the independence of scientific advisors is necessary and timely. Close cooperation with industry or industry-dominated bodies like the International Life Science Institute (ILSI) may be regarded as incompatible with the degree of independence required for advisory bodies.

Transparent and reliable documentation of possible conflicts of interest has not yet been achieved in all cases.

Performing or reviewing risk assessments for public agencies is time-consuming. Experts have to be paid adequately for doing this work. This would allow attracting the best qualified and independent scientists. Both testing and assessment can be financed by charging industry a fee. The employers of these qualified members of the scientific community (universities, research institutions) should be required by government agencies to decrease the workload of these scientists so that they can perform this important service to society.

10.12 Lessons learned

The intense discussion and scientific work on BPA have slowly contributed to a process of improving test strategies. While traditional toxicology has relied on a monotonic increasing dose-response relationship as evidence that the effect is caused by the test agent, studies on BPA and other endocrine disruptor chemicals (EDCs) have demonstrated the limitations of this approach and adjustments have been made in some cases. For example, the US NTP Expert Panel report on BPA (NTP-CERHR, 2007) and the report of the French ANSES 2011 included both single dose and multiple dose studies in their compilations of studies that are useful for evaluating the risks of BPA (Arnich et al., 2011). It has also been widely accepted that effects cannot be predicted by simply thinking of BPA as a weak oestrogen and extrapolating from what is observed for more potent endogenous oestrogens, and this lesson is widely evident in the intense pharmaceutical interest in selective oestrogen response modifiers (SERMs), although some investigators persist in referring to BPA simply as a weak oestrogen.

Under its testing guideline programmme, OECD is currently modifying its guidelines and incorporating many new endpoints that are sensitive to hormonal perturbation, such as timing of vaginal opening, and anogenital distance.

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11 DDT: fifty years since *Silent Spring*

Henk Bouwman, Riana Bornman, Henk van den Berg and Henrik Kylin ([1])

'There was a strange stillness. The birds for example — where had they gone? Many people spoke about them, puzzled and disturbed. The feeding stations in the backyards were deserted. The few birds seen anywhere were moribund: they trembled violently and could not fly. It was a spring without voices ... only silence lay over the fields and woods and marsh.'

The book *Silent Spring* by Rachel Carson is mainly about the impacts of chemicals (in particular in particular dichlorodiphenyltrichlorethane also known as DDT) on the environment and human health. Indeed, the close association between humans and birds remains very apt. Representing the only two warm-blooded groups of life on Earth, mammals and birds share the same environments and threats.

Carson's claim that she lived in 'an era dominated by industry, in which the right to make a dollar at whatever cost is seldom challenged' still resonates strongly with the problems that societies face all over the world. One chapter heading, 'The obligation to endure', derived from the French biologist and philosopher Jean Rostand's famous observation that, 'the obligation to endure gives us the right to know'. United States President John F. Kennedy responded to the challenge posed by Carson by investigating DDT, leading to its complete ban in the US. The ban was followed by a range of institutions and regulations concerned with environmental issues in the US and elsewhere, driven by public demand for knowledge and protection.

DDT was the primary tool used in the first global malaria eradication programme during the 1950s and 1960s. The insecticide is sprayed on the inner walls and ceilings of houses. Malaria has been successfully eliminated from many regions but remains endemic in large parts of the world. DDT remains one of the 12 insecticides — and the only organochlorine compound — currently recommended by the World Health Organization (WHO), and under the Stockholm Convention on Persistent Organic Pollutants, countries may continue to use DDT. Global annual use of DDT for disease vector control is estimated at more than 5 000 tonnes.

It is clear that the social conscience awakened by Rachel Carson 50 years ago gave momentum to a groundswell of actions and interventions that are slowly but steadily making inroads at myriad levels. Chapter 17 of her book, 'The other road' reminds the reader of the opportunities that should have been seized much earlier. With more than 10 % of bird species worldwide now threatened in one way or another, it is clear that we missed early warnings or failed to act on them. Will we continue to miss signposts to 'other roads'? Are our obligations to endure met by our rights to know? As Carson said 50 years ago: 'The choice, after all, is ours to make.'

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11.1 Introduction

> 'There was a strange stillness. The birds for example — where had they gone? Many people spoke about them, puzzled and disturbed. The feeding stations in the backyards were deserted. The few birds seen anywhere were moribund: they trembled violently and could not fly. It was a spring without voices. ....only silence lay over the fields and woods and marsh.'

This narrative by Rachel Carson in *Silent Spring* (1962) ([2]) of an imagined town and surroundings, representing thousands such all over America, frames the context of one of the 20th century's most powerful books on humans and the environment. Fifty years on, with an enduring and strengthening message, Rachel Carson's *Silent Spring* is an unmistakeable icon for early environmental awareness and current concern.

Silent Spring is mainly about the impacts of chemicals — with an emphasis on dichlorodiphenyltrichloroethane (DDT) — on the environment and human health. Its impact is as strong now as then. Indeed, the close association between humans and birds remains very apt; representing the only two warm-blooded groups of life on earth — mammals and birds — we share the very same environments and threats. Carson's realisation of humankind-in-nature, arguably as important as humankind-in-cosmos, contributed significantly to modern and enduring environmental and even social movements, resulting in regulations and restrictions on activities and practices that now exceed chemicals alone. In her second chapter, *The obligation to endure*, Carson points a finger which then, and indeed still now, resonates strongly with problems that societies face all over the world, 'it is also an era dominated by industry, in which the right to make a dollar at whatever cost is seldom challenged'. Carson took her chapter heading and context from the French biologist and philosopher Jean Rostand's famous thought, 'the obligation to endure gives us the right to know'. United States President John F. Kennedy responded to the challenge posed by Carson by investigating DDT, eventually leading to its complete ban in the United States. Despite many counter-claims and arguments from various sources, the ban on DDT and other chemicals resulted in the return of the bird chorus to affected areas. The ban was followed by a range of institutions and regulations concerned with environmental issues in the United States and elsewhere, driven by a public demand for knowledge and protection.

The right to know and the willingness to endure, so crucial to advancing civilisation and freedom, poses interesting and challenging issues that continue to face humanity on many economic, political, social, and environmental fronts. Indeed, DDT remains part of the conundrum of 'enduring yet knowing', a situation described in more detail below.

11.2 History

The DDT molecule was first synthesized in 1873 (Zeidler, 1874), a time when organic chemistry was still a young discipline, and the synthesis was performed to study what happens when different reagents are mixed under specific conditions with no notion of what the product could be used for. It was not until 1939 that Paul Müller showed the insecticidal property of DDT (Nobelprize.org, 2012a). The first DDT formulations marketed in the United States against a variety of insect pests drew the attention of the military; means to combat insect-borne diseases in the theatres of World War II were in great demand. The key event to popularise DDT was an outbreak of typhus in Naples, Italy, in October 1943. By January 1944, and after treating 1 300 000 people over a three week period with DDT, the epidemic was brought under control (Nobelprize.org, 2012b). Based on work by De Meillon (1936), indoor residual spraying (IRS) with DDT to interrupt malaria transmission was introduced in South Africa in 1946, achieving complete coverage of malaria areas by 1958 (Sharp and le Sueur, 1996).

Paul Müller was awarded the Nobel Prize for Medicine or Physiology in 1948, but already in the prize presentation speech, problems with flies developing resistance to DDT were mentioned. However, resistance development was not viewed in any environmental light but rather as an opportunity to develop new chemical pesticides to solve the problem (Nobelprize.org, 2012b). There was no mention in the prize presentation speech of potential environmental concerns, rather, the persistence of DDT, today considered as one of the main environmental concerns, was viewed as positive for the practical use of the insecticide (Nobelprize.org, 2012b), and the early recommendations on how to use DDT were, to modern eyes, staggeringly

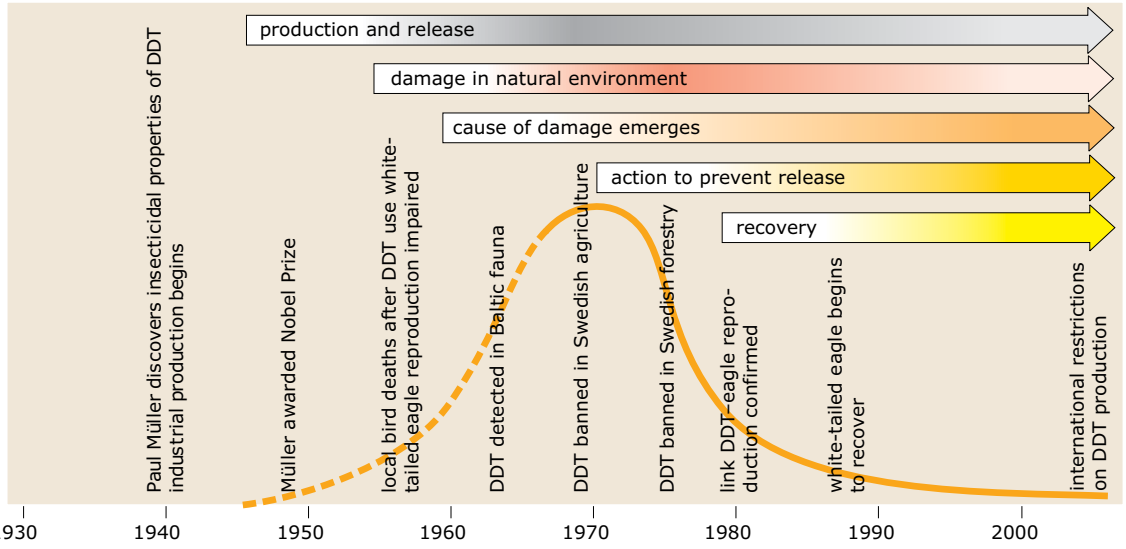
([2]) All quotations are taken from the 1972 reprint of *Silent Spring* by Hamish Hamilton, London.

indiscriminate, with much dusting of both individuals and food without any precaution (West and Campbell, 1946). However, some restrictions on indiscriminate use came already in 1948, the same year as the Nobel Prize, when use of DDT inside dairies was prohibited (American Journal of Public Health, 1949). In Sweden, cases in the 1950s were reported of flies dying after contact with dairy products with very high DDT content (Löfroth, 1971).

Arguably, the publication of *Silent Spring* (Carson, 1962) triggered the development of environmental chemistry as an academic discipline. Technical developments in analytical chemistry during the 1950s were prerequisites for development of the discipline, and, indeed, for the writing of the book, as these instrument developments were necessary to identify DDT and other organochlorine pesticides as potential environmental problems. However, it was *Silent Spring* that made the potential environmental problems everyone's concern and pressured resource allocation into environmental chemistry. In Sweden, for example, the government gave special funding to Stockholm University to set up a laboratory for the analysis of DDT in the environment (Bernes, 1998). These activities started in 1964, less than a year after the book was published in Swedish, and led, inter alia, to the identification of polychlorinated biphenyls (PCB) as environmental contaminants in 1966 (Jensen, 1966). It is difficult to envisage this development had it not been for the impact of *Silent Spring*.

That DDT was the first organic environmental pollutant that came under scrutiny was probably not only due to it being the first organochlorine pesticide to gain wide use. Another reason was probably that the negative effects first reported were on birds as many people were (and are) interested in birds, particularly large birds, and declines in the populations of birds of prey were observed in many places of the world and tied to eggshell thinning after bioaccumulation of DDT (Bernes, 1998; Bernes and Lundgren 2009). In addition, DDT was a pesticide deliberately released into the environment, which is why its presence in the environment was no great surprise. In comparison, PCB was put into production earlier than DDT, but as it was used in industry and not actively released into the environment, its presence in the environment was much of a surprise. In addition, there was no great incentive among the public to observe the negative effects of PCB as these were most severe in fish-eating mammals such as seals (Bernes, 1998; Bernes and Lundgren, 2009). The only people to regularly observe seals were fishermen, who mainly regarded them as a pest that competed for the fish. Thus, looking at the time-line for DDT and PCB (Figure 11.1), DDT was identified as a

Figure 11.1 The development of DDT concentrations in the Baltic Sea in relation to historical events, the development of environmental awareness and legal measures restricting their use



Note: The dashed portion of the line is estimated from museum material (seals), while the solid lines are based on data on Guillemot eggs analysed in the Swedish National Environmental Programme. Most uses of DDT were banned in Sweden around 1970.

Source: Bernes and Lundgren, 2009.

possible environmental problem much sooner after it was taken into use than PCB. In addition, although DDT and PCB were banned at about the same time in Sweden, the decline of DDT concentrations was more rapid as there were many remaining diffuse sources of PCB contamination, but for DDT the only use was as an insecticide (Bernes, 1998; Bernes and Lundgren, 2009).

Based on the increasing amount of data on environmental effects, restrictions on the use of DDT were put in place in different countries from the early 1970s, but the use and misuse of DDT continued. In Bangladesh, for example, fish intended for human consumption was until recently dried in DDT to avoid fly infestation in the market (Amin, 2003), even though DDT was banned in Bangladesh. With the Stockholm Convention on Persistent Organic Pollutants (Stockholm Convention, 2004), which came into force in 2004, new means to assist developing countries to reduce problems with DDT and other persistent organic pollutants (POPs) have come into place. However, the convention recognises the need to use DDT for malaria vector control until other practical and economically viable methods have been developed.

11.3 Current uses

11.3.1 DDT and malaria control

DDT was the primary tool used in the first global malaria eradication programme during the 1950s and 1960s. The insecticide was used to spray the walls and ceilings of houses and animal sheds with coverage of entire populations. Early mathematical modelling had convincingly shown that indoor residual spraying with insecticides, such as DDT, to kill adult mosquitoes had a major impact on malaria transmission (MacDonald, 1956). The insecticides prevented the female mosquitoes from surviving long enough to become infective, since it takes around 12 days for malaria parasites to migrate to the mosquito's salivary glands and, hence, only mature female mosquitoes can infect humans. Malaria has been successfully eliminated from many regions, but remains endemic in large parts of the world (Mendis et al., 2009).

The development of insect resistance to DDT, reported as early as 1951 (with even earlier indications in 1948 house flies in Sweden), became an obstacle in the eradication of malaria, and was one of the reasons behind the abandonment of the global malaria eradication campaign in 1969 (Najera et al., 2011). Amidst concerns about the safety of DDT during the 1970s, the insecticide was banned for use in agriculture in many countries. Nevertheless, DDT remained effective in a number of countries and continues to be used for malaria control today (van den Berg et al., 2012).

The negotiations that led to the inclusion of DDT as one of the initial twelve chemicals restricted under the Stockholm Convention sparked a debate about the continued need for DDT to control malaria (Curtis and Lines, 2000). An important series of developments took place over the same period. After South Africa had banned the use of DDT for malaria control in 1996, the highly effective malaria vector *Anopheles funestus* was able to reinvade the country because it had developed resistance to the pyrethroids that were being used, but not to DDT (Hargreaves et al., 2000). This situation, which was unique to South Africa, resulted in serious outbreaks of malaria, forcing the government to revert to DDT, after which the number of malaria cases declined. When simultaneously a global ban on DDT use was being proposed, fierce debates emerged over the benefits and adverse effects of DDT (The Lancet, 2000). In the final negotiations that led to the Stockholm Convention, an exception was made for DDT with an acceptable purpose for use in disease vector control. Thus, under the Stockholm Convention, countries may continue to use DDT, in the quantity needed, provided that the guidelines and recommendations of the World Health Organization (WHO) and the Stockholm Convention are met, and until locally appropriate and cost-effective alternatives become available for a sustainable transition from DDT.

DDT is one of the 12 insecticides, and the only organochlorine compound, currently recommended by the WHO for use in indoor residual spraying for disease vector control (WHO, 2006). Other recommended compounds are organophosphates, carbamates and pyrethroids. DDT has the longest residual efficacy, reportedly from 6–12 months, when sprayed on the walls and ceilings of traditional housing and, hence, one or two applications per year suffice to provide continuous protection to populations at risk. In the past few years, however, increased monitoring has shown that resistance of malaria vectors to DDT, and to other available insecticides, is now widespread in sub-Saharan Africa and India (WHO, 2011a).

11.3.2 Trends in production and use

Currently, DDT is produced only in India, from where it is exported as a pure (also called 'technical')

or as a commercially formulated product to other, mostly African, countries (UNEP, 2010). China has recently stopped production of DDT but South Africa formulates DDT using technical product from India, and exports the formulated product to several other African countries. DDT can be produced at low cost, which is relevant because it has been recommended for use at a dosage that is on average 60 times higher than that for pyrethroid insecticides. As a consequence of these differences in application rates, 71 % of the global annual amount of insecticides used for vector control is DDT, even though pyrethroids are much more widely used in terms of surface area covered (van den Berg et al., 2012). DDT is used mostly for malaria control, but 19 % of the global share is sprayed to control leishmaniasis transmission by sandflies.

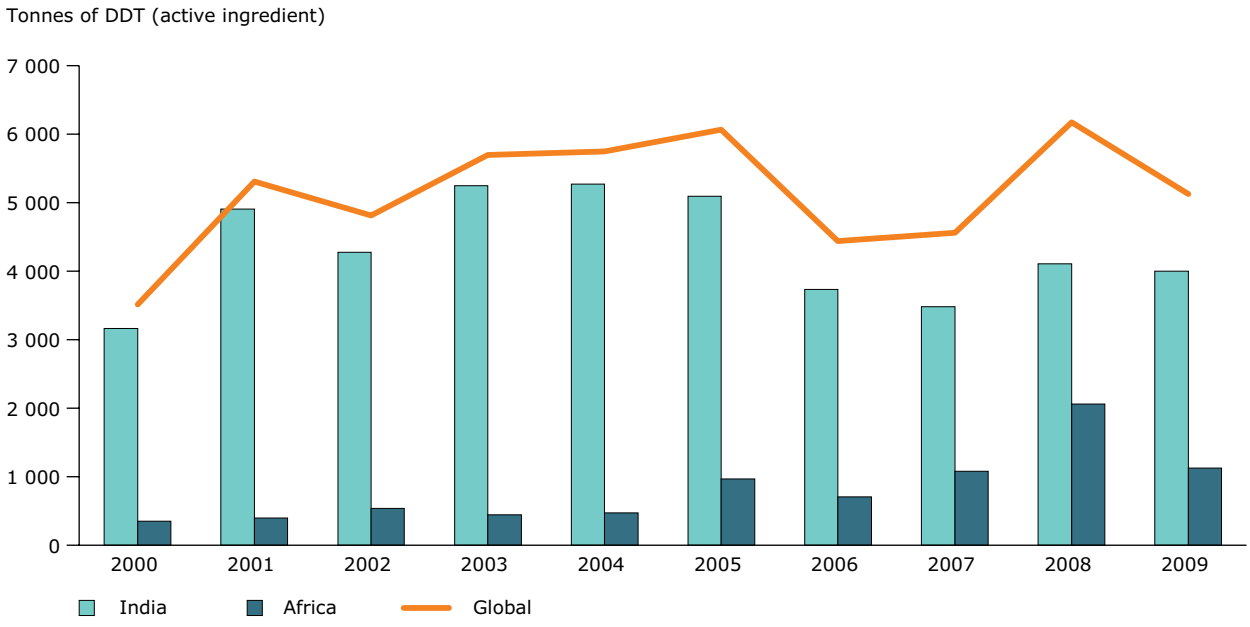
Global annual use of DDT for disease vector control is estimated at more than 5 000 tonnes of active ingredient. The amount has fluctuated during the past decade but has not declined substantially since the Stockholm Convention was enacted (van den Berg et al., 2012). India has the lion's share, with 82 % of global use. African countries also significantly increased their DDT use until 2008 (Figure 11.2) because of countries either scaling-up indoor residual spraying programmes using DDT or re-introducing its use. Only four African countries reported using DDT in 2000, compared to nine in 2008: Eritrea, Ethiopia, Mauritius, Mozambique, Namibia, South Africa, Swaziland, Uganda and Zimbabwe (WHO, 2011b). More recently, however, Ethiopia, Mozambique, and Uganda have reportedly stopped using DDT because of either policy change away from DDT or the development of insecticide resistance. It remains to be seen whether the decline in DDT use in Africa in 2009 is part of a new trend.

In DDT-using countries, it is of utmost importance that DDT is used for its acceptable purpose only. However, a recent global survey in countries at risk of vector-borne diseases revealed critical deficiencies in the capacity for regulatory control and management of pesticides, which include DDT, thus increasing the risks of adverse effects on human health and the environment (Matthews et al., 2011; van den Berg et al., 2011). For example, there are clear indications that DDT has been illegally traded on local markets for use in agriculture and termite control and there is also information to suggest that DDT is, or has been, widely used in agriculture in the Democratic People's Republic of Korea (van den Berg, 2009).

11.4 Current human health concerns

Carson (1962) devoted Chapter 12 of *Silent Spring* to a summary of the environmental health

Figure 11.2 Trends in the global use of DDT



Source: van den Berg et al., 2012.

effects associated with DDT, as then known. Very perceptively, Carson said, 'even research men suffer from the handicap of inadequate methods of detecting the beginnings of injury. The lack of sufficiently delicate methods to detect injury before symptoms appear is one of the great unsolved problems in medicine'. Since then, research men and women have added much to the arsenal of tools available, and a short summary of some follows.

The Agency for Toxic Substances and Disease Registry (ATSDR) report on DDT (2002) discussed in detail the acute exposure effects on the nervous system, the effects of chronic exposure to small amounts of DDT being almost limited to changes in liver enzymes. However, in the environment DDT is transformed to DDE which is even more persistent, leading to concerns that elevated concentrations of *p,p'*-DDE in human breast milk shortened the period of lactation and increased the chances of a pre-term delivery (see Box 11.1 for terminology on DDT and its related compounds). The International Agency for Research on Cancer (IARC) classified DDT as possibly carcinogenic to humans. Two recent publications extensively reviewed the human health consequences of DDT exposure (Eskenazi et al., 2009) and the human health aspects of IRS associated with DDT use (WHO, 2011). When the transplacental transfer of DDT and the exposure of the new-born child through breast milk became clear, there were concerns that DDT or its metabolites might affect, in particular, the reproductive and nervous systems. Moreover, some of these health effects may not become evident immediately but only long after exposure. Carson said, 'when one is concerned with the mysterious and wonderful functioning of the human body, cause and effect are seldom simple and easily demonstrated relationships. They may be widely separated in space and time'.

11.4.1 Breast cancer

The human female breast seems particularly vulnerable to environmentally-induced carcinogenesis during several critical periods such as *in utero* and before puberty (Eskenazi et al., 2009). Evidence that adult DDT exposure is associated with breast cancer was equivocal until Cohn et al. (2007) reported DDT levels in archived serum samples collected between 1959 and 1967, peak years of DDT use, from pregnant women participating in the Child Health and Development Studies (CHDS). Considering women ≤ 14 years old in 1945 when DDT was introduced, subjects with levels in the highest tertile were five times more likely to develop breast cancer than those in the lowest tertile. Moreover, in women exposed after the age of 14, there were no associations between the risk of breast cancer and *p,p'*-DDT levels. Therefore, exposure to *p,p'*-DDT during the pre-pubertal and pubertal periods is the critical exposure events to risk the development of breast cancer later in life.

11.4.2 Endometrial cancer

Sturgeon et al. (1998) reported on possible associations between endometrial cancer (cancer that starts in the lining of the uterus) and DDT serum levels, but the findings were inconclusive (Sturgeon et al., 1998). However, Hardell et al. (2004) found weak but significant associations with serum DDE levels and the topic needs further investigation.

Box 11.1. DDT-compounds

When DDT is produced the technical mixture, 'technical DDT', mainly consists of two compounds, approximately 80% *p,p'*-DDT (1,1,1-trichloro-2,2-*bis*(4-chlorophenyl) ethane), the insecticidal component, and 15% *o,p'*-DDT (1,1,1-trichloro-2-(2-chlorophenyl)-2-(4-chlorophenyl) ethane). The major degradation products in the environment of *p,p'*-DDT are *p,p'*-DDE (1,1-dichloro-2,2-*bis*(4-chlorophenyl) ethene) and *p,p'*-DDD (1,1-dichloro-2,2-*bis*(4-chlorophenyl) ethane). The major degradation products of *o,p'*-DDT are *o,p'*-DDE (1,1-dichloro-2-(2-chlorophenyl)-2-(4-chlorophenyl) ethene) and *o,p'*-DDD (1,1-dichloro-2-(2-chlorophenyl)-2-(4-chlorophenyl) ethane).

In environmental samples the concentrations of all these compounds are often added to a total DDT (ΣDDT) concentration. Generally, the *p,p'*-isomers are more persistent than the *o,p'*-isomers, and *p,p'*-DDE is the most persistent of all these compounds. Therefore, high DDT/DDE or DDT/ΣDDT ratios indicate a recent release of DDT while low ratios are typical of old releases of DDT or that DDT has undergone long-range transport.

11.4.3 Male reproductive effects

There is increasing evidence suggesting that DDT and metabolites have harmful effects on the quality of human semen and sperm function, particularly in young adult healthy men from an endemic malarial area with very high DDT and DDE levels (Aneck-Hahn et al., 2007). Sperm DNA integrity in this population was also adversely affected (De Jager et al., 2009).

Bornman et al. (2010) determined the association of external urogenital birth defects (UGBD) in newborn boys from DDT-sprayed and non-sprayed villages in a malarial area. Between 1995 and 2003, mothers living in villages sprayed with DDT had a 33 % greater chance of having a baby with a UGBD than mothers whose homes were not sprayed. A stay-at-home mother significantly increased the risk of having a baby boy with a UGBD to 41 %. Further studies are necessary to determine possible causal relationships with DDT and any possible genetic or epigenetic predispositions.

11.4.4 Testicular germ cell tumours

Concentrating on a selection of recent studies, McGlynn et al. (2008) found some evidence of an association between DDE and testicular germ cell tumours. There was a positive, but not statistically significant, association between DDE and testicular cancer. However, similar associations were also found for other chemicals such as chlordane, PCB, and some insecticides (Purdue et al., 2009). Therefore, the implications of DDE associated with testicular germ cell tumours need further studies. Cohn et al. (2010) examined maternal serum levels of DDT-related compounds in relation to sons' risk of testicular cancer 30 years later. Mothers of testicular cancer cases had lower levels of *p,p'*- DDT, *o,p'*-DDT and *p,p'*-and DDE, but a higher DDT/DDE ratio, than their matched controls. However, the possible role of DDT in the development of testicular cancer is still not clear (Hardell et al., 2006).

11.4.5 Diabetes

Various studies reported findings suggesting that body burdens of DDT and/or DDE may be associated with the prevalence of diabetes (1980 Morgan et al., 1980; Rylander et al., 2005; Rignell-Hydbom et al., 2007). However, a variety of other persistent environmental chemicals are also associated with diabetes prevalence and the WHO (2011d) concluded that the evidence is inconclusive. Nevertheless, the findings of Turyk et al. (2009) of an association between DDE exposure and diabetes incidence warrants further research to define the specific contributions of DDT and DDE.

Ukropec et al. (2010), in a cross-sectional study from Eastern Slovakia, investigated possible links between environmental pollution and pre-diabetes/diabetes (Type 2 diabetes). The prevalence of pre-diabetes and diabetes increased in a dose-dependent manner, with individuals with highest DDT levels showing striking increases in prevalence of pre-diabetes. PCBs showed comparable associations, but increased levels of hexachlorobenzene (HCB) and β-hexachlorocyclohexane β-HCH seemed not to be associated with increased prevalence of diabetes. The synergistic interaction of industrial and agricultural pollutants in increasing prevalence of pre-diabetes or diabetes is likely. For Type 1 diabetes, Rignell-Hydbom et al. (2010) found no evidence that in utero exposure to DDT could predispose the development of the disease.

11.4.6 Pregnancy

Women exposed to DDT had shorter menstrual cycles (Onyang et al., 2005) and both DDT and DDE reduced progesterone and estrogens (Windham et al., 2005; Perry et al., 2006). Other studies, however, found no relationship between menstrual abnormalities or cycle length and DDE or DDT exposure (Yu et al., 2000; Chen et al., 2005). There is limited evidence that DDT/DDE can increase the risk of miscarriage and the risk of preterm delivery. In the U.S. Collaborative Perinatal Project, high DDE concentrations were associated with an increased risk of foetal loss in previous pregnancies (Longnecker et al., 2005). Each 1 ng/g increase in serum DDE was associated with a 1.13 increased odds of miscarriage (Korrick et al., 2001). Venners et al. (2005) studied Chinese textile workers with comparable DDE concentrations and reported a similar increased odds of 1.17 for each 10 ng/g serum increase in total DDT. Together the two cohort studies (Longnecker et al., 2005; Venners et al., 2005) indicated an association between increasing DDT and DDE levels and foetal loss. In the Longnecker et al. (2001) study, the odds of preterm delivery were 3.1 times higher in women with serum DDE ≥ 60 μg/L than in those with DDE < 15 μg/L during pregnancy. Inconsistent results on the possible association between DDT/DDE levels and gestational age were reported in other studies.

Taken together, the positive dose-response relationships for these endocrine-regulated

end-points raise concern for effects of exposure to DDT on female reproductive health. It should be noted that the 'high' DDE serum may be substantially lower than in populations where indoor residual spraying is still occurring, emphasising the need for research in the context of IRS (WHO, 2011d). In some studies the onset of menopause was associated with DDT/DDE studies (Cooper et al., 2002; Akkina et al., 2004; Eskenazi et al., 2005), but in the Agricultural Health Study DDT exposure was associated with slightly older age at menopause (Farr et al., 2006).

11.4.7 Breast milk

DDT may shorten (Gladen and Rogan, 1995; Kostyniak et al., 1999; Rogan et al., 1987; Rogan and Gladen, 1985), prolong (Weldon et al., 2006), or have no effect (Cupul-Uicab et al., 2008) on the duration of lactation, due to the endocrine disruptive properties of DDT isomers (Wetterauer et al., 2012). It is not clear whether DDT or DDE exposure per se is linked to the duration of lactation. However, a recent study from an area where DDT is sprayed as IRS for malaria control showed no differences in lengths of lactation between three DDT sprayed villages and a reference village where no DDT has ever been applied (Bouwman et al., 1012).

Infant exposure to DDT is directly related to intake through breast milk and milk levels are linked to IRS spraying for malarial vector control. Bouwman et al. (1990b) analysed breast milk from mothers visiting baby clinics, in one regularly IRS controlled area and in a control area, ten years after DDT use in agriculture was banned in South Africa. Parity, maternal age, infant age, and percentage of milk fat between the two groups were similar. DDT was detected in all samples analysed, while DDE levels were significantly lower in the non-exposed group. It should be noted that in South Africa, as in many parts of Africa, extended periods of breastfeeding (up to two years) seems the norm in rural communities (Bouwman et al., 2006). Since there is no maximum residue level (MRL) for breast milk (FAO, 2005), comparing it to bovine milk MRLs found that, based on the volume of 800 mL of breast milk consumed by a 5-kg infant, the MRL for total DDT (ΣDDT) in cow's milk is notably exceeded (Bouwman et al., 2006).

First-born infants receive much higher levels of DDT in breast milk than their siblings (Bouwman et al., 2006; Gyalpo et al., 2012; Harris et al., 2001), but recently it became clear that there are also differences in pollutant levels and effects on male and female infants (Gascon et al., 2011; Grimalt et al., 2010; Jackson et al., 2010; Jusko et al., 2006; Ribas-Fitó et al., 2006). Therefore, infant gender may somehow affect levels of pollutants in breast milk by a mechanism that is not immediately clear. One gender being exposed to higher levels than the other would add to concern about possible effects of DDT on development as result of endocrine-disruptive properties of DDT chemicals, a situation already suspected in South Africa (Bornman et al., 2010). A recent study has shown indications of gender involvement (Bouwman et al., 2012).

11.4.8 Neurodevelopment

The main mode of action of DDT as an insecticide is disruption of the nervous system. In other animal studies, DDT is a neurodevelopmental toxicant (ATSDR 2002). In mice, particular exposure to DDT during sensitive periods such as prenatal (Craig and Ogilvie, 1974) and neonatal periods (Eriksson and Nordberg, 1986; Eriksson et al., 1990; Johansson et al., 1996) affected development of the nervous system and caused behavioural and neurochemical changes into adulthood (Eskenazi et al., 2009). Eskenazi et al. (2006) was the first study to show that prenatal exposure to DDT, and not only to DDE, was linked to neurodevelopmental delays during early childhood. Ribas-Fito et al. (2006) assessed neurocognitive development relative to DDT levels in cord serum of 475 children. At age 4, the level of DDT at birth was inversely associated with verbal, memory, quantitative and perceptual performance skills, and the associations were stronger among girls. Torres-Sanchez et al. (2007) found that the critical window of exposure to DDE *in utero* may be the first trimester of the pregnancy, and that psychomotor development in particular is targeted by the compound. The authors also suggested that residues of DDT metabolites may present a risk of developmental delay for years after termination of DDT use.

Sagiv et al. (2008) demonstrated an association between low-level DDE exposures and poor attention in early infancy. In a follow-up study, they found that prenatal organochlorine DDE was associated with attention deficit hyperactivity disorder (ADHD) behaviour in childhood (Sagiv et al., 2010).

11.4.9 Immune effects

Cooper et al. (2004) demonstrated that DDE modulates immune responses in humans with evidence of potential immunosuppression and

immune-mediated health effects such as infectious diseases and autoimmune diseases. Higher levels of prenatal DDE were associated with an increased incidence of otitis media in a study of Inuit infants (Dewailly et al., 2000). Workers directly exposed to DDT and lindane for 12–30 years, compared to a control population of individuals, had a higher prevalence of infectious diseases and of upper respiratory tract infections such as tonsillitis, bronchitis, and pharyngitis (Hermanowicz et al., 1982).

11.4.10 Recent health assessments of DDT

Two recent assessments of DDT and human health indicated issues that need attention. Eskenazi et al. (2009) found after reviewing 494 recent studies: 'The recent literature shows a growing body of evidence that exposure to DDT and its breakdown product DDE may be associated with adverse health outcomes such as breast cancer, diabetes, decreased semen quality, spontaneous abortion, and impaired neurodevelopment in children'. Focusing on DDT used in IRS, Bouwman et al. (2011) found that: 'The evidence of adverse human health effects due to DDT is mounting. However, under certain circumstances, malaria control using DDT cannot yet be halted. Therefore, the continued use of DDT poses a paradox recognized by a centrist-DDT position. At the very least, it is now time to invoke precaution. Precautionary actions could include use and exposure reduction.' They concluded that 'There are situations where DDT will provide the best achievable health benefit, but maintaining that DDT is safe ignores the cumulative indications of many studies. In such situations, addressing the paradox from a centrist-DDT position and invoking precaution will help design choices for healthier lives.' This was however, challenged by others (Tren and Roberts, 2011).

11.4.11 Carson on human health

The following quotations from Carson (1962) on the relationship between humankind and chemicals illustrate the concerns that are still with us today, but care should be taken not to interpret them out of context.

'Their [chemicals including pesticides] presence casts a shadow that is no less ominous because it is formless and obscure, no less frightening because it is simply impossible to predict the effects of lifetime exposure to chemical and physical agents that are not part of the biological experience.'

'The whole problem of pesticide poisoning is enormously complicated by the fact that a human being, unlike a laboratory animal living under rigidly controlled conditions, is never exposed to one chemical alone.'

'Some of the defects and malformations in tomorrow's children, grimly anticipated by the [US] Office of Vital Statistics, will most certainly be caused by these chemicals that permeate our outer and inner worlds.'

'The most determined effort should be made to eliminate those carcinogens that now contaminate our food, our water supplies, and our atmosphere, because these provide the most dangerous type of contact — minute exposures, repeated over and over throughout the years.'

11.5 Current human exposure

11.5.1 DDT used for indoor residual spraying

Following the essentially global ban on DDT use in agriculture, the only remaining repeated exposure of people to DDT is via IRS. It is otherwise assumed that illegal use is irregular and decreasing as stocks are dwindling. With between 2–3 grams of DDT applied per square metre on indoor walls, rafters, and outside under eaves, an average house may receive between 64–128 g/year, applied prior to the malaria transmission season. As DDT is long-lasting, the residual effect interrupts malaria transmission from an infected to an unaffected person by killing the female mosquito vector that rests indoors. It also acts as a contact irritant or spatial repellent (Grieco et al., 2007).

Arguably, the millions of people living in dwellings treated by DDT to protect them from malaria could be the largest non-occupationally exposed community in the world. The exposure is non-intentional, but inevitable (Bouwman et al., 2011). A closer look at how people are exposed in a domestic environment may indicate options for reduction in exposure and amounts applied. Such an exercise would be generic for any chemical used in similar ways. Again, despite the decades of DDT used as IRS, very little has been published on this subject.

11.5.2 DDT in air

DDT in ambient air is decreasing worldwide as its production and use has decreased dramatically

with the ban on its use in agriculture (Schenker et al., 2008). Background levels in air for the general population are therefore low, with a concomitant reduction in risk. However, DDT, applied repeatedly on various indoor and associated surfaces of dwellings as IRS, remains continuously available. Because DDT has to interrupt transmission by the vectors, it must remain bio-available for six months or longer. Sereda et al. (2009) proposed a process of continuous indoor sublimation, revolatilsation, and re-deposition of DDT, effectively redistributing the DDT throughout the treated dwelling. Transport via air, airborne dust, as well as regular sweeping and removal of house dust to the outside results in DDT pollution of the outdoor environment. Applied DDT therefore, does not remain stationary. For spatial repellence of mosquitoes to remain effective for months also implies that DDT remains in the indoor air for substantial periods. Van Dyk et al. (2010) presented evidence that DDT remains detectable in indoor air for at least 84 days after application. DDT in indoor air, and probably at lower concentrations in outdoor air near the homesteads, therefore remains chronically available for inhalation by all homestead residents. Recently, Ritter et al. (2011) modelled air and human intake in an IRS situation and found inhalation exposure to DDT as an important route of uptake. A particular concern are individuals who remain close to home for long periods, such as infants, children, the elderly, pregnant mothers, and those with domestic responsibilities.

11.5.3 DDT in food and water

Van Dyk et al. (2010) reported on levels of DDT in various environmental matrixes, food, and human serum from a DDT-sprayed village in South Africa. High levels of DDT were found, especially in food items such as chickens and outdoor soil, but less so in vegetables and water. The patterns of DDT, DDD, and DDE (breakdown products of DDT; DDD is dichlorodiphenyldichloroethane) were also such that it seems far more likely that DDT in humans was derived from home-produced animal foods and outdoor soil rather than from air, indoor dust, and water. Elsewhere it was also found that DDT in fish was less likely to contribute towards DDT burdens in humans under IRS conditions (Barnhoorn et al., 2009; Bouwman et al., 1990a). DDT uptake by humans living in dwellings treated by IRS with DDT is therefore mainly through DDT entering the food chain in the immediate environs of the sprayed dwellings themselves. This differs from the situation where DDT is used on crops as insecticide, and the human route of uptake is mainly via treated crops, dairy products, or contaminated fish. A situation can be envisaged where both types of exposures occur, but large commercial agriculture was and is rarely found in malaria areas. It seems that people living in DDT-treated dwellings have a greater DDT burden than those exposed otherwise (Eskenazi et al., 2009). Gyalpo et al. (2012) using models based on data showed that primiparous mothers have greater DDT concentrations than multiparous mothers, which causes higher DDT exposure of first-born children. The DDT in the body mainly was found to be mainly from diet, likely derived from the immediate environment of the homestead (van Dyk et al., 2012).

The results presented in the previous paragraph point towards options for exposure reduction to all chemicals used in IRS, not only DDT. For such options to be investigated, the dynamics of the IRS chemicals, inhabitants, and vector mosquitoes need to be better understood. The procedures involving IRS have remained static since their introduction in the early 1940s. In the meanwhile, much more knowledge has become available about environmental chemistry, health impacts, and vector behaviour. It is clear that, where possible, all measures should be taken to reduce the exposures of the inhabitants to IRS chemicals as far as possible. A Total Homestead Environment (THE) approach has been proposed whereby these interactions are studied with the aim of identifying opportunities of exposure reduction (Bouwman et al., 2011; Bouwman and Kylin, 2009; Sereda et al., 2009).

11.5.4 Legacy issues

Except for use in disease vector control, any other current use of DDT is illegal (Section 1.3.2). Although global production of DDT may gradually be declining, legacy sources remain a problem. With vast amounts of DDT having been manufactured in industrial countries, it comes as no surprise that wastes and emissions resulted in large pollution problems near factories that are now closed down. On the Pine River in Michigan, United States, for instance, even though a Superfund site, DDT is still found in the environment, and health concerns persist (Eskenazi et al., 2009). A no-consumption of fish advisory is still in effect, and clean-up of nearby residential properties is scheduled for 2012, among a whole range of other protective and mitigating measures (EPA, 2012c). Likewise, previous mitigation of sediments at the DDT formulation site of United Heckathorn Co. in Richmond Harbor, California,

which went bankrupt in 1966, seems not to have been as effective as anticipated and high levels of DDT in sediments and water persist (EPA, 2012b). An advisory against fish consumption (initially due to mercury but now for multiple pollutants) has been in effect since 1972. A search of the EPA Superfund site (EPA, 2012a) reveals 213 sites under United States jurisdiction that list DDT in one way or another at various stages of intervention.

Other legacy issues remain. DDT can undergo long-range transport via, air, water, and biota, contaminating areas where it has not been used or released (Bailey et al., 2000; Beyer et al., 2000; Iwata et al., 1993; O'Toole et al., 2006). Residues in glaciers are now being released as a result of climate change (Bettinetti et al., 2008; Geisz et al., 2008).

11.5.5 Effects of mixtures of chemicals

Legacy situations relating to DDT and malaria control hardly ever concern DDT only. With many commercial chemicals available, DDT now occurs together with many other pollutants in all manner of media and biota. Carson, after deliberating on combinations of pesticides in a common salad bowl said: 'Residues well within legally permissible limits may interact.', then said: 'What of other chemicals in the normal human environment? What in particular of drugs?' Later she brought in other chemicals: 'Added to these are the wide variety of synthetic oestrogens to which we are increasingly exposed — those in cosmetics, drugs, food, and occupational exposures. The combined effect is a matter that warrants the most serious concern.' Now, 50 years later, the issue of mixture effects, referred to in the Stockholm Convention as 'toxicant interactions', pharmaceuticals and personal care products (PPCPs) is a major area of research.

Scientific advances are finding ever more effects associated with chemicals in more and more biological systems; some effects such as endocrine disruption was barely understood at the time of Rachel Carson. This is evident from her statement: 'The ultimate answer is to use less toxic chemicals so that the public hazard from their misuse is greatly reduced. Such chemicals already exist. … the pyrethrins, rotenone, ryania, and other derived from plant substances.' We now know that even pyrethroids have health concerns (Bouwman and Kylin, 2009) and may interact with DDT (Eriksson et al., 1993). Even if DDT is not the major component of the cocktail of pollutants in many areas, it poses a legacy that cannot be ignored. Now that DDT is universally distributed in the biosphere, its interactions with other pollutants cannot be ignored, and will occupy science for many years to come, long after the final batch of DDT has been produced.

11.6 Future directions

11.6.1 Malaria, DDT, and the Stockholm Convention

Carson devoted relatively little space to DDT and malaria, but highlights the problem of development of resistance to DDT: 'Malaria programmes are threatened by resistance among mosquitoes.', and describes a number of instances around the world, including behavioural resistance. 'Apparently the adult mosquitoes had become sufficiently tolerant of DDT to escape from sprayed buildings.' The reverse of this situation, of pyrethroid-resistant mosquitoes re-invading South Africa when DDT was withdrawn, puts this issue into a new context. DDT had to be re-introduced to return to pre-1996 levels of morbidity and mortality. DDT resistance in South Africa and many other African countries was absent, not detected, or not strong enough to result in a breakdown of control. Whether behavioural resistance to DDT — where mosquitoes leave treated houses or fail to enter — effectively interrupts transmission is still not adequately resolved.

As described in Sections 11.2 and 11.3.1 above, DDT is one of the chemicals restricted by the Parties to the Stockholm Convention. The text of the convention is provided in Box 11.2. The provisions in the Convention regarding DDT can be seen as balancing the need for the continued use of DDT for malaria control where alternatives are not yet effective or proven, with an (undated) eventual aim of banning it. However, the experience in South Africa with pyrethroids (Maharaj et al., 2005) failing as an alternative to DDT in IRS has probably increased the threshold of expectation of proof of sustainability, especially regarding the requirements of viable alternatives listed in paragraph 5 (b) of the Stockholm Convention (see Box 11.2). No Party would want to revert to DDT if the alternatives are not as effective or better, measured by increased morbidity and mortality. The Stockholm Convention is driving various activities that can be followed on their website (www.pops.int).

11.6.2 Integrated vector management

The urgency of developing and establishing suitable alternatives to DDT for disease vector control is now widely recognised. Indeed the need for alternatives

Box 11.2 DDT in the Stockholm Convention, Annex B. Restriction, Part II

1. The production and use of DDT shall be eliminated except for Parties that have notified the Secretariat of their intention to produce and/or use it. A DDT Register is hereby established and shall be available to the public. The Secretariat shall maintain the DDT Register.
2. Each Party that produces and/or uses DDT shall restrict such production and/or use for disease vector control in accordance with the World Health Organization recommendations and guidelines on the use of DDT and when locally safe, effective and affordable alternatives are not available to the Party in question.
3. In the event that a Party not listed in the DDT Register determines that it requires DDT for disease vector control, it shall notify the Secretariat as soon as possible in order to have its name added forthwith to the DDT Register. It shall at the same time notify the World Health Organization.
4. Every three years, each Party that uses DDT shall provide to the Secretariat and the World Health Organization information on the amount used, the conditions of such use and its relevance to that Party's disease management strategy, in a format to be decided by the Conference of the Parties in consultation with the World Health Organization.
5. With the goal of reducing and ultimately eliminating the use of DDT, the Conference of the Parties shall encourage:
   (a) Each Party using DDT to develop and implement an action plan as part of the implementation plan specified in Article 7. That action plan shall include:
      (i) Development of regulatory and other mechanisms to ensure that DDT use is restricted to disease vector control;
      (ii) Implementation of suitable alternative products, methods and strategies, including resistance management strategies to ensure the continuing effectiveness of these alternatives;
      (iii) Measures to strengthen health care and to reduce the incidence of the disease.
   (b) The Parties, within their capabilities, to promote research and development of safe alternative chemical and non-chemical products, methods and strategies for Parties using DDT, relevant to the conditions of those countries and with the goal of decreasing the human and economic burden of disease. Factors to be promoted when considering alternatives or combinations of alternatives shall include the human health risks and environmental implications of such alternatives. Viable alternatives to DDT shall pose less risk to human health and the environment, be suitable for disease control based on conditions in the Parties in question and be supported with monitoring data.
6. Commencing at its first meeting, and at least every three years thereafter, the Conference of the Parties shall, in consultation with the World Health Organization, evaluate the continued need for DDT for disease vector control on the basis of available scientific, technical, environmental and economic information, including:
   (a) The production and use of DDT and the conditions set out in paragraph 2;
   (b) The availability, suitability and implementation of the alternatives to DDT; and
   (c) Progress in strengthening the capacity of countries to transfer safely to reliance on such alternatives.
7. A Party may, at any time, withdraw its name from the DDT Registry upon written notification to the Secretariat. The withdrawal shall take effect on the date specified in the notification.

to DDT has been one of the drivers that led the WHO to develop a global strategic framework on integrated vector management (IVM) (WHO, 2004). IVM is a strategy for the optimal use of vector control methods, procedures and resources aiming to improve the efficacy, cost-effectiveness, ecological soundness and sustainability of vector control (WHO, 2012). Development of alternative insecticides is one way to address the problem of insecticide resistance, and it is probable that improved formulations of existing insecticide molecules will be available soon although new insecticide molecules will take considerably longer to come to the market (Hemingway et al., 2006). However, evolutionary selection for resistance will continue against any new modes of action unless the selection pressure on vector populations is substantially reduced (Read et al., 2009).

It is therefore critical that the choice of vector control methods should be carefully based on the evidence of their effect on transmission reduction and their appropriateness in the local context. Combinations of methods, including house screening, environmental management, repellents, trapping, and biological

control, with insecticide-treated bed nets or indoor residual spraying, may provide superior control while reducing reliance on single modes of action (Takken and Knols, 2009). For example, the use of IRS or insecticidal bed nets could usefully be complemented by larval source management or repellents, particularly where part of the vector population bites outdoors (Fillinger et al., 2009; Hill et al., 2007).

In its implementation, vector control should not be combined only with disease control programmes. Integrated vector management would benefit substantially from integration within the health sector, collaboration between sectors and active participation of communities (WHO 2012; Chanda et al., 2008; Beier et al., 2008).

11.6.3 Malaria, DDT, and the World Health Organization

The WHO has a major commitment to combating malaria using prompt treatment of cases, and vector control by insecticide-treated bed nets and IRS, implemented within an integrated vector management strategy. The summary of the latest WHO position statement on DDT (WHO, 2011c) is provided in Box 11.3, confirming that DDT is still required for malaria control. The WHO also introduced a global strategic framework for integrated vector management, expanded on in the previous section.

Recent unease with safety issues about DDT also prompted the WHO to reassess the potential health impact of DDT used for IRS (WHO, 2011d). The Consensus statement concluded: 'For households where IRS is undertaken, there was a wide range of DDT and DDE serum levels between studies. Generally, these levels are below potential levels of concern for populations. Considering the ranges of exposures in treated households that are summarised in Table 11.1, in some areas, the exposures in treated residences have been higher than potential levels of concern. Efforts are needed to implement best practices to protect residents in treated households from exposures arising from IRS. Of particular concern would be women of childbearing age who live in DDT IRS-treated dwellings and transfer of DDT and DDE to the fetus in pregnancy and to the infant via lactation.' The WHO has a number of initiatives and programmes relating to malaria control and IRS, which can be followed on their website (http://www.who.int/malaria/en/).

11.6.4 Likely future developments

It is clear that there is a roadmap for the exit of DDT. There remains the need to find, further refine, convincingly demonstrate sustainability, and implement alternatives. Although there is a roadmap, there is no timetable. The pieces need to be found and fitted within the budgetary constraints and competing agendas. Given the current climate regarding research and development budgets and interfacing political agendas, the final demise of DDT still seems some way off. However, DDT has taught us a lot. It is probably the most widely known quintessential environmental pollutant. It will remain a model molecule and benchmark against which many others will be compared. It has shown the good and bad side of what can be done by chemicals. One thing is for certain — DDT will remain a source of contention for some time to come. It will probably remain in inert environmental media for decades to come, but there may come a time when it will only be found in books, such as *Silent Spring*, to be read in gardens with birds.

11.7 The legacy of Rachel Carson

It is clear that the social conscience awakened by Rachel Carson 50 years ago gave momentum to a groundswell of actions and interventions that is

Box 11.3 Global Malaria Programme: The use of DDT in malaria vector control. WHO position statement, 2011

DDT is still needed and used for disease vector control simply because there is no alternative of both equivalent efficacy and operational feasibility, especially for high-transmission areas. The reduction and ultimate elimination of the use of DDT for public health must be supported technically and financially. It is essential that adequate resources and technical support are rapidly allocated to countries so that they can adopt appropriate measures for sound management of pesticides in general and of DDT in particular. There is also an urgent need to develop alternative products and methods, not only to reduce reliance on DDT and to achieve its ultimate elimination, but also to sustain effective malaria vector control (WHO, 2011e).

slowly but steadily making inroads at a myriad of levels addressing human and environmental concerns about chemicals. Reading *Silent Spring*, one is struck by how modern and current many of the issues that she raised are, although some are now described by other terminology. Resistance development, genetic damage, genetic modification, cancer, effects of mixtures, the need for more and improved biomarkers, sterile male techniques, push-pull biological control, ethical choices, and the need for concerted action at all levels, are just some of these. Although not yet aware of endocrine disruption as a mode of action of pesticides, effects such as cancer involving reproductive hormones was one of the issues she addressed. Not only did she attack the indiscriminate use of pesticides, she also proposed forms of integrated pest/vector management and biological control in chapter 17 that seem so modern and obvious today, but conceptually are more than 50 years old. Long-range transport of chemicals through air was also not well understood at the time of *Silent Spring*.

The heading of Chapter 17 — The Other Road — elicits a strong feeling that we have not taken the road that we should have taken much earlier on, an opportunity that was missed, an option not taken that will resonate for decades to come. Carson opined in her last sentence of *Silent Spring*: 'The concepts and practices of applied entomology for the most part date from the Stone Age of science. It is our alarming misfortune that so primitive a science has armed itself with the most modern and terrible weapons, and that in turning them against the insects it has also turned them against the earth.' Applied entomology has long since incorporated pest control measures other than chemicals and one can but ponder how much this was due to *Silent Spring*?

With more than 10 % of bird species worldwide now threatened in one way or another, and some already gone since *Silent Spring*, the silence that Carson called upon to illustrate the impact of chemicals has now also crossed into other realms of environmental impact. Radiation (also addressed by Carson), climate change, habitat destruction, economic mismanagement of the environment, human population expansion, and more — all of them have Other Roads, and we missed the obvious early signposts or failed to act upon them. Will there be more signposts to Other Roads that we will miss? Two final thoughts on this. Paraphrasing Jean Rostand; are our obligations to endure met by our rights to know? As Carson said 50 years ago: '*The choice, after all, is ours to make*.'

Table 11.1 Early warnings and actions

1873	The DDT molecule was first synthesised
1939	Paul Müller showed the insecticidal property of DDT
1943-44	Typhus broke out in Naples, Italy in October 1943. By January 1944, and after treating 1 300 000 persons over a three week period with DDT, the epidemic was brought under control
1946	Indoor residual spraying (IRS) with DDT to interrupt malaria transmission was introduced in South Africa
1948	Paul Müller was awarded the Nobel Prize for Medicine or Physiology. Already in the prize presentation speech problems with flies developing resistance against DDT was mentioned
1948	Use of DDT inside dairies in the US was prohibited
1950s-60s	DDT was the primary tool used in the first global malaria eradication programme. The insecticide was used to spray the walls and ceilings of houses and animal sheds with coverage of entire populations
1951	First reports of the development of insecticide resistance to DDT. This became an obstacle in the eradication of malaria, and was one of the reasons behind the abandonment of the global malaria eradication campaign
1958	Complete coverage of malaria areas in South Africa via indoor residual spraying with DDT achieved
1962	The novel *Silent Spring* was published, drawing attention to the impacts of chemicals on the environment and human health. Special emphasis was given to DDT
1964	Stockholm University, Sweden, set up a laboratory for the analysis of DDT in the environment. These activities led, inter alia, to the identification of polychlorinated biphenyls (PCB) as environmental contaminants
1970s	Based on the increasing amount of data on environmental effects, restrictions on the use of DDT were set in place in different countries, but still, the use and miss-use of DDT continued. Amidst concerns about the safety of DDT, the insecticide was banned for use in agriculture in many countries
1996	South Africa discontinued the use of DDT for malaria control and introduced pyrethroids on a large scale
2000	South Africa re-introduced DDT after failure of pyrethroids in many areas. Pyrthroids are used where viable
2004	The Stockholm Convention on Persistent Organic Pollutants came into force eliminating the production and use of DDT except for disease vector control where safe, effective and affordable alternatives are not available
2010	DDT is now only produced in India, from where it is exported to other, mostly African, countries. China has recently stopped its production of DDT. South Africa formulates DDT with the technical product from India, and exports the formulated product to several other African countries.

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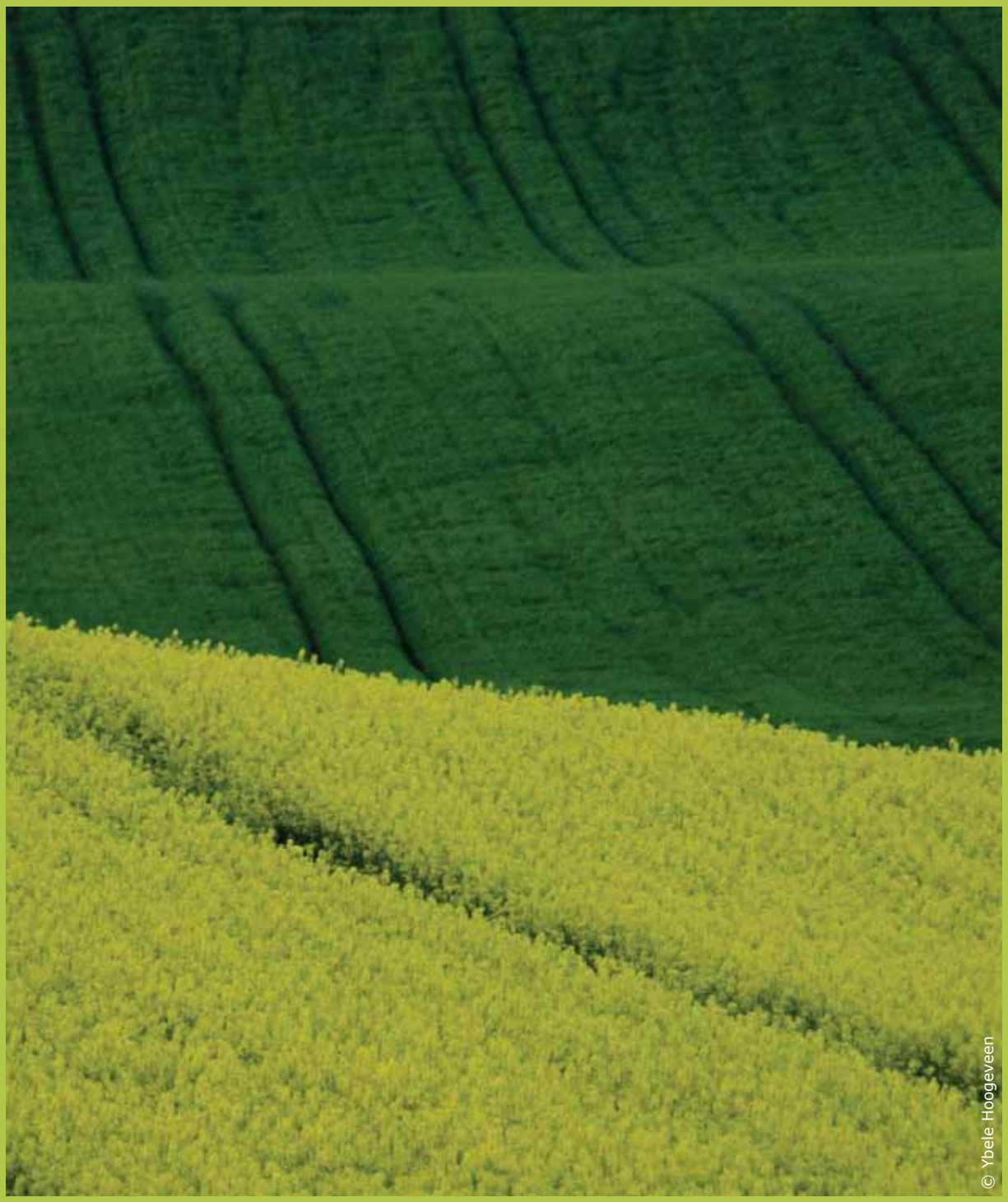
Part B Emerging lessons from ecosystems



Contents — Part B

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12 Booster biocide antifoulants: is history repeating itself?

Andrew R. G. Price and James W. Readman

Tributyltin (TBT) was widely used as an effective antifouling agent in paints for ships and boats until the European Community restricted its use in 1989 because of its proven harm to the environment and shellfisheries. Thereafter, booster biocides were introduced to enhance the performance of antifouling paints. They were believed to be less damaging to aquatic life than TBT. Subsequently, however, it has been established that booster biocides can also create significant environmental risks.

This chapter outlines the background to booster biocide use, the early warnings about their potential physiological and ecological impacts on non-target species, and the actions taken in response. The science that set some alarm bells ringing is described, along with lessons that could influence the future of an industry still searching for less environmentally invasive solutions.

Booster biocide antifouling agents threaten a variety of habitats — from coral reefs and seagrass beds to open moorings — within the EU and globally. Their primarily herbicidal properties mean that coral zooxanthellae, phytoplankton and periphyton are particularly vulnerable. Compared to TBT, an antifouling agent with a quite specific action, booster biocides have more broad-spectrum impacts. The wider ecological effect of shifting to booster biocides remain poorly understood but of considerable concern because they may affect the base of marine food chains.

From a toxicological viewpoint, booster biocides do not threaten to have endocrine disrupting properties similar to TBTs. At current environmental concentrations, however, some can damage primary producers and some are persistent. While legislation has been introduced to control their use, the rigour of regulations varies between countries. These geographical disparities need to be addressed, and future biocidal products and novel approaches to antifouling should be better appraised.

For policymakers, the challenge is to protect non-target biological communities from selective change resulting from booster biocide use. Persistence, bioaccumulative and toxic (PBT) criteria can be used to evaluate the relative potential impact from the available biocides, and consequently target appropriate legislation. Nevertheless, lateral thinking, aiming to identify novel materials and strategies to address antifouling, could pay dividends in the future.

12.1 Introduction

12.1.1 The need for antifoulants

Preventing plants and animals from growing on and fouling the hulls of boats is essential for the shipping industry and boating communities. The application of coatings to vessel hulls to prevent fouling organisms from settling dates back to Ancient Greece (Yebra et al., 2004) and possibly even earlier.

Protecting the hull was initially the principal concern and the earliest antifoulants often acted more as physical barriers than chemical toxicants. They prevented the isopod crustacean 'gribble' (*Limnoria*) and the infamous *Teredo* worm (actually a mollusc) from reducing hardwood planking to pulp within a matter of months. However, hull damage was not the only concern. Fouling organisms made sailing ships sluggish and severely limited their capacity to sail to windward. For naval and fighting ships, severely reduced speed and impaired manoeuvrability could mean losing sea battles ([1]).

Fouling organisms create 'hull roughness', increasing friction between the hull and the water (Evans et al., 2000). Combined with the weight of fouling organisms attached to the hull, this can lead to considerable increases in fuel consumption. A layer of algal slime only 1 mm thick will increase hull friction by 80 % and cause a 15 % loss in ship speed, while a 5 % increase in fouling for a tanker weighing 250 000 deadweight tonnes will increase fuel usage by 17 % (MER, 1996; Evans et al., 2000).

Antifouling agents, applied as paint, are the most economically efficient solution found so far. Yet they come at an environmental cost, as graphically illustrated by the organotin compound tributyltin (TBT).

12.1.2 The rise and fall of TBT

Shortly after World War II, TBT became a common additive in antifouling paints, especially in 'self-polishing' formulations which, by design, release toxic persistent substances into the environment. The use of powerful antifoulants enabled the periods between dry-docking for repainting to be extended and TBT was particularly valued because it does not cause galvanic corrosion to aluminium hulls. By the 1980s, however, TBT had been recognised as a global pollutant and its environmental effects on non-target organisms are now infamous (Santillo et al., 2002).

TBT's effects include shell malformations in oysters, which can render the produce worthless. In Arcachon Bay (France) alone TBT caused an estimated loss of USD 147 million through reduced production of the oyster *Crassostrea gigas* (Alzieu, 1991). A more serious and pervasive impact was 'imposex' — the development of male sexual organs in female marine gastropods. Worldwide, imposex has been documented for around 150 species (Vos et al., 2000). This endocrine disruption was first discovered in the early 1970s (reviewed in Santillo et al., 2001). Because of limited analytical capabilities, however, the physiological and ecological consequences were only attributed to TBT in the 1980s when many gastropod populations had declined. Importantly, mollusc species can be affected at very low concentrations — less than 10 billionths of a gram per litre (10 ng/L). By the late 1980s, the TBT problem was global.

Steps were taken to ban TBT because of its unacceptable toxic effects on commercial shellfish (especially oysters) and other non-target organisms. Regulatory controls included the EC Directive 89/677/EEC (1989) banning TBT use on small boats (< 25 m, primarily pleasure craft). Important legislation to phase out TBT use on larger vessels includes the International Maritime Organization (IMO) International Convention on the Control of Harmful Anti-fouling Systems (IMO, 2008). Santillo et al. (2001) provide further insights into the complexities surrounding TBT, its ban and the delay in controls

Barnacles on a boat. Application of coatings is used to prevent plants and animals from fouling on the hulls of boats.

Photo: © istockphoto/Carsten Madsen

([1]) Yebra et al. (2004) provide additional information on the historical development of antifouling systems.

coming into force. The extent of hazard was initially underestimated for both technical and socioeconomic reasons. Specifically:

- it was incorrectly assumed that an environmental quality target (EQT) of 20 ng/l would be sufficiently protective;
- persistence, accumulation and wider dissemination in the environment were underestimated;
- organotin bioaccumulation was underestimated (Labare et al., 1997);
- the geographical scale of the problem was not fully appreciated (inadequate data collection);
- imposex observed in 1970 in predatory gastropods in Arcachon Bay was considered acceptable — it had no immediately obvious economic cost — whereas the failure of the oyster stocks soon after was not acceptable;
- the transboundary nature of the problem was not fully appreciated until continuing TBT problems in Japan (despite a national ban in the late 1990s) highlighted the issue.

Many of these findings from TBT are useful reminders for managing booster biocides. They highlight the value of recognising potential environmental hazards early, and introducing protocols for monitoring and appropriate regulatory measures.

12.1.3 Effects of the TBT ban

EU and national legislative prohibitions on using TBT for small craft reduced pollution substantially. In Arcachon Bay, for example, concentrations fell from 900 ng/L in 1983 to below 10 ng/L in the late 1980s. The oyster beds recovered and commercial harvesting resumed during the same period. The (limited) controls imposed were hailed by some as a 'solution' to the TBT problem. Evans et al. (2000) reported a general recovery of dogwhelk populations in the United Kingdom, partially confirming this claim. However, in other European areas recovery appears to have been mixed, or slower than expected, despite the imposition of regulations for small craft (see Santillo et al., 2001).

Experience in New Zealand is one of several examples illustrating the complex interactions between TBT inputs, concentrations, accumulation and biological effects and, most importantly, the beneficial effects of legislation (Table 12.1).

On the other hand, the ban on TBT does not seem to have been very effective everywhere. Levels are still going up in Asia, implying either that it is still being used or that there are issues surrounding persistence and transportation that are not yet fully understood.

12.2 Early warnings, actions and inactions

Booster biocides were developed, at least initially, for the 'small boat' market, following the European Community ban on TBT for vessels of less than 25 m in 1989. A wide range of booster biocide compounds have been used or promoted (Box 12.1). Whilst the list is substantial, not all products have been marketed and some newly introduced compounds such as phenylborane pyridine, Econea, capsaicin and medetomidine (Thomas and Brooks, 2010) are not included.

For example, in the United Kingdom during the 1990s, antifouling agent use was massively dominated by copper(I) oxide, followed by (in order of use) diuron, Irgarol 1051, zinc pyrithione and dichlofluanid. Some of these are now banned (see Section 12.4.1). The organic biocides included agrochemicals (e.g. diuron), other compounds that were previously registered as biocides (e.g. Irgarol 1051) and personal care products such as the anti-dandruff agent zinc pyrithione.

Contamination of coastal waters by booster biocides was first reported in the early 1990s. Irgarol 1051 concentrations of up to 1700 ng/L were reported around the Cote d'Azur on the French Riviera (Readman et al., 1993). These high levels were actually discovered during a survey of agricultural triazine herbicides, which are measured using the same analytical protocol. That study triggered subsequent research, which confirmed broad contamination of boating areas in Europe, Bermuda, the United States of America, Japan, Singapore and Australia (Konstantinou and Albanis, 2004; Readman, 2006; Scarlett et al., 1999). Interestingly, Irgarol 1051 was detected in Australia, despite not being used in Australia's boating industry.

Readman et al. (1993) was followed by the pioneering studies of Dahl and Blanck (1996) on Irgarol 1051's toxicity to periphyton communities. These algae and microbes live in a surface film attached to submerged surfaces including plants,

Table 12.1 Complexities associated with TBT accumulation and legislative controls for leisure boats and ships in New Zealand from studies in 1988/1989 and 1994/1995

Issue	Environmental and governance implications
Imposex measured at different resolution (% imposex, or penis length in females relative to males)	Judging the effect of TBT on gastropods depends partly on the sensitivity of the measure used
Re-release of TBT residues in sediments and long half-life of TBT (2.5–3 years) in sediments	Can obscure actual TBT levels and the effectiveness of legislation
1989 legislation (TBT ban on < 25 m leisure craft)	No fall in % imposex at Evans Bay marina in Wellington harbour, despite TBT ban for small craft, due to close proximity of commercial Burnham Warf and leaching of TBT. Continual monitoring needed to determine the effectiveness of legislation for larger ships
1993 legislation (TBT banned completely for New Zealand vessels but not for foreign ships)	
Sampling strategy (e.g. presence of commercial ships near leisure craft)	

Source: Smith, 1996.

rocks and the hulls of boats. Periphyton is also an important indicator of water quality. The authors demonstrated the potential for ecological effects to occur at the concentrations of Irgarol 1051 present in coastal waters. Together, these studies raised concerns and inspired other scientists to conduct more in-depth research.

Besides antifouling paints, however, booster biocides in aquatic environments derive from a variety of other sources, including:

- agricultural and domestic uses of chlorothalonil, dichlofluanid and diuron as agents to deal with weeds, fungi and other unwanted plant growth;
- some anti-dandruff shampoos, in which zinc pyrithione (ZPT) is the active agent against the scalp fungus, *Malasseziaglobosa*.

A comprehensive picture of booster biocide distributions and concentrations in European waters emerged from the Assessment of Antifouling Agents in Coastal Environments (ACE) project, which ran from 1999 to 2002. In the course of the project, water samples (and sediments from some areas) were collected from marinas, harbours,

Box 12.1 Examples of booster biocides used or promoted as agents in antifouling paints

- 2-methylthio-4-tertiary-butylamino-6-cyclopropylamino-s-triazine (Irgarol 1051)
- 1-(3,4-dichlorophenyl)-3,3-dimethylurea (diuron)
- 4,5-dichloro-2-n-octyl-4-isothiazolin-3-one (Sea-Nine 211)
- N-dichlorofluoromethylthio-N', N'-dimethyl-N-phenylsulphamide (dichlofluanid)
- 2,4,5,6-tetrachloro isophthalonitrile (chlorothalonil)
- bis(1hydroxy-2(1H)-pyridethionato-O,S)-T-4zinc (zinc pyrithione)
- 2-(thiocyanomethylthio)benzthiazole (TCMBT)
- 2,3,5,6-tetrachloro-4-(methyl sulphonyl) pyridine (TCMS pyridine)
- cuprous thiocyanate
- 4-chloro-meta-cresol
- arsenic trioxide
- cis1-(3-chloroallyl)-3,5,7-triaza-1-azonia adamantanechloride
- zineb
- folpet
- thiram
- oxy tetracycline hydrochloride
- ziram
- maneb

estuaries and coastal waters, covering diverse European coastal systems (ACE, 2002; Readman, 2006). Of the major booster biocides, diuron was found in the greatest mean concentrations, with the highest levels in north-western Europe. Irgarol 1051 was present at lower mean concentrations than diuron, with Mediterranean coastal environments the most contaminated. Chlorothalonil, dichlofluanid and Sea-Nine 211 were sporadically encountered, primarily in the Mediterranean. In isolated cases, however, high concentrations were recorded. Measurable concentrations of the degradation products of Irgarol 1051 and diuron were also recorded, albeit at lower levels than the parent compounds.

Globally, data for the most common biocides (diuron, Irgarol 1051 and Sea-Nine 211) are available for Europe, North America and Japan, while negligible data are available for other regions. Konstantinou and Albanis (2004) summarise data on Irgarol 1051 levels in water and sediment samples reported in the literature. More recently, booster biocides have been detected in the remotest part of the Indian Ocean, although at negligible concentrations. Indeed, of the substances sought, only Irgarol 1051 was detected. Moreover, it was only encountered in two of the 31 samples analysed, at concentrations of 2 ng/L and 8 ng/L (Guitart et al., 2007).

12.3 Early warnings: the science on antifouling agents

12.3.1 Persistence and toxicity

Concerns about the potential environmental impacts of booster biocides arose because of the high concentrations reported at an increasing number of areas, coupled with findings regarding their toxicity to periphyton (at equivalent concentrations). The high concentrations in coastal environments are maintained by leaching from vessels, although dilution and degradation act to reduce concentrations (see below). While some antifouling biocides have other uses (e.g. as agrochemicals), in marinas and harbours antifouling use normally dominates the total input (Konstantinou and Albanis, 2004). Compounds can be removed from the water column through, for example, biotic degradation, photo-degradation, chemical hydrolysis, attachment to particulates followed by sedimentation, volatilisation or bioaccumulation (Readman, 2006).

The MAM-PEC model (van Hattum et al., 1999) was developed to predict environmental concentrations of antifouling agents in the marine environment. It has been validated using the data set collected during the ACE project and can now be applied to predict future concentrations.

The half-lives of booster biocide compounds vary and can be considerable. The abiotic and biotic half-lives for these booster biocide agents, examined in laboratory studies and under controlled field conditions, indicated that diuron and Irgarol 1051 were substantially resistant to degradation in comparison with other agents. Thomas et al. (2002) and Thomas and Brooks (2010) have reported the following highly variable half-lives for booster biocides:

- Irgarol 1051: 100 days;
- dichlofluanid: 18 hours;
- chlorothalonil: 1.8 days;
- Sea-Nine 211: < 24 hours;
- zincpyrithione: < 24 hours;
- TCMTB: 740 hours;
- zineb: 96 hours;
- diuron: no degradation over 42 days in seawater when associated with antifouling paint particles (without this particle association it has a 14-day half-life).

More worrying still were the toxic effects that scientists were beginning to identify, reviewed in studies such as Jones (2005), Yamada (2006) and more recently by Thomas and Brooks (2010). The herbicidal properties of most antifoulants mean that marine plants appear to be particularly vulnerable to many of these biocides. As noted above, the first published study on the herbicidal properties of booster biocides was by Dahl and Blanck (1996), addressing the toxicity of Irgarol 1051 to periphyton communities. Long-term effects were detected at 0.25–1 nM (63–250 ng/L), which is within the range of concentrations reported for coastal waters. Later studies (Okamura et al., 2003; Jacobson and Willingham, 2000; Fernandez-Alba et al., 2002) have confirmed the vulnerability of algae/phytoplankton to booster biocides.

Using natural populations of phytoplankton, Readman et al. (2004) reported toxic effects of Irgarol 1051 at low concentrations with a 72-hour half maximal effective concentration (EC50) of

70 ng/L ([2]). The endpoint used in this study was the selective reduction in 19'-hexanoyloxyfucoxanthin. Again, this concentration is well within the range of concentrations reported in coastal waters.

Devilla et al. (2005) provide some insights into relative susceptibilities to a range of booster biocides. Growth inhibition results following 72 hours of exposure indicated that *Synechococcus* sp. was more tolerant to zinc pyrithione (NOEC ([3]) of 1 000 ng/L) and Sea-Nine 211 (NOEC of 900 ng/L) than *E. huxleyi* (EC50 of 540 and EC50 of 350 ng/L, respectively). In contrast, *Synechococcus* sp. was more sensitive to diuron (EC50 of 550 ng/L) than *E. huxleyi* (EC50 of 2 260 ng/L), whereas exposure to Irgarol 1051 similarly impacted both species (EC50 of 160 and 250 ng/L, respectively).

Endocrine disruption was also assessed within the ACE Project. None of the antifoulants evaluated (Irgarol 1051, Sea-Nine, chlorothalonil, diuron, dichlofluanid, maneb and ziram) showed a strong estrogenic response. Thomas et al. (2001) identified persistence and toxicity as critical features in the risk evaluation of booster biocides.

Despite accumulating substantial information, Voulvoulis et al. (2002) considered that additional data would still be required to properly evaluate the risks associated with widespread use of the booster biocides Irgarol 1051, diuron, Sea-Nine 211 and chlorothalonil. They cautioned against the use of TCMS pyridine, TCMTB and dichlofluanid, although again identified a lack of appropriate data. And in their initial risk evaluation, zinc pyrithione and zineb appeared to be the least hazardous options for the aquatic environment. However, analytical constraints for these latter booster biocide compounds render environmental assessment difficult.

12.3.2 Adverse ecological effects on corals

The herbicidal (chlorophyll photosystem II-inhibiting) mode of action of Irgarol 1051 also raises concerns regarding the potential impact on zooxanthellae — the symbiotic microalgae that live within warm water corals to the mutual benefit of both the coral polyps and the algae. This has important implications for the growth, survival and health of corals, already rendered vulnerable by events such as the 1998 coral bleaching episode in the Indian Ocean. That event arose from exceptional seawater warming in 1997–1998 and led to massive coral mortality. Most island archipelagos were severely affected, with mortality of over 90 % to considerable depths in the Maldives, Seychelles and Chagos (Sheppard et al., 2002).

During bleaching events coral expel, to a greater or lesser extent, their symbiotic algae known as zooxanthellae. In extreme events, as occurred in 1998, zooxanthellae are totally evicted from their host. All that remains is dead white coral skeletons or, worse still, rubble and debris — something very different from a vibrant, living reef attached firmly to the seabed (see Price, 2009). Recent publications have shown that Irgarol 1051 inhibits the photosynthesis of both zooxanthellae isolated from the coral tissues and also zooxanthellae still within the host (coral) tissues (i.e. in symbio) at environmentally relevant concentrations (as low as 60 ng/L) (Owen et al., 2002; Owen et al., 2003; Jones, 2005). Studies at many harbours in the world report concentrations of Irgarol 1051 at or above this level (Konstantinou and Albanis, 2004). This creates the possibility that antifouling agents will disperse to offshore sites, including coral reefs.

'Coral bleaching' — the dissociation of symbiosis between corals and algae — is a common but significant sub-lethal stress response requiring many months to recover. It is generally considered to be caused by elevated water temperatures but diuron and Irgarol 1051 will also cause bleaching and, like warm water bleaching, they may operate by affecting algal/zooxanthellae photosynthesis (Jones, 2005). The notion that Irgarol and diuron contamination could exacerbate bleaching caused by elevated water temperatures has not yet been tested.

Jones (2005) points out that at low levels and over short exposure periods, the coral-bleaching effects of herbicides can be reversible (i.e. when corals are returned to clean seawater) and vary according to type of herbicide. However, on exposure to higher concentrations in the light or over longer exposure periods, sustained long-term reduction of the photochemical efficiency of the algae (symptomatic of chronic photo-inhibition) follows.

Corals and reefs in European waters lack symbiotic microalgae, meaning that booster biocide toxicity

([2]) The EC50 is the concentration of a toxicant that induces a response halfway between the baseline and maximum after a specified exposure time.
([3]) NOEC denotes 'no observable effect concentration'.

to coral microalgae is not directly relevant within the EU. However, several European countries have dependent territories with significant coral reefs. In some cases (e.g. France, the Netherlands and some UK dependent territories), the environmental legislation of the dependent territories is closely allied to that of the European country. In others, such as Chagos, British Indian Ocean Territory, environmental legislation is more independent.

Chagos happens to lie in the remotest part of the Indian Ocean and studies more than 10 years ago revealed that these atolls and islands were virtually pristine and contaminant free (Everaarts et al., 1999; Readman et al., 1999), despite the fact that the biggest atoll and island, Diego Garcia, is an important military base. Booster biocide concentrations from the atolls of Chagos were determined during early 2006 as part of an international environmental research effort (Guitart et al., 2007). This has provided a useful international baseline or standard, against which biocide concentrations in European waters and elsewhere could be compared. More generally, studies have recently highlighted the scientific importance of Chagos as a 'clean' control site for monitoring environmental change (SOFI, 2009; Sheppard et al., 2009). Environmental monitoring is also an important requirement of national, European and international agreements to which the British Indian Ocean Territory is party.

12.4 The lessons drawn

12.4.1 Permitted agents

Controls and legislation have been developed to address the accumulation of booster biocides in the marine environment and the marked toxicity of certain agents. The booster biocides permitted in European waters and the legislative situation, as of 2002, are listed in Tables 12.2 and 12.3. This shows that several agents previously permitted for small craft in the United Kingdom, including diuron and Irgarol 1051, are now prohibited. In the United Kingdom, only three organic booster biocides are permitted. In Sweden there is even greater restriction. In the Netherlands, France, Greece and Spain, a greater number of agents are permissible. In the Netherlands, files for antifouling agents are being reviewed. In Denmark, diuron and Irgarol 1051 were banned for use on pleasure craft in 2000. Results from an environmental risk analysis of Sea-Nine 211 and zinc pyrithione in Danish waters demonstrated that, in most cases examined, the PEC/PNEC (predicted environmental concentration/predicted no effect concentration) ratio was less than 1, indicating an acceptable risk.

The Biocidal Products Directive (98/8/EC) provides for the authorisation of biocidal products within the European Union. The Directive harmonises the data requirements for existing and new biocides within the EU, including antifouling agents (product type 21). Any company seeking to register an antifouling agent was required to submit a notification in 2002 and provide a base set of data. Time scales for submitting additional necessary data have not been established.

National legislative positions on antifoulings are presented in IYP (2008) and Thomas and Brooks (2010) provide a review of the current legislative position.

Experiences in Bermuda provide insights that may have useful applications elsewhere. Within a period of 10 years, harmful booster biocides were identified in some harbour areas and, because of their potential harm to corals, were banned in the entire territory (Box 12.2).

Box 12.2 Case study — Bermuda

In June 1995, Readman visited Bermuda and analysed seawater samples for antifouling agents including booster biocides. Levels of Irgarol were high in some harbour areas and sparked fears of damage to coral endosymbiotic algae (Readman, 1996). Extended data were later published (Connelly et al., 2001).

The Bermuda Government (Ministry of the Environment) funded toxicological studies at the Bermuda Biological Station for Research that demonstrated the vulnerability of the corals (Owen et al., 2002 and 2003). On 1 July 2005, Irgarol- and diuron-based antifouling paints were banned in Bermuda by amendment to the Bermuda Statutory Instrument BR 20/1989 Fisheries (Anti-Fouling Paints Prohibition) Regulations 1989.

Table 12.2 Use of metallic antifoulants and organic booster biocides on yachts < 25 m in European waters

	United Kingdom	France (a)	Greece (a)	Spain (a)	Sweden	Denmark (b)	Netherlands (b)
Copper(I) oxide	+	+	+	+	+ (c)	+	+
Copper thiocyanate	+	+	–	–	+ (c)	+	+
Cu powder	–	–	–	–	+ (c)	+	–
Chromium trioxide	–	–	–	–	–	–	+
Diuron	–	+	+	+	–	–	+
Irgarol 1051	–	+	+	+	+	–	+
Zinc pyrithione	+	+	+	+	–	+	
Dichlofluanid	+	+	+	+	–	–	+
TCMTB	–	–	–	–	–	–	–
Chlorothalonil	–	+	+	–	–	–	–
TCMS pyridine	–	–	–	–	–	–	–
SeaNine 211	–	–	–	+	–	+ (d)	–
Ziram	–	–	+	–	–	–	+
Zineb	+	–	–	–	–	–	+
Folpet	–	–	+	–	–	–	–
Total (booster biocides)	3	5 (a)	7 (a)	5 (a)	1	2	5

Note: (+) Agent permitted.
(–) Agent not permitted.
(a) Very limited/no approval scheme (in principle, all can be used).
(b) Regulations currently under debate.
(c) Leach rate regulated on west coast; banned on east coast.
(d) Although approved, product not used on pleasure craft.

Source: ACE, 2002, cited in Readman, 2006.

Table 12.3 Legislative position of EU Member States, October 2008 update

European Union Member States	Antifoulings applied in EU Member States must be notified or authorised for use. Products sold in Austria, Belgium, Finland, Ireland, Malta, the Netherlands, Sweden and the United Kingdom must be registered under national pesticide laws. The Biocidal Products Directive (98/8/EC) is now in force and a review of all antifouling biocides submitted for approval is well under way. Decisions on the acceptability of these biocides are expected shortly. If a biocide is deemed 'acceptable' under the directive, EU Member States will then re-review the antifouling products containing biocides that are on the market. If acceptable, a product registration will be issued allowing sale and application of the product. Products deemed 'unacceptable' will be removed from the EU market. In the interim period before all products on the market are reviewed, the directive has required manufacturers of antifouling paints to notify details of antifouling products on the market in each EU Member State.
Restrictions	Application of TBT antifoulings to all vessels is forbidden in all EU Member States under the Marketing and Use Directive (76/769/EEC). Under Regulation (EC) No 782/2003, application of TBT antifoulings on all ships and boats flying flags of EU countries are also banned and those with active TBT antifoulings are forbidden from entering European ports and harbours. Ships over 400 gross tonnage flying flags of EU Member States must be surveyed and carry certificates of compliance with the Regulation. Ships over 24 m in length and less than 400 gross tonnage must self-certify as compliant.
Sweden	Use of antifouling products is evaluated on a case-by-case basis using risk assessment to determine if the paint's use is acceptable.
Denmark	Import, marketing and use of biocidal antifouling paint with release of copper exceeding 200 µg Cu/cm^2 after the first 14 days and 350 µg copper/cm^2 after the first 30 days are banned for pleasure crafts of 200 kg and above that are mainly used in saltwater. Import, marketing and use of biocidal antifouling paint for use on pleasure crafts less than 200 kg and mainly used in salt water is banned. This does not apply for wooden boats and it does not apply for pleasure craft belonging to harbours classified as A or B for insurance purposes. Use of Irgarol 1051 and diuron in antifoulings applied to pleasure craft is banned.
United Kingdom	Use of the organic biocides Irgarol 1051 and diuron in antifoulings is banned.
Netherlands	Use of diuron in antifoulings is banned.

Source: IYP, 2008.

12.4.2 Effects of banning selected booster biocide agents

While the positive impact of banning TBT has been well demonstrated in European waters and elsewhere, the effectiveness of legislation outlawing specific booster biocides has been determined only recently. The following summarises key findings of a study by Cresswell et al. (2006).

In 2001, the United Kingdom introduced legislative measures restricting the antifouling agents that could be used in paints for small (< 25 m) vessels to three substances: dichlofluanid, zinc pyrithione and zineb. This removed the previously popular booster biocides diuron and Irgarol 1051 from the market (for small vessels) on the grounds of environmental concerns. To investigate the impact of this legislation, water samples were taken from locations where previous biocide levels were well documented. Results from analyses demonstrate a clear reduction in water concentrations of Irgarol 1051 (by 10–55 % of levels in pre-restriction studies), indicating that the legislation appears to have been effective (Cresswell et al., 2006). No comparable data were reported for diuron. Although other booster biocides were screened for (chlorothalonil, dichlofluanid and Sea-Nine 211), they were below the limits of detection (< 1 ng/L) in all samples. It is unclear whether the Irgarol 1051 remaining resulted from some ongoing use, continued presence on pre-painted hulls, continued use on non-UK vessels entering UK ports or simply persistence of the chemical in the environment, even after use stopped completely. It is likely to be a combination of all these factors.

The reduced concentrations are attributed to changes regulating the distribution, advertising, sale and use of the booster biocide. A survey of antifouling paint retailers revealed that small amounts of Irgarol 1051-based paints were still being sold and that there was no routine monitoring of retailers. However, by regulating the production and distribution of Irgarol 1051 at the manufacturer level, the UK Health and Safety Executive has been successful in reducing environmental concentrations of the compound to below the proposed Environmental Quality Standard, EQS, of 24 ng/L. The survey of chandlers and discussions with legislative authorities supports these results and concurs with removing Irgarol 1051-based paints from the market using simple regulations targeted at manufacturers (Cresswell et al., 2006).

12.4.3 History repeats itself?

The development and use of booster biocides has followed a very similar pattern to the evolution and demise of organotin and earlier antifoulants:

- identification of new antifouling agents to replace older supposedly more toxic or less effective products (although the relative efficacy and toxicity of antifouling paints can only be determined by subsequent monitoring to establish whether initial suppositions/hypotheses were correct);
- monitoring of distribution, accumulation and toxicity of the new agent(s) to determine whether the initial supposition or hypotheses about the net benefits of new products were correct;
- concern, debate and review of the new antifouling agent(s);
- banning of the most harmful agents;
- search for less toxic solutions to the problem of biofouling communities on hulls of small craft and ships.

Detailed toxicity tests have not been undertaken for all booster biocides. There is evidence, however, for example for diuron and Irgarol 1051, that non-target organisms are exposed and potentially vulnerable. Concern arises because, as noted above, photosynthesis can be affected by booster biocides at extraordinarily low concentrations, i.e. in the 'parts per trillion' (ng/L) range. Effects may be reversible over short exposures, but higher concentrations and long-term exposure can lead to reduced photochemical efficiency of algae (Jones, 2005). In corals this may lead to breakdown of the coral-zooxanthellae symbiosis (bleaching), demanding lengthy recovery times. This has certainly been the case following coral bleaching induced by seawater warming, for example in 1998. Hence, booster biocides can impact the base of food chains, which are linked to seafood production and many other ecosystem services.

A particularly significant aspect of booster biocides is that the most popular ones act herbicidally. Both diuron and Irgarol 1051 act at the herbicide binding site (by definition) of PSII, affecting the primary photochemical reactions of photosynthesis via the QB binding site on the D1 protein. This is a remarkably conserved area (the amino acid sequence of D1 has a 98 % homology between different higher plants and 85–90 % between PSII containing species). This

conservation, and the fact that it is the base of the food chain, means that, like TBT, booster biocides can potentially have far-reaching consequences. Whereas TBT acted quite specifically in causing imposex and shell abnormalities, through endocrine disruption, the booster biocides that replaced TBT have more broad-spectrum impacts.

The wider ecological impacts of the above finding and the transition to booster biocides remain poorly understood but of considerable potential concern. The message is clear: there is a need to develop and apply non-toxic and less toxic solutions to the problem of biofouling on vessel hulls.

12.4.4 Why monitoring should continue

Monitoring should continue for several reasons: the legacy of TBT, our understanding now that booster biocides are far from 'risk free', and the recognition that developing non-toxic alternatives may take years or decades. One key lesson is that there is a need to monitor at least selected constituents of the newer antifouling agents. Both the chemical and ecological aspects are, and will remain, an important marine and environmental indicator within European waters. Monitoring design will need to be sufficiently robust to identify, and quantify, temporal and spatial trends with an appropriate degree of precaution. This is necessary to ensure that any 'clean bill of health' given to existing and new booster biocides is environmentally warranted. And while several booster biocides have already been banned in parts of Europe, monitoring of both banned and permitted antifouling agents will help determine whether further legislation is needed as an additional measure of precaution.

The present report's chapter on methyl mercury pollution in Minamata Bay, Japan, demonstrates that it is not always easy to identify pollution-free sites to serve as an 'international baseline'. For booster biocides, one possible reference area has recently been established in Chagos (Guitart et al., 2007), one of the world's essentially pristine and remotest marine areas. In Chagos, concentrations of Irgarol 1051 and other booster biocides screened for were extremely low. Over the coming years, monitoring of these antifouling agents will be necessary in both affected and reference or 'control' areas.

Price and Readman (2006) outlined an approach for establishing a monitoring procedure and an indicator for booster biocides in European waters. Essentially this could be a scaled down version of the ACE project (ACE, 2002). Sampling is recommended in sites in the regions of Norway and the Faroe Islands, the Baltic, the North Sea, the Mediterranean (north and south), the Black Sea, the Barents Sea, the English Channel, the Celtic region and Irish Sea, and the Iberian Peninsula.

Monitoring efforts should focus initially on Irgarol 1051, in view of its widespread use, marked toxicity and other factors. Extensive data are available for Irgarol 1051 and it can be traced to antifouling paints since it is not used as a herbicide (unlike diuron). The 800 samples collected and analysed during the ACE project represent a valuable resource, providing baseline data that should help determine temporal and spatial patterns in booster biocide accumulation and toxicity. Sampling from one of the world's least contaminated ocean areas (Guitart et al., 2007) might provide a valuable international standard or benchmark to determine the contamination of other marine and coastal areas.

Any future monitoring programme should be firmly linked to an action plan and catalyse management activities if contaminant levels or other metrics of ecosystem health fall to some predetermined threshold level(s). Otherwise, monitoring can easily become an essentially scientific or academic pursuit. For example, physical, chemical, ecological and visual criteria have been developed to determine when (if at all) to begin and when to end oil spill clean-up. Monitoring therefore informs clean-up, by helping determine environmental situations in which clean-up is and is not appropriate. Similar considerations may be needed for regulating and controlling biocides. On the other hand, the detection of imposex at least partly resulted from initially academic work, rather than monitoring of toxic effects. Academic activities may thus play a role, not least in identifying possible emerging issues.

12.4.5 New-age antifouling: is there a non-toxic way?

Given the undeniable (and necessarily) toxic nature of biocidal antifouling agents, there is a case for further research and fast-track development of more environmentally benign solutions. The controlled, slow release of agents regulated through polymer design (Readman, 2006) is seen as one approach. However, this represents only a 'stop-gap' and far from an optimal environmental solution given the undesirability of releasing toxic substances into the water column and environment, even slowly. Arguably, it might be better for these substances to be retained permanently in the paint, assuming they could still be sufficiently effective, to enable recovery and disposal on land.

An alternative strategy makes use of natural products (or synthesised analogues). These compounds normally act enzymatically by interfering with the metabolism of fouling organisms or dissolving their adhesive materials. Structures include terpenoids, steroids, heterocyclics, alkaloids and polyphenolics. This approach to preventing fouling has not, however, been commercially exploited (Readman, 2006). Although not all natural products are hazard-free — strychnine and aflatoxins are two examples that are not used in antifouling preparations — the release and occurrence of natural antifoulant compounds derived from marine organisms is not perceived to pose a serious environmental threat by the general public.

Non-stick fouling-residue coatings that prevent adhesion by fouling organisms are another approach. At present the choice of materials is restricted to fluoro-polymers and silicones (Readman, 2006). From an environmental perspective, this option is appealing. Results from performance tests for currently available coatings indicate modest performance, requiring relatively high speeds to remove fouling organisms. A number of such formulations are already on the market and in use for some classes of vessels. Coupled with expense, however, poor adhesion qualities to the hull and susceptibility to damage mean that widespread commercial application seems unlikely without further advances in technology (Readman, 2006).

The Biocidal Products Directive (98/8/EC) and other legal instruments give consideration to substitutes and alternatives. However, it is normally existing manufacturers of antifouling products that seek to innovate in response to such instruments and they tend to devise solutions with which they are familiar — typically more biocide. The result is incremental change, such as the shift to booster biocides after TBT use was outlawed. As noted, relatively undeveloped alternatives exist, such as non-stick coatings and polishing robots, but the companies that could develop more innovative solutions are generally unaware of the emerging market.

12.4.6 Hindsight, foresight and conclusions

Table 12.4 provides a summary of the historical use of antifouling agents and the main early environmental warnings and actions. TBT, now in demise, has been a highly effective antifouling agent but is among the most toxic synthetic compounds ever produced. Use on small crafts was banned in European waters in the late 1980s and early 1990s. Prohibition has taken longer on ships. Through an international convention, and European legislation linked to this, a total ban has come into force.

For technical and socioeconomic reasons, the extent of TBT hazards was initially underestimated. Many of the warnings serve as important reminders for booster biocides, in terms of the value of early recognition of potential environmental hazards, protocols for monitoring and appropriate regulatory measures. Uncertainties regarding the geographical scale of the problem of TBT (e.g. the limited sensitivity of analytical methods and imperfect baseline data) do not constrain understanding of antifouling residues as they did twenty or more years ago.

Recent research has demonstrated the significant toxicity of booster biocides at extremely low concentrations. Of the major booster biocides, diuron has been encountered in the highest mean concentrations, particularly in north-western Europe (ACE, 2002). Irgarol 1051 has normally been identified at lower mean concentrations, with most contamination in Mediterranean coastal environments. Globally, data are available for the biocides most commonly used in Europe, North America and Japan (i.e. diuron, Irgarol 1051 and Sea-Nine 211), while negligible data are available for other biocides. Significant endocrine disruption, the major problem associated with TBT, was not found for booster biocides (ACE, 2002). Instead, booster biocides are often photosystem II inhibitors; by impairing photosynthesis they can impact the base of food chains and their dependencies (e.g. symbiotic algae and host corals).

Despite accumulating substantial information on adverse environmental side effects, some experts (Voulvoulis et al., 2002) consider that additional data are needed to evaluate properly the risks of widespread use of Irgarol 1051, diuron, Sea-Nine 211 and chlorothalonil. They caution against using TCMS pyridine, TCMTB and dichlofluanid, again identifying a lack of appropriate data. In their initial risk evaluation, zinc pyrithione and zineb appeared the least hazardous options for the aquatic environment.

Like several other countries, the United Kingdom has taken precautionary action, introducing legislation in 2001 to restrict the use of antifouling agents in paints on small (< 25 m) vessel to dichlofluanid, zinc pyrithione and zineb. The previously popular booster biocides diuron and Irgarol 1051 were banned. Recent research (Cresswell et al., 2006) indicates that this legislation appears to have been effective in reducing environmental concentrations.

Even for prohibited (but still used) toxic substances, it is fair to assume that a release into the environment is often inevitable. The preference should always be for non-toxic, competitively priced alternative approaches, rather than adding toxic contaminants to the environment.

Booster biocides must be monitored to gather more data on accumulation, toxicity and the impact of legislation. Given the undeniable (and necessarily) toxic nature of antifouling agents, however, there appears to be a strong case and market demand for further research and fast-track development of more environmentally benign solutions to biofouling, such as natural products and non-stick coatings.

Thomas and Brooks (2010) indicate that even today DDT is used in China as an antifoulant. Meanwhile, novel compounds, such as phenylborane pyridine, Econea, capsaicin and medetomidine, are almost uninvestigated, with very little information available on them in the public domain.

In conclusion, booster biocide antifouling agents threaten a variety of habitats — from coral reefs and seagrass beds to open moorings — within the EU and globally. Their primarily herbicidal properties mean that coral zooxanthellae, phytoplankton and periphyton are particularly vulnerable. Compared to TBT — an antifouling agent with a quite specific action — booster biocides have more broad-spectrum impacts. The wider ecological effect of shifting to booster biocides remain poorly understood but of considerable concern because they may affect the base of marine food chains.

For policymakers, the challenge is to protect non-target biological communities from selective change resulting from booster biocide use. Policy has proven effective in, for example, Bermuda and the United Kingdom, where banning selected agents lowered concentrations and limited adverse ecological impacts. Clearly persistence, bioaccumulative and toxic (PBT) criteria can be used to evaluate the relative potential impact from the available biocides, and consequently target appropriate legislation. Nevertheless, lateral thinking, aiming to identify novel materials and strategies to address antifouling, could pay dividends in the future.

Table 12.4 Early warnings and actions

Early maritime to late-1600s ~ 2–3 thousand years	Ancient Greece: lead sheathing and copper nails caused no environmental concern
~ 800 AD	Arab ships: lime and mutton fat coating caused no environmental concern
Late 1400s	Columbus: pitch and tallow coating caused no environmental concern
1600s	UK navy: tar, grease, sulphur pitch coating caused no environmental concern
Late 1700s	Copper sheathing caused no environmental concern
Mid 1800s →	Copper paints caused no or limited environmental concern
Mid 1900s	Copper, arsenic and mercury paints caused no or limited environmental concern
Late 1950s/early 1960s–1990s	Organotin compounds such as tributyl tin (TBT) caused increasing environmental warnings and actions (see EEA, 2001, Ch. 13)
1989	EC Directive 89/677/EEC bans TBT on small boats (< 25 m), triggering the development and use of booster biocides
1993	First report of booster biocides in coastal waters (Irgarol 1051)
1996	First report on the toxicity of booster biocides at environmental levels (Dahl and Blanck, 1996)
1997	Previous events trigger expanded environmental research
1999	European Commission funds ACE Project (ACE, 2002)
2000	Under the Biocidal Products Directive (98/8/EC) the European Commission began reviewing all biocides used in all biocidal products, including antifouling paints. It entered into force on 14 May 2000
2000	UK Health and Safety Executive began phasing out all booster biocides except dichlofluanid, zinc pyrithione and zineb for small vessels (< 25 m)
2002–2005	Concern raised over toxicity of booster biocides to coral zooxanthellae at extremely low concentrations (e.g. Owen et al., 2002, 2003; Jones, 2005) leading to bans on specific agents in several countries
Today	Development of new technologies/non-toxic alternatives: • potential for natural products (disturbing foulant metabolism or dissolving foulant adhesives) • potential for fluoro-polymers and silicones (non-stick coatings)

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13 Ethinyl oestradiol in the aquatic environment

Susan Jobling and Richard Owen

Many decades of research have shown that when released to the environment, a group of hormones known as oestrogens, both synthetic and naturally occurring, can have serious impacts on wildlife. This includes the development of intersex characteristics in male fish, which diminishes fertility and fecundity. Although often sublethal, such impacts may be permanent and irreversible.

This chapter describes the scientific evidence and regulatory debates concerning one of these oestrogens, ethinyloestradiol (EE2), an active ingredient in the birth control pill. First developed in 1938, it is released to the aquatic environment via wastewater treatment plants. Although it is now clear that wildlife species are exposed to and impacted by a cocktail of endocrine disrupting chemicals, there is also reasonable scientific certainty that EE2 plays a significant role, and at vanishingly low levels in the environment.

In 2004 the Environment Agency of England and Wales accepted this, judging the evidence sufficient to warrant consideration of risk management. In 2012, nearly 75 years after its synthesis, the European Commission proposed to regulate EE2 as a EU-wide 'priority substance' under the Water Framework Directive (the primary legislation for protecting and conserving European water bodies). This proposal was subsequently amended, delaying any decision on a regulatory 'environmental quality standard' until at least 2016.

This is in part because control of EE2 will come at a significant price. Complying with proposed regulatory limits in the environment means removing very low (part per trillion) levels of EE2 from wastewater effluents at considerable expense.

Is this a price we are willing to pay? Or will the price of precautionary action be simply too high — a pill too bitter to swallow? To what extent is society, which has enjoyed decades of flexible fertility and will also ultimately pay for the control and management of its unintended consequences, involved in this decision? And what could this mean for the many thousands of other pharmaceuticals that ubiquitously infiltrate our environment and which could have sublethal effects on aquatic animals at similarly low levels?

13.1 Introduction

A large body of scientific data built up over many decades indicates a cause-effect link between exposure to a complex cocktail of chemicals and the feminisation and demasculinisation of wildlife species, particularly those living in or around the aquatic environment (reviewed in Lyons, 2008). Some scientists also relate exposure to hormonally active chemicals (so-called 'endocrine disruptors', including alkylphenols, bisphenol-A, phthalates, flame retardants and many other chemicals in everyday use) to declining sperm counts, increased incidence of male genital abnormalities, testicular, breast and prostate cancer in human populations (Lyons, 2008; Sharpe, 2009), breast growth in young men (Henley et al., 2007), and early onset of puberty in young girls (Den Hond and Schoeters, 2006; Jacobson-Dickman and Lee, 2009).

Over the last 50 years, since the publication of *Silent Spring* by Rachel Carson in 1962, we have learned that chemicals in food, household products, medicines and cosmetics, can be and are harmful to wildlife at very low levels. Many of these chemicals, each present at vanishingly low (parts per trillion) concentrations, can together have additive biological effects — producing 'something from nothing' in the words of Silva et al. (2002). Awareness of this reality has awoken scientists and the public to an era of possible harms from low-level, chronic chemical pollution (e.g. from human pharmaceuticals).

These chemicals may not have obvious catastrophic effects such as those observed for the endocrine disrupting anti-foulant tributyltin (TBT), which devastated commercially important oyster populations (see EEA, 2001, Ch. 13 on TBT and Gee, 2006). They can, however, have less obvious effects that nonetheless cause irreversible harm to individual organisms. This raises difficult questions concerning the relationship between these damaging but sub-lethal impacts on wildlife and their connections to ecological (e.g. population level) impacts, and to human health. It also raises issues for the precautionary principle, which states that where there is evidence of damage and irreversible harm, lack of full scientific certainty should not excuse inaction (UN, 1992). As we shall describe, the evidence suggests that it is entirely reasonable to invoke the precautionary principle and introduce regulation to limit aquatic exposure to EE2. But this is no trivial matter, and the reasons for this raise serious questions for the precautionary principle itself.

This is the story of one of these chemical pollutants, the contraceptive pill hormone 17α-ethinyloestradiol (EE2) as it has unfolded in the United Kingdom from the 1970s to today

13.1.1 The contraceptive pill

The first orally active synthetic steroidal oestrogen, EE2 ([1]), was synthesised by Hans Herloff Inhoffen and Walter Hohlweg at Schering AG in Berlin (Inhoffen and Hohlweg, 1938; Maisel, 1965) in 1938. EE2 was invented at a time when scientists across the world were intensifying their research into sex hormones as a means of controlling fertility and gynecological disorders. They were inspired by the remarkable successes achieved during the 1920s in using insulin to treat diabetes, thyroxine to alleviate thyroid deficiencies and metabolic disorders, and by the discovery of progesterone, the ovulation preventing hormone in 1934 (Sneader, 1985).

At a similar time, Edward Charles Dodds, a British medical researcher, discovered the potent oestrogenic properties of diethylstilbesterol (Dodds et al., 1938; EEA, 2001, Ch. 8) and those of bisphenol-A and 4-nonylphenol (Dodds et al., 1936), now well known endocrine disrupting chemicals. While BPA (see Chapter 10 on BPA) and 4-nonylphenol never found uses as drugs (their future was to be in plastics and detergents, respectively), for many medical practitioners and scientists there seemed no limit to the extent to which artificial oestrogens could be put to good medical use. EE2 was first marketed by Schering as Estinyl in 1943 and initially used to manage menopausal symptoms and female hypogonadism. It appeared to be readily absorbed orally and very resistant to degradation and metabolism by the gut. The stability and effects of EE2 paved the way for developing oral contraceptive pills ('the pill'), which eventually occurred in the 1950s and 1960s (Medical News, 1961).

The development of the pill was powerfully intertwined both with concerns about overpopulation and the 'sexual revolution' of the 1960s. Symbolically, it was much more than a tool for contraception. From the start it was linked with the hopes that it could curb population growth and bring about world stability. The first version of the contraceptive pill (Enovid) contained the hormones mestranol (the methyl ether of ethinyl oestradiol) and norethynodrel (a progesterone-like

([1]) 17α-ethinyloestradiol is the 17α-ethinyl analogue of the natural female hormone, 17β-oestradiol.

hormone). As Dr John Rock, a catholic obstetrician-gynecologist who ran some of the first clinical trials of the birth control pill, noted in 1967, 'If taken as it should be … it will stop ovulation 100 per cent' (CBC digital Archives, 1964).

Today the mechanisms of action of synthetic oestrogens and progestogens ([2]) are well understood. They are taken up by the cells in the reproductive system, pituitary, bone, liver and other tissues and bind to oestrogen and progesterone receptors, triggering increases or decreases in the expression of genes regulated by these hormones, in turn controlling gender, sexual development and reproduction. When taken correctly in the contraceptive pill, they interfere with the normal monthly cycle of a woman, preventing pregnancy by stopping the ovaries from releasing an egg, making it difficult for sperm to enter the womb (by thickening mucus in the cervix) and making the lining of the womb too thin for a fertilised egg to implant.

The American Food and Drug Administration approved the pill for use in the US in early 1961 and on 4 December 1961, Enoch Powell, then Minister of Health, announced that it could be prescribed through the UK National Health Service at a subsidised price of two shillings per month (Time, 1961). Take up of the pill was fast. Between 1962 and 1969, the number of UK users rose from approximately 50 000 to one million (out of an estimated 10 million users worldwide), generating an enormous social impact and earning it a place on the front cover of Time Magazine in April 1967 (Time, 1967) ([3]). The pill is hailed as playing a major role in the women's liberation movement and greater sexual freedom (Asbell, 1995; Goldin and Katz, 2002). Its availability, particularly in the developed world, has made a significant and dramatic impact on women's lives: giving unprecedented control over fertility, preventing pregnancy, and so avoiding the mortality and morbidity associated with pregnancy, childbirth and termination.

The pill now comes in 32 different forms and is used by more than 100 million women worldwide. Usage varies widely by country (UNPD, 2006; Leridon, 2006), age, education, and marital status. One quarter of women aged 16–49 in Great Britain currently use the pill — either the combined pill, progesterone-only pill or 'minipill' (Taylor et al., 2006) — compared to only 3 % of women in Japan (Hayashi, 2004; Hayes, 2009), which, in 1999, became the last country in the developed world to legalise the pill.

13.1.2 Evidence of environmental harm from 'the pill'

In the 1970s some scientists began speculating that using the contraceptive pill might cause environmental problems (e.g. Tabak and Bunch, 1970). They realised that oral medications, including contraceptives, are in fact rather inefficient methods for administering drugs to the body, since it takes a lot of drug administered orally to get a little into the bloodstream. The rest of the medicine passes right through the body and into wastewater in urine and faeces. Since water and waste treatment plants were not designed to remove pharmaceuticals (or indeed other man-made chemicals), it was likely that the contents of our medicine cabinets were unintentionally being passed on directly into the environment, and eventually, even into drinking water supplies.

EE2 is excreted as conjugates of sulphates and glucuronides, along with the natural steroid hormones oestrogens oestrone (E1), 17β-oestradiol(E2) and oestriol(E3) that occur naturally in humans. The synthetic EE2 shares a common hormonal mode of action with these natural oestrogens, which also means that, when released into the environment, the oestrogenic endocrine disrupting effects of EE2, and the natural steroid oestrogens in combination are additive. EE2, the synthetic oestrogen, is however by far the most potent of the four.

The data supporting the need for risk management of EE2 and the most potent of the three other steroid oestrogens (E2 and E1), due to their endocrine disrupting effects in the environment, are now comprehensive and compelling (Gross-Sorokin et al., 2006; Caldwell et al., 2008). Based on data amassed over many decades, the mechanism of toxicity of EE2, E2 and E1 is now well understood. They are continuously, and widely, released into the aquatic environment and are persistently present, having a half life in fresh water of between less than a day and approximately 50 days under aerobic conditions.

([2]) Progestogens (also spelled progestagens or gestagens) are a group of hormones including progesterone.
([3]) Front cover of Time Magazine's April 1967 edition can be viewed at: http://www.time.com/time/covers/0,16641,19670407,00.html.

They have been shown to cause endocrine disrupting effects at environmentally relevant concentrations in controlled laboratory studies (e.g. Lange et al., 2001; Nash et al., 2004, reviewed in Caldwell et al., 2008), in field studies of fish placed downstream of sewage treatment works with various types of secondary treatment technologies (Harries et al., 1996 and 1997) and in whole experimental lake studies dosed with EE2 (Kidd et al., 2007).

In some UK rivers, 100 % of wild male fish of the species *Rutilus rutilus* (roach, a common freshwater fish of significance to anglers) sampled between 1995 and 2002 had female characteristics (Jobling et al., 1998) and intersex has now been reported in many fish of a number of freshwater and marine species, in more than 10 countries (Tyler and Jobling, 2008; Hinck et al., 2009). Models predicting exposure of riverine fish to EE2, E2 and E1 in the United Kingdom have also been shown to correlate well with impacts observed in fish populations in the field (Jobling et al., 2006). These impacts damage fish reproductive health, for example affecting fertility and fecundity (Jobling et al., 2002a and 2002b; Harries, Hamilton et al., 2011) and are in some cases irreversible (Rodgers-Gray et al., 2001).

Risk characterisation of EE2 and the other two non-synthetic steroid oestrogens, E2 and E1, in the aquatic environment is possibly one of the most comprehensive for any chemical pollutant. Many millions of euro have been spent on this research over many decades. The chemical industry has concluded that 'endocrine disruption is undoubtedly occurring in wild fish populations' and that the evidence that wildlife has been impacted adversely following exposure to endocrine disrupting substances is 'extensive' (Webb et al., 2003). The pharmaceutical industry, in particular, has carried out and funded some of the key lab studies showing that EE2 plays a key role in causing these effects (e.g. Lange et al., 2001).

In response to this evidence, in 2004 the Environment Agency of England and Wales (EA) concluded that risk management was needed for steroid oestrogens (Gross-Sorokin et al., 2006). In 2012 the European Commission proposed EE2 as a Priority Substance (i.e. a substance requiring control across Europe) under the Water Framework Directive, one of the most important pieces of legislation for protecting European surface and ground waters, proposing regulatory limits in the aquatic environment for EE2. At present, this is only a proposal, with formal processes of agreement required before regulation can occur. In July 2012 an amendment to this proposal was tabled. This delays review of a proposal for a regulatory limit until 2016 (rather than 2012), which (if adopted) would then have to be complied with by 2027. Nevertheless nearly 75 years after its initial development, during which time some of the most comprehensive and compelling evidence of environmental impact for any chemical has been amassed, a decision to regulate of EE2 is finally under serious consideration. Why has this taken so long? And what lessons can we learn?

The example of EE2 and endocrine disruption in the aquatic environment, and the questions and dilemmas it raises, is in many ways a test case for many thousands of low-level pollutants that infiltrate our environment ubiquitously, many of which have chronic impacts that go beyond the acute polluting effects of past industrial chemicals.

13.2 Early warnings

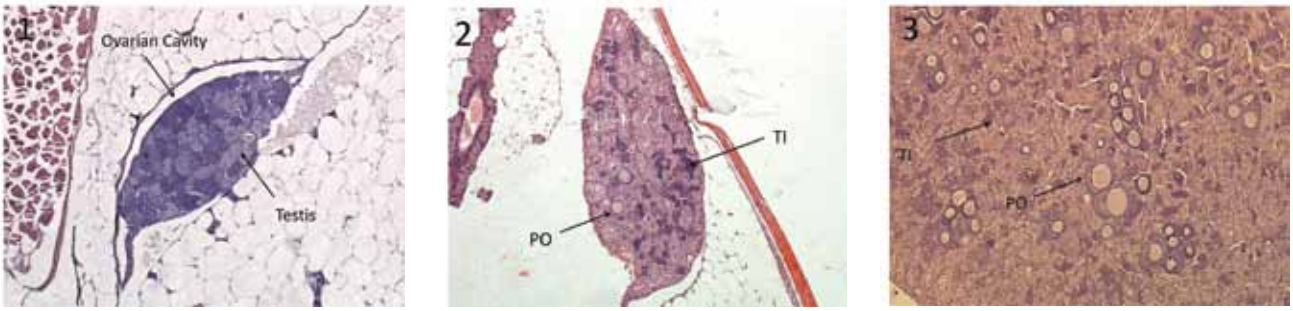
13.2.1 Early warnings from wildlife: the UK experience

The earliest concerns about possible hormone contamination of water (from contraceptive pills and other sources) related to impacts on male fish reproductive health in UK rivers. In 1978, Tony Dearsley, a Thames water area biologist in the United Kingdom, found eggs developing in the testes of five out of 26 male fish of the commonly caught species *Rutilus rutilus* (the roach) while conducting a routine health check on a small sample of fish from the River Lea.

As Dearsley's manager, Roger Sweeting, then Senior Scientist at Thames Water, noted, 'It was amazing to see macroscopically hermaphrodite fish that were both male and female all at the same time'(Sweeting, pers. comm.). It was not until a year later, however, after reading a paper by Jafri and Ensor (1979), that Sweeting telephoned David Ensor, who confirmed that the findings were highly unusual. Jafri and Ensor had reported a normal incidence of hermaphroditism of 1 in 1 000, in the same species of fish (Jafri and Ensor, 1979), more than 100 times lower than found in the fish collected from the Lower River Lea (see Figure 13.1).

Larger samples of fish confirmed the earlier observations. It was also observed that the incidence of feminisation varied with the age of the fish, with the highest proportion (20 %) found

Figure 13.1 Histological sections showing intersex phenotypes in roach



Note: Image (1) shows a female-like ovarian cavity in an otherwise normal testis. Image (2) shows a severely intersex gonad following exposure to sewage effluent with a testis containing a large number of primary oocytes at a single focus. Image (3) shows the intersex gonad of a wild fish caught from the River Aire, the United Kingdom. TI denotes 'testis lobule'. PO denotes 'primary oocyte'.

in the older fish (aged more than six years). Roger Sweeting reported that this suggested a 'cumulative effect with time' (Sweeting, 1981).

Thames Water, at the time a government-owned company, was proactive in researching the matter further to gain a better understanding of its relevance to public health. It was reasoned that 'some risk of endocrine disturbance in human consumers of the water could be implied' (Sweeting, 1981) as it was known that the River Thames received discharges from numerous wastewater treatment plants (352 according to Williams et al. (2008)) and that it also served as a major potable water source for North London. Water abstracted from the river was purified, used by people, or industry, and then disposed of to sewage treatment works, where it was 'cleaned' before being discharged (as effluent) back into the river, only to be abstracted, used and cleaned a second or subsequent time downstream. (For this reason, it is a commonly said that when you drink a glass of water in London, the water has already passed through several pairs of kidneys).

Thames Water's concerns for public health led to further studies (never published) under a research contract given to Liverpool University. Water samples were taken directly from the River Lea at the drinking water abstraction point and transported on a train to Liverpool University, where they were given to rats to drink. Derek Tinsley (a PhD student at the time who now works for the Environment Agency of England and Wales) recalls visiting the station at regular intervals to collect the water. The studies showed clearly that giving female rats this water to drink for 12 months induced persistent oestrous.

Further studies showed, however, that water samples taken part way through the drinking water treatment process had no effects on the rats. Moreover autopsies of small mammals (water voles and wild rats) trapped around the sewage works revealed no obvious gross reproductive abnormalities. Derek Tinsley recalls that he felt 'relief that there were no signs of any effects of the treated drinking water on the rat reproductive system, and therefore no apparent risks to the consumer' ([4]).

Thames Water officials felt confident enough to present Tinsley and Ensor's results to a standing committee of the Department of Health, which, after conducting further studies, agreed that there was enough information to discount any possibility of risk to human consumers of water abstracted from the Lower Lea. It is striking that such a rapid decision was made on the basis of this small set of studies. This, as we will go on to discuss, is in stark contrast to decision-making regarding protection of aquatic wildlife from the effects of EE2 and other oestrogens, despite the many studies indicating adverse health effects related to oestrogen exposure.

The possibility that the contraceptive pill hormone might well be causing intersex in fish was not formally stated in any of the scientific reports circulated between the government and the water industry. Nor was any link made with the reports of occurrence of steroidal oestrogens in wastewater, river and potable waters (Tabak and Bunch, 1970;

([4]) Personal communication from Derek Tinsley.

Tabak et al., 1981; Aherne et al., 1985). At least one of those studies had recognised that steroidal oestrogens could potentially have adverse effects, even if none were identified:

> 'the concentrations found are far below therapeutic doses and there appears to be no evidence of adverse effects from reused water resources which may be contaminated from the normal use of such highly active therapeutic agents' (Aherne et al., 1985).

Aherne and colleagues could not have known about the Thames Water studies as they were confidential. Moreover, the significance of their work and the earlier studies by Tabak and colleagues was not recognised, because the human health agencies responsible for international drug regulation at the time usually had limited expertise in environmental issues; consideration of these was not formally required. The situation is today very different, with environmental exposure now recognised as a key consideration (for example in European Medicines Agency guidelines (EMA, 2006) ([5]). Moreover, until the 1990s, any concerted chemical analytical efforts to look for drugs in the environment achieved limited success. This is because the requisite chemical analysis tools (with sufficiently high separatory powers to identify the drugs amid a plethora of other natural and anthropogenic substances in the environment, and sufficiently low detection limits (i.e. nanograms per litre or parts per trillion)) were not commonly available.

Now there is considerable concern about the increasing amounts of pharmaceuticals that are being consumed and found in the environment (Kümmerer, 2004 and 2007; Apoteket AB et al., 2006 and 2009; EEA, 2010; German Advisory Council on the Environment 2007; Mistrapharma, 2011). With an ageing population the UK Office of National Statistics predicts that the country's medicine usage will more than double by 2050 (Nature, 2011).

13.2.2 More evidence of an environmental problem

In the mid-1980s, fisheries scientists working for the UK Ministry of Agriculture Fisheries and Food, or MAFF (Dr Colin Purdom, Dr Vic Bye and Dr Alex Scott) were asked to comment on the evidence collected to date. Quite independently, one of their colleagues, Dr John Sumpter, had found high levels of a female-specific yolk protein (vitellogenin or VTG) in the blood of male fish kept at an experimental fish farm rented by MAFF. VTG is under strict oestrogen control and as males have extremely low (often undetectable) levels of oestrogen in their blood, they can only produce VTG if they are exposed to an oestrogen (Sumpter and Jobling, 1995). The scientists wondered whether the fish were being supplied with water contaminated with oestrogens originating from the treated sewage effluent entering the river upstream of the fish farm, and whether oestrogens in the water might also explain the discovery of feminised wild male fish in the River Lea.

Field trials in the late 1980s, funded by the Department of the Environment (DoE), confirmed that VTG levels in male trout placed for just two weeks in the sewage treatment plant effluent from Rye Meads sewage treatment works (which entered the River Lea) underwent a 100 000 fold increase, reaching levels equivalent to those in mature females. These results provided the impetus for a nationwide survey of effluents (conducted between 1987 and 1990) by Brunel University (John Sumpter and Charles Tyler) and MAFF (Colin Purdom, Vic Bye, Sandy Scott and Peter Hardiman), with funding from the DoE. The results of this survey proved beyond doubt that oestrogenic effluents entering rivers were widespread throughout England and Wales (Purdom et al., 1994).

By the late 1980s, therefore, there was already evidence that wastewater from sewage treatment plants was having harmful effects on aquatic wildlife, and that at least one possible culprit was EE2. This information was not widely circulated beyond government and industrial organisations. Indeed, the results were not published until 1994 (Purdom et al., 1994), because of the contractual agreement between the DoE, MAFF and Brunel University. There was little action: policymakers of that era perhaps preferred to wait until the level of proof linking cause with effect was beyond reasonable doubt, reflecting a wider resistance at the time to precautionary action in the absence of higher levels of proof.

Subsequent research has proven EE2's presence in effluents and natural waters, and established that it

([5]) More recent guidance from the European Medicines Agency states that if the estimated environmental concentration (i.e. predicted surface water concentration) of a medical product is below 0.01ppb and 'no other environmental concerns are apparent' then no further actions are needed in terms of environmental risk assessment, i.e. no action needed by a pharmaceutical company.

is highly likely that it is contributing significantly to the damaging effects seen in wild fish (Caldwell et al., 2009). Moreover, studies carried out in Canada have confirmed large effects associated with very low concentrations in a multi-year study in which fish living in a large experimental lake were exposed to introduced EE2 (Kidd et al. (2007): 6.1 ng/L (+/– 2.8) during the first year, 5.0 ng/L (+/– 1.8) during the second year and 4.8 ng/L (+/– 1.0) during the third year of. This low level introduction of oestrogen provoked a large surge in fish plasma VTG levels, followed by complete collapse of the fish population. The fundamental conclusion, that EE2 and other hormones in wastewater, both natural and synthetic, are harming aquatic wildlife, particularly downstream of wastewater plants with low dilution, has not changed since the late 1980s. Only the level of uncertainty has reduced.

13.2.3 Widespread endocrine disruption in wild fish and growing evidence of problems in other wildlife

The discovery in the 1980s that oestrogenic effluents were widespread led logically to more caged fish trials that illustrated the extent of the oestrogenic pollution at greater distances from the sewage treatment works (Harries et al., 1996 and 1997). Extensive field trials in the United Kingdom between 1995 and 2000 also showed unequivocally that intersex in wild roach was widespread and especially prevalent up to 10 km downstream of medium- to large-sized sewage treatment works (serving populations of 50 000 to 675 000) and where dilution of their effluents in receiving river waters was less than 10-fold (Jobling et al., 1998).

In addition, studies on estuarine species of fish illustrated clearly that the effects of oestrogenic contaminants extended beyond the rivers into estuaries (Lye et al., 1997 and 1998; Allen et al., 1999) Feminisation and sub-fertility were also reported in additional wildlife species, especially those living in or around the aquatic environment (reviewed in Lyons, 2008). Specifically:

- amphibians were found to have abnormal production of VTG by males and ovotestes/ intersex features;
- reptiles were found to have abnormal production of VTG by males: sex hormone disruption; ovotestes; smaller phallus in alligators and shorter estimated penis length in turtles; decreased hatching; and decreased post hatch survival;
- birds were found to have abnormal VTG production in males; deformities of the reproductive tract; embryonic mortality; reduced reproductive success including egg-shell thinning and poor parenting behaviour;
- otters and mink were found to have reduced penile bone length; smaller testes; and impaired reproduction;
- seals and sea lions were found to have impaired reproduction (including implantation failure, sterility, abortion, premature pupping);
- cetaceans were found to have reduced testosterone levels; impaired reproduction; and hermaphrodite organs;
- polar bears were found to have intersex features and deformed genitals; reduced testes and baculum length; low testosterone levels in adult males; and reduced cub survival.

In none of these cases was a link with exposure to EE2 investigated and/or proven.

13.2.4 Wildlife as sentinels for human reproductive health

Beyond the aquatic environment, the feminising syndromes found in wildlife appeared to mirror reports of male infertility, genital abnormalities and testicular cancer observed in the human male population, collectively termed Testicular Dysgenesis Syndrome (TDS; see Box 13.1). If testicular dysgenesis syndrome was occurring in humans due to environmental pollutants, then genital disruption should have been found in wildlife exposed to those pollutants. This did indeed seem to be the case. The question arose whether the effects seen in wildlife and in humans shared a common cause: environmental oestrogens including EE2. There had already been evidence of human health impacts associated with another synthetic oestrogen created in the same year as EE2: diethylstilbestrol (DES). From the 1940s to the early 1970s, pregnant women in the US (and beyond) were commonly prescribed DES in the mistaken belief that it could prevent miscarriage. Some of the sons of these DES mothers developed low sperm counts, undescended testicles and deformations of the penis (Ibaretta and Swan, 2001).

The steepest declines in male reproductive health appear to have taken place in most countries between the 1960s and the 1980s, coinciding not only with the introduction and take up of the contraceptive

Box 13.1 Human health concerns

The first indications that something might be wrong with human sperm came in 1974, when Kinloch Nelson and Bunge produced a small study of the semen quality of men who were about to undergo vasectomies. They found that only 7 % had sperm concentrations above 100 million (Kinloch Nelson and Bunge, 1974), which is well below the 65 % reported earlier by pioneering andrologist, John Macleod (MacLeod and Heim, 1945).

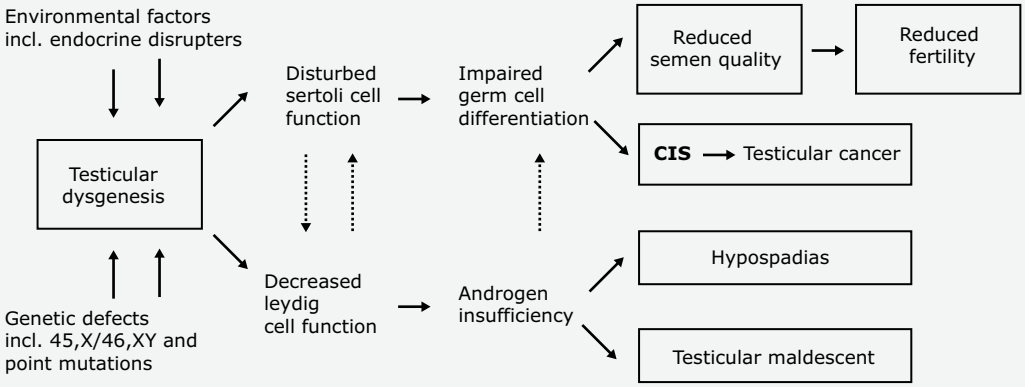
Kinloch Nelson and Bunge speculated that 'an environmental factor to which the entire population has been exposed' might be causing the low sperm counts. These studies were discredited by John MacLeod himself in 1979. While acknowledging a decline in sperm counts in fertile males since the 1930s, MacLeod and Wang (1979) rejected the notion of a larger, overall decline, citing analytical errors in the Nelson and Bunge study and suggesting a concentration of 20 million per ml should be the lower limit for the normal sperm count. This limit was adopted in the WHO guidelines for semen analysis in 1980 (WHO, 1980).

Nothing more was reported until 1992, when Danish clinician Niels Skakkebaek and Elizabeth Carlsen published their ground-breaking paper on studies of sperm counts around the world. In 61 studies going back as far as 1938, they found a decline in average sperm density from 113 million per millilitre in 1940 to 66 million in 1990 (Carlsen et al., 1992). These findings made some scientists wonder whether the human species was approaching a fertility crisis. Debate on this issue was intense and opinion was divided regarding the validity of the apparent fall in global sperm counts (e.g. Swan et al., 1997; Paulsen et al., 1996; Fisch et al., 1996).

The approach taken in Europe (led by Skakkebaek) followed the reasoning that 'if sperm counts have fallen then the average should be lower in men born most recently than they were in the past'. More recent investigations in seven European countries involving more than 4 000 young men have shown that in most of the countries investigated 20 % or more of young men have a subnormal sperm count (less than 20 mn per ml) and the average sperm count is 45–65 million (Jorgensen et al., 2006). This is consistent with sperm counts having fallen, as suggested by the meta-analysis studies. More importantly, it shows that male subfertility is likely to be a common issue for current and future generations, with widespread societal and economic consequences.

The importance of declining semen quality lies partly in its possible link with other problems of male reproductive organs, especially the rise in the incidence of testicular cancer (Adami et al., 1994; Wanderas et al., 1995; Bergstrom et al., 1996; Moller, 2001; McGlynn et al., 2003; Richiardi, 2004) and in congenital malformations of the male reproductive system such as cryptorchidism (undescended testis) and hypospadias (penis malformation) (Hohlbein, 1959; Sweet et al., 1974; WHO, 1991; Matlai and Beral, 1985; Paulozzi et al., 1997; Lund et al., 2009). These diseases often occur together (Prener, 1992; Berthelsen, 1984; Petersen et al., 1999; Schnack et al., 2009) and may have the same underlying pathology — testicular dysgenesis syndrome (TDS) (Sharpe and Skakkebaek, 1993; Skakkebaek, 1998) with a common origin in fetal life (see Figure 13.2).

Figure 13.2 Testicular dysgenesis syndrome



Source: Sharpe and Skakkebaek, 1993.

Box 13.1 Human health concerns (cont.)

Unlike in the case of intersex in fish, there has never been one widely accepted theory regarding the cause of the decline in male reproductive health. Instead, a bewildering array of hypothetical culprits have been posited, including not only the residues of birth control pills in drinking water or inadvertent pill taking during pregnancy, but also a range of anti-androgenic industrial chemicals (male hormone lowering or blocking) and non-chemical stressors that have been shown in laboratory studies to induce TDS when exposure takes place during early pregnancy (Sharpe, 2009). The research in this field has been challenged by the lack of human exposure information and the absence of results of past testing of industrial chemicals for endocrine disruption and other adverse effects that may affect the development of the male reproductive system. Even if animal testing is performed, the results cannot directly be translated to humans because, for example, a chemical may reduce sperm counts by 80–90 % in rats before male fertility is affected.

The net result is that no systematic effort has been made to prevent infertility, despite the substantial potential societal consequences associated with its widespread occurrence. Indeed, the official WHO response to male infertility has been to redefine the ill people as 'normal' by changing the lower reference value for a 'normal' sperm concentration first from 60 mn/ml in 1940s to 20 mn/ml in 1980 and then to the current 15 mn/ml (WHO, 2010), making it of little use in helping society recognise that there is a problem (Skakkebaek, 2010).

pill but also with the entry of many other synthetic chemicals into the environment, the Clean Water Act in 1972 and subsequent upgrading of sewage treatment plants to secondary treatment. Thus, endocrine disruption in the developing child could have occurred through the inadvertent consumption of pills in the first trimester of pregnancy (Smithells, 1981, although refuted by Joffe, 2002). Alternatively, or additionally, it could have resulted from drinking water containing residues of contraceptive pill hormones and a whole plethora of industrial chemicals. Or it could have resulted from inadvertent exposure to these chemicals via application to the skin (cosmetics), inhalation or diet. A more recent report highlights a relationship between modern contraceptive pill use and prostate cancer (Margel and Fleshner, 2011), another hormone-dependent male reproductive disease.

In the case of the contraceptive pill, one might expect the exposure to have been higher in the 1960s, 1970s and 1980s than in later years as the first pill formulations contained up to 100 μg of oestrogen, at least five times higher than current formulations. If exposure to the contraceptive pill was a significant risk factor in causing TDS, the effects should show up in statistics on male reproductive health.

Examination of historical contraceptive pill usage in various countries does indeed suggest higher rates of use (allowing a 30–35 year time lag between exposure of the developing child and the later appearance of testicular cancer) in some countries where rates of testicular cancer and hypospadias are higher, such as Denmark, Germany, Hungary, the United Kingdom and USA, than in countries where rates are lower, such as Bulgaria, Finland, Italy, Poland, Portugal, Romania and Spain and Japan (Leridon et al., 2006). These associations may well be coincidental, however, as the available evidence in support of the oestrogen theory is not entirely convincing (Raman-Wilms et al., 1995; Toppari et al., 1996; Martin et al., 2008). Indeed, recent animal experimental studies suggest that industrial chemicals that block the action of male hormones (anti-androgens) are more likely culprits of declines in male reproductive health and could even act in combination with oestrogens to induce a proportion of the cases of TDS seen in humans. So far, however, 'there is no human or experimental animal data to support this' (Sharpe, 2009). The lack of cause-effect, especially in human epidemiological studies, could easily be wrongly interpreted as ruling out involvement of endocrine disruptors in TDS. Several factors complicate analysis, including the long latency between exposure and effect and the possibility that the effects may be caused by multiple chemicals in combination, while exposure to each chemical individually may not be insufficient to cause damage. This is also why Bradford Hill's criteria, when invoked in the 2002 WHO report on endocrine disruption (WHO, 2002), rejected the hypothesis of an impact on male reproductive function. These criteria are not suited for determining causation by environmental toxicants because such exposures are simply too complex. Perhaps we should abandon the unrealistic hope of achieving more certainty prior to

policymaking about human male reproductive health and use wildlife as sentinels instead?

The case for endocrine disrupting chemicals causing male sterility in humans and wildlife, showing wildlife were sentinels for human health, was beautifully presented in the British Broadcasting Company's award-winning Horizon documentary 'Assault on the male', written and produced by Deborah Cadbury and screened in 1993. The world began to sit up and take notice. Mounting concern in Europe was such that between 1998 and 2007 the European Commission invested over EUR 150 million into researching endocrine disruption. This research provided the basis for testing both existing chemicals and those planned for introduction to the market in the future for their endocrine disrupting effects. It also furthered understanding of the effects of mixtures of endocrine disrupting chemicals, identification of vulnerable life stages and impacts on male reproductive health. The new data showed that a wide range of chemicals could have endocrine disrupting effects, with a wide range of health impacts.

13.3 The hunt for the culprit chemicals

Against the backdrop of growing global awareness of endocrine disruption, attention focused on the chemicals responsible for the feminised male fish observed in UK rivers. Laboratory studies showed clearly that male fish were extremely sensitive to the presence of EE2 in the water at low ng/L concentrations (Sheahan et al., 1994). Until the mid-1990s, however, few were convinced that this or any other hormone was present in wastewater in sufficient amounts to cause the effects seen in fish.

Coincidentally, during that time information was emerging from the US that, in addition to pharmaceuticals, industrial chemicals in everyday use could mimic oestrogens. Although this was first shown by Charles Dodds in the 1930s (Dodds et al., 1936), widespread awareness of this possibility was instigated by John McLachlan, one of the pioneers of research into environmental oestrogens and the organiser of the first meeting on the topic in 1979 (McLachlan, 1980).

It now seemed possible that effects seen in aquatic and other wildlife were actually more likely to be a result of exposure to cocktails of 'endocrine-disrupting' industrial chemicals, (Clement and Colborn, 1992) than to the contraceptive pill hormone. In 1988 Theo Colborn, in her research on the environmental condition of the North American Great Lakes, showed that persistent, man-made chemicals were being transferred from top predator females to their offspring, undermining the construction and programming of their youngsters' organs before they were born. In 1991, Theo convened a meeting ('The Wingspread Meeting') of 21 international scientists from 15 different disciplines to share relevant research on the topic and it was during this meeting that the term 'endocrine disruption' was coined.

It was also in 1991 that Dr Ana Soto published a paper about the oestrogenic effects of nonylphenol, a chemical compound used in manufacturing a large group of industrial detergents (Soto et al., 1991). Some detective work by Susan Jobling (then a student of John Sumpter) at Brunel University revealed that the environmental chemist Walter Giger had identified these chemicals in sewage treatment works effluents, sewage sludge and river water (Giger et al., 1984) at concentrations that Jobling later confirmed were oestrogenic to fish exposed to the chemicals in the laboratory (Jobling and Sumpter, 1993; Jobling et al., 1996).

An earlier report of the oestrogenic activity of 4-nonylphenol, was published in 1936 by Charles Dodds when he was trying to synthesise one of the first synthetic oestrogens, diethylstilbesterol ([6]). The detergent industry may have been unaware of this literature when it embarked on the largescale manufacture and sale of nonylphenol ethoxylates as detergents in the 1940s, leading to the contamination of many rivers and estuaries with these oestrogenic chemicals.

While the causal links between exposure to industrial chemicals and endocrine disruption in most wildlife species were still unclear in the 1990s, further research in the United Kingdom and other European countries showed that nonylphenolic chemicals were causing at least part of the problem in wild fish in some, but not all, areas (Sheahan et al., 2002a and 2002b). However, more sophisticated studies employing chemical fractionation and screening of effluents using an *in vitro* oestrogenicity screen showed that naturally occurring and synthetic steroid oestrogens (EE2, E2

([6]) Interestingly, Dodds identified another controversial compound at the same time — the environmental endocrine disruptor bisphenol-A (Dodds, 1938). See also Chapter 10 on BPA.

and E1) were in fact the most potent oestrogenically active substances present in domestic effluents (Desbrow et al., 1998; Routledge et al., 1998; Snyder et al., 2001), responsible for much of the oestrogenic activity found in wastewaters and rivers throughout most of the world. Of these, EE2 was by far the most potent: the pill was once again under the spotlight.

13.4 Government and industry action in the 1990s

Enormous efforts were made in the 1990s to assess and manage the risks of alkyphenols, not only because of their endocrine disrupting effects but also their wider toxicity to aquatic life:

Following recommendations of the UK Chemicals Stakeholder Forum, the UK government negotiated a voluntary agreement with the suppliers of nonylphenols, octylphenols, and their respective ethoxylates. Suppliers thereby agreed not to promote octylphenol (another endocrine disruptor also found in sewage effluent) as a substitute for nonylphenols, not to manufacture or import new formulations or products containing those substances, and to reformulate existing products to remove those substances as a matter of urgency. This was a constructive application of the precautionary principle (Lokke, 2006), which has not been extended to EE2.

Similarly, in mainland Europe, the European Union undertook a risk assessment of nonylphenols and, as a result, restrictions on using nonylphenol have been imposed across Europe.

At the same time, continued uncertainty about exposure to chemical pollutants in the environment and their effects on the human population (particularly regarding reproductive health) were highlighted during discussions at a major European workshop at Weybridge, the United Kingdom ([7]), on endocrine disrupting chemicals held in December 1996 and jointly sponsored by the European Commission, the European Environment Agency, the European Centre for Environment and Health and the WHO (EU, 1996). An EU strategy on endocrine disruptors was launched in 1999 to begin to address the problem (EU, 1999) but still no action was taken on EE2.

13.5 The last decade of research

Since the mid-1990s, oestrogenic sewage-treatment works effluents have been identified more widely across Europe, and globally, e.g. in Denmark (Bjerregaard et al., 2006), Germany (Hecker et al., 2002), the Netherlands (Vethaak et al., 2005), Portugal (Diniz et al., 2005), Sweden (Larsson et al., 1999), Switzerland (Vermeirssen et al., 2005), China (Ma et al., 2005), Japan (Higashitani et al., 2003) and the United States (Folmar et al., 1996). More extensive evidence has also emerged from around the world showing widespread endocrine disruption in fish in rivers (Hinck et al., 2009; Bjerregaard et al., 2006; Blazer et al., 2007; De Metrio et al., 2003; Hinck et al., 2009; Penaz et al., 2005; Vajda et al., 2008), estuaries (Allen et al., 1999) and oceans (Cho et al., 2003; Ohkubo et al., 2003; Fossi et al., 2004; Kirby et al., 2004; Scott et al., 2006 and 2007).

In general, the situation in other countries appears to match that found in the United Kingdom. The incidence and severity of endocrine disruption appears to relate largely to the size of the sewage works (treatment type is also important), most importantly, and the dilution of its effluent in the receiving water. This leads to generally lesser effects in fish inhabiting large rivers with high dilution factors (a common scenario in the US and parts of Europe, for example) compared with those in smaller rivers with little dilution (a common scenario in the United Kingdom and other parts of Europe). In Japan, where contraceptive pill hormone use is probably the lowest anywhere in the developed world and where endocrine disruption in fish is reported to be quite rare (Tanaka et al., 2001; Higashitani et el., 2003), the greater mean river flow, and hence available dilution per capita (five times more than in the United Kingdom), suggests that combined steroid estrogen potency will be less across its rivers than in the United Kingdom. Even if the Japanese population were to take up the contraceptive pill to the extent of use in England then widespread endocrine disruption in fish would still not be predicted because of the large amount of available dilution (Johnson et al., 2012).

A growing body of evidence also shows that the harm caused by exposure to endocrine disrupting chemicals early in development is, in many cases, irreversible. In fish, as in humans and rodents, feminisation of the male reproductive tract occurs early in development and produces a fish with

([7]) In 2006 the 10th anniversary of Weybridge was marked with a conference organised by the Academy of Finland, the European Commission (DG Research), and the EEA. The EEA has updated and published the papers from that meeting (EEA, 2012).

both an oviduct and a sperm duct. Depuration in clean water does not correct this condition, indicating that feminised ducts seen in wild roach are likely to be a permanent feature (Rodgers-Gray, 2001). Considerable evidence also shows that both the prevalence and the severity of feminisation in wild roach increases with age (Jobling et al., 2006), in extreme cases resulting in a 100 % female population after three years of continuous exposure to treated sewage effluents or EE2 (Lange et al., 2009).

Population-relevant effects of EE2 have also been documented, including a complete fish life cycle test carried out by the original manufacturers of EE2, Schering (Lange et al., 2001), which showed inhibition of breeding at concentrations exceeding the environmentally relevant concentration of 2 ng/L and full sex reversal of males producing an all female population at 4 ng/L. This effect was corroborated by Kidd et al., (2007), who (as we have already noted) dosed an entire lake with EE2, causing a population collapse at concentrations of approximately 5–6 ng/L.

Improvements in analytical power, lower analytical instrument detection limits and innovative modelling approaches have led to the discovery of other steroid oestrogens in the environment, such as equine oestrogens used in hormone replacement therapies (Tyler et al., 2009). There are now also more accurate measurements (Williams et al., 2003; Kanda and Churchley, 2008) and credible modelled estimates (Hannah et al., 2009) of steroid oestrogen concentrations present in sewage effluents and in rivers . This has caused a mixture of doubt and amazement at the possibility that EE2 could be causing endocrine disruption at the very low concentrations at which it is present.

The last decade has also brought the realisation that risk assessments for mixtures of hormonally active chemicals are not adequately protective if based on data for individual substances. Mixtures of synthetic and natural oestrogens (EE2, E2, E1) each at or below their individual 'no effect' concentration were shown to be particularly potent when present in combination (Silva et al., 2002; Thorpe et al., 2003; Brian et al., 2005 and 2007) or with other industrial chemicals with anti-androgenic (male-hormone blocking) activity. These findings confirmed concerns originally mooted by Rachel Carson in 1962 in her book, *Silent Spring*.

More recent reports show an almost concurrent incidence of anti-androgenic chemicals and oestrogens in treated wastewater throughout the United Kingdom. Statistical modelling of exposure and effect data suggest that these chemicals (although not yet identified) could play a pivotal role in causing feminising effects in male fish in UK rivers. Until now it was thought that such effects were caused only by oestrogens found in contraceptive pills and some industrial chemicals (Jobling et al., 2009).

There may be a further twist in the story. Synthetic progesterones (which complement synthetic oestrogen in the contraceptive pill) have been identified in natural waters (Standley et al., 2008; Kuster et al., 2008) and reported to cause effects in fish when present at ng/L concentrations (Paulos et al., 2010; DeQuattro et al., 2012). Ironically, despite the history of their combined use, oestrogens and progesterones have yet to be tested in fish 'in combination', despite the fact that human females have been carrying out this 'test' for 50 years.

13.6 From risk assessment to risk management

In 2004, some 25 years after initial observations of intersex in fish, the UK government accepted the weight of evidence that EE2, E2 and E1 in combination posed a significant risk to aquatic life through their endocrine disrupting effects (Gross-Sorokin et al., 2006). The long journey to this point was passionately championed by Geoff Brighty, Science Manager at the Environment Agency of England and Wales. His team, in collaboration with others, built and defended the evidence-based case against steroid oestrogens and other endocrine disrupting chemicals in UK rivers.

As Brighty remarked in 2004, 'We now have enough data to act as a policy trigger for taking action' (ScienceBlog, 2004).

End-of-pipe treatment of effluent by water companies was chosen as the risk management approach, in comparison to alternative approaches (such as pharmaceutical industry action to develop substitutes for the active ingredient (EE2) in the pill). This may have partly reflected awareness of the public health benefits of the oral contraceptive, the fact that both naturally-excreted and synthetic oestrogens posed risks via their endocrine disrupting effects (i.e. that both would need to be removed) and that other priority hazardous chemicals would also be reduced with the end-of-pipe treatment approach.

This would place the responsibility for risk management on the water industry and (ultimately) the cost of treatment of the tax paying public. In

2007 the Environment Agency began to develop a (draft) technical environmental quality standard (EQS) — a target concentration which could be used for regulatory compliance for EE2- based on a predicted no effect concentration of 0.1ng/L (Young et al., 2004, Figure 13.3). The Environment Agency also identified the EU Water Framework Directive (WFD) as an appropriate legislative mechanism within which the EQS could be enforced. Options for control under the WFD might be to propose EE2 either as a nationally important 'specific pollutant, or an EU-wide 'priority substance' requiring control across Europe. The WFD is the most important EU legislation for managing water resources and had already been used to regulate other endocrine disrupting chemicals such as TBT and nonylphenol. Since additional endocrine disrupting chemicals were likely to be proposed as 'specific pollutants' or 'priority substances' in order to decrease their overall environmental burden, this was a reasonable option for the steroid oestrogens. At this point, no other country in the world had Environmental Quality Standards for any of these substances ([8]).

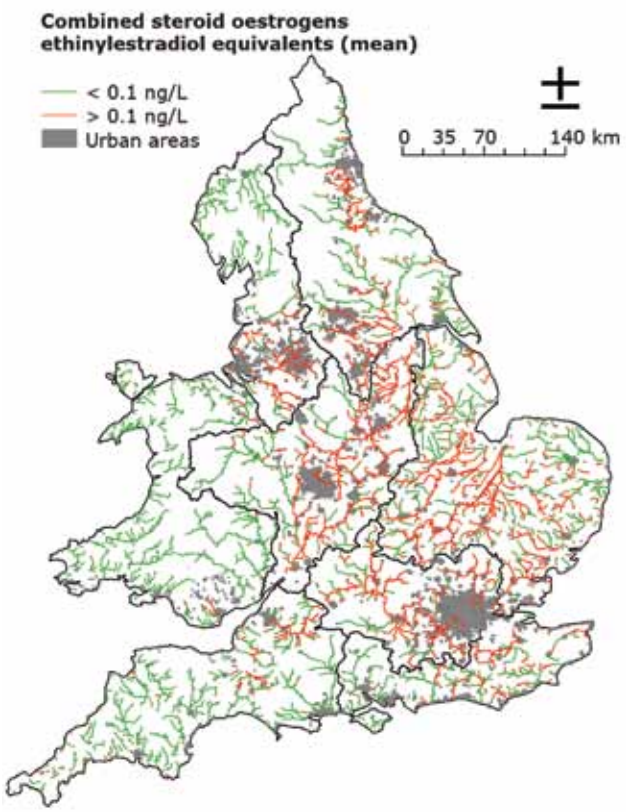
Before introducing risk management of this type there is an important step known as risk evaluation, which quantifies the wider consequences and costs to society of the proposed management approach and balances them against the benefits. The various options on how to proceed are then evaluated and a decision made. For example, a regulatory impact assessment may be undertaken to evaluate the implications of bringing in regulation and implementing an EQS.

In the case of EE2 and the other two steroid oestrogens it was necessary to understand the efficiency of various treatment approaches in removing these substances from sewage treatment plant final effluents. The approaches included both existing and new (advanced) treatment methods: these would need to be quantified in terms of both financial and carbon costs.

In 2004 the UK water industry, in collaboration with the Environment Agency and the UK government, and under the watchful eye of the independent auditor Ofwat, commenced a comprehensive and lengthy work programme to address this goal. The so-called 'National Demonstration Programme' (Gross-Sorokin, 2006) was budgeted at GBP 25–40 million and was not welcomed by the UK water industry, which financed most of the costs. All ten water companies in England and Wales were involved.

In the first phase of the programme fourteen sewage treatment plants were used to evaluate the efficiency of oestrogen removal through 'conventional' treatment technologies. These consisted of primary or chemically aided primary sedimentation with secondary treatment by nitrifying, non-nitrifying activated sludge (ASP) or biological filtration and in some cases tertiary sand or biologically aerated filtration. In the second phase, two so-called 'full-scale' plants were used to evaluate the most promising new technology as an additional

Figure 13.3 UK rivers and streams exceeding the Predicted No Effect Concentration (PNEC) for EE2



Note: In rivers and streams coloured red the suggested Predicted No Effect Concentration (PNEC) for EE2 of 0.1 ng/L is exceeded. In rivers coloured green the combined concentrations of steroid oestrogens (in EE2 equivalents) are less than the suggested PNEC.

([8]) In the US, for example, the FDA regulates pharmaceutical manufacture and the EPA regulates discharge under the Clean Water Act. However, these limitations may not be strict enough to protect the environment because they are technology-based and do not rely on environmental data. As explained later, there is no treatment technique currently available that comprehensively deals with EE2.

advanced tertiary effluent treatment: granular activated carbon (GAC).

The first phase of the Demonstration Programme was completed in mid-2008 (UKWIR, 2009). Results showed that while existing treatment approaches were effective for removal of oestrone and oestradiol, particularly using nitrifying activated sludge treatment, EE2 was far harder to remove. The most efficient treatment, nitrifying ASP, removed some 54 %, with tertiary treatments accounting for a further reduction of 0–38 % of that remaining, depending on the form of tertiary treatment.

These results are completely in line with the consensus seen in current international scientific literature, as comprehensively reviewed by Racz and Goel (2010). Wastewater treatment plants with long retention times (greater than 10 days), especially those performing nitrification, seem to be generally more effective at removing oestrogens because they allow the enrichment of slow-growing bacteria, such as nitrifying bacteria, and the establishment of a more diverse ecological community including species capable of degrading EE2. For this reason, expensive membrane bioreactors with microfiltration and ultrafiltration as well as long retention times have been shown to effectively degrade and reduce the concentrations of oestrogens in effluents, including EE2.

In general, however, EE2 is not nearly as easily biologically removed as the other oestrogens. The ethinyl group of EE2 is thought to hinder EE2 sorption and metabolism. Furthermore, EE2 often exists in the aquatic environment at concentrations below those at which a substrate can support bacterial growth. Biodegradation studies at EE2 concentrations greater than those found in natural environments (mainly conducted at such concentrations due to limitations in analytical chemistry techniques) may therefore lead to erroneous conclusions about the occurrence, rates and products of microbial transformation of EE2 and the other steroid oestrogens.

As a consequence of removal inefficiencies, the proposed EE2 Predicted No Effect Concentration (PNEC) of 0.1 ng/L is exceeded in many UK final effluents entering the aquatic environment, irrespective of conventional treatment type (see Figure 13.3). The results of the second phase of the UK Demonstration Programme were reported in May 2010 (NDP, 2010). They showed that additional treatment using a novel approach called granular activated carbon (GAC) can be effective at removing EE2, producing final effluents below the EE2 PNEC and with no significant induction in fish VTG or intersex (Filby et al., 2010; Baynes et al., 2012). GAC could therefore offer the most promising route for preventing EE2's entry into the aquatic environment at harmful levels (noting that in one study reproduction in fish was slightly, but significantly impacted by effluent subjected to GAC treatment). The Demonstration Programme showed, however, that GAC suffers from a fundamental problem: it is expensive to implement.

For a small town with a 50 000 population equivalent (PE) sewage treatment plant, the capital costs alone of setting up additional GAC were calculated as being over EUR 3 million. That rose to over EUR 8 million for a 250 000 PE works serving a large town such as Swindon, which was one of the sites chosen in the United Kingdom for assessing the technology. Operating costs per annum were calculated as being EUR 800 000 for a 250 000 PE sewage treatment plant, but this would depend on the life of the granular activated carbon. Costs were calculated to approximately 14 kg of CO_2 per person per year. Provisional estimates by the UK government showed that, in total for England and Wales, this would translate into costs of between EUR 32 and 37 billion for the approximately 1 360 sewage treatment works that would require additional treatment (Owen and Jobling, 2012). Again, these findings are in line with the findings of Racz and Goel (2010), who concluded that 'Much attention has also been placed on studying methods of removing oestrogens prior to discharging effluent or disposing waste sludge. While advanced treatment systems such as chemical removal, activated carbon, chlorination, ozonation, ultraviolet irradiation, membrane separation, and other novel approaches may be effective, their current capital and operation costs may make them not viable options.'

Faced with this information, those tasked with implemention of an EQS for EE2 (for example as a 'priority substance' under the Water Framework Directive, see below) increasingly began to worry about two important considerations: technical feasibility and disproportionate cost. It confirmed what they had suspected for many years: EE2 was potent and hard to get rid of.

Evaluation of risk management costs, which have to be calculated at a national scale given the widespread nature of endocrine disruption (Figure 13.4), is however only one half of the cost benefit equation. They must be balanced against the (often intangible) benefits of risk management to key stakeholders, such as the angling community,

Figure 13.4 Extent of sexual disruption in roach in English rivers

Note: Intersex was present at 44 (86 %) of 51 sites surveyed, with an aggregate incidence of intersex of 23 % of sampled males. Coloured symbols indicate incidence of intersex at the different river sites surveyed.

Source: Taylor et al., 2005.

and the public, who will ultimately have to pay for it. This has been a highly contested and often acrimonious area of debate, with highly charged discussions about what constitutes harm at the level of individual fish and what it means for (more ecologically important) fish populations. Adding to this debate is the fact that the costs associated with removing EE2 and E2 should not be seen in isolation: treatment such as GAC would also quite possibly serve to reduce/remove other substances posing risks to the environment and requiring control. Why should such removal costs not be considered for all such chemicals as a whole: is it scientifically incorrect to blame just EE2 for the costs?

Another consideration is how such costs might scale at an EU-wide level, where EU-wide regulation might occur. One European Commission estimate for this is EUR 11–18 per person per annum (EC, 2012). EUREAU (European Federation of National Associations of Water and Wastewater Services) however estimates that these costs are much higher; 25–50 % of the current annual sewerage charges per year (EUREAU initial position paper on amending Directives 2000/60/EC and 2008/105/EC as regards priority substances in the field of water policy). There is clearly considerable uncertainty here.

The costs at an individual country level are likely to vary on a country by country basis, for example varying with the population density, status of wastewater treatment and size of rivers. In some cases individual country costs may be substantially lower than those estimated for the United Kingdom (e.g. see EU project Neptune and the Swiss project Micropoll; Eawag, 2009). Many European countries have lower population densities and much greater dilution of effluents in their receiving rivers than seen in the United Kingdom. Consequently, the total national costs of complying with any regulation concerning EE2 could be considerably lower in these countries than in the United Kingdom. In addition, the quality of treatment plants in mainland Western Europe is in general higher than in the United Kingdom. In Germany, for example, most sewage treatment plants have three stages and some even have a fourth stage, whilst in the United Kingdom, two stages are most commonly encountered. As we have already noted, the addition of a third stage, whether it be GAC, mild ozonation or simple sand filtration could cause dramatic reductions in estrogen concentrations and their biological effects on fish. As recently demonstrated by Baynes et al. (2012) using biological effects rather than chemical concentrations as measures of effective risk reduction, sand filtration following activated sludge treatment was almost as effective as GAC at preventing the feminisation of male fish albeit it was two thirds cheaper.

For a number of years the decision of whether or not to regulate EE2 appeared to stall in the still waters of cost-benefit analysis, with little chance of resolution and little movement forward. Then, in January 2012, the European Commission proposed a revised list of 'priority substances' for the Water Framework Directive (EC 2012). This included the oestrogens 17β-oestradiol and 17α-ethinyloestradiol. The proposed regulatory EQS for EE2 was 0.035 ng/L for inland surface waters (e.g. rivers and lakes): this is the annually-averaged limit in these water bodies. If this proposed EQS is adopted (a first vote on which occurs in the European Parliament's Environment, Public Health and Food Safety Committee in November 2012), it could be taken into account in the 2015 updated River Basin Management Plans and associated 'Programmes of Measures' across Europe, with enforcement required by 2021. But even now, nearly 75 years after its

initial manufacture in 1938, and decades of research concerning its environmental endocrine disrupting effects, this remains a proposal requiring agreement: the decision to regulate or not is yet to be made and may be stalled by recent representations to the EC from both the water and pharmaceutical industries (EUREAU, 2012).

Indeed in July 2012 an amendment to this proposal was tabled, stating 'It is appropriate not to specify the EQS for certain substances of pharmaceutical relevance that have been added to the list of priority substances' and that 'The Commission should propose the EQS for these substances in the next review of the list in 2016, and appropriate measures should be introduced…with the aim of meeting the EQS by 2027' ([9]).

13.7 Late lessons

Ethinyloestradiol, the active ingredient in the birth control pill, has allowed women to control their fertility reliably on a global scale. But it has come at a price to the environment. As mixtures, EE2 and other oestrogens, both synthetic and natural, have been shown to have serious impacts on wildlife — impacts that can be associated with early life exposure but manifest themselves later in adult life. Such impacts are often sub-lethal but may be permanent and irreversible. They may also serve as sentinels for impacts on human health via environmental oestrogen or other endocrine disrupting chemical exposure.

Since wildlife is exposed to a cocktail of endocrine disrupting chemicals, it is naive to conclude that EE2 alone is the culprit. It is, however, the most potently oestrogenic of the steroid oestrogens, occurring widely in effluents entering the environment, at concentrations that can frequently exceed the Predicted No Effect Concentration of 0.1 parts per trillion (UKWIR, 2009). There is reasonable certainty, based on sufficient scientific evidence, that EE2 plays a significant role in causing the reproductive health impacts observed in fish. The need for risk management has been accepted by both the Environment Agency of England and Wales (Gross-Sorokin et al., 2006) and by the European Commission through its proposal for EE2 to become a priority substance requiring control (EC, 2012).

But this is a story that is far from over, and is one that continues to raise important questions that will apply not only to EE2 but to any other pollutants exerting damaging but often sub-lethal effects at very low concentrations. For a decision to regulate EE2 has not been agreed. A critical question is whether we as a society are willing to pay a potentially very high premium to be precautionary and exclude EE2 from the environment. Alternatively, would we, as a society, prefer to live with the impacts of EE2 and other oestrogens on wildlife; are they acceptable risks? To what extent is society, which ultimately bears the benefits of flexible fertility but also the costs of cleaning up its unintended consequences on the environment, having a say on this decision?

This historical retrospective allows us to identify several important lessons, which are central not only to regulation of EE2 and other steroid oestrogens but also for many other low-level chemical pollutants in the environment with sublethal effects, alone or in combination, now and in the future.

13.7.1 Lesson 1: for low-level pollutants in the environment, is the price of being precautionary simply too high?

With regulation of EE2 now a serious proposal in Europe, the water industry, regulators and national governments are faced (as will be the case with many other low-level pollutants) with risk management that will be a costly process if EE2 is to be removed from sewage treatment works final effluents to the vanishingly low levels that will be required for compliance. The target level proposed by the EC for EE2 as an annual EQS has been set at 0.035 ng/L for inland surface waters (e.g. rivers and lakes). This is the regulatory concentration *in the water body itself,* not in the final effluent discharged from the sewage treatment works. However, as the UK Demonstration Programme has shown, reducing levels of EE2 in final effluents via end-of-pipe treatment to enable compliance with this EQS (e.g. for those water bodies with low dilution receiving large volumes of oestrogenic effluent) will be extremely difficult, The most promising technology, granular activated carbon, might achieve this, but it is expensive and may have a potentially large carbon footprint. Mild ozonation may also be

([9]) Draft report on the proposal for a directive of the European Parliament and of the Council amending Directives 2000/60/EC and 2008/105/EC as regards priority substances in the field of water policy (17.07.2012). Proposer Richard Seeber, European Member of Parliament.

effective, but this will still be expensive in terms of capital set up costs ([10]).

Measuring compliance with the low EQS for EE2 and E2 will also be a significant challenge. The techniques available to measure such very low levels of EE2 in natural waters and effluents are hardly routine. Some efforts have been made to develop more amenable enzyme-linked immunoassay analysis methods but these have been fraught with issues around selectivity and sensitivity at the very low levels of detection required. This leaves both the water industry and regulators with a fundamental problem: it will be costly to remove EE2 to enable compliance with the target EQS, and costly to monitor and demonstrate legal compliance itself. So while it is technically possible to develop an EQS, in practice it may be very hard to implement. The widespread nature of contamination has only added to the problem: this is unlikely to be an issue in one isolated location, but one with significant cost implications across Europe and beyond.

What other options might there be? Since EE2 is both the most potent of the steroid oestrogens and, seemingly, the most difficult to remove by conventional sewage treatment, could there be an argument for substituting this as the active ingredient in the contraceptive pill, leaving the remaining oestrogens to be removed conventionally at less cost? But what would replace it? If there were sufficient demand or need, the pharmaceutical industry could continue to provide women with access to birth control and reproductive choice while substantively altering the design of pharmaceuticals to protect the environment from unnecessary harm. This would represent a constructive precautionary approach ([11]). Is this option preferable?

13.7.2 Lesson 2: low-level pollutants with sublethal effects present fundamental issues for the precautionary principle

A number of definitions and interpretations of the precautionary principle exist (see Weiner and Rogers, 2002; Gee, 2006), of which the Rio Declaration (UN, 1992) is one that is widely cited:

> 'Where there are threats of serious or irreversible damage, lack of full scientific certainty shall not be used as a reason for postponing cost-effective measures to prevent environmental degradation' ([12]).

The chapter on the precautionary principle (PP) in this volume, provides different definitions of the PP taken from other international treaties and the European Court of Justice, including the working definition proposed by the EEA which is designed to improve common understanding about the meaning and application of the PP.

However, for this chapter it will be useful to consider the constituent parts of the Rio definition, the first of which deals with threats of serious or irreversible damage.

It is not in dispute that intersex in fish represents both serious and irreversible damage to fish and that exposure to environmentally relevant levels of EE2 has adverse effects on fish reproduction, an ecologically relevant measure of impact. Uncertainties remain, particularly around fish population level effects, but the precautionary principle aims to promote action in the face of such uncertainties, when there is evidence of serious environmental damage that is irreversible. In fact, the level of scientific certainty concerning the risks (or threats) posed by oestrogens as mixtures to aquatic life, mediated through their endocrine disrupting effects is extremely high and there seems to be little or no doubt that there is sufficient evidence to justify applying the precautionary principle (Gross-Sorokin et al., 2006). Responding to this evidence of harm, the water and chemical industries (and indeed some scientists) have increasingly asked the question, 'so what?' There may be male fish with eggs in their testes and this might be unpleasant, irreversible and widespread. But does it seriously damage fish populations? (Webb et al., 2003). Why pay potentially vast sums

([10]) It should be noted that some European countries have decided to clean up wastewater, even in the absence of regulation of EE2 and E2, but in recognition of contamination of wastewater by pharmaceuticals, pesticides and endocrine disruptors. Full-scale treatments will be installed on more than 100 Swiss WWTP treating about 80 % of the Swiss municipal wastewater. The first full-scale ozonation plant will go in operation in Spring 2013 and will cost only 5 EUR/person/year including both capital and operational costs, because sand filtration already exists on this plant.

([11]) There has been some research towards development of contraceptive formulations such as the progesterone-only pill, which do not contain oestrogen and instead target the female reproductive cycle more specifically (Lakha et al., 2007).

([12]) A European Commission Communication on the Precautionary Principle (EC, 2000) sets out guidance on when to apply the precautionary principle e.g. 'where there are reasonable grounds for concern'. The Communication sets out a set of general principles underpinning application of the PP This includes 'examining costs and benefits' which 'entails comparing the overall cost to the Community of action and lack of action, in both the short and long term. This is not simply an economic cost-benefit analysis: its scope is much broader, and includes non-economic considerations, such as the efficacy of possible options and their acceptability to the public' (p. 4). It also includes the need for the decision-making process to be 'transparent'.

of money for risk management when the seriousness of such population — level effects is uncertain? These populations might collapse in the future, as indicated in the Great Lakes study of EE2 (Kidd et al., 2007), but maybe they will not. Is intersex an unpalatable but acceptable harm?

But even if the seriousness of the harmful threats is accepted, the precautionary principle's Achilles heel, however, as defined in the Rio Declaration, lies in the words 'cost effective'. The central issue for oestrogens (and quite possibly for many other chemicals that cause sublethal impacts at very low levels) is that any risk management measures are likely to be very costly, and as we have discussed above, this may be a price too high to pay.

The potentially high costs of risk management have combined with protracted debates about what constitutes acceptable harm to seriously delay decision-making about the regulation of EE2 and other steroid oestrogens. This has been compounded by a precautionary principle whose definition includes issues of disproportionate cost and cost effectiveness, either explicitly or implicitly ([13]). Defined in this way the precautionary principle may be logical and rational, but it can also paradoxically become a perfect excuse for inaction or, at best, seriously delayed action. It is therefore perhaps no surprise that eight years after the UK government officially recognised EE2 and other steroid oestrogens as posing a risk to wildlife that should be managed, and some 30 years after the first observations of their effects in wild fish populations, that the regulation of EE2 is still undecided. And even if the EC proposal is agreed, it will not come into force until at least 2015.

Such long delays have, one might argue, been completely within the spirit of the precautionary principle at least as defined in the Rio declaration. The precautionary principle is well intended and should expedite decision-making in the face of uncertainty. But in reality decision-making has been painfully slow. We are left with the uncomfortable knowledge of a serious environmental issue that has been, and continues to be, unresolved: one which we may have to live with if the price of precaution is deemed too high. This is a bitter pill to swallow.

13.7.3 Lesson 3: the need for an open debate on precaution and decision-making

Our environment is full of low-level pollutants present as mixtures that cause sublethal effects. The European Inventory of Existing Commercial Chemical Substances (EINECS) lists over 100 000 chemical compounds and little is known about the toxicity of about 75 % of them. Several hundred new substances are marketed each year after some basic premarket toxicity testing and these are registered in the European List of Notified Chemical Substances (ELINCS), which currently contains about 2 000 chemicals.

In 2007 the new chemicals EU regulation, REACH (Registration, Evaluation, Authorisation and restriction of CHemicals) was enacted. This reformed chemicals laws and set up procedures and responsibilities to address the backlog of untested chemicals, focusing on some 30 000 substances now being evaluated by industry and the new EU chemicals agency ECHA. Hazard identification and quantification is challenging however, and implementing monitoring programmes and conducting risk assessments for this whole 'chemicals universe' is unfeasible. Moreover, we do not have the tools to fully analyse how mixtures of these chemicals behave. The only logical way forward seems to be to reduce exposure as much as possible — to be precautionary. But this comes at a price and raises ethical questions of where responsibility should lie. Do we want the water industry to reduce exposure through costly treatment? Do we want the pharmaceutical industries to invest in developing new, less harmful contraceptive pills? Either way, are we as a society, prepared to pay for it? Do we care?

The average fish in a stream or person in the street now has hundreds of novel compounds in their bodies that were not there 60 years ago. We can measure them in adult and foetal tissue. We know they have detrimental effects such as intersex in fish. We have changed the chemical environment of the developing organism. EE2 is a perfect case study of how we are responding as a society to difficult decisions regarding the need for, and challenges of, risk management for these low-level pollutants with chronic sublethal effects.

([13]) The EU communication on the precautionary principle also recommends an 'Examination of the benefits and costs of action and lack of action'. This 'examination of the pros and cons should include an economic cost benefit analysis where this is appropriate and possible.However, such an 'examination of the pros and cons cannot be reduced to an economic cost-benefit analysis'. It is wider in scope and includes non-economic considerations (EC, 2000). The EEA working definition of the PP also uses the broader 'pros and cons' rather than 'costs and benefits' for similar reasons, including the importance of the non-quantifiable 'cons' such as the melt down of public trust in scientists and polictic ians which occurred in the BSE saga (see EEA, 2001, Ch. 15 on BSE).

A key observation from this case study is that the public has been and continues to be silent witnesses. A key lesson learnt from previous case studies (EEA, 2001; Gee, 2006; Lokke, 2006) has been that the process of applying precaution must encourage public participation, such that the costs of action (e.g. risk management) and potential costs of inaction are debated. This enables value judgements and decisions to be made in an open and democratic way. Transparency of decision-making and the need to involve all interested parties as early as possible is a central tenet of the European Commission communication on the precautionary principle (EC, 2000), which states that:

> 'All interested parties should be involved to the fullest extent possible in the study of various risk management options that may be envisaged once the results of the scientific evaluation and/or risk assessment are available.'

The US National Academy of Sciences has also repeatedly stressed the importance and need for stakeholder involvement at all stages of the risk-based decision-making process (NAS, 2009.) Prior to this, in 1998 the UK Royal Commission on Environmental Pollution published a report on Setting Environmental Standards (RCEP, 1998) in which it emphasised that decisions must be informed by an early understanding of peoples values, with a process that ensures transparency and openness. This is a view that is shared by the chemicals industry (Webb et al., 2003).

The Royal Commission also identified specific mechanisms by which this could be achieved. It stated that those affected have a right to make their views known before a decision is made and that 'it is no longer acceptable for decisions to be negotiated privately between the regulator and polluter' (RCEP, 1998). This was fully endorsed by the UK government in their response to the Commission's report. But this endorsement is yet to translate into action. Opportunities for engagement and consultation that do exist are insufficient ([14]).

Decisions regarding regulation of EE2 and its sister oestrogens, and the dilemmas and issues these pose, have been, and continue to be undertaken in a poorly understood, closed process that has little engaged the public. It is vitally important that decision-makers understand about the acceptability of risk, appetite for precaution and the willingness to pay for being precautionary. The views and concerns of the public have to date however gone largely undocumented. This is not an academic exercise: it is fundamental to making a decision on such a complex and potentially costly issue, a point emphasised by the Royal Commission in 1998 and the European Commission in 2000. Without public support the costs of risk management, of regulation of EE2, may be seen by policy makers as disproportionate. It might be that the weight of evidence suggests that public opinion is not on the side of risk management, that we are prepared to live with endocrine disruption in the environment as collateral damage associated with flexible fertility in our own species. But what is very clear is that without asking the public it will be far easier to come to a conclusion based largely on costs alone. This loads the dice before they are thrown.

([14]) For example in the development of the next round of River Basin Management Plans across the EU under the Water Framework Directive.

Table 13.1 Early warnings and actions

1938	17α-ethinyl estradiol (EE2) synthesised
1943	EE2 marketed as a contraceptive
1962–1969	USFDA approve the birth control pill and the United Kingdom allows it to be prescribed through its National Health Service
1970	Pill users increase in number from 50 000 to 1 million
1976	First speculation that oral contraceptives might pass through sewage treatment works (STWs) into the aquatic environment
1979	Kinloch Nelson and Bunge publish a study showing low sperm counts in 93 % of men about to undergo vasectomies
1982	Routine health checks of male fish (roach) in a UK river show the presence of oocytes in testes (intersex). The rate of hermaphroditism is very high in comparison to the norm
Mid-1980s	First reports of contraceptive pill hormones in river water
1985	High levels of female-specific yolk protein (vitellogenin) found in blood of male fish in a fish farm receiving effluent containing river water
1985	Nonylphenols discovered in sewage effluents and in sludge
1991	National survey shows that oestrogenic effluents are widespread in England and Wales
1991	4-Nonylphenol is rediscovered as an oestrogen
1992	Meta-analysis of 61 studies shows sperm counts have declined 50 % in the preceding 50 years
1993	Theo Colborn and Clement publish 'The Wildlife Human Connection' suggesting widespread endocrine disrupting effects in wildlife and humans as a result of exposure to chemicals
1994–1996	Sharpe and Skakkebaek publish a hypothesis that testicular cancer, hypospadias, cryptorchidism and lowered semen quality are part of a syndrome caused by exposure to environmental oestrogens during foetal life
1993	BBC Horizon screens the award-winning documentary 'Assault on the male'
1995–1996	Surveys show that intersex is widespread in roach and is especially prevalent downstream of STWs with low effluent dilution. Feminising syndromes in other wildlife species are reported
1996	Major European workshop on endocrine disruptors are held, jointly sponsored by the European Commission, the European Environment Agency, the European Centre for Environment and Health and the World Health Organization
1998	Steroid oestrogens, and EE2 in particular, are shown to be the most potent oestrogenically active substances in domestic effluent
1998	Royal Commission on Environmental Pollution publishes a report *Setting environmental standards*, in which it emphasises that decisions must be informed by an early understanding of people's values. It is endorsed by the United Kingdom government
1999	European Union launches a Strategy on endocrine disrupters
2001	Feminisation is shown to be a permanent phenomenon that is progressive with age i.e. duration of exposure
2001	Schering publish a whole life-cycle study showing EE2 causing full sex reversal of males to females at concentrations > 2 ng/L
2002	Silva et al. show additive effects of oestrogenic endocrine disrupting chemicals *in vitro*: 'something from nothing'
2002-2003	More widespread surveys show intersex fish are present throughout the United Kingdom. Widespread anti-androgenic activity is discovered in sewage effluents
2003	Nonylphenol and nonyphenol ethoxylates are banned in the European Union as a hazard to human and environmental safety. Serious evaluations of other endocrine disruptors such as BPA take place
2004	Predicted No Effect Concentration (PNEC) of 0.1 ng/L derived for EE2
2004	UK Endocrine Disruption Demonstration Programme commences, evaluating the efficiency of removing oestrogens from sewage treatment processes
2007	Draft environmental quality standard for EE2 prepared by the Environment Agency of England and Wales
2008	Experimental lakes study in Canada reports a population crash of fish after exposure to EE2 at 6 ng/L
2009	UK Demonstration Programme reports first phase results showing difficulty removing EE2 to the PNEC using conventional sewage treatment approaches
2012	European Commission publishes proposals to regulate EE2 as a 'Priority Substance' under the EU Water Framework Directive, which if accepted may come into force after 2015. An amendment to this proposal is tabled in July 2012 which proposes delay of setting EQS until 2016, with the aim of meeting this by 2027'

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14 Climate change: science and the precautionary principle

Hartmut Grassl and Bert Metz ([1])

The first scientifically credible early warning about the possible dangers of climate change due to carbon dioxide (CO_2) emissions from burning fossil fuels came in 1897. While the basic physical principles of global warming are simple, however, the more detailed science of climate change is exceedingly complicated. Even now, more than a hundred years since the first early warning, many important details of climate change cannot be predicted with certainty. It is therefore unsurprising that the science of climate change and questions about the true value of burning fossil fuels have fostered sustained scientific and political controversy.

When the first volume of *Late lessons from early warnings* was drafted there appeared to be too much legitimate controversy about climate change for the issue to be included. A case study could have led to arguments that distracted attention from the valuable and robust lessons from more established issues such as asbestos, polychlorinated biphenyls (PCBs), chlorofluorocarbons (CFCs) and the ozone-hole, X-rays and acid rain. This decision was taken despite the then widespread acceptance that 'the balance of evidence suggests a discernible human influence on global climate' (IPCC, 1995a).

Over a decade later and after two more reviews by the Intergovernmental Panel on Climate Change (IPCC) of a much greater volume of climate change science it seemed appropriate to include climate change in this volume, despite some continuing controversy. The evidence that human activities are having a dangerous impact on the climate has strengthened since 1995. By 2007, the IPCC was able to conclude with 'very high confidence that the global net effect of human activities since 1750 has been one of warming' (IPCC, 2007a). Given the size and irreversibility (on human time scales) of many of the harmful effects of human-induced climate change, there is an urgent need for action to reduce CO_2 emissions and other greenhouse gases. Some contrarian views persist, however, as the authors illustrate.

This chapter summarises the history of growing knowledge about human-induced climate change and of the main actions, or inactions that accompanied it. Like many other chapters, it reflects the lifelong commitment of both authors to trying to understand and mitigate the effects of human-induced climate change. It concludes with some lessons and insights that are relevant to many other environmental and health issues.

Also included is a panel text describing how the IPCC's approach to assessing uncertainty evolved between its first to its fifth assessment reports.

([1]) The authors would like to acknowledge EEA staff members John van Aardenne, Hans-Martin Füssel, André Jol and Paul McAleavey for helping to prepare the manuscript.

14.1 Introduction

The climate provides the background for the development of human civilisation. Historically, it has been a decisive factor determining where and how people live, what they eat, how they clothe themselves, how they structure their activities, where and why they travel, what hazards they face, and how they organise their response to those hazards. In fact, almost every aspect of human and social life is closely linked to climatic factors.

At the same time, the goal of becoming less dependent on the climate's vagaries has been an important driver for the development of human civilisation. Humans have learned how to construct shelters to protect themselves and their belongings from cold and rain, how to build irrigation systems that allow food production despite erratic rainfall, how to conserve and store food to prevent starvation at times when there are few natural food sources available, and so on.

Growing use of fossil fuels since the industrial revolution has arguably been the key factor enabling humankind to separate decisions about where and how to live from the local climatic conditions. Today, fossil fuels allow a significant fraction of humankind to heat or cool a building at the press of a button, to pump water over long distances and even between watersheds, to transport food across continents, often in artificially cooled environments, and to fly to holiday destinations with particularly attractive climates.

During recent decades, a rapidly increasing body of scientific knowledge has identified unexpectedly close links between these two major driving forces of social and economic development: the climate and burning fossil fuels. We now know that the use of fossil fuels, which has allowed the wealthy part of humankind to become less dependent on climate factors, is substantially changing the radiative properties of the atmosphere. It is thereby causing changes to the global climate system that are unprecedented at least since the end of the last ice age.

Ironically, or tragically, the societies that have contributed most to the problem of anthropogenic (i.e. man-made) climate change are generally least affected by its impacts, and vice versa. The massive use of fossil fuels — and the economic wealth that typically goes with it — allow fossil fuel-intensive societies to largely protect themselves from the vagaries of climate variability and weather extremes. In contrast, poor people who use little fossil fuels and who have contributed least to the problem have limited resources to cope with the hazards brought about by anthropogenic climate change. Worse still, they often live in regions with an already marginal climate.

It is not surprising that the strong links between these two fundamental drivers of human societies and their evolution have brought about an unprecedented level of interest, debate and conflict in the public, the media and at all political levels. Climate change policy has become a key item on the agenda of many high-level international meetings. In fact, the fifteenth session of the Conference of the Parties to the United Nations Framework Convention on Climate Change (COP15) in Copenhagen in December 2009 was the second largest assembly of Heads of State and Heads of Government ever to occur outside the New York Headquarters of the United Nations (after the Earth Summit in Rio de Janeiro in 1992).

Anthropogenic climate change is in many ways a unique problem. First, the anticipated (and increasingly observed) effects of climate change and of climate protection policies are very large and widespread. Second, the expected 'winners' and 'losers' from climate change and from climate policies are very unequally distributed across the world and across time, which raises difficult questions of international and intergenerational equity. Third, the science of climate change and its interactions with other social and economic developments is extremely complex, which prevents clear-cut answers on many questions of particular relevance for decision-makers (e.g. on specific local and regional impacts of climate change).

Against the backdrop of an increasingly charged public and political environment, the science of climate change is continuously developing, producing robust results and identifying key uncertainties. In parallel to the evolution of science, unique institutions have been created to facilitate the transfer of scientific knowledge to decision-makers. Other forces have developed to obstruct this knowledge transfer by creating unfounded confusion even around robust scientific findings. As a consequence, climate scientists find themselves in an increasingly politicised environment.

Climate change is, of course, not the only global problem undermining the planet's ecosystems and economies. The loss of biodiversity, increasing water scarcity, dispersion of toxic chemicals, loss of productive land due to erosion and overgrazing, and the depletion of natural resources are, like climate

change, the result of human societies' unsustainable practices. A global response was formulated at the UN Conference on Environment and Development (the Earth Summit) in Rio de Janeiro in 1992, with the adoption of Agenda 21 for sustainable development (UN, 1992). The subsequently adopted Millennium Development Goals (UN, 2000) establish a clear link between eradicating widespread poverty (Goal 1) and ensuring environmental sustainability (Goal 7). This development dimension is fundamental to dealing effectively with climate change, although in practice much of the scientific and policy discussion on climate change has been narrowly focused.

This chapter attempts to shed light on the co-evolution of climate change science and international climate policy by presenting key events, important actors and institutions, and the main conflicts. The focus is on the science-policy interface, the role of the precautionary principle in helping to deal with scientific and social uncertainties of long-term climate change, the link with the broader sustainable development agenda and the lessons that can be drawn so far.

14.2 Early development of the scientific knowledge base on human-induced climate change until the 1970s

First hints of the greenhouse gas effect

The greenhouse effect, as currently understood, is described in Box 14.1. The first hint of its existence dates back to the 1800s. Based on observations by Saussure from the late 18th and early 19th century, the Frenchman Joseph Baptiste Fourier correctly understood the observed atmospheric vertical temperature gradient (i.e. the observation that upper layers of the atmosphere are colder than lower layers) to be similar to the observed strong heating caused by a glass plate on an insulated box (Fourier, 1824). Up until that time, the absorption properties of atmospheric gases had been completely unknown.

Absorption of heat radiation by atmospheric trace gases

Nearly 40 years later, in 1863, John Tyndall, an Irishman working in Great Britain, published a remarkably precise description of the atmospheric greenhouse effect, which comes close to modern definitions:

> 'The solar heat possesses the power of crossing an atmosphere, but, when the heat is absorbed by the planet, it is so changed in quality that the rays emanating from the planet cannot get with the same freedom back into space. Thus the atmosphere admits the entrance of the solar heat but checks its exit, and the result is a tendency to accumulate heat at the surface of the planet' (Tyndall, 1863a).

Tyndall based his definition on his own observations of the absorption characteristics of atmospheric trace gases, including the key absorption bands of water vapour and carbon dioxide, which account for about 80 % of the total atmospheric greenhouse effect according to current knowledge.

The first scientist identifying fossil fuel use as a potential reason for climate change

In 1896, the Swede Svante Arrhenius used the knowledge of carbon dioxide absorption bands published by American scientist Samuel Langley to

Box 14.1 The greenhouse effect (IPCC definition)

Greenhouse gases effectively absorb thermal infrared radiation, emitted by the Earth's surface, by the atmosphere itself due to the same gases, and by clouds. Atmospheric radiation is emitted to all sides, including downward to the Earth's surface. Thus greenhouse gases trap heat within the surface-troposphere system. This is called the *greenhouse effect*. Thermal infrared radiation in the troposphere is strongly coupled to the temperature of the atmosphere at the altitude at which it is emitted. In the troposphere, the temperature generally decreases with height. Effectively, infrared radiation emitted to space originates from an altitude with a temperature of, on average, – 19 °C, in balance with the net incoming solar radiation, whereas the Earth's surface is kept at a much higher temperature of, on average, + 14 °C. An increase in the concentration of greenhouse gases leads to an increased infrared opacity of the atmosphere, and therefore to an effective radiation into space from a higher altitude at a lower temperature. This causes a radiative forcing that leads to an enhancement of the greenhouse effect, the so-called *enhanced greenhouse effect*.

Source: IPCC, 2007d.

argue that increased combustion of coal — at that time mainly in Great Britain — could lead to higher surface temperatures. He stated:

> 'if the quantity of carbonic acid [i.e. carbon dioxide] increases in geometric progression, the augmentation of the temperature will increase nearly in arithmetic progression' (Arrhenius, 1896).

The modern formulation of this still valid relationship is that 'the temperature increase is proportional to the logarithm of the carbon dioxide increase'. Arrhenius's estimate that the global surface temperature would rise by 3–5 °C if atmospheric carbon dioxide concentrations doubled is close to present day knowledge. For example, the Intergovernmental Panel on Climate Change (IPCC, 2007a) has projected a 2.0–4.5 °C increase.

Arrhenius was not alarmed about the warming due to an enhanced atmospheric greenhouse effect, since his initial concern was the negative consequences for Scandinavia if cooling were to occur.

Early anthropogenic climate change debates until 1940

The issue of anthropogenic climate change was raised in the late 19th century by Eduard Brückner, although his interest was not the greenhouse effect. Instead his focus was the effects of deforestation and cultivation of land on the reflectivity of the land surface and its evaporation, given the huge changes people have made to vegetative cycles (Penck and Brückner, 1901–1909). Arrhenius, as already described, was the first to consider anthropogenic emissions and the greenhouse effect but the lack of accurate measurements of trace gas concentrations prevented a continuing debate except for a few follow-up papers by Arrhenius (e.g. in 1899). Even some decades later Callendar (1938) was only able to give a range of 274 to 292 parts per million volume (ppmv) for the atmospheric CO_2 concentration at the turn of the century.

Guy Stewart Callendar's 1938 paper published in the Quarterly Journal of the Royal Meteorological Society marked a milestone in the history of understanding anthropogenic climate change. He was the first to establish the full link from trace gas concentration change, observed only for carbon dioxide, via changed radiation fluxes from the atmosphere to the surface, to observed global mean warming for the period from 1900 to 1938. The following year he went further, stating:

> 'As man is now changing the composition of the atmosphere at a rate which must be very exceptional on the geological time scale, it is natural to seek for the probable effects of such a change. From the best laboratory observations it appears that the principal result of increasing carbon dioxide […] would be a gradual increase in the mean temperature of the colder regions of the Earth' (Callendar, 1939).

Callendar's paper failed to raise a major scientific debate even though the first (albeit rather inaccurate) measurements of CO_2 concentration changes were available, a major global mean warming episode had occurred between 1900 and 1940, and spectroscopy of trace gases had advanced. One reason why Callendar did not succeed in spreading his message, even among the scientific community, was because his meteorological colleagues did not believe the CO_2 concentration changes he claimed to have been observed ([2]). A second reason was the poor knowledge that most meteorologists then had of radiative transfer of heat radiation (also called terrestrial, or thermal infrared, or long-wave radiation) through the atmosphere.

From theoretical considerations on the transfer of energy in the global atmosphere to quantification in computer models

While the mechanisms underlying the transfer of energy around the global atmosphere are simple to understand in principle, quantifying this in a computer model remains far from easy. Accurate radiative transfer calculations in a spherical atmosphere require sophisticated numerical codes, as the basic equation fully established by Chandrasekhar (1950) is a so-called integro-differential equation that can only be solved numerically, demanding high performance computing facilities. Even today a comparably large amount of computing time is devoted to the 'brute force' calculation of a still very simplified radiative transfer in a climate model.

([2]) For accurate trace gas measurements, groups of laboratories have to measure concentrations of gases in samples given to them within an international comparison in order to eliminate larger systematic errors. Reliable change estimates for CO_2 were not available until the 1960s and data for the other two naturally occurring long-lived trace gases, N_2O and CH_4, were not available until the late-1980s.

Chandrasekhar's work allowed a more accurate calculation (at first only in atmospheres without clouds) of the increased downward thermal radiation and hence the global mean warming estimates, following any increase in greenhouse gases. In the second half of the 1950s and early 1960s such estimates for a doubling of CO_2 concentrations evolved steadily from original estimates without cloud influence reaching 2.5 °C (Plass, 1956). Adding the influence of clouds reduced this to less than 2 °C (Kaplan, 1960) but attempts to account for water vapour influence, via fixed relative humidity led to very high temperature increases (Möller, 1963). These were strongly disputed because the positive water vapour effect amplified the estimated impact of a doubling of CO_2 concentrations to nearly 10 °C warming.

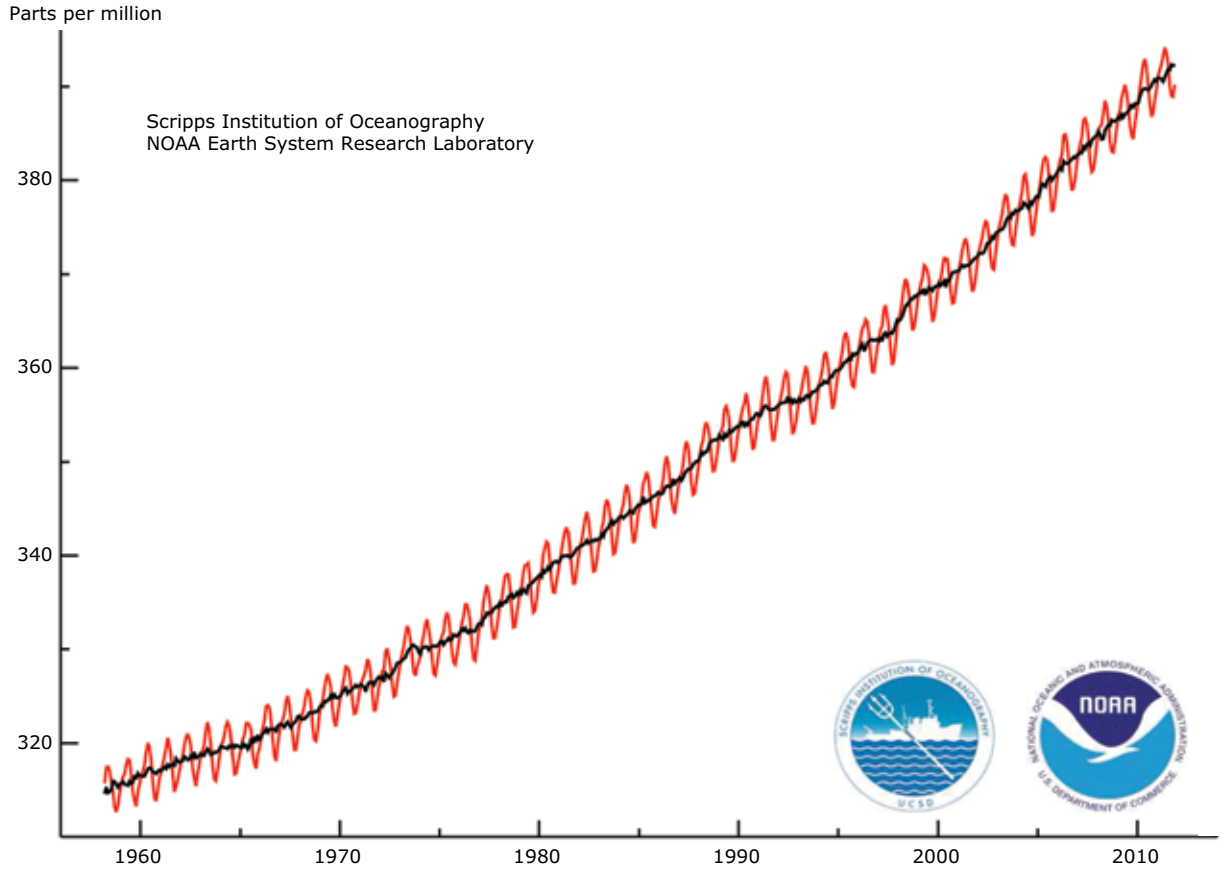
Establishment of long-term time series of greenhouse gas measurements

The International Geophysical Year from 1957 to 1958 marked the start of long-term monitoring of the most important anthropogenic greenhouse gas, carbon dioxide (CO_2). The US scientist David Keeling established two monitoring stations in very remote locations — Mauna Loa on Hawaii (Figure 14.1) and Antarctica — to measure the background concentration of CO_2 without the influence of nearby anthropogenic sources. These time series soon revealed the annual seasonal 'breathing' of the northern hemisphere (caused by the growth of biomass during the warm months and its decay during cold months). This annual cycle is weak at the South Pole, at the point furthest from the seasonal influence. It was this time series which, by 1970, had demonstrated a clear rising trend in global CO_2 concentration of some 0.4 % per year. The full trend curve can be found in NOAA (2011).

First calculations with global circulation models

Computers have had a huge impact on our ability to understand the atmospheric greenhouse gas effect. The advent of the first global three-dimensional atmospheric general circulation

Figure 14.1 Carbon dioxide (CO_2) mixing ratio at the Mauna Loa station on Hawaii



Note: The yearly averages and the annual cycle rise continually in the 50 year period. The annual cycle is caused by biomass growth during the Northern Hemisphere summer and the decay of biomass in the winter.

Source: NOAA, 2011.

models (AGCMs) for weather forecasting came with the first electronic computers in the late 1950s. By the early 1960s, an AGCM roughly representing the present day climate had also been run with doubled or quadrupled atmospheric CO_2 concentration.

These AGCMs rapidly reached a new higher equilibrium for surface temperature because the effect of the ocean, represented merely as a rather thin boundary of several 10s of metres in the model, was a poor representation of reality. Oceanic circulation — particularly vertical mixing — has a major impact, delaying the rise in global mean warming by at least several decades under present CO_2 concentration increases. Climate system sensitivity — the change in temperature resulting from a net change in incoming and outgoing energy at the top of the atmosphere ([3]) — has been investigated ever since such the first AGCM efforts of the mid-1960s.

The role of clouds

Simulations by AGCMs consistently indicated a surface temperature increase of around 1 °C for a net increase in energy flux of one watt per square metre at the top of the atmosphere, if the effect of clouds were trivial. Clouds cover more than 60 % of the Earth's surface, however, and their effect is far from trivial. They can reflect up to 80 % of solar radiation and they decouple thermal infrared emission from the surface into space. High clouds very often add to the greenhouse effect but low clouds lower it. Schneider (1972) was the first to realise that increasing cloud top height by 600 m is equivalent to a temperature increase of 2 °C. Reducing cloud cover by 8 % has a similar effect. Clouds are also influenced by air pollution, leading to higher reflectivity for geometrically thin water clouds and lower reflectivity for geometrically and optically thick water clouds, if they contain some black carbon.

It rapidly became evident that understanding cloud properties and the consequences of any changes in these, was a crucial element in predicting greenhouse gas effects. However, it proved very difficult to quantify what the net effect of these various changes would be.

Air pollution and climate change

The absence of obvious atmospheric warming from the late 1940s until the 1970s, despite the increase in greenhouse gases, revealed yet another facet of the anthropogenic climate change 'puzzle': that surface cooling could occur as a result of increased atmospheric turbidity, both in clear and cloudy atmospheres. This is because turbidity arising from anthropogenic air pollution affects the radiative transfer of energy in the following, sometimes unexpected, ways:

- it increases local planetary albedo (reflectivity) over dark surfaces like the ocean but decreases local planetary albedo over bright surfaces like sand dunes and snow (Yamamoto, 1972; Eschelbach, 1973);
- it strongly reduces solar irradiance at the Earth's surface — also called 'global dimming';
- it enhances cloud reflectivity for water clouds, especially for weakly absorbing minute, so-called 'aerosol' particles — the Twomey effect (Twomey, 1972 and 1974) — and reduces cloud reflectivity for optically thick water clouds, if black carbon or soot particles are part of the aerosol particles (Grassl, 1975).

As stated in IPCC's fourth assessment report (IPCC, 2007a), the latter two effects have remained a key uncertainty within the anthropogenic climate change debate, and are now estimated to mask the enhanced greenhouse effect by about one third.

Summary

By the end of the 1970s, it was known that the CO_2 concentration in the atmosphere was increasing by about 0.4 % per year; that a doubling of CO_2 concentration in climate models would lead to a mean global warming of several degrees centigrade; and that the water cycle contains two positive feedbacks (increasing the key greenhouse gas, water vapour, and lowering the reflectivity of earlier ice and snow surfaces), which act as an amplifier.

With that, most of the main elements of our current technical understanding of the issues were in place. It was not known, however, whether systematic

([3]) Radiative forcing is the rate of energy change per unit area of the globe as measured at the top of the atmosphere or at the tropopause level (the latter has been adopted by IPCC), if a certain radiatively active constituent of the atmosphere is altered and others remain fixed. It is measured in watts per square metre (Wm^{-2}), and positive values lead to surface warming. According to the IPCC, 'The radiative forcing of the surface-troposphere system due to the perturbation in or the introduction of an agent (say, a change in greenhouse gas concentrations) is the change in net (down minus up) irradiance (solar plus long-wave; in Wm^{-2}) at the tropopause AFTER allowing for stratospheric temperatures to readjust to radiative equilibrium, but with surface and tropospheric temperatures and state held fixed at the unperturbed values.'

changes of methane (CH_4) and nitrous oxide (N_2O) concentrations were taking place. Nor could CO_2 concentrations before industrialisation be determined.

14.3 Scientific breakthroughs regarding human-induced climate change during the 1980s

The 1980s brought scientific breakthroughs with respect to a number of the remaining uncertainties. As outlined below, these included historical greenhouse gas concentrations derived from air bubbles in ice cores, the emergence of coupled three-dimensional ocean-atmosphere-land models, and the clear signal of observed global mean warming in near-surface temperatures. These breakthroughs were largely the result of global change research coordination, as discussed in Section 14.4.

Trace gas history from air bubbles in ice cores
The air inside a snow pack in areas without summer melt, i.e. in the large inner parts of the two major ice sheets in Greenland and Antarctica, is trapped in small air bubbles within older snow that becomes progressively compacted. These tiny bubbles still exist in deep layers of an ice shield after several hundred thousand years.

During the 1980s, Swiss and French scientists (Neftel et al., 1985; Jouzel et al., 1987) were the first to determine the CO_2 concentration in these air bubbles of ice cores with enough precision to reconstruct the long-term history of greenhouse gases (CH_4 and N_2O concentrations could also be determined later). These findings established the strong correlation between CO_2 concentrations and the temperature at precipitation formation. However, the processes causing this correlation are still debated today. Greenhouse gases were clearly a global player in glacial cycles but the lower and upper limits of CO_2 concentration at about 190 to 200 ppmv for glacial maxima and about 280 ppmv during interglacials are still unexplained today.

It also became clear that the start and end of 'glacial' periods were initiated by the insolation changes in the Northern Hemisphere caused by long-term changes in the Earth's orbit around the sun. The consequences of these changes in the Northern Hemisphere climate are then amplified and made global by changing levels of greenhouse gases and by the ice-albedo feedback (Hansen, 2010).

Emergence of coupled atmosphere-ocean models
At the end of the 1980s, the first coupled atmosphere-ocean models emerged. These models included a three-dimensional representation of the ocean, which for the first time allowed simulations of the dynamic interactions between atmosphere and ocean under increasing greenhouse gas concentrations. The models, based on natural laws, are the only way for a look into the future, based on assumptions about human behaviour with respect to population changes, energy supply systems, land use change and global economic development.

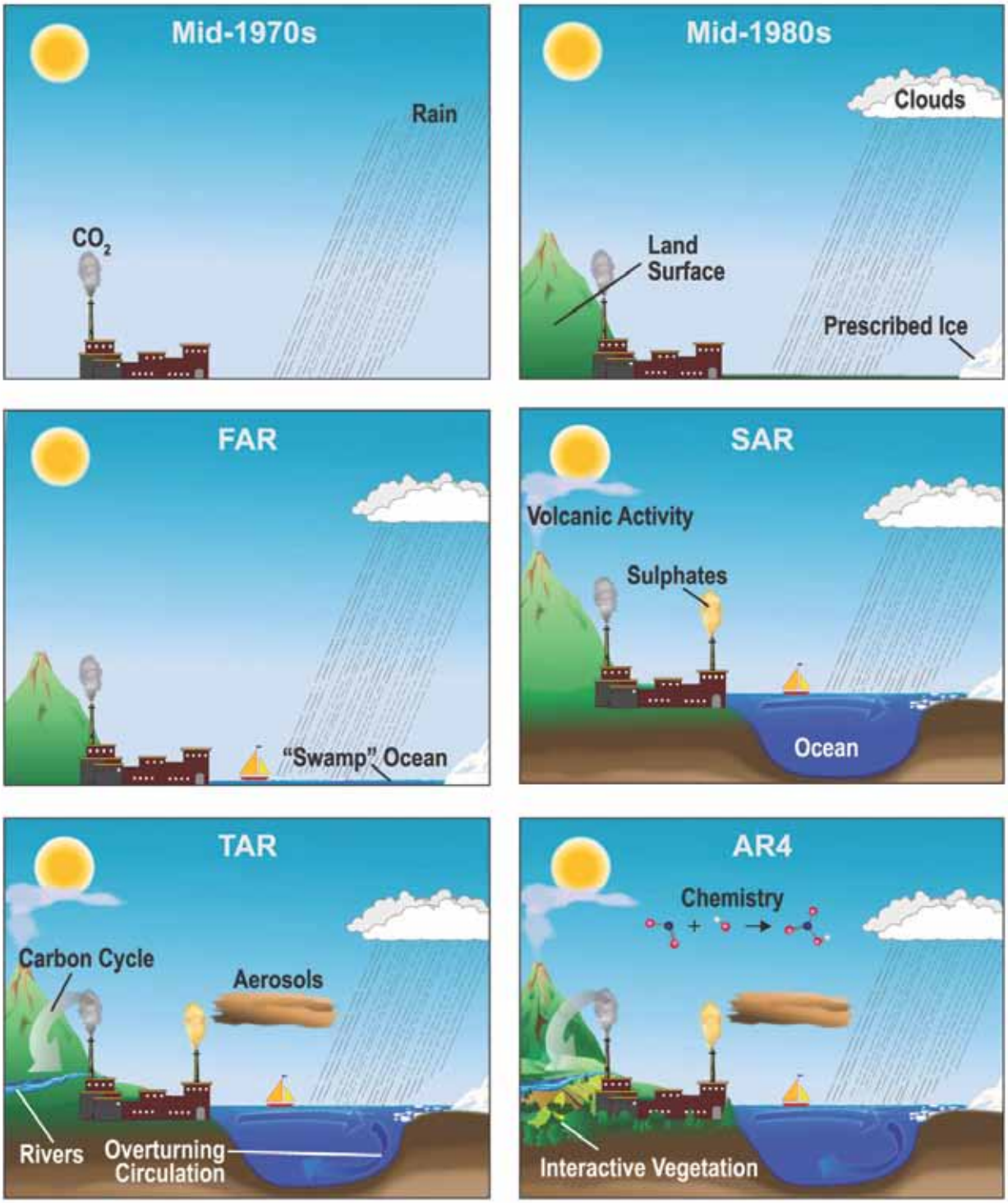
These first coupled models were, however, in need of 'flux corrections'. Flux corrections imply deliberately changing the energy and momentum fluxes at the air-ocean interface to prevent climate drift, i.e. a change in climate, in a constant greenhouse gas concentration scenario. It was not until the IPCC's third assessment report in 2001 that these flux corrections were no longer needed by some more advanced climate models.

One robust and anticipated result of these early coupled models was the delay of the full climate change signal by many decades compared to AGCMs due to the high heat capacity of the ocean. The models predicted that in a period with strong greenhouse gas concentration increase, such as now, less than two thirds of the mean warming that is inevitable due to the past concentration increase can be seen. Another important implication of the considerable inertia in the global climate systems is that the effects of policy measures taken now can only be detected after several decades. The progress in climate modelling during recent decades is depicted in Figure 14.2.

Detection of increased global mean air temperature
A further major development during the 1980s concerned temperature trends. While various regional air temperature trends had been published over the years, the first global trend analyses covering a full century only emerged during the 1980s (Groisman et al., 1987; Hansen et al., 1988). They were still rather uncertain, partly because there were gaps in the 'quality assurance' of observations from thousands of stations. Temperature time series can be inhomogeneous for many reasons, including changes in instrumentation, changed vegetation or buildings in the neighbourhood of the station, changed observers and infrequent calibration.

Other developments
Also in the mid-1980s, the 14th Ozone Report (WMO, 1984) provided the first more or less comprehensive list of the many artificial substances found in the atmosphere, subsequently known as the 'greenhouse gang', that apparently were very

Figure 14.2 Evolution of global climate change models



Note: The complexity of climate models has increased over the last few decades. The additional physical, chemical and biological processes incorporated in the models are shown pictorially by the different features of the modelled world.

Source: IPCC, 2007a.

strong greenhouse gases. Amongst them were the chlorofluorocarbons (CFCs), which were later found to be responsible for the hole in the ozone layer over Antarctica. That phenomenon became widely known only in 1985, although it had started several years earlier. That 14th Ozone Report could not, however, quantify the increase of methane and nitrous oxide concentration because the monitoring time series were too short given the accuracy of concentration measurements at that time.

14.4 Start of global coordination or climate change research and dissemination of findings on human-induced climate change

During the 1980s the climate change issue 'broke out' from being a largely scientific issue to a matter of concern for environmental policymakers. That is not to say that governments had totally ignored the issue previously. Much of the research on climate change had, in fact, been funded by governments. However, the warnings of global anthropogenic climate change by groups of leading scientists, speaking as an increasingly coordinated and unified voice, often reinforced and broadcasted by environmental non-governmental organisations such as the Climate Action Network, played a crucial role in raising the issues prominence. This knowledge transfer from science to policy became formalised with the establishment of a then unique, remarkable and authoritative scientific global climate change assessment body — the IPCC — in November 1988.

14.4.1 World Climate Research Programme

The first World Climate Conference in 1979, organised by the World Meteorological Organization (WMO), a specialised UN agency, agreed a World Climate Programme (WCP). Its research component, the World Climate Research Programme (WCRP), started in 1980 based on an agreement between WMO and the International Council for Scientific Unions (now named the International Council for Science) to organise and co-finance the first global change research programme.

The International Geosphere Biosphere Programme (IGBP), established in 1986, together with WCRP, now provides the main global organising and coordinating framework underpinning the bulk of scientific progress in understanding the functioning of the global system. A large part of the research assessed today by the Intergovernmental Panel on Climate Change (IPCC), was initiated in 1980 under the WCRP, which, for example, had by 1997 completed the first global survey of the physical status of the world oceans via its World Ocean Circulation Experiment (WOCE). The observations from this survey in turn allowed it to determine that the oceans absorb about 2 billion tonnes of carbon from anthropogenic carbon dioxide emissions per year, as presented in the IPCC's third assessment report (IPCC, 2001a, 2001b and 2001c).

14.4.2 Villach Conferences in 1980 and 1985

After two scientific conferences in the Austrian town of Villach in the early and mid-1980s, groups of high-ranking scientists issued initial warnings of the potential consequences of anthropogenic climate change. The scientists had been invited to Villach by the United Nations Environment Programme (UNEP), the World Meteorological Organization (WMO) and the International Council for Scientific Unions. In October 1985, these warnings culminated in the observation that:

> 'Many important economic and social decisions are being made today on long-term projects [...], all based on the assumption that past climatic data, without modification, are a reliable guide for the future. This is no longer a good assumption since the increasing concentrations of greenhouse gases are expected to cause a significant warming of the global climate in the next century. It is a matter of urgency to refine estimates of future climate conditions to improve these decisions' (WMO, 1986).

This paragraph captured one of the key threats of global climate change, namely that important features of our society, such as key infrastructure, may no longer be well adapted to prevailing climate conditions. Scientists, such as Scientific Committee on Problems of the Environment (SCOPE 29, 1988) highlighted that anthropogenic climate change could affect not only average conditions but also climate variability and weather extremes. Many extreme weather events might become more frequent and even new, more devastating extremes might occur as a result of changes in the distribution of climate parameters.

Box 14.2 Why do most policymakers accept IPCC statements as the most authoritative voice on climate change?

In all areas of science, reviews by authoritative groups of established scientists have for a long time been the preferred method of informing the scientific community and the public at large about the current state of knowledge. In the case of the IPCC, however, such assessments were lifted to a level never reached before in any field of science. The reasons primarily structural but also related to individuals, most notably the first IPCC chairman, Bert Bolin.

The structural advantages of the IPCC include the following:

- it is sponsored by well accepted institutions of the United Nations: the World Meteorological Organization (WMO), a technical agency in charge of climate matters, and the United Nations Environment Programme (UNEP);
- it is intergovernmental, i.e. government representatives are members of the national IPCC delegations;
- scientists and governments select the groups of authors for each chapter drawing from lists given by countries and accepting contributions by other experts in a certain subsector of climate research;
- the reviewing process is elaborate and involves the scientific community first and government-named experts in a second round, with all critical remarks and proposals for improvement judged by established scientists who are not authors of the chapters themselves.

A further essential part is the approval of the summary for policymakers 'sentence by sentence'.

14.4.3 Establishment of the Intergovernmental Panel on Climate Change

The IPCC originated from proposals of presidents of national meteorological services, put forward at the Tenth Congress of the World Meteorological Organization (WMO) in Geneva in May 1987. That Congress established an intergovernmental mechanism charged to deliver an authoritative assessment of knowledge about anthropogenic climate change, without which government attention was unlikely.

The Executive Council of WMO proceeded jointly with the United Nations Environment Programme (UNEP) towards establishing an intergovernmental panel of experts. This led, in November 1988, to the first meeting of the IPCC at the Geneva Congress Centre. Three working groups were formed. Working Group I assesses the physical scientific aspects of the climate system and climate change. Working Group II assesses the vulnerability of society and nature to climate change, and means of adaptation, while Working Group III examines mitigation measures for limiting or preventing the effects of greenhouse gases.

More specifically the IPCC's tasks are:

- to identify human induced influences on the climate and to compare these with other external influences and natural variability.
- to address, through process studies and observations, effects on the climate system of important feedbacks, both positive (enhancing change) and negative (reducing change), for instance those due to water-vapour, clouds and ocean circulation.
- to combine these influences and effects by means of numerical computer models simulating past and present climates and projecting future climate.
- to compare model simulations from different modelling groups with observations related to past and present climates, and so estimate the contributions to climate change from natural and human induced influences, together with their associated uncertainties. These computer models provide the only means of adding together all the non-linear processes involved in the evolution of climate.
- to describe the likely future impact on human communities and ecosystems.

All chapters of IPCC reports are reviewed, first by a limited number of expert scientists, then by the international community of climate scientists and others with an interest in reviewing, and finally by governments.

When the working groups meet in plenary, they consist of government representatives, generally both scientists and policymakers, which is a remarkable development in itself. However, the actual assessment work is done by selected scientists only. The overall IPCC structure has been judged successful and has been retained (see Bolin, 2008) although in 2010–2011 several changes were implemented to address criticism (see Section 14.6.4).

The creation of the IPCC represented a decisive turning point in recognition of the scale of the climate change problem, at least amongst technical and policy experts. The IPCC was immediately under pressure to publish its first full assessment of knowledge on (anthropogenic) climate change in time for the Second World Climate Conference (SWCC), scheduled for October 1990.

The IPCC first assessment report, 1990
The IPCC finished its first assessment report in June 1990. The report stated that:

- there is a natural greenhouse effect of the atmosphere which already keeps the Earth warmer than it would otherwise be;
- there is a strong increase of concentrations of all three long-lived naturally occurring greenhouse gases (CO_2, CH_4, N_2O), which is due to anthropogenic activities;
- global mean near-surface air temperature has risen by 0.3 to 0.6 °C during the 20th century;
- in the past there has been a strong correlation between greenhouse gas concentrations and the global mean temperature, as shown by concentrations of greenhouse gases in air bubbles from the last 160 000 years contained in ice cores in Antarctica.

In addition, the IPCC report also pointed to other observed changes in the climate system, including a rise in the mean sea level, the retreat of mountain glaciers in most regions, changes in the regional redistribution of precipitation, and other significant changes in climate parameters. On the basis of the evidence before them, however, and the level of proof that is required to conclude that observed climate change is significantly beyond the level of natural variability, the IPCC could not yet state that observed climate change has a man-made origin.

The IPCC Response Strategies Working Group concluded in 1989 that the potentially serious consequences of climate change justified the immediate adoption of response strategies, such as limiting emissions and preparing adaptation measures. The Working Group suggested that the United Nations agree on a framework convention that later could be supplemented with specific protocols, following the approach taken with the Vienna Convention on Protecting the Ozone layer and its Montreal Protocol. It also suggested setting goals for reducing emission levels in an equitable manner and listed many specific options for doing so across economic sectors.

The IPCC second assessment report, 1995
In 1995, the IPCC published its second assessment report. The Working Group I volume (IPCC, 1995a), agreed in November 1995, stated that 'The balance of evidence suggests a discernible human influence on global climate.' This was the first time that scientific evidence enabled the human-induced change signal to be perceived against the background of natural climate variability. This conclusion strengthened the urgency of calls to address climate change.

Box 14.3 Evidence of anthropogenic climate change

In March 1995, a pre-print of a peer-reviewed scientific paper (Hegerl et al., 1997) claiming that anthropogenic climate change had been detected was announced at a press conference in Hamburg, Germany. The founding director of the Max Planck Institute for Meteorology, Klaus Hasselmann, presented the work of his research group, which was based on four types of evidence: time series of long-lived greenhouse gas concentrations, observed geographical patterns of temperature anomaly time series, transient runs of a coupled atmosphere-ocean-land model, and the so-called fingerprint method (Hasselmann, 1997) searching for anomaly patterns attributable to distinct processes. The wide media coverage of this very unusual event emphasised the significance of the findings.

The Working Group II volume, covering impacts, adaptation and mitigation of climate change (IPCC, 1995b), presented a wealth of information. It indicated that impacts of anthropogenic climate change were already occurring and would pose serious risks in the future.

The Working Group III report, covering the economic and social dimensions of climate change, showed that there were many options available, both in terms of low-emitting technologies and available policy instruments to reduce GHG emissions significantly in all countries and economic sectors. The report also pointed to the importance of early mitigation efforts to improve flexibility in stabilising atmospheric greenhouse gas concentrations as a risk management approach.

The IPCC third assessment report, 2001

The IPCC published its third assessment report in 2001 (IPCC, 2001a, 2001b and 2001c). The role of human activity in causing climate change was further clarified: 'There is new and stronger evidence that most of the warming observed over the last 50 years is attributable to human activities.' Evidence of climate change impacts around the world had strongly increased and projections of climate change impacts in the future were much more serious than in the past. The potential for strong reductions in global GHG emissions was clearly demonstrated and the costs of these reductions were shown to be modest compared to the projected increase in wealth. Insights into effective climate policies had grown significantly.

The IPCC fourth assessment report, 2007

On 2 February 2007 Working Group I of IPCC (2007a) stoked the political debate by clearly pointing out humankind's responsibility for the observed mean global warming:

> 'The understanding of anthropogenic warming and cooling influences on climate has improved since the third assessment report, leading to very high confidence that the global net effect of human activities since 1750 has been one of warming, with a radiative forcing of 1.6 Wm^{-2} (uncertainty range 0.6 to 2.4 Wm^{-2})'.

This statement strengthened the claim that an anthropogenic climate signal had been detected in the second and third assessments. The IPCC's Working Group II report in April 2007 (IPCC, 2007b) concluded that the extent of climate impacts on natural systems had further increased and that risks of future impacts were considered higher than in previous assessments, including an onset of negative impacts at lower temperature changes (see also Smith et al., 2009) than previously assumed. It included for instance the observation that:

> 'Approximately 20–30 % of plant and animal species assessed so far are likely to be at increased risk of extinction if increases in global average temperature exceed 1.5–2.5 °C.'

In May 2007 Working Group III on mitigation of climate change (IPCC, 2007c) made it clear that global emissions need to peak not later than 2015 to have a 50 % chance of keeping long-term temperature increase below 2 °C above pre-industrial levels. If peaking were delayed to 2025 the world would be committed to at least 3 °C warming in the long term. The report confirmed that ample options for reducing GHG emissions are available at modest costs. The report also suggested that the costs and benefits of mitigation are broadly comparable, even for the most stringent stabilisation of GHG concentrations studied (i.e. 450 ppm CO_2-eq.).

The *Stern review on the economics of climate change* (Stern, 2007) published at about the same time was more unequivocal. It stated that the costs of aggressive mitigation action are substantially lower than the costs of climate impacts and adaptation measures. It should be noted that the benefits of avoided climate change are notoriously difficult to estimate, since many impacts cannot easily be translated into monetary terms. In addition, co-benefits of reducing emissions, such as health benefits due to reduced air pollution from coal or increased energy security due to lower imports of fossil fuels, are not included in these calculations.

The outcomes of the Stern review were influenced by the choice of discount rates, which determine the weighting of future benefits and costs in decision-making. The Stern review employed very low discount rates and argued why that was the right choice. Not all economists agree with the approach used (e.g. Nordhaus, 2007).

One of the reasons for the stark messages about the urgency of reducing emissions was the higher estimate for so-called 'climate sensitivity', compared to previous reports. Working Group I stated that the 'best estimate' for a doubling of the CO_2 concentration compared to pre-industrial levels is a 3 °C increase in the mean global temperature, with a lower bound of + 2 °C and an upper bound of + 4.5 °C at two standard deviations. More recent studies confirmed this range (Rummukainen et al., 2010). The third assessment report had estimated

climate sensitivity as 2.5 °C (without providing upper and lower bounds). As a consequence, GHG concentration levels for avoiding a particular temperature increase have to be lower than previously indicated. In particular, the European Union had originally estimated that a CO_2 concentration of 550 ppmv would be compatible with its goal of limiting the increase in global mean temperature to 2 °C above preindustrial levels. According to the new assessment, staying within this temperature limit requires greenhouse gas concentrations to remain below about 450 ppm CO_2-eq., which in turn implies a maximum concentration for CO_2 alone of about 400 ppm (compared to measured 380 ppm in 2007). To achieve that, CO_2 emissions would have to be reduced by 50–85 % from 2000 to 2050 globally, and by 80–95 % in industrialised countries.

Such a goal may appear Herculean. Nevertheless, many scenarios have been developed that achieve such a low carbon future using different portfolios of measures. Some scenarios still allow for relatively high shares of fossil fuels (coal and gas) for electricity production but require power plants to be equipped with CO_2 capture and storage. Other scenarios rely on a large share of nuclear power and yet others bring emissions to very low levels by moving to producing 80–100 % of electricity from renewable sources (e.g. WBGU, 2003; Greenpeace/EREC, 2007; van Vuuren, 2007; IEA, 2009 and 2010; IPCC, 2011).

IPCC special report on renewable energy sources and climate change mitigation

The Working Group III special report, *Renewable energy sources and climate change mitigation* (IPCC, 2011), is an assessment of the literature on the scientific, technological, environmental, economic and social aspects of the contribution of six renewable energy sources to mitigating climate change, published in 2011. Some of the main messages are:

- 'A significant increase in the deployment of renewable energy by 2030, 2050 and beyond is indicated in the majority of the 164 scenarios reviewed in this special report';
- In 2008, total renewable energy production was roughly 64 EJ/year (12.9 % of total primary energy supply) with more than 30 EJ/year of this being traditional biomass. The global primary energy supply share of renewable energy differs substantially among the scenarios. More than half of the scenarios show a contribution from renewable energy in excess of a 17 % share of primary energy supply in 2030 rising to more than 27 % in 2050. The scenarios with the highest RE shares reach approximately 43 % in 2030 and 77 % in 2050.

14.5 Emerging climate change policy

The foregoing sections of this chapter presented the evolution of science regarding the enhanced greenhouse gas effect and its projected impacts. The remainder focuses on how the political process dealt with this emerging scientific knowledge base. The power to determine the ends and means of public policy is widely though not equally shared, and different groups will of course seek to shape perceptions of truth, information or analysis (Gregory, 1989). Among the various stakeholders that seek to influence government policy development are environmental NGOs and business organisations. Their influence is mentioned briefly here but is not analysed in detail in order to limit the length of the chapter.

Some environmental NGOs like the Climate Action Network (CAN, 2012) aim to influence the United Nations Framework Convention on Climate Change (UNFCCC) policy process directly by providing detailed feedback through newsletters during the negotiations. Others focus on awareness campaigns (e.g. Greenpeace, 2012) and others provide summary information on scientific aspects (e.g. WWF, 2012). Some businesses (e.g. parts of the fossil fuel industry) have aimed to influence the negotiations directly or through lobby groups (e.g. the former Global Climate Coalition) or have questioned the underlying science (as discussed below). Other businesses have focused on the opportunities provided by climate policy, for example members of the World Business Council on Sustainable Development (WBCSD, 2012). It appears that the perspective of many businesses has changed somewhat over the years from being against action on GHG emission reductions to being in favour of measures such as regulation, either to provide investment security or because certain industries see opportunities (e.g. the renewable energy industries).

14.5.1 The 1980s: initiatives to stimulate political debate on how to deal with climate change

The late-1980s saw several initiatives to stimulate political debate on how to deal with climate change. There was intense public debate in some industrialised countries on climate change, illustrated by reports from some national advisory bodies to governments and legislative bodies, such

as in Germany (WBGU, 1993) and other countries (Oppenheimer and Petsonk, 2005). In 1987, scientists and policymakers discussed matters at workshops in Villach and Bellagio, leading to recommendations to formulate policy targets (Oppenheimer and Petsonk, 2005).

Two conferences in Toronto (1988) and Noordwijk (1989) provided opportunities to enhance the scientific input into political decision-making and came up with proposals that would become the heart of the legal climate change regime later on. This was made possible by the mix of government representatives, international agency staff and scientists participating in these conferences.

Encouraged by the international agreement on the Montreal Protocol on protecting the ozone layer in 1987, which set targets for phasing out ozone-depleting substances, many of which are also powerful greenhouse gases (IPCC, 2005a), the Canadian government hosted an international conference in Toronto in 1988. The Toronto Declaration (WMO, 1989) makes extensive reference to the signals of a changing climate and the projections of future changes. It calls for an action plan, including a framework convention on climate change and the stabilisation of GHG concentrations in the atmosphere, and calls for domestic action on reducing CO_2 emissions. The action plan set a political target of a 20 % reduction of global CO_2 emissions by 2005 from 1988 levels, with industrialised countries taking responsibility for most of it. It further called for the establishment of a global atmosphere fund.

The Noordwijk conference, bringing together a group of 67 concerned countries at ministerial level in November 1989, was provided extensive scientific information on climate change, its impacts and strategies to bring it under control. This led to a ministerial declaration, which called for atmospheric GHG concentrations to be stabilised 'within tolerable limits', reflecting the concern about increasing negative impacts of climate change. It asked the IPCC (which was working on its first assessment) to report on the best scientific knowledge to help define what that level should be. It also stated that GHG emissions should be reduced and sinks increased to a level consistent with the natural capacity of the planet, allowing for ecosystems to adapt naturally, food production not to be threatened and economic activity to develop in a sustainable manner (Oppenheim and Petsonk, 2005). This would provide the foundation for the later United Nations Framework Convention on Climate Change.

These events demonstrate the willingness of some political actors to take action based on emerging, but certainly not complete knowledge on climate change and its impacts: the precautionary principle in action.

14.5.2 The 1990s: establishment of the framework of international law for dealing with climate change

In the field of climate policy, the 1990s saw the establishment of the framework of international law for addressing climate change.

United Nations Framework Convention on Climate Change

The IPCC finished its first assessment report in June 1990 and was asked to present its findings at the Second World Climate Conference (SWCC), which took place in Geneva, Switzerland, in October 1990. The World Meteorological Organization (WMO) had changed the earlier main topic of the SWCC, climate variability, to anthropogenic climate change, indicating the increasing priority being given to the issue. The presentation of the first full assessment of scientific knowledge on climate change by the IPCC during the first part of SWCC in 1990 had a major impact on the later ministerial part.

As a result, ministers from 134 countries called for a framework convention on climate change, to be ready for signature at the Earth Summit in Rio de Janeiro, in June 1992. They urged the inclusion of a global objective of stabilising GHG concentrations in the atmosphere at a level that would prevent 'dangerous interference with climate' (language used in the Noordwijk Declaration) and, as a first step, to halt the growth of global GHG emissions.

As a result of the Ministerial declaration of the SWCC, the UN General Assembly decided in December 1990 to set up an international negotiating committee, consisting of government representatives of all UN member countries, to work out an agreement. To serve the negotiations, the IPCC brought out a supplementary report in early 1992 (IPCC, 1992) to provide a synthesis of the latest scientific knowledge about climate change. The work of the negotiating committee resulted in agreement on the text of the United Nations Framework Convention on Climate Change (UNFCCC, 1992) in May 1992, just before the World Summit in July 1992, where it was signed by 153 countries and the European Communities.

Interestingly, the Convention explicitly mentions several underlying principles, including, in Article 3.3, the precautionary principle:

> 'The Parties should take precautionary measures to anticipate, prevent or minimize the causes of climate change and mitigate its adverse effects. Where there are threats of serious or irreversible damage, lack of full scientific certainty should not be used as a reason for postponing such measures, taking into account that policies and measures to deal with climate change should be cost-effective so as to ensure global benefits at the lowest possible cost.'

The central goal (or 'ultimate objective') of the UNFCCC reads as follows:

> 'The ultimate objective of this Convention […] is to achieve […] stabilization of greenhouse gas concentrations in the atmosphere at a level that would prevent dangerous anthropogenic interference with the climate system. Such a level should be achieved within a time frame sufficient to allow ecosystems to adapt naturally to climate change, to ensure food production is not threatened and to enable economic development to proceed in a sustainable manner.'

This article clearly shows the central role given to science, which was supposed to inform politics about the level of action to be taken. Specifically, this article raises four major questions (Box 14.4). Science had not progressed to provide definite and clear information on all these questions, so they were essentially unanswered when the UNFCCC came into force.

Operationally, the UNFCCC contains clauses in which industrialised countries commit themselves to:

> 'adopt national policies and take corresponding measures on the mitigation of climate change, by limiting its anthropogenic emissions of greenhouse gases and protecting and enhancing its greenhouse gas sinks and reservoirs. These policies and measures will demonstrate that developed countries are taking the lead in modifying longer-term trends in anthropogenic emissions consistent with the objective of the Convention, recognising that the return by the end of the present decade to earlier levels of anthropogenic emissions of carbon dioxide and other greenhouse gases not controlled by the Montreal Protocol would contribute to such modification'.

This text is a complicated and not really legally binding way of saying that developed countries will try to stabilise GHG emissions by the end of the century at the level of some prior year. The vague formulation already reflected the trouble of getting all industrialised countries (and particularly the US) to agree on a binding formulation to stop the growth of emissions. Box 14.5 sets out the other key elements of the Convention. The UNFCCC was rapidly ratified. It became binding on 21 March 1994, 90 days after the threshold of 55 countries had been reached on 21 December 1993.

Box 14.4 Four major science questions associated with the central goal of the UNFCCC

- What is dangerous interference with the climate system? In other words, what climate change impacts constitute a danger? This is obviously a value judgement that cannot be made on scientific grounds alone but science has an important role to play in providing relevant information.
- How fast may the climate change while still allowing for ecosystems to adapt naturally? This seems largely a scientific question. However, any level of change will cause responses in ecosystems. Whether these responses are still considered as 'adaptation' or already as 'impacts' is partly a value judgement, which in turn may be influenced by considerations about how much these responses matter — e.g. fish stocks that we eat versus marine species that we do not.
- At which redistribution of precipitation and at which warming level is food production threatened? Again, it initially seems a scientific question but in effect it also requires value judgements, asking for political decisions related to e.g. food distribution and the population size of an area facing food insecurity.
- At what degree and rate of climate change is economic development going to be affected negatively? But also, what is the speed at which emissions reduction and adaptation measures can be taken so as to avoid disrupting economic development? Here scientific and economic knowledge is needed to inform politics.

Box 14.5 Key elements of the UNFCCC

Principles:
- 'common but differentiated responsibility'
- special consideration for vulnerable developing countries
- 'precautionary principle'
- 'polluter pays'
- promoting sustainable development

Goals: the ultimate goal (Article 2) is to 'stabilize greenhouse gas concentrations in the atmosphere at a level that would prevent dangerous anthropogenic interference with the climate system. Such a level should be achieved within a time frame sufficient to allow ecosystems to adapt naturally to climate change, to ensure that food production is not threatened and to enable economic development to proceed in a sustainable manner.'

Participation: almost universal (191 countries and the European Union, as of 1 September 2008).

Actions required:

- All countries must minimise emissions and protect and enhance biological carbon reservoirs, so called 'sinks'. Industrialised countries ('Annex I countries') must take action to stop growth of emissions before 2000.
- All countries must promote development, application and transfer of low-carbon technologies. Annex I countries must assist developing countries.
- Cooperate in preparing for adaptation.
- Promote and cooperate in research and development.
- Report on emissions and other actions (so called 'national communications'), annually for Annex I countries and less frequently for others.
- Rich industrialised countries ('Annex II countries') must assist developing countries financially in their actions.

Compliance: reports are reviewed by the secretariat and by visiting expert review teams.

Institutions:

- The Conference of the Parties (COP) is the supreme decision-making body. Its rules of procedure for decisions have never been agreed.
- The Bureau (comprising officials elected by the COP) is responsible for overall management of the process.
- Two subsidiary bodies (for implementation and for scientific and technological advice) prepare decisions of the COP.
- The financial mechanism is operated by the Global Environment Facility of the World Bank, the United Nations Development Programme (UNDP) and UNEP, and replenished by Annex II countries on a voluntary basis. Two special funds — a least developed country fund and a special climate change fund — mainly finance adaptation plans and capacity-building but also provide for technology transfer and economic diversification.
- Expert groups exist on technology transfer, developing country national communications, least developed country national adaptation plans.
- The Secretariat is located in Bonn, Germany.

Other elements: a requirement to review the need for further action regularly.

Source: Metz, 2010.

Kyoto Protocol

At the time the UNFCCC entered into force (end-1994), the IPCC was still working on its second assessment report. Enhanced scientific understanding of climate change and stronger evidence of its man-made causes was becoming more widely known. At the first session of the Conference of the Parties to the UNFCCC (COP1), in Berlin from end-March to the early-April 1995, the vague and not legally binding commitment of industrialised countries to try to stabilise emissions by 2000 was recognised as being far from sufficient.

The Conference of the Parties therefore adopted the so-called Berlin Mandate, which contained as its key provision the need for a legally binding intergovernmental agreement to reduce greenhouse gas emissions by industrialised countries, ready in time for COP3 in 1997.

Developing countries pushed hard to be left out of this strengthening of commitments. Under the UNFCCC they are only subject to general obligations on matters such as taking national action to combat climate change and reporting their emissions. Their arguments were based on the principle of 'common but differentiated commitments and respective capabilities' in UNFCCC Article 3.1. The COP agreed that in the UNFCCC context this approach implied that industrialised countries should take the first step but that all countries would step up their commitments to address the problem over time, albeit maintaining proper differentiation of actions.

The demand expressed in the 'Berlin Mandate' for a binding legal agreement for greenhouse gas emission reductions was met at COP3 in Kyoto, Japan, with the unanimous adoption of the Kyoto Protocol to the UNFCCC by more than 150 countries on 10 December 1997 (UNFCCC, 1997). Industrialised countries agreed to reduce their GHG emissions, using a basket of six GHGs, to about 5 % below their 1990 level by the 2008–2012 period. This was a substantial deviation from the business as usual situation which, despite the commitments made in the UNFCCC, still showed strongly increasing GHG emissions from industrialised countries. The aggregate 5 % reduction was to be achieved by differentiated emission targets for each country, taking into account specific national circumstances. The principles of the Convention, including the precautionary principle and the principle of 'common but differentiated responsibilities and respective capabilities' apply to the Protocol. Other key elements are presented in Box 14.6.

Implementation of the Kyoto Protocol

Four years of negotiations and four further sessions of the Conferences of the Parties to the UNFCCC (COP4 to COP7) were needed to get the full 'small print' of the Kyoto Protocol finalised. It was not until ratification by the Russian Federation on 16 February 2005 that the 1997 Kyoto Protocol became binding, which required ratification by 55 countries representing more than 55 % of the total emissions in 1990 from countries with reduction commitments. Ratification by Russia was critical for the Kyoto Protocol to enter into force after the single most important emitter, the US, withdrew from the Protocol in 2001.

Will industrialised country ('Annex B') Parties achieve their collective target of reducing greenhouse gas emissions by 5 % below 1990 on average over the 2008 to 2012 period? Projected emission levels in the period 2008–2012, based on country reporting as of 2007 show that, other than Canada and New Zealand, most Parties are likely to meet their targets after accounting for emissions and removals from land-use change and credits from the Kyoto flexible mechanisms (UNFCCC, 2011a). Emission levels in 2009 of all Annex B Parties to the Protocol were about 22 % below the base year, in part due to the economic recession of 2008 (Figure 14.3).

The EU-15 ([4]) is on track to achieve its commitment under the Kyoto Protocol of reducing emissions by 8 % compared to base-year levels. This is due to a combination of domestic measures, EU-wide policies and measures, carbon sinks and Kyoto mechanisms. The closing of coal mines in the United Kingdom in 1985 and the German reunification after the fall of the Berlin wall in 1989 have helped these countries deliver on their respective 12.5 % and 21 % individual reduction targets. In recent years emissions were also reduced because of the short-term effects of the global economic crisis.

EU actions have included establishing the EU Emissions Trading Scheme; promoting renewable energy sources; promoting energy efficiency increases in the energy, transport and industry sectors; reducing methane from landfills; and cutting emissions of industrial fluorinated gases (EC, 2010; EEA, 2010; EEA, 2011).

Countries of the former Soviet Union and eastern European countries are significantly overachieving their targets because emissions fell dramatically after the breakup of the Soviet bloc and the expected rebound of emissions after economic recovery did not occur as a result of changes in their economic structure and modernisation of their industries. Collectively they are at around 35 % below their 1990 level.

([4]) The EU comprised 15 Member States when it agreed to a collective 8 % reduction target in 1997. That is still the basis for compliance with the Kyoto Protocol obligations, although the EU now has 27 Member States.

Box 14.6 Key elements of the Kyoto Protocol

Principles: same as the Convention

Goals: same as the Convention

Participation: 180 countries and the European Union (United States are not a Party)

Actions:

- Annex I countries jointly reduce emissions to 5 % below the 1990 level, on average over the period 2008–2012. Specific emission caps are set for individual countries (UNFCCC, 2012).
- Option to use flexible mechanisms, i.e. international trading of emission allowances (not to be confused with domestic emission trading systems), using the emissions reductions from projects in developing countries (through the Clean Development Mechanism, CDM) or other Annex I countries ('Joint Implementation').
- Option to develop coordinated policies and measures.
- Strengthened monitoring and reporting requirements for countries with reduction obligations.

Compliance: failures to achieve emission reduction targets are to be compensated in the period after 2012, with a 30 % penalty.

Institutions:

- COP of the UNFCCC, acting as the Meeting of the Parties of the Protocol, serves as the primary decision-making body.
- All other UNFCCC institutions are used.
- Compliance Committee, with consultative and enforcement branch.
- Executive Board for the Clean Development Mechanism.
- Joint Implementation Supervisory Committee.
- Adaptation Fund, managed by the Adaptation Fund Board and administered by the GEF. The Fund gets its money from a 2 % levy on CDM projects.

Other elements: a requirement to review the need for strengthening actions.

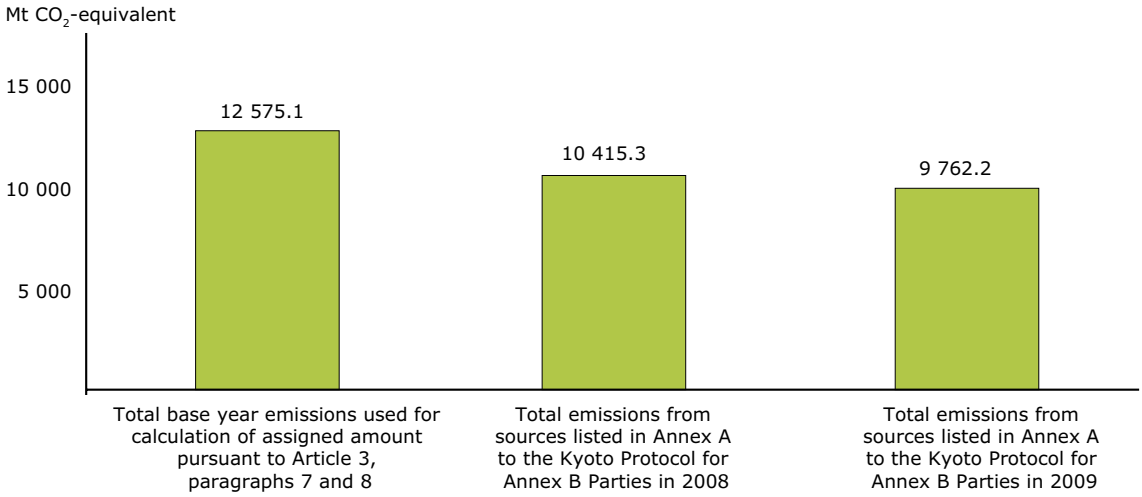
Source: Metz, 2010.

At the same time, however, global emissions increased from about 38 Gt CO_2-equivalent in 1990 to about 50 Gt CO_2-equivalent in 2010 (UNEP, 2011b), largely because developing countries increased their emissions as a result of spectacular economic growth. Compared to developing country emissions growth, the fact that the US stayed out of the Kyoto Protocol played a minor role in aggregate emissions growth. The global increase till 2012 was deliberately accepted (although underestimated at the time) in the design of the Kyoto Protocol, in line with the 'polluter pays' principle and the need to deal with equity concerns on the side of developing countries. The expectation was that in subsequent periods all countries would strengthen their actions to bring global emissions under control.

The Clean Development Mechanism of the Kyoto Protocol was increasingly employed. It allows developing countries to 'sell' reductions obtained from specific projects to industrialised countries and aims to support sustainable development in the 'selling' developing country. As of 1 January 2009, there were 4 474 CDM projects in the pipeline (i.e. either submitted to or registered by the CDM Executive Board). Of these, 1 370 had been registered and 465 certified emission reductions (CERs) had been issued. Together they equate to a reduction of about 0.3 Gt CO_2-equivalent per year in the period 2008–2012 and about 0.7 Gt CO_2-equivalent per year from 2013 to 2020. Given their relatively low price, it is very likely that Annex I countries will buy all the CERs originating from the CDM to meet their obligations.

To put things in perspective: the 0.3 Gt CO_2-equivalent per year is about 50 % of the total emission reduction (compared to the base year) that Kyoto Annex I countries are supposed to achieve. In other words, domestic emissions reductions in these countries will be only half of what they would have been without the CDM, if all available CERs are indeed bought (Metz, 2010).

Figure 14.3 Emission levels of Kyoto Protocol Annex B Parties in 2008 and 2009 (excluding land-use change emissions), compared to the base year



Source: UNFCCC, 2011b.

CDM projects cover a wide range of mitigation activities. The number of projects on renewable energy is the highest, with much smaller numbers for landfill gas (methane) recovery and destruction of HFC-23 at HCFC plants and N_2O at chemical plants. In terms of tonnes of CO_2-equivalent reduction expected before the end of 2012, however, renewable energy projects represent 36 % and HFC-23 and N_2O projects 26 %, which reflects the high global warming potential of HFC-23 (Metz, 2010).

Although the CDM is one of the successes of the Kyoto Protocol there are also some weaknesses. An example is the approval of some renewable energy projects (e.g. hydropower) but also efficient ('super critical') coal-fired power plants projects, where it is hard to prove that emission reductions are 'additional'. In other words, these projects possibly would have happened anyway without CDM credits. Another example is the approval of various industrial destruction projects of HFCs, which are emitted as a by-product of manufacturing the refrigerant gas HCFC-22, for companies that thus made profits selling credits. Such weaknesses are being addressed in current negotiations on a new international agreement for the period after 2012.

The US went its own way in dealing with climate change, as did Australia until December 2008 when it ratified the Protocol. Domestic climate action at federal level was given low priority in the US until the Bush administration concluded at the end of 2008. Although some action was taken at State and local level across the US, GHG emissions kept rising and net emissions were about 15 % above 1990 levels in 2008 (EPA, 2010b). After the election of President Obama at the end of 2008 there was hope that federal US GHG emission reduction policy would change, but this has not happened. Australia, although not part of the Kyoto Protocol until December 2008, nevertheless took domestic action in line with its Kyoto commitment. Australia is more or less set to meet its Kyoto target.

The ultimate objective of the UNFCCC and the EU two-degree target

It seems highly probable that the statement that 'The balance of evidence suggests a discernible human influence on global climate' in the IPCC second assessment report and the information on climate impacts and emission reduction options both played a strong role in facilitating the adoption of the Kyoto Protocol in 1997 by all countries attending the third session of the Conference of the Parties to the UNFCCC. The resistance that emerged in the US Congress prior to COP3 was primarily focused on the design of the Protocol, particularly its exemption of countries like China, and on the perceived risk for the US economy if significant emissions reductions were made (Byrd-Hagel Resolution, 1997).

In terms of the precautionary principle, political action was indeed strengthened at a time when scientific knowledge had improved but was still far from certain on the causes of climate change, the expected impacts and the feasibility and costs of emission reductions. It was not possible, however, to achieve political agreement on the exact meaning

of the ultimate objective of the UNFCCC, i.e. what constitutes a 'safe' level of GHG concentrations in the atmosphere. In other words, there was no clear idea how big the challenge actually was and how fast global emission reductions would have to occur.

In 1996 an important decision was taken by the Council of Environment Ministers of the European Union. They decided that in the light of the scientific evidence as reflected in the IPCC second assessment report, global average temperatures should not be allowed to rise more than 2 °C above the pre-industrial level. This was a political decision, based on scientific evidence about the risk of expected climate change impacts on one hand and the perceived feasibility of deep emission reductions on the other. It would become the focus for EU climate policy for the next decade and beyond.

The decision was based on the following global risk management approaches (Metz, 2010):

- **Cost-effectiveness approach**: first determine what a 'tolerable' risk of climate change impacts is (a political judgement based on scientific evidence), then determine how this level can be achieved at the lowest possible costs, and finally consider whether this is politically feasible.

- **Cost-benefit approach**: perform a cost-benefit analysis that attempts to compare the monetised climate change damages with the cost of taking action, ensuring that the benefits of an action exceed its costs. As noted in Section 14.4.3, estimating these future costs and benefits poses some significant challenges.

The EU's 2 °C decision was arguably based on a mix of the two approaches. It was obvious that a 2 °C warming would still mean a significant increase of the risks of climate change with serious consequences in vulnerable countries. It was regarded as unrealistic, however, to turn around global emission trends fast enough to limit the temperature increase further. It was also felt that setting a maximum tolerable level of warming should not be based on an uncertain and disputed comparison with the monetised costs of climate change impacts. The precautionary element was to set a clear limit, despite the continuing scientific uncertainty about climate change impacts, and the costs and feasibility of drastic emission reductions.

Scientific literature published since the IPCC second assessment report confirmed that limiting global warming to less than 2 °C above pre-industrial temperatures would considerably reduce the risk of triggering irreversible large-scale changes in the climate system, such as a complete melting of the Greenland ice sheet, which would lead to large adverse impacts in many world regions. Nevertheless, significant risks would remain even in the event of a 2 °C increase above pre-industrial temperatures (IPCC, 2007b; CCSEG, 2010). This recently led to a large group of developing countries challenging the adequacy of the 2 °C limit, arguing for the necessity of a 1.5 °C limit, as discussed in the next section.

14.6 Debate on further international action after 2012

14.6.1 The post-Kyoto UNFCCC process

At COP11 in 2005 a decision was taken to start two processes: a negotiation among Kyoto Parties about a second commitment period (following the first period from 2008–2012), and a so called 'dialogue' among all UNFCCC Parties about the future evolution of international climate action under the UNFCCC.

The IPCC published its fourth assessment report in 2007 and was awarded the Nobel Peace Prize in November 2007, together with Al Gore. With the messages from IPCC being discussed widely, it was possible at COP13 in Bali in December 2007 to formally start negotiations on a new agreement for the period after 2012. A complex two-track negotiating structure emerged. The negotiations on a second commitment period of the Kyoto Protocol continued with all countries except the US. A new track was also started, known as the 'long-term cooperative action', which covered all countries and aimed to enhance national and international action to achieve the ultimate objective of the UNFCCC. COP13 agreed the 'Bali Action Plan', which called for negotiations to be completed at COP15 in Copenhagen in December 2009.

14.6.2 Copenhagen 2009

COP15 in Copenhagen failed to reach agreement on a legally binding agreement for the post-2012 period, jeopardising effective global action. The COP 'took notice' of the Copenhagen Accord (UNFCCC, 2010), a political declaration by more than 140 countries. The Accord includes the goal of keeping global temperature increase below 2 °C or possibly even 1.5 °C, it promises substantial

financial resources from industrialised countries, and it contains an annex in which countries can include their intended national actions.

Although the COP did not formally endorse the Accord, it does reflect some significant progress regarding the policy response to climate change, including the endorsement of the 2 °C limit. It demonstrated the almost unanimous support for the 2 °C limit first proposed in 1996 by the EU. And the Accord even recognises that the climate change risks implied in this limit may already be going beyond what vulnerable regions, countries and people can tolerate and that a 1.5 °C limit might be needed.

The specific actions that have subsequently been pledged by almost 100 industrialised and developing countries show the intent of many countries to take domestic action to combat climate change. The EU specified internally agreed climate and energy targets to be met by 2020: reducing EU greenhouse gas emissions to at least 20 % below 1990 levels; providing for 20 % of EU energy consumption from renewable resources; and reducing primary energy use by 20 % compared with projected levels, to be achieved by improving energy efficiency (EU, 2012). It also pledged a 30 % reduction of emissions, provided other major emitters would made comparable efforts.

Unfortunately, the sum of these national emission reduction pledges for 2020 does not add up to what is needed to be on track to limit global temperature increase to 2 °C. In fact, current pledges imply a 2.5–5 degree trajectory, depending on how pledges for 2020 are implemented and what happens after 2020 (UNEP, 2010a and 2010c).

In Figure 14.4, the top coloured bands illustrate emission pathways over the 21st century, generated using integrated assessment modelling (IAM). The pathways were grouped based on ranges of likely temperature increase in the 21st century. Emissions corridors correspond to the 20th to 80th percentile range of emissions. The median of the Copenhagen Accord Pledge cases in 2020 is represented by the black bar.

The two bottom figures illustrate temperature increases associated with the different emissions pathways in the years 2020 (left) and 2050 (right): Thick, black lines show the median values, dark shaded areas represent the 20th to 80th percentile range, and light shaded ones the minimum/maximum range.

14.6.3 Cancun and Durban

COP16 in December 2010 took place in Cancun, Mexico. It was the culmination of a year of very active diplomacy and consensus was reached among all Parties to the UNFCCC on a series of decisions that formalised the elements of the Copenhagen Accord as official UNFCCC decisions and agreed a number of organisational provisions on finance and technology transfer. This meant that the long-term goal for limiting global warming and the pledges made by countries to reduce their emissions were formally decided. However, the most contested issues in the negotiations, such as the future of the Kyoto Protocol, the legally binding character of a new treaty, commitments from major developing countries, the provisions on monitoring, reporting and verification and the provision of financial support to developing countries, were not addressed.

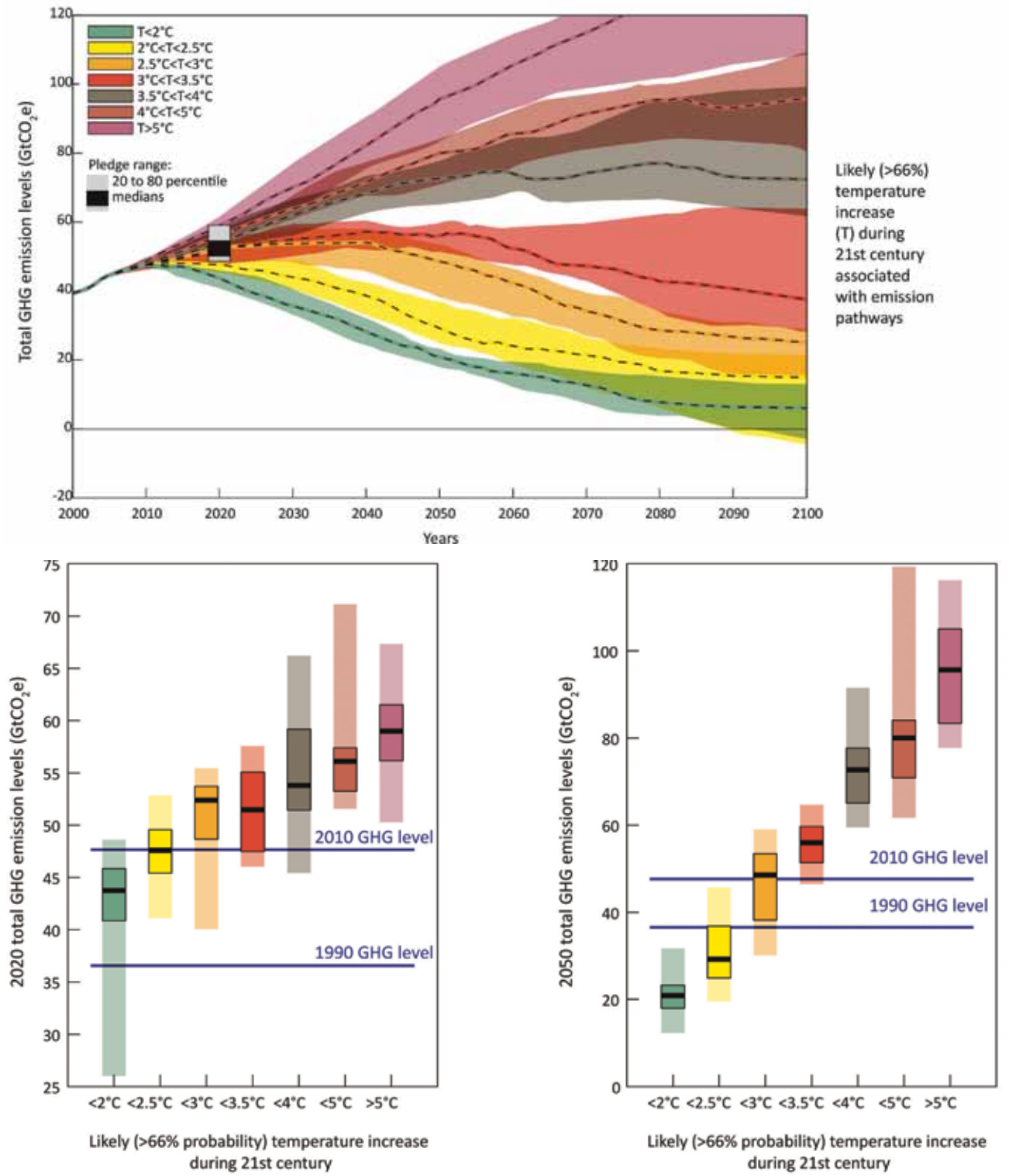
Despite difficult preparations, the next COP17 in Durban in 2011 delivered a series of decisions, although these did not include a new agreement for the period 2012–2020. Many countries were satisfied with the voluntary pledges that had been made in Copenhagen and Cancun. Only some Annex B countries agreed to put these pledges into a second commitment period under the Kyoto Protocol. It was agreed to hold workshops to clarify the pledges and were encouraged to strengthen the pledges, since the existing commitments would lead to a 3–4 °C trajectory, making it impossible to meet the 2 °C limit (UNEP, 2011b).

COP17 decided to start negotiations for a new legally binding agreement that would cover the period after 2020 and to complete negotiations by 2015 (UNFCCC, 2011d). Businesses require long-term agreements extending beyond 2020 to inform their investment decisions. Governments likewise need time to translate international agreements into national legislation and policies. In the short term, however, there is also a need for more ambitious action in the period up to 2020 if the 2 °C limit is to be taken seriously.

14.6.4 Creating doubt on the scientific knowledge base

Looking back at the 2000–2010 decade we see that international political action on climate change is moving forward only slowly. This is at odds with the increasingly strong messages from the scientific community about the man-made causes of climate change, the current and expected impacts of climate change, the urgency of deep reductions of global

Figure 14.4 Projected emission pathways over the 21st century



Note: In the above figure, the top coloured bands illustrate emission pathways over the 21st Century, generated using integrated assessment modelling (IAM). The pathways were grouped based on ranges of likely temperature increase in the 21st Century. Emissions corridors correspond to the 20th to 80th percentile range of emissions. The black bar represents emissions in 2020 resulting from pledges.

The two bottom figures illustrate temperature increases associated with the different emissions pathways in the years 2020 (left) and 2050 (right): Thick, black lines show the median values, dark shaded areas represent the 20th to 80th percentile range, and light shaded ones the minimum/maximum range.

Source: UNEP, 2011b.

GHG emissions and the feasibility of specific actions and technologies to realise such reductions.

One factor that caused this, although not the only one, is the doubt that was created about scientific knowledge on climate change. Other reasons, such as global economic and political developments and the growing ineffectiveness of the current approach to international agreements, have certainly contributed but are beyond the scope of this chapter.

Proper scientific conduct requires assumptions and findings to be challenged continuously in order to advance scientific knowledge. The IPCC has invested a lot in accurately reflecting in its assessments the certainty of findings and the continuing uncertainties (see Panel 14.1 on the IPCC and Uncertainty) — and it is important that these uncertainties be explored. While scientific method demands close scrutiny of certainties and uncertainties alike, however, honest scientists would not blatantly deny where the preponderance of evidence leads (Schneider, 2009). That is precisely what 'climate change deniers' or 'contrarians' are doing.

The science of climate change in general and the conclusions of the IPCC in particular have often been attacked by interested political actors and in the past years increasingly through a range of internet blogs, often in order to create doubt about the scientific basis for climate protection policies. These attacks have occurred despite significant scientific progress and despite the IPCC having stimulated research on topics that were identified as key uncertainties in earlier IPCC reports. Political lobbies supported by very few scientists — mostly from fields unrelated to climate change and without a publication record on climate issues — have often received prominent attention in the media, merely by opposing settled knowledge. Media in Anglo-Saxon countries have been much more inclined to support such attempts than in other countries (Painter, 2011). These campaigns have been able to delay the political process, in particular in the US, but also at the global level. It seems that the message that nothing has to be done is preferred to a call for global action.

The fossil fuel industry, for example, financed the 'Global Climate Coalition' in the US from 1989 to 2002. This group ran multi-million dollar advertising campaigns just before the Kyoto negotiations, which certainly had an impact on public opinion. These efforts have continued in different forms until now, the latest incarnation being a full 'denial industry' (Hoggan and Littlemore, 2009; Dunlap and McCright, 2010). Parallels between the climate change debate and earlier controversies over tobacco smoking, acid rain and the hole in the ozone layer have been identified, showing that spreading doubt and confusion was a basic strategy of those opposing action in each case (Oreskes and Conway, 2010).

Another line of attack on addressing climate change has come from economists who argue that climate change is not the most important problem ('not the end of the world') and that tackling it would divert scarce resources from resolving problems such as poverty, hunger, malaria and HIV/AIDS that claim more lives (Lomborg, 2007; Copenhagen Consensus Center, 2009).

Just before COP15 in Copenhagen, another attack on climate science was launched, accusing climate scientists that had worked for the IPCC of manipulating their results and keeping unwanted papers from scientists with different views out of the IPCC report. This accusation, dubbed 'Climategate' in the press, was based on a series of hacked emails from the computers of the University of East Anglia (UEA) in the United Kingdom. This attack was followed soon by the discovery of two mistakes in the Working Group II contribution to the 3 000 page IPCC fourth assessment report. Due to an erroneous statement on the melting rate of Himalayan glaciers, this problem became known as 'Glaciergate'. Attackers suggested that IPCC authors had deliberately manipulated the assessment to make it scarier than was warranted. A delayed and defensive reaction from the IPCC management to these accusations made things worse.

A number of different investigations in the United Kingdom of the behaviour of the involved scientists at the Climatic Research Unit (CRU) of the UEA cleared them from scientific misconduct (Russell et al., 2010; Oxburgh et al., 2010; House of Commons Science and Technology Committee, 2010). One of the recommendations given by the investigators was that climate scientists should take even more steps to make all their supporting data available — right down to the computer codes they use — in order to make research findings properly verifiable. The CRU (and other organisations) have meanwhile started activities to make more climate data accessible (e.g. UEA, 2010).

Investigations of the claimed mistakes in the IPCC report showed that only very few things needed correction and that they did not have any impact on the major conclusions contained in the Synthesis Report and the summaries of the working group reports (e.g. NEEA, 2010; EPA, 2010a). A review of the IPCC procedures and management structure requested by the UN Secretary-General and the IPCC suggested several changes to avoid similar problems in the future (InterAcademy Council, 2010).

Panel 14.1 The evolution of the IPCC's approach to assessing 'uncertainty'

Malcolm MacGarvin

Dealing with uncertainty has been a fundamental issue in assessing and communicating climate change. The IPCC generally distinguishes between 'statistical', 'value' or 'probabilistic' uncertainty (referred to as 'quantifiable risk' in *Late lessons from early warnings*) and 'systemic' or 'structural' uncertainty (termed 'unquantifiable uncertainty', 'ignorance' and 'indeterminacy' in *Late lessons from early warnings*).

The first and second IPCC assessments use terms such as 'almost certain', 'likely' and 'doubtful' inconsistently, even within each assessment. In preparation for the third assessment report, the IPCC therefore produced guidance for authors addressing the issue of reporting uncertainty. This included material on underlying theory, the practical pitfalls for authors and editors, and the communication of uncertainty to the wider world. The IPCC has since revisited its guidance on uncertainty for both the fourth and fifth assessments. This panel charts the various landmarks in the IPCC's evolving approach to uncertainty.

Guidance for the third assessment

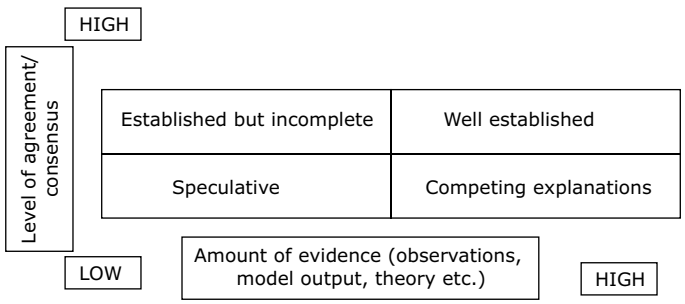
The third assessment report's guidance on uncertainties (Moss and Schneider, 2000) — which lists 37 reviewers, including some still influential in IPCC work — noted that uncertainty results from a lack of information, and disagreement about what is known or even knowable. Uncertainty exists even in carefully controlled laboratory studies. For climate research, however, this is compounded by factors such as the global scale and low frequency variability, with characteristic times greater than the length of most instrumental records; the impossibility of before-the-fact experimental controls; and the (particularly tricky) issue of long time lags between climate forcing and response. According to the third assessment report guidance, assessing the probability of events will inevitably be subjective. It reflects the 'degree of belief that exists among lead authors and reviewers that the event will occur, given the observations, modelling results and theory currently available.'

Other challenges include how best to represent differences in expert opinion; how to alert readers to 'long tail' events (outcomes believed to be unlikely but with serious implications should they occur); and 'poorly managed' projected ranges in impact assessments that may propagate a 'cascade of uncertainty'. Evidently there are communication and credibility challenges in emphasising quantified probabilities, while simultaneously communicating these as provisional and liable to (perhaps dramatic) change. The guidance stresses that it is vital that the specialists should **quantify** the probabilities to the best of their abilities because otherwise others, less expert, would do so on their behalf. The guidance introduced a five-point scale to categorise quantitative probabilities (presented on the left side of Figure 14.5).

The guidelines acknowledged that some reviewers and potential users of the guidelines were 'uncomfortable' with the quantitative ranking of uncertainty. It therefore proposed a qualitative scheme, based on the amount and strength of evidence of various types, and the level of consensus between experts (as shown on the right side of Figure 14.5). Together, these could be used to express high, medium or low confidence in particular findings, with specific formulations of words for various combinations. The guidance maintained, however, that this should be supplementary to the quantitative assessment, because qualitative terms 'do not always map well onto a quantitative scale', increasing the likelihood of inconsistent usage.

Figure 14.5 Quantitative and qualitative expressions of uncertainty as categorised in the third assessment report guidance

(0.95)–(1.00) 'Very High Confidence'
(0.67)–(0.95) 'High Confidence'
(0.33)–(0.67) 'Medium Confidence'
(0.05)–(0.33) 'Low Confidence'
(0.00)–(0.05) 'Very Low Confidence'



Source: Moss and Schneider, 2000.

Panel 14.1 The evolution of the IPCC's approach to assessing 'uncertainty' (cont.)

A separate practical dimension of the third assessment report guidelines is their acknowledgement of human shortcomings in producing assessments. The guidance notes that the means for ensuring consistency in assessing and reporting on uncertainty had not previously received much attention in IPCC reports and that lead authors need to be aware of bias. Group dynamics add complexity to report drafting and that lead authors 'need to guard against the potential for 'gaming' or strategic behaviour' from contributors negotiating a text. Uncertainty within a group arising from conflicting strongly held individual views is qualitatively different from that of a group of collectively uncertain individuals, and report users need this information. Moreover, lead authors should be aware of history, that overconfidence biases experts' judgements: experts 'are correct less often than their confident assessments imply'.

For all these reasons, the third assessment report guidelines advise the preparation of a 'traceable account', describing the 'reasons for adopting a particular probability distribution, including important lines of evidence used, standards of evidence applied, approaches to combining/reconciling multiple lines of evidence, explicit explanations of methods for aggregation, and critical uncertainties.' For particularly important outcomes, the guidelines suggest the use of formal decision analytic techniques, which may achieve 'a more consistent assessment of the subjective probability distribution'.

Learning from third assessment report and preparing for the fourth

Following the third assessment report, an IPCC workshop on uncertainty and risk again reviewed the issues (Manning et al., 2004). The workshop report states that:

> 'probability is the basic language of uncertainty and was originally developed to describe the chance of different outcomes for processes that are stationary over time (such as throws of dice) where observed frequencies are equivalent to probabilities. In general, assigning probabilities to future outcomes cannot assume stationarity or be based entirely on past observations. This leads to the subjective view of probability as a statement of the degree of belief that a person has, that a specified event will occur given all the relevant information currently known by that person. Such subjective probabilities have wider utility and are more relevant to the climate change context.'

Nevertheless, 'cognitive bias' will exist, influenced by a person's (selective) awareness of past events and future expectations; the roots of their perceptions; and the analogies that spring to their mind. A distinction was also drawn between 'likelihood' and 'levels of confidence'. Likelihood was 'the chance of a defined occurrence or outcome' whereas the 'level of confidence' refers to a broader 'degree of belief or confidence in a science community of the amount of evidence or information available and the degree of consensus in the interpretation of that information'.

The workshop also reported on how the third assessment report working groups had diverged from the guidance. Working Group I (addressing the physical science basis) had generally used mathematical-statistical methods and estimates of uncertainty in raw data, using likelihood 'as a basis for approaching uncertainty focused on the probability of outcomes'. It 'was clearly intended to be interpreted in that way despite the definition in the Working Group I Summary for Policymakers as 'judgemental estimates of confidence''. Working Group I never used the qualitative confidence terms introduced in the guidance because of 'discomfort' with the wording. Members agreed, however, that it was appropriate to provide separate indications of the amount of information and the degree of unanimity in the expert community on its interpretation.

Working Group II (addressing impacts, adaptation and vulnerability) addressed less material based on statistical methods, instead giving levels of confidence focused on the degree of understanding and consensus among experts. At times this was used as a proxy for the probability of outcomes. Chapter authors had exercised discretion in using qualitative or quantitative assessments.

Working Group III (addressing mitigation of climate change) did not adopt the guidelines, asserting that it was challenging for economists and social scientists to attempt to use a scale such as those employed by Working Groups I and II, and that there was very little literature to support such estimates for mitigation potentials and estimates of future emissions or drivers.

Panel 14.1 The evolution of the IPCC's approach to assessing 'uncertainty' (cont.)

According to the workshop report, 'structural' uncertainty had not been adequately addressed in the third assessment report. This applied to physical measurements (such as interpreting temperature trends from satellite data) and to biological consequences (such as significant differences between crop yield models, indicating structural uncertainties). Even less account had been taken of structural uncertainties for natural (unmanaged) ecosystems. Similarly, socio-economic structural uncertainties underlying future scenarios and the treatment of adaptive and mitigated capacity had not been explained well in the TAR.

While acknowledging that assessing structural uncertainty 'is generally more difficult and can normally only be done to a limited extent', the workshop concluded that there had nevertheless been a demonstrable tendency for it 'to be overlooked by expert groups'. Indeed 'structural uncertainties associated with analysis techniques … were not considered explicitly. This may have lead to more apparent certainty being given to results where only one or very few independent analyses had been carried out'. There is 'an obligation to identify what we are unlikely to be able to know before the changes actually occur'. So far 'the assessment community has not done very well' in addressing this point.

The workshop was clear that decision-makers need to be aware of events with low probabilities but large impacts, even though these are 'necessarily based on subjective views, usually of a group of experts, on how the future may evolve'. Qualitative explanations of uncertainties associated with costs and benefits, mitigation and adaptation potentials, and scenarios, may be more appropriate than quantitative confidence or likelihood estimates. Providing context will sometimes be more relevant to policymakers than trying to quantify the uncertainties. This includes indicating how robust predictions are, under different assumptions; identifying and explaining sources of uncertainty, including how the variables are defined; assumptions regarding system boundaries; and competing conceptual frameworks. Indeed, giving statements about confidence in probabilistic projections of likelihood raises basic issues, such as how do we measure confidence in unfalsifiable probabilities of future climate change, and to what extent convergence of models can actually be assumed to indicate increasing confidence. Given such deep uncertainties, it was argued, robust strategies that appear to work reasonably well across a wide range of outcomes should be favoured.

Fourth assessment guidance

Following the workshop, the *Guidance note on addressing uncertainties for the fourth assessment report* (IPCC, 2005) was drafted. In part drawing on the earlier work, the fourth assessment guidance was intended to 'assist' lead authors to have a consistent approach to uncertainty 'where possible', while acknowledging that there will be a 'diversity of approaches'. These, the guidance suggested, should be considered early, using a balanced process that reflects any divergence of views, and addressing value and structural uncertainty as well as fundamental unpredictability. Where expert judgements are made, their basis and the critical assumptions, should be traceable. Lead authors should be aware of group dynamics converging and becoming overconfident in an expressed view, or unjustifiably anchored on previous versions or values.

The guidance noted that the appropriate level of precision should be used to describe findings and it proposed a six-point **linear 'typology of uncertainties'**. This ranged from (A) 'Direction of change is ambiguous or the issue assessed is not amenable to prediction' to (F) 'A probability distribution can be determined for changes in a continuous variable either objectively or through use of a formal quantitative survey of expert views'. Three sets of terminology were given 'to describe different aspects of confidence and uncertainty and to provide consistency across the fourth assessment report':

- The first was essentially the same qualitative assessment of confidence (evidence versus level of agreement) set out in the third assessment report guidance, although this time accompanied by instruction that this should only be used to supplement quantitative assessment.
- Similarly, the second was the five-point quantitative confidence scale ranging from 'very high confidence' to 'very low confidence' from the third assessment report guidance. This could 'be used to characterise uncertainty that is based on expert judgement as to the correctness of a model, an analysis or a statement'.
- The third was a 'likelihood' scale, intended to serve as 'a probabilistic assessment of some well defined outcome having occurred or occurring in the future', based on 'quantitative analysis or expert views'. This ranged from 'virtually certain, greater than 99 % probability of occurrence' to 'exceptionally unlikely, less than 1 % probability'.

Panel 14.1 The evolution of the IPCC's approach to assessing 'uncertainty' (cont.)

The guidance did not specify how to ensure that the third assessment report's weaknesses in addressing structural uncertainty were rectified in the fourth report, other than to repeat the third assessment report guidance that 'structural uncertainty tends to be underestimated by experts'. Indeed, the proposed linear 'typology of uncertainties' proposed has the potential to contribute to this confusion as any classification will contain contingent elements of structural uncertainty. A situation classified as (F) inevitably includes elements of classification (A) — categorisation is neither linear nor exclusive.

That such dilemmas exist should not lead to policy paralysis, nor necessarily mean that the best option is further research to 'reduce' uncertainty. Moss and Schneider (2000), the 2004 IPCC workshop report, volume 1 of *Late lessons from early warnings* and the general literature on uncertainty all contain numerous proposals, such as weighing up the pros and cons of action or inaction.

Inter-Academy Council (IAC) review

Following 'Climategate', a critical Dutch review, and the revelation of an error regarding the fate of Himalayan glaciers (actually raised but unaddressed during the fourth assessment report review process) the IPCC asked the IAC to review the IPCC process. Issues raised (IAC, 2010) relevant to uncertainty included the need to improve on transparent selection criteria for authors; demonstrably improved and formalised handling of alternative viewpoints; the advantages of an open review process; policies and resources for handling the volume of comments likely to arise, including any orchestrated efforts, by those with strong views, to overwhelm the system; and demonstrable independence of the review process. Structural uncertainty was not raised.

The IAC recommended that all working group reports should use the qualitative level-of-understanding scale in their summaries for policymakers and technical summaries, 'as suggested in' the fourth assessment report guidance. Actually the guidance was ambiguous on this (c.f. paragraphs 7 and 11–12).

The IAC concurred with the IPCC's aspiration that the basis of the assessments should be fully traceable — although this has resource implications for expert authors and for recovering the information if queried. The IAC also argued that requiring quantitative levels of overall confidence, and a likelihood scale for specific observations, was redundant, noting 'One could have high confidence that obtaining two sixes when rolling a pair of fair dice is extremely unlikely. But why not just say that obtaining two sixes when rolling a pair of fair dice is extremely unlikely'.

Fifth assessment guidance

The IPCC has now produced a *Guidance note for lead authors of the IPCC fifth assessment report on consistent treatment of uncertainties* (Mastrandrea et al., 2010), taking into account the recommendations of the IAC review. The guidance states that:

'The fifth assessment report will rely on two metrics for communicating the degree of certainty in key findings:

- Confidence in the validity of a finding, based on the type, amount, quality, and consistency of evidence (e.g. mechanistic understanding, theory, data, models, expert judgment) and the degree of agreement. Confidence is expressed qualitatively.
- Quantified measures of uncertainty in a finding expressed probabilistically (based on statistical analysis of observations or model results, or expert judgment).'

To avoid any doubt about the strength of this guidance, the IPCC subsequently stated, in a response to the IAC report (IPCC, 2011), that working groups were now 'instructed to make this evaluation of evidence and agreement the basis for any key finding, even those that employ other calibrated language (level of confidence, likelihood), and to provide a traceable account of this evaluation in the text of their chapters.' This, nominally at least, represents a significant evolution in the approach to uncertainty by IPCC since the third assessment report guidelines.

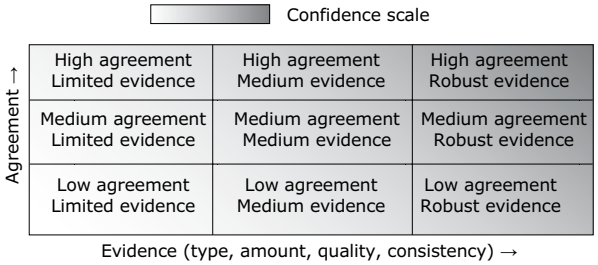
The approach to communicating the certainty of key findings in the fifth assessment report is presented in Figure 14.6. The accompanying explanation in the guidance describes this as 'A depiction of evidence and agreement statements and their relation to confidence.

Panel 14.1 The evolution of the IPCC's approach to assessing 'uncertainty' (cont.)

Confidence increases towards the top-right corner as suggested by the increasing strength of shading. Generally, evidence in most robust when there are multiple, consistent independent lines of high-quality evidence.'

Whereas the fourth assessment report guidance employed three sets of terminology to describe confidence and uncertainty, this is reduced to two for the fifth assessment. The five-point quantitative confidence scale is deleted, leaving only the likelihood scale to 'provide calibrated language for describing quantified uncertainty'.

Figure 14.6 Fifth assessment report scheme for communicating confidence in key findings



Source: Mastrandrea et al., 2010.

For the first time, the fifth assessment report guidance asks authors to 'be aware that findings can be constructed from the perspective of minimising false positive (type I) or false negative (type II) errors'. Traditionally, academic science places its emphasis on avoiding false positives (falsely concluding that a result is significant, when it is not), and these form the basis of most statements of quantitative likelihood or confidence. Although the fifth assessment report guidance does not discuss it in such terms, from a precautionary perspective one is also interested in type II errors (concluding that a result is not significant, when it is), which requires a different approach. In essence, it can mean assuming that it is more important to be safe than to be right.

In other respects, as might be expected given the earlier effort, the fifth assessment report guidance largely reflects previous IPCC guidance, with some differences of emphasis and re-ordering of text. The guidance again refers to the importance of communicating low probability outcomes with significant impacts; the need to communicate the full range of views where expressing collective viewpoint is inappropriate; the need to make expert judgements and provide a traceable account of their derivation; the tendency of groups to converge on a viewpoint and become overconfident in it; the need to be wary of how the wording of statements affects interpretation by the reader; and the need for lead authors to ensure that they have considered all 'plausible' sources of uncertainty and to be aware that experts underestimate structural uncertainty arising from incomplete understanding.

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The IPCC has started implementing reforms based on these suggestions. In May 2011 the IPCC adopted guidance on a communications strategy; recommendations on how best to handle 'grey' literature; protocols on how to handle scientific uncertainties and corrections of errors in reports; and a conflict of interest policy. The IPCC also agreed to establish an Executive Committee to strengthen the overall management structure (IPCC, 2010).

Polls have shown that these attacks and other developments have had an impact on public opinion regarding the urgency of taking action, even though the accusations were shown to be unsubstantiated. In Europe in 2011 only 34 % of citizens consider climate change to be one of their five major concerns, compared to 57 % in 2007 (EC, 2011a), although 95 % of EU citizens still feel that protecting the environment is important to them personally. Media coverage of climate change has also decreased since 2009, although there are differences across the world (CSTPR, 2011). A survey in 15 countries (covering about 50 % of the global population) shows that climate change was still one of the top three concerns in 2010 (HSBC, 2010). But doubts about the reality of climate change have increased in the general population, and the pressure on politicians to take action on climate change has decreased.

This is not to say that the scientific community is completely free of blame for the situation. Scientists and the IPCC should be open to consider criticism seriously, even if it appears to be scientifically unfounded. In the attacks on the IPCC mentioned above, the response of the IPCC and individual scientists was defensive, which was one reason why the Inter-Academy Council recommended a more transparent communication practice for IPCC. Scientists in general are not necessarily good communicators, lacking understanding on how to communicate effectively to decision-makers and the general public. A lot can be improved here (Bowman et al., 2010).

14.7 Discussion

Can the evolution of climate change policy be understood as an application of the precautionary principle?

Climate change science has evolved over time. The IPCC was established to provide comprehensive policy-relevant assessments of the scientific knowledge relevant for developing climate change policies. These developments clearly had an effect on climate policymaking. IPCC assessment reports played an important role in raising awareness of risks as well as explaining potential solutions and their estimated costs.

At the international level, however, this science-policy dialogue can only be regarded as a partial success. Current policies will not achieve the emission reductions that scientists consider necessary to achieve the ultimate objective of the UNFCCC, as confirmed in the Cancun agreements concluded at COP16. Hence, the sum of international political action over the last 20 years is inconsistent with a strict interpretation of the precautionary principle, which would require taking necessary action in the absence of full information.

A key question is the level of scientific certainty that the international policymaking community needs to act to address climate change. The five criteria presented below correspond to increasing evidence that humankind is significantly altering the climate on a global scale, starting with the most basic criterion and ending with the most demanding one. The more society and its leaders are willing to adopt a precautionary approach, the fewer criteria have to be fulfilled before actions are implemented.

- Criterion 1: Observation of a long-term increase of long-lived greenhouse gas concentrations in the atmosphere.
- Criterion 2: Observation of mean global warming derived from nearly global long-term nearsurface air temperature measurements.
- Criterion 3: Paleo-climatic evidence of global warming caused by an enhanced greenhouse effect of the atmosphere.
- Criterion 4: Detection of a significant anthropogenic contribution to observed mean global warming using validated climate models and statistical fingerprint methods.
- Criterion 5: Attribution of specific aspects of climate change to anthropogenic causes. Examples include attributing thermal expansion of ocean water, the most important contribution to sea level rise, to mean global warming at the surface and strong cooling of the upper stratosphere and the mesosphere due to increased CO_2 concentration.

Criterion 1 was satisfied as far back as the late-1960s, although only for CO_2. For concentration increases of the other two long-lived greenhouse gases, CH_4 and N_2O, the 1990 report of IPCC Working Group I (climate science) presented the evidence. The

halocarbons as new, artificial long-lived greenhouse gases became known as contributors to the enhanced greenhouse effect in the ozone assessment reports by WMO and NASA (WMO, 1986).

Criterion 2 was satisfied by the first assessment report of IPCC (IPCC, 1990). Criterion 3 was arguably also fulfilled by the first IPCC report from 1990, which showed very high correlation between greenhouse gas concentrations and temperatures (during snow-formation) for a 160 000 year record of air bubble composition and oxygen isotope content in Antarctic ice cores.

Criterion 4 was fulfilled by the sentence 'the balance of evidence suggests a discernible human influence on global climate', published in December 1995 in the Working Group I's summary for policymakers in the IPCC's second assessment report.

Criterion 5 was fulfilled by the IPCC's third assessment report in 2001. This report showed that the observed cooling in the lowest stratosphere is predominantly caused by depletion of ozone as a consequence of chlorofluorocarbon decomposition in the stratosphere and less by the enhanced greenhouse effect, which is the key reason for cooling in the upper stratosphere (above 30 km height) and mesosphere (above 50 km height). In addition, the IPCC fourth assessment report of Working Group I, published in February 2007, cites several new links such as 'sea level rise is largely a consequence of the warming of sea water in the upper ocean layers' (IPCC, 2007a).

An important factor in the IPCC successfully fulfilling the criteria above was the development of guidelines for assessing and expressing uncertainty systematically. As a result, important statements on the knowledge about changes in the climate system could be given qualifications such as 'as likely as not' (33–66 % probability it is true), 'likely' (67–90 % probability), 'very likely' (90–99 % probability) or 'virtually certain' (99–100 % probability).

In summary, for all these criteria scientific proof is by now largely or completely available at a high confidence level. Hence we are far beyond the knowledge level where the precautionary principle would still be needed for any action in the global climate change context — at least, if the precautionary principle is interpreted as referring to major anthropogenic changes to the global climate system.

Obviously, the list above considers neither the impacts of changes in the climate system on humans and ecosystems nor the costs and impacts of climate change policies. Some would say that attempts to consider the costs and impacts of alternative policies (including doing nothing) go beyond the precautionary approach — instead being characteristics of a comprehensive risk management approach. However, most authorities accept that precautionary policy actions need to take account of the pros and cons of action and inaction (See Chapter 27 on the precautionary principle).

It seems that when the precautionary approach has been applied in environmental policymaking in the years since the Rio Declaration, it has mostly occurred at regional scales and addressed air and water pollution. The stakes were much lower than in the case of global climate change and those implementing policies were generally also the ones benefitting from them. Global climate change is very different in many ways:

1. Climate change and climate policies have strong impacts on all of us. There is no readily available solution that could easily reduce the problem to a safe level.

2. Climate change is a global problem and efforts to reduce GHG emissions are cost-effective only if they are part of an agreement with others to act in a comparable manner. Furthermore those countries and population groups most negatively affected by climate change are generally poor countries and population groups who have contributed little to its causation. Hence, the motivation for reducing greenhouse gas emissions can differ substantially depending on the underlying ethical perspective. In the particular case of climate change, it appears that increasing information on the expected distribution of impacts, i.e. on expected 'winners' and 'losers', has unfortunately decreased the momentum for international climate policy.

3. Climate change is a problem characterised by the very long atmospheric life times of many greenhouse gases (from a decade to millennia) and a long inertia in the climate system (mostly due to the large heat capacity of the ocean). As a result, emissions reductions of long-lived greenhouse gases now will only have significant climatic effects after several decades. Hence, the moral dilemma outlined in the previous bullet point is even larger: the costs and benefits of emission reductions are not only unequally distributed across countries but also over time. Primarily self-interested high emitters have little incentives for costly emission reductions because they will experience only a small fraction of their benefits, if their scope is only the present

generation. However many emission reductions provide substantial non-climatic benefits in the short term, including reduced air pollution and reduced costs for importing fossil fuels. Contrastingly, self-interested motivation is particularly low for GHG reduction measures such as carbon capture and sequestration that do not provide large non-climatic benefits.

Apparently the precautionary principle did play a role when the UNFCCC was agreed after the IPCC first assessment report in 1990 (criteria 4 and 5 above were not yet fulfilled). If the UNFCCC had already contained binding emission reduction goals for industrialised countries, it would have provided evidence of full acceptance of the principle in the climate change context. The influence of the precautionary principle diminished however with subsequent actions. Now precautionary arguments appear to have only little, if any, effect on internationally coordinated climate policy action.

Is a risk management framework better for understanding the evolution of climate policy?

The history of climate change policy suggests that arguments based on a risk management framework had a much stronger impact on political action than arguments based mainly on a precautionary framework. In a risk management framework, it is necessary to know the risks of climate change impacts and the risks, costs and benefits of taking mitigation and adaptation action, including their distribution across regions and over time. Countries have only committed to significant action at the national level (in the context of the Kyoto Protocol and the subsequent pledges under the Copenhagen Accord) after having satisfied themselves that emissions reductions are technically feasible, and that they can be implemented at reasonable costs and in a politically acceptable way. In addition, cost-benefit analysis (such as the Stern review) is sometimes applied to evaluate how far mitigation measures should go in the light of the avoided climate change impacts.

So risk management approaches have been applied but other key factors are also important, including the perception of risk. Risks, costs and benefits of climate change depend on assumptions about future social, economic and technical developments and on the evaluation of uncertainties that cannot be presented in strict scientific terms. Perceptions of risks, costs and benefits of climate change and climate protection policies vary significantly across different people and stakeholders. In addition, risk perception depends on factors such as how the scientific community communicates its findings and interacts with stakeholders, how credible it is perceived to be, how the media handle the information, as well as human psychology and behaviour, cultural background, world views and political affiliations (Weber and Johnson, 2012; McCright and Dunlap, 2011).

The importance of risk perception became obvious in the uproar surrounding the attacks on climate science and the IPCC in 2009–2010. The public in several countries became less concerned about climate change and this affected the political prioritisation of action. The 'blogosphere' generates a huge amount of (dis)information, in which scientific arguments often are characterised as 'just another opinion'. This undermines the authority of bodies like the IPCC (Giddens, 2009), further altering risk perception. Misperceptions of risk partially, but not wholly, explain why climate change policy has so far been inadequate.

From threat to opportunity

Perhaps the biggest problem with establishing effective climate policy at the national and international levels has been the focus on avoiding climate change risks. Climate policy appears to require short-term sacrifices from particular economic actors and changes in the costs of services and human activities. Benefits accrue decades later in the form of avoided climate change impacts. Even if the benefits in monetary terms outweigh the costs measured over a long period of time, such propositions are not very attractive or understandable for many people. Those that could be worse off in the short term will lobby against a proposed policy. The focus on avoiding climate change risks does not appeal to immediate self-interest, at least not directly. A lot rests on solidarity with future generations.

What could be highlighted more both at the international and national levels is the fact that many interventions to stimulate development, wellbeing and economic growth, if well targeted, can contribute to a low emissions and climate resilient economy. Energy efficiency in industry, transport and buildings is good economic policy, leading to lower energy bills and lower greenhouse gas emissions. Renewable energy can provide much needed modern energy in rural areas, improve air quality and health, reduce dependency on imported energy, create new jobs and contribute to emissions reduction. Building new infrastructure, development of coastal areas, increasing food production — all good investments in development — can be done in such a way that they are more resilient against future floods and drought that result from climate change, and maximise the preservation of carbon stocks.

So if climate change is integrated into the agenda of development and economic growth, it aligns the benefits for the stakeholders interested in positive economic activities with the benefit of avoiding climate change damage. Climate change can be more mainstreamed into core economic decisionmaking, making it more likely that the necessary action will be taken. Rather than looking at positive economic and social effects as a co-benefit of reducing climate change risk, climate change risk reduction becomes a co-benefit of development and economic growth.

There is now a trend emerging to consider climate change as an integral element of socio-economic decisionmaking. New paradigms of 'low carbon growth' or 'low emissions development', 'climate compatible development' or in a broader sense 'green growth' are being adopted in many countries. The European Commission's statement in October 2011 is a good illustration:

> 'Just two weeks ago, the European Commission announced proposals on resource efficiency. Together with our proposals on a low carbon economy, they set out what is needed to transform Europe's economy to be sustainable by 2050. This package is our approach to green growth, and it builds on the efficient and sustainable management of our resources.' (EC, 2011b).

More and more countries see low-carbon growth, low emissions development or green growth as a promising way of integrating climate change action into core socio-economic decision-making. The green economy was one of the key issues for the Rio+20 meeting in 2012. UNDP, UNEP, the Organisation for Economic Co-operation and Development (OECD) and the World Bank, among others, have set up strong programmes to promote this development (OECD, 2011; UNDP, 2011; UNEP, 2011a; World Bank, 2009 and 2010a).

As a result, the main question for policy becomes 'how can we achieve the socio-economic goals of growth and development, while addressing climate change risks?' This question in turn demands answers to scientific questions: 'how can dependence on energy imports be reduced by developing domestic renewable energy resources?', 'how can air quality be improved to eliminate health hazards by shifting from fossil fuel-based energy production and transport systems to clean energy and electric cars?' and 'how can agriculture be made more productive and less vulnerable to climate change by sequestering more carbon in agricultural soils?' These questions require a more integrated analysis and assessment than earlier questions that regarded climate change mitigation as largely separate from other policy areas.

Such questions are also critical for determining the different technological pathways to the 2050 goal of a green economy that is not dependent on fossil fuels — pathways that must be determined, in part, by means of greater public engagement.

Table 14.1 Early warnings and actions

1896	Svante Arrhenius (Sweden) calculated that a doubling of CO_2 in the atmosphere from coal burning could lead to an increase in average global temperature of 3–5 °C. (In 2007 IPCC estimated that this would be 2.4–4.5 °C).
1938	Guy Stewart Callendar (United Kingdom) concluded that 'the principle result of increasing CO_2 … would be a gradual increase in the mean temperature of the colder regions'.
1958–1970	David Keeling (US) established two long term monitoring stations in 1958 in Mauna Loa on Hawaii and at the South pole to measure the background concentration of CO_2 without the influence of nearby anthropogenic (human) sources. By 1970 the Mauna Loa monitoring station showed clear rising trend in global CO_2 of 0.4 % per year.
1970s	Schneider, Twomey and Grassl identified critical interactions of clouds and air pollution that amplified or dampened the human induced greenhouse effect.
1980	The World Climate Research Programme organised and co-financed by the World Meteorological Organization and the International Council for Scientific Unions became the first global change research programme.
1980s	Models of atmospheric changes showed that both greenhouse effects and measures to avert them would take decades to be clearly seen because of inertia in the systems caused principally by the oceans.
1985	Neftel et al. (Switzerland) and Jouzel et al. (France) were the first to determine the CO_2 concentration in air bubbles of ice cores with enough precision to reconstruct the long-term history (160 000 years) of greenhouse gases.
1987/1988	Groisman and Hansen publish the first trend analyses of global mean air temperature covering a full century.

Table 14.1 Early warnings and actions (cont.)

1980 and 1985	At two scientific conferences at Villach (Austria) climate change scientists concluded that 'the increasing concentrations of greenhouse gases are expected to cause a significant warming of the global climate in the next century'.
1987	The global Montreal Protocol on protecting the ozone layer sets targets for phasing out ozone-depleting substances, many of which are also powerful greenhouse gases
1988	The Intergovernmental Panel on Climate Change (IPCC) was formed focusing on climate change science, the vulnerability of society and nature to climate change and means of adaptation, and on mitigation measures for limiting or preventing greenhouse gases and their effects.
1988	SCOPE scientists warn that human induced climate change could cause increases in climate variability and of extreme weather events.
1988/1989	Scientific conferences in Toronto and Nordwijk call for a global action plan, a Framework Convention from 1988 levels and for a reduction of 20 % in global CO_2 by 2003.
1990	The IPCC published its first assessment report concluding that: 'there is a natural greenhouse effect of the atmosphere which already keeps the Earth warmer than it would otherwise be'; 'there is a strong increase of concentrations of all three long-lived naturally occurring greenhouse gases (CO_2, CH_4, N_2O), which is due to anthropogenic activities, global mean near-surface air temperature had risen by 0.3 to 0.6 °C during the 20th century, there was evidence of a rise in mean sea level, of retreats in mountain glaciers and changes in regional precipitation'.
1990/1992	The UN 2nd World Climate Conference called for a Framework Convention on Climate Change (UNFCCC) which was later signed by 153 countries and the European Communities in Rio in 1992.
1995	The IPCC published its second assessment report stating that 'The balance of evidence suggests a discernible human influence on global climate.' This was the first time that scientific evidence enabled the human-induced change signal to be perceived against the background of natural climate variability. It also stated climate change impacts were happening and could pose serious risks in the future; and that policy measures were available to reduce GHG emissions.
1995	At the first session of the Conference of the Parties to the UNFCCC (COP1) the Berlin Mandate was adopted, which recognised the need for a legally binding intergovernmental agreement to reduce greenhouse gas emissions by industrialised countries, to be ready in time for COP3 in 1997.
1996	The Council of Environment Ministers of the European Union decided that global average temperatures should not be allowed to rise more than 2 °C above the pre-industrial level.
1997	The Kyoto Protocol to the UNFCCC was adopted by more than 150 countries. Industrialised countries agreed to reduce their GHG emissions, using a basket of six GHGs, to about 5 % below their 1990 level by the 2008–2012 period.
2001	IPCC's third assessment report in 2001 concluded that 'There is new and stronger evidence that most of the warming observed over the last 50 years is attributable to human activities.' Projections of climate change impacts in the future were much more serious than in the past. The potential for strong reductions in global GHG emissions was clearly demonstrated and the costs of these reductions were shown to be modest compared to the projected increase in wealth.
2001	The USA withdrew from the Kyoto Protocol.
2005	The Russian Federation ratified the Kyoto Protocol which then became binding having required ratification by 55 countries representing more than 55 % of the total emissions in 1990 from countries with reduction commitments.
2007	IPCC fourth assessment report concluded that 'the understanding of anthropogenic warming and cooling influences on climate has improved ... leading to very high confidence that the global net effect of human activities since 1750 has been one of warming'.
2007	The UK Stern Review of the Economics of Climate Change stated that the costs of aggressive mitigation action are substantially lower than the costs of climate impacts and adaptation measures.
2008	Australia signs the Kyoto Protocol.
2010/2011	Some minor errors, and deficiencies in the handling of scientific uncertainty, in the 3 000-page 2007 IPPC report were identified but these did not affect its main conclusions. Recommendations were made to make all climate change data freely available so that research findings can be further verified. IPCC improves its communications and its guidance on handling scientific uncertainties.
2011	COP17 in Durban in 2011 agreed to start negotiations for a new legally binding agreement for after 2020 and to complete negotiations by 2015; acknowledged that businesses require long-term agreements extending beyond 2020 to inform their investment decisions and recognised the need for more ambitious action by 2020 if the 2 °C limit is to be taken seriously.
2011	Canada withdraws from the Kyoto Protocol.

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15 Floods: lessons about early warning systems

Zbigniew W. Kundzewicz ([1]) ([2])

Floods are an increasingly acute problem. Intense precipitation has become more frequent and more intense, growing manmade pressure has increased the magnitude of floods that result from any level of precipitation, and flawed decisions about the location of human infrastructure have increased the flood loss potential.

Unlike most other case studies presented in this report, this chapter focuses on flooding as a phenomenon and the requirements for effective early warning systems, rather than addressing a particular event and the lessons that can be learned.

Flooding cannot be wholly prevented. The occurrence of a flood need not be considered a 'failure' and, conversely, minimisation of losses may constitute a 'success'. There are lessons to be learned from every flood and it is important to use them in preparing for the next flood. Once we accept that no flood protection measures can guarantee complete safety, a general change of paradigm is needed to reduce human vulnerability to floods. The attitude of 'living with floods' and accommodating them in planning seems more sustainable than hopelessly striving to eradicate them.

Flood forecasting and warning systems fail because links in the chain perform poorly or fail completely. A single weak point in a system that otherwise contains excellent components may render the overall system performance unsatisfactory. A successful system requires sufficient integration of components and collaboration and coordination between multiple institutions.

The chapter deals primarily with the challenges of fluvial (river) floods. It is complemented by three short supplementary texts. The first highlights the complex, dynamic and diverse ecosystems of river floodplains, which are often degraded during construction of flood defences. Despite their huge economic value, near-natural floodplains are among the most threatened ecosystems globally.

The second discusses uncertainties in anticipating rainfall patterns and intensity, and their relationship to flood levels during extreme flows. Such uncertainties present challenges for scientists and decision-makers alike.

The third addresses the increasing risks of coastal flooding due to factors such as climate change and sea-level rise, and reviews European experience with precautionary action.

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'And the rain was upon the earth forty days and forty nights … And the waters prevailed exceedingly upon the earth; and all the high hills that were under the whole heaven were covered' (Genesis 7:12, 19).

'We have first raised the dust and then complain we cannot see' (George Berkeley).

15.1 River floods and early warnings

The term 'flooding' denotes a potentially destructive abundance of water in a normally dry location. Various categories of flood exist. They include, for example, situations where intense precipitation overwhelms urban sewer and drainage systems. In contrast, groundwater flooding occurs when the water table reaches the ground surface in a location where it does not normally do so. And coastal and estuary flooding occurs when high sea levels (due to high tides, storm surges or tsunamis) cause the coastal line to recede.

This chapter addresses river (fluvial) floods, although Panel 15.3 contains information on coastal flooding. River floods occur when water inundates areas outside the river channel, where there is potential to cause damage. They can be caused by several mechanisms, such as rain (intense or long-lasting), snowmelt (possibly with rain), glacier melt, glacial lake outbursts, dam breaks (breach) and tidal surges. Unexpected flow obstructions such as landslides, ice jams, beaver dams or debris can also cause flooding upstream.

Floods differ considerably from some of the other hazards addressed in this report. Floods are intermittent events. They usually recur rarely in a given location, although they can be commonplace at some sites, for example occurring every spring when snow cover melts. This contrasts with hazards that affect the environment continuously and can impose cumulative 'pressures'.

River floods are natural phenomena, manifesting the natural spatial and temporal variability of the river water level and discharge, which can take on extremely high values from time to time. River floods, jeopardising settlements located in floodplains, have been a continued hazard for humanity and can be identified in old myths and narratives. For millennia, people have settled in river valleys to till fertile soils, benefit from flat terrain, access water supplies easily and use water for transport. Riparian people have historically lived in harmony with nature, benefiting from benign floods and the valuable services they provide to fisheries, wetlands, wildlife and agriculture.

The notion of 'early warning of floods' can be interpreted in at least two ways that are relevant to this chapter. The first refers to a short-term flood preparedness system, where a 'flood warning' is a technical term, denoting a means of reducing flood damage to people and property. In this sense, a flood warning contains specific timely information, based on a reliable forecast, that a high water level is expected at a particular location and time. It aims to ensure that emergency actions, such as strengthening dikes or evacuation, can be undertaken.

A 'flood alert', usually issued before a 'flood warning', is less specific and has the broader aim of raising vigilance. A warning should be issued sufficiently early prior to the potential inundation to allow adequate preparation. The appropriate timeframe is affected by the catchment size relative to the vulnerable zones. The warning should also be expressed in a way that persuades people to take appropriate action to reduce damage and costs of the flood.

The other interpretation of 'early warning' in the context of floods is a statement that a high water level or discharge is likely to occur more frequently in the future. Technically, this constitutes a 'prediction' of a change in flood frequency compared to a reference period, such as the 30-year climate normals 1961–1990. An early warning of this type could, for example, predict that at a site of concern the current 100-year flood (river flow exceeded once in 100 years on average) may become a 50-year flood within some defined future time horizon. Such an early warning, over a longer time scale, is (or should be) an important signal for decision-makers that the required level of protection is unlikely to be maintained in the future unless flood preparedness is improved.

Floods continue to be a problem and we clearly do not cope with them satisfactorily. In fact, they are an increasingly serious problem. Flood risk has been greatly intensified by humans, who — to use the language of mechanics — have increased the load and decreased the resistance of the system. In many places, humans have increased the flood magnitude for any level of precipitation and have amplified the flood damage potential. Severe floods cause rising material damage worldwide and continue to cause a considerable death toll. Annual global economic losses from extreme weather events, including floods, increased ten-fold between the 1950s and

Panel 15.1 Managing river flood plains as ecosystems of global strategic importance

Klement Tockner

River floodplains (including deltas) extend from the edge of permanent water bodies to the edge of uplands. Because of their unique position at the deepest location in the landscape, floodplains integrate and accumulate upstream and catchment processes.

In their natural state, floodplains are disturbance-dominated ecosystems tightly linked to fluvial and geomorphic processes, thereby creating some of the most complex, dynamic and diverse ecosystems globally — landscapes that were once comparable in diversity with tropical rain forests or coral reefs (Junk et al., 1989; Naiman et al., 2005; Tockner et al., 2002 and 2008). This diversity has, and continues to be, deeply degraded, a fact that has so far captured remarkably little attention at the policy level. Paradoxically, a good deal of this damage is done by hydrological engineering for flood defences that reduces the ecological integrity of floodplains, while other actions (in the floodplains and elsewhere in the catchments) simultaneously remove natural flood-mitigation features.

Worldwide, floodplains cover only about 2 % of the land surface (although an accurate estimation of their extent remains difficult). Nevertheless, they are calculated to provide about 25 % of all continental ecosystem services, which is more than any other continental ecosystem type (Costanza et al., 1997; Oppermann et al., 2008; Tockner et al., 2008). Major services include flood regulation, drinking water supply (including recharging groundwater) and waste treatment. Daily nitrogen removal ranges from 0.5 to 2.6 kg N per ha (although wasting nutrients is undesirable, current systems would otherwise require considerable expenditure to remove them, e.g. from drinking water). Floodplains also provide opportunities for recreation and, in areas such as the Danube Delta Biosphere Reserve, fishing. In Europe and elsewhere, benefits also include natural fertilisation, providing grazing land and firewood.

The multiple services provided by floodplains have favoured the development of civilisations along the Nile, Euphrates, Indus, Amazon, Yangtze, and Mississippi Rivers; and many indigenous human societies are well adapted to the conditions of flooding. Floodplains continue to be preferred sites for human occupation. For example, about half of the human population in Europe and Japan lives on (former) floodplains (Nakamura et al., 2006, Tockner et al., 2009). Bangladesh, the most densely populated country worldwide, is almost entirely covered by a vast deltaic floodplain (accounting for about 80 % of the country's area).

As described in the present chapter, floods are among the most costly natural disasters worldwide (see also Tockner et al., 2008). To reduce these costs, Switzerland has declared the remarkable intention (probably unique in Europe) to restore the ecological integrity of its river floodplains and their natural flood mitigation properties. This commitment was made because flood-related costs in Switzerland have been increasing since 1970, resulting in an accumulated cost of more than CHF 15 billion over the past 35 years (BUWAL and BWG, 2003). At the same time, Switzerland had the highest global expenditure per capita on traditional hydraulic engineered flood control measures (CHF 45 billion between 1970 and 2005). This was unaffordable.

In response, the Swiss government fundamentally altered its river management strategy. Future flood control measures are now required by law to be linked to a concurrent improvement of the integrity of river floodplain ecosystems. It has been estimated that about 22 000 ha of cultivated land need to be converted back to dynamic floodplains; about 11 000 km of streams and rivers need to be restored. The current restoration rate ranges between 15 and 28 km per year; and 50 000 barriers must be removed (Armin Peter, personal communication; EAWAG, 2006). At present, more than 95 % of former floodplains have been converted to industrial, agricultural, and urban areas.

Despite their huge economic value for flood mitigation and other services and benefits, near-natural floodplains are among the most threatened ecosystems globally. In Europe, North America, and Japan, more than 90 % of former floodplains are functionally extinct or have been converted into cropland and urban areas. Conserving the remaining unimpaired floodplains as strategic global resources and restoring degraded floodplains are of the highest priority for future ecosystem management. There are major limitations, however, in implementing successful conservation and restoration strategies. Today, many river floodplains have been altered to such an extent that they must be considered as novel or emerging ecosystems where a mixture of native and non-native species, assemblages lacking a joint evolutionary

Panel 15.1 Managing river flood plains as ecosystems of global strategic importance (cont.)

history, dominate. For example, up to 80 % of the benthic invertebrates collected along the Upper Danube, the Rhine or the Elbe Rivers are already of non-native origin (Sommerwerk et al., 2010).

The rapid biotic turnover observed along regulated river corridors results from a combination of species decrease, species spread, and climate-induced species distribution shifts, although the relative contribution of these three components to the total turnover rate remains largely unknown. In central Europe, 28 000 km of navigation canals and navigable rivers connect 24 countries, creating a biological 'super-catchment' covering an area of 2.45 million km^2. This dense navigation network artificially facilitates the exchange of organisms across biogeographic barriers, thereby contributing to the increasing homogenisation of the European freshwater fauna and flora.

There is an urgent need to develop a comprehensive overview of river floodplains, their environmental state and anticipated pressures. Such an overview is a prerequisite for prioritising conservation and management. Further research should focus on:

- understanding the formation and dynamics of novel, emerging ecosystems and associated biotic communities;
- quantifying the ecological and evolutionary consequences of novel communities;
- quantifying the ecosystem services provided by novel ecosystems;
- measuring and predicting the resilience of ecosystems and species assemblages along human impact gradients;
- assessing the evolutionary potential of an ecosystem, i.e. its genetic diversity and genetic connectivity, as a complementary tool in biodiversity conservation planning;
- developing and testing new indicators of biodiversity change and impacts.

One of the best documented examples of a long-term and fundamental modification of a river floodplain is the Upper Rhine valley between Basel (Switzerland) and Worms (Germany). More than 150 years ago, Tulla's regulation of the Upper Rhine was a technical masterpiece and one of the largest construction projects worldwide during the nineteenth century. The river was shortened from 345 to 273 km, 2 200 islands were removed — an area of more than 100 000 ha between Basel and Strasbourg alone — and 240 km major dikes were constructed (Blackbourn, 2006). As a consequence, the Rhine floodplain has been converted from a fishery and waterfowl paradise to a productive agricultural area. Reconstruction of the native biodiversity is difficult because a first systematic inventory of the benthic invertebrate community was compiled at the beginning of the twentieth century, decades after the end of the 'rectification' of the Upper Rhine valley (Lauterborn, 1905). The rich biodiversity that still exists in the remnant floodplain channels and riparian forests along the Upper Rhine is most likely a legacy of past hydrogeomorphic processes. At the same time, however, the reduction in natural retention areas has led to an increase in flood peaks in the downstream sections of the Rhine valley.

A lack of adequate reference conditions restricts the development of guiding images for conservation and restoration, and limits implementation of the Water Framework Directive (EU, 2000), which strongly depends on defined reference standards for assessing alterations. Even the best protected floodplains in Europe such as the Alluvial Zone National Park (Danube, A), the Odra National Park (Odra, D) or the Danube Delta Biosphere Reserve, have been irreversibly modified. Traditional conservation and restoration strategies will simply not maintain their rich biodiversity and ecosystem processes and services in a sustainable way. Adaptive management strategies must manage these floodplains actively as coupled ecological-social-technological systems for the benefit of humans and nature. Active manipulation to deliver multiple ecosystem services is also needed to create the environmental conditions for rich (albeit largely non-native) floodplain communities (Dufour and Piegay, 2009).

At the European level, it is crucial to establish synergies among the partly contradictory requirements of the Water Framework Directive, the Habitats Directive (EU, 1992) and the Floods Directive (EU, 2007). Furthermore, we urgently need a European competence network that focuses on large rivers, including their role as long-distance migration and dispersal corridors linking various biomes; as key storage and transformation areas for carbon and nutrients; as centres for evolutionary processes; and as coupled social-ecological ecosystems.

1990s in constant prices (IPCC, 2001b). Data compiled by Munich Re (Kron, 2005) indicate that the number of great flood disasters (requiring international or interregional assistance) has grown significantly in recent decades, as have the economic impacts and the insured damage.

Several recent river flood events have caused material losses exceeding USD 10 billion. The death toll has been considerable, with individual events in less developed countries causing more than 1 000 fatalities (Kundzewicz et al., 2010a). The highest material losses, in the order of USD 30 billion, were recorded in China in the 1998 floods. Destructive floods are commonplace in many developing countries, in particular in the Asian continent (especially Bangladesh, China and India) and South America, yet numerous deluges have hit virtually all parts of the world, including Europe. As reported by Barredo (2007), a rising number of flood disasters have been observed in Europe in recent years and high-impact floods are occurring more frequently. The material flood damage recorded in Europe in 2002 (above EUR 20 billion) was higher than in any previous year.

Recognising that flood damage has increased worldwide, it is interesting to understand the reasons for this growth. Several factors may be responsible, including changes in socio-economic, terrestrial and climate systems:

- **Socio-economic changes** include increasing exposure and potential damage due to population growth and economic development in flood-prone areas; land-use change (such as urbanisation and deforestation) and changing perceptions of risk.

- **Changes in terrestrial systems** include changes in hydrological systems and ecosystems, driven by land-cover change, the regulation of river flow through such measures as channel straightening and shortening, and the construction of embankments. Conditions that determine the transformation of precipitation into runoff in the river basin also change. Draining wetlands and eliminating natural vegetation, alongside expanding impermeable areas, lead to reduced water storage capacity and consequently a higher flood peak and a shorter time to peak.

- Finally, **climate changes** are important, even if they may not always be detectable in the historical record. They include increased water-holding capacity and water content of the atmosphere in a warmer climate, increases in the frequency of heavy precipitation, changes in snow cover, and changes in seasonality and in atmospheric circulation patterns.

Human encroachment into floodplains has increased exposure to floods. Encroachment may increase as people become wealthier and technology or economic imperatives help populate more flood-prone areas. Many flawed decisions have increased the flood loss potential. The assets at risk from flooding can be enormous. For instance more than 10 million people live in areas at risk of extreme floods along the Rhine and the potential damage from floods there has been estimated at EUR 165 billion (EU, 2007). In some less developed countries, the portion of the population living in flood-prone areas is very much higher. The hope of overcoming poverty drives poor people to migrate to informal settlements in endangered, flood-prone zones around mega-cities in developing countries, which have previously been left uninhabited on purpose because effective flood protection cannot be assured.

Future changes in flood risks may be complex. In many places, flood risk is likely to grow due to a combination of anthropogenic and climatic factors. Quantifying flood statistics is difficult, however, and subject to high uncertainty. As stated in IPCC (2001a), 'the analysis of extreme events in both observations and coupled models is underdeveloped'. Recent modelling studies show that plausible climate change scenarios project future increases of both amplitude and frequency of rain-caused flooding events. Yet no conclusive and ubiquitous climate change trend in the flood behaviour has been found, based on the global data on high river flows observed so far (Kundzewicz et al., 2005; Svensson et al., 2005).

Detecting climate change at global or regional scales (let alone within catchments) is inherently difficult because of the low signal-to-noise ratio. The relatively weak climate change signal (if any) is superimposed on a strong natural variability of rainfall and river discharge, which is further confounded by land-use change. Hence, Wilby et al. (2008) speculate that statistically robust trends are unlikely to be apparent for several decades.

Although land use management and land cover change have an important effect on flood risk, it is less significant in the case of very high-intensity rainfall, which causes high flood runoff in both urban and forested basins.

There is always potential for floods that are higher than those recorded in the past, even under stationary conditions — i.e. without climate change. This is simply a sampling effect and its significance

depends on the length of the historic record; as records get longer, the probability of record high precipitation occurring in an area with high damage potential increases. Flood defences are typically designed to withstand an event with a return period of 100 years, perhaps with some additional safety margin. However, the discharge for this return period is generally estimated from records gathered over an inadequately short interval and is therefore uncertain.

The highest point precipitation amounts ever recorded for different time intervals are 1 340 mm in 12 hours, 1 825 mm in one day and 3 847 mm in eight days (WMO, 1986). If precipitation of a similar scale occurred over (or directly upstream from) a large city, the result could be expected to be utter destruction.

It is important not to forget that, in addition to negative effects, floods can generate benefits. For example, the fertile Nile floods were crucial to the development of ancient Egypt. In some areas, floods are an important means of recharging groundwater aquifers. Floods may strengthen community solidarity and can enhance economic activity (related to flood preparedness and recovery). Any benefits that could be lost also need to be taken into account when considering flood prevention measures and options.

15.2 Flood forecasting and warning

Flood alerts, forecasts, warnings and responses are very important components of modern flood preparedness systems. They fall into the category of non-structural flood protection measures, which can save lives and reduce material losses and human suffering. An effective system should embrace detection of the risk of a flood-triggering situation, quantitative flood forecasting (with adequate lead time), development of a reliable warning message, issuing and disseminating the warning to communities at risk, adequate actions by communities to reduce losses and, finally, post-hoc audits to learn lessons and improve the system for the future.

Flood warning has existed for thousands of years. The Old Testament mentions the oldest 'early warning', received by Noah from God; archaeologists have revealed other, even earlier, accounts of a similar story. For centuries, floods were believed to be a divine punishment for the sins of mankind. In 1523, a forecast anticipating a flood in February 1524 was published in Augsburg, based on a quasi-scientific speculation: a peculiar conjunction of planets in the constellation Pisces. The forecast turned out to be false (Brázdil et al., 2005).

15.2.1 Flood forecasts

A flood forecast should ideally deliver reliable and accurate information on the future development of an event, enabling an alert and warning to be issued. A forecast expresses when a flood is expected to occur (ranging from minutes to days or even weeks ahead), its location and its intensity. Flood magnitude is determined by the stage, discharge, inundated area and duration of flooding. A forecast also conveys how a flood will travel downstream and evolve and what secondary effects it may cause.

In order to detect the risk of a flood-triggering situation occurring, a meteorological and hydrological monitoring system should be in place. Forecasting, based on mathematical modelling, allows experts to convert the information on rainfall, hydrological status of soil moisture and snow cover into a forecast of river discharge, water level and inundated area for a future time horizon.

For small or urban catchments and for flash floods in steep and rapid mountain streams, the time lag between an intense precipitation and the resulting river flood peak is very short (minutes to hours). In these circumstances, observations of rising river water levels may come too late for a useful flood forecast. Weather radar data (which brings its own issues) or quantitative precipitation forecasts are therefore required to estimate future river flows with sufficient lead time to provide a useful warning.

At the other extreme, the formation of a flood wave in a large river may take several weeks, allowing ample time for response to a flood forecast. A hydrodynamic flood-routing model can be used, allowing visualisation (via GIS) of the forthcoming inundation in downstream cross-sections of the river. Many activities are under way to improve forecast accuracy and to extend the forecast lead time. In this context, two important factors are data assimilation and adaptive forecasting, which makes use of current measurements to reduce forecast errors (Young, 2002).

15.2.2 Flood warnings

Flood warnings should contain more information than flood forecasts. This includes recommendations or orders for affected populations to take actions, such as evacuation or emergency flood-proofing, specifically designed to safeguard life and property (Smith and Ward, 1998). According to Nigg (1995), warning systems must fulfil two basic functions:

- assessment (from the moment that a specific hazard is detected to the point when a risk message is developed for the threatened locality);

- dissemination (issuing and transmitting the warning message to a target audience).

A warning, converting scientific forecasts into lay language, is a communication that a hazard will produce specific risks for a specific population (Nigg, 1995). Affected communities should not just be told about the hazard but also informed in such a way that they are persuaded to take specific remedial action in time. Such warnings should be 'populist' in tone and communication but their design is actually a skilled task requiring careful forethought and design.

There is an important difference between flood alerts and flood warnings. The latter have much shorter lead times that must be accurate to maintain public confidence. In Vaison-la-Romaine in 1992, Meteo-France issued two (accurate) flood alerts based on heavy rainfall predictions 12 and 24 hours ahead but because the local authorities did not know which catchment would be affected no warning was issued and many people died. The European Flood Alert System (EFAS) at the European Commission's Joint Research Centre (JRC) now produces flood alerts for the whole of Europe (JRC, 2011).

It is often noted that forecasts have advanced markedly, while progress in warnings has lagged behind despite recent advances in some countries, such as automatic telephone and text-messaging services and the provision of detailed forecasting services on the internet.

Nigg (1995) argues that to formulate warning messages:

- the basis of the warning must be credible;

- the warning message must explain the degree to which a specific area is at risk;

- people must be told what they can do to reduce their exposure to danger.

Speed of reaction to warnings is essential because there may be a short time to implement emergency pre-flood actions, such as strengthening or deploying

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defences and evacuation, before the risk becomes high. Other useful criteria or indicators of warning quality are the penetration of the warning (the proportion of those who need information that receive it) and degree of satisfaction.

15.2.3 Flood warning errors

Two types of warning errors occur:

- first, when a warning is issued but the risk does not materialise;
- second, when no warning is issued but a risk and the ensuing disaster occur.

The first does not include situations where the risk has materialised but the disaster has not. For instance, flood warning in the Netherlands in January 1995 resulted in massive evacuation. A disaster did not arrive, as the levees withstood the high water load but the warning and the evacuation were justified and perceived by the population as the right decision. The risk of dike failure was high. Similarly, during the summer 1997 flood on the Odra (see Box 15.1), the Polish town Słubice was evacuated due to high risk of inundation. As a result of major dike-strengthening action, however, and dike breaches upstream in Germany, which reduced the load, Słubice was not inundated.

As noted by Nigg (1995), officials often hesitate to issue warnings due to fear of error, especially when warning systems are just developing or when there is still a great deal of uncertainty about the occurrence of the future event.

15.2.4 Credibility and efficiency of flood warnings

The more personal the manner in which a message is delivered, the greater its credibility. In principle, person-specific warnings may trigger more urgent responses than communication directed at the general public. There can be challenges, however, in establishing more focused communication mechanisms. In the United Kingdom people in flood risk zones can sign up to receive warnings by telephone, text message or email but the take-up has not been high. This is partly because many people do not want to recognise that they are in a flood risk zone because of a fear of reduced house prices or the inability to acquire insurance.

Factors influencing the efficiency of message dissemination include the credibility of the source (which may vary according to the recipient of the message); the accessibility of the chosen communication channel; the usefulness or redundancy of the information; and the communication of a system's resistance to floods. Essentially, the information should be conveyed in wording that the public can understand and empathise with and via channels that the public finds credible.

15.2.5 Long-term early warnings

In addition to short-term (real-time) warnings related to a specific, forthcoming flood event, recent work has also emphasised the need to issue another type of early warning if the projections (predictions) of flood hazards in the more distant future indicate considerable changes in the anticipated risk (Hall et al., 2003, 2005; Hirabayashi et al., 2008; Dankers and Feyen, 2008; Kundzewicz et al., 2010a, 2010b). Early warnings of increasing flood risk in the decades ahead are necessary to upgrade defence strategies, for example by undertaking the time-consuming and resource-intensive task of strengthening levees.

Climatic and non-climatic factors affect future flood risk and adaptation needs. For example, land-cover changes and urbanisation can increase flood risk regardless of any change in climate. Observations and climate projections show widespread increases in the contribution of very wet days to total annual precipitation in the warming atmosphere (Trenberth et al., 2007). Increasing flood magnitudes are projected in areas where floods result from heavy rainfall; decreasing flood magnitudes are anticipated where they result from spring snowmelt. Winter (rain-caused) flood hazard is likely to rise for many catchments under several climate scenarios. However, global warming may not necessarily reduce snowmelt flooding everywhere. Since an increase in winter precipitation is expected, snow cover may actually increase in cold areas where the temperature remains below 0 °C.

Floods corresponding to a 100-year return in the control period may become more or less frequent in the future climate. Where they increase, upgraded flood prevention measures will be needed to ensure the required protection level. Projections by Hirabayashi et al. (2008) and by Dankers and Feyen (2008) indicate that in much of Poland, France, the United Kingdom, southern Sweden and northern Italy, today's 100-year floods will occur more frequently in 2071–2100. They are projected to occur less frequently over most of Finland and the European part of the Russian Federation. These two

studies show that, in aggregate terms, the control 100-year flood is projected to become more frequent over more than 40 % of Europe, and that over 30 % of Europe the mean recurrence interval of such floods is projected to decrease from 100 years to below 50 years by 2071–2100 (Kundzewicz et al., 2010b).

Systems continue to be designed and operated assuming stationarity (the past is the key to the future). Since this assumption is clearly incorrect due to both non-climatic and climatic changes (Milly et al., 2008), existing design procedures need to be revised, accounting for land-cover change, climate change and other changes of relevance. Otherwise, systems will be under- or over-designed and either not serve their purpose adequately or be overly costly (with excessive safety margins).

Difficulties in isolating the greenhouse signal in river flow observation records, coupled with the large uncertainty in projections of future precipitation and related variables, mean that no precise quantitative information can be delivered for long-term flood preparedness planning. Nevertheless, water managers in some countries, including Germany, the Netherlands and the United Kingdom, have begun to take account of these early climate change warnings explicitly in flood protection design codes.

In Bavaria, for example, flood design values now take into account projections of a 40–50 % increase in small and medium flood discharges by 2050, and an increase of around 15 % in 100-year floods. In the United Kingdom, the precautionary allowance of the Department for Environment, Food and Rural Affairs (Defra, 2006) includes projections of increased peak river flow volumes (10 % up to 2025 and 20 % after 2085), to reflect the possible effects of climate change, based on early impact assessments. A 'climate change factor' is to be reflected in any new plans for flood control measures in the Netherlands. Measures are planned to manage the Rhine's increased discharge in the Netherlands resulting from climate change. By 2015, the measures implemented should increase the design discharge from 15 000 to 16 000 m^3/s and this should increase further to 18 000 m^3/s in the longer term (Kundzewicz et al., 2007).

15.3 Flood preparedness systems — the science and its use

Complete flood safety is impossible in low-lying areas adjacent to rivers. Flood risk can be considerably restricted, however, if an adequate preparedness system is built, consisting of a site-specific mix of measures. Flood-related research, financed by regional, national and international funding institutions, administrative authorities, water agencies, and the insurance and reinsurance industry, is indispensable to optimise preparedness systems.

In Europe, important research initiatives have been undertaken at the international and national levels. A prominent example of integrated international action is the interdisciplinary FLOODsite project (Klijn, 2009) within the Sixth Framework Programme of the European Union. FLOODsite developed integrated flood risk analysis and management methods, covering the physical, environmental and socio-economic aspects of floods from rivers, estuaries and the sea. It integrated different scientific disciplines, spatial planning and management and considered flood risk as a combination of hazard sources, pathways and consequences for people, property and the environment.

The EU Floods Directive (EU, 2007; Box 15.2) explicitly refers to FLOODsite as the largest ever EU flood research project. The FLOODsite project dealt with detection and forecasting of hydro-meteorological conditions and timely warning of the relevant authorities and the public. The research aimed to enhance the performance and shorten the lead time of flash-flood forecasting by linking rainfall-runoff models to real-time remotely sensed (radar and satellite) data. A system for detecting and estimating extreme storm rainfall was developed and tested and the uncertainty of the radar rainfall estimates was assessed.

15.3.1 Protect, adapt, retreat

An example of national flood-related research initiatives is the UK's Foresight Project (Evans et al., 2004; Hall et al., 2005), dealing with flood and coastal defence. The project's aim was to forecast changes in flood risks in the United Kingdom over the next 100 years and to identify the best options for responding to future challenges. The key finding was that if existing policies are continued the flood risks in 2080 could increase substantially. Projected changes range from little increases above current expected annual damage in an optimistic scenario to a 20-fold increase under another scenario. The projections suggest that it will be necessary to choose between investing more in sustainable approaches to flood management or learning to live with increased flooding. An integrated portfolio of responses can reduce future risk by an order of magnitude, although the relative effectiveness of response measures depends very much on the scenario considered.

The current strategy for flood preparedness in Europe can be summarised as 'protect as far as technically possible and affordable' and otherwise 'adapt and accommodate'. This has also been expressed as 'living with floods' (Germany, Netherlands) and 'making space for water' (Netherlands, the United Kingdom). If a necessary level of protection cannot be achieved and accommodation (living with floods) is not possible, then another option is retreat.

Decisions have to be made about how to design protection systems and how to control the damage potential, for example by enforcing zoning, banning floodplain development and moving out of the harm's way. Flood protection measures may either modify flood waters or modify the system susceptibility. They depend on the rate of recurrence of floods: natural measures (such as enhancing wetlands and floodplains) are appropriate for frequent floods; engineering measures are suitable for rare floods; residual risk management is essential for very rare floods (Kron, 2005). This latter category contains extreme but possible floods, and those beyond the limits of past experience.

15.3.2 Structural and non-structural flood protection measures

A range of flood protection and management measures exist, falling into structural ('hard') or non-structural ('soft') approaches. The former refer to large-scale defences, such as dikes, dams and flood control reservoirs, diversions and floodways, and improving drainage channel capacity. Structural defences have a very long tradition, with dams and dikes having been built for millennia. Constructing reservoirs where excess water can be stored allows a regulated temporal distribution of streamflow, reducing the natural peak flow.

The physical dimensions of structural flood protection measures, such as levees, are based on probability theory to withstand a predicted 'design flood' of a certain magnitude, e.g. a 100-year flood (although this is difficult to determine in practice), in a given location. The longer the assumed return period of the design flood, the better the level of protection and the greater the costs. This raises various value judgements, such as whether to design dikes to withstand a 100-year flood or perhaps a 1 000-year flood. The latter solution would give better protection but be far more costly. Moreover, it is misleading to expect complete flood protection or total certainty of outcomes.

Dikes protect well against small- and medium-size floods but when a deluge is of disastrous size and dikes break, losses in a levee-protected landscape can be higher than in the absence of a levee due to the false feeling of security that levees can generate among the riparian population and the high damage potential in apparently (but not completely) safe areas. No matter how high a design flood is, there is always a possibility of a greater flood occurring, inducing losses. A dike designed for a 100-year flood is likely to fail if a 1 000-year flood occurs.

In the United Kingdom, the 2005 Carlisle flood occurred when the plans for the new Carlisle flood defences were out for public consultation. The planned defences would have met the UK standard of the 100-year return period and if built they would have been breached because the 2005 event had a return period in excess of 150 years. After the event, the defences were therefore redesigned to address a 200-year return period.

Several developed countries have costly structural protection facilities to withstand a high, rare flood. Reinforced dikes or super-dikes of 300–500 meters width play an important part in flood protection of major cities in Japan, where a very high level of safety must be assured (Kundzewicz and Takeuchi, 1999). Even higher protection levels are achieved in the low-lying Netherlands. The Flood Defence Act of 1996 set high safety standards with the return period of design flood set at 1 250 years for middle to upper rivers in the Netherlands and 2 000 years for lower river reaches (Pilarczyk, 2007).

'Soft' non-structural flood protection measures include source control (watershed management), laws and regulations, zoning, economic instruments, efficient flood forecast warning systems, flood risk assessment systems, awareness-raising information and flood-related databases. Source control modifies the formation of floodwater by catching water where it falls, enhancing infiltration, reducing impermeable areas and increasing storage in the watershed. These measures counteract the adverse effects of urbanisation, such as reduced storage potential, growth in the runoff coefficient and flood peak, and acceleration of a flood wave. Restoring, retaining or enhancing water storage capacity in the river system (floodplains, polders and washlands) is also important.

Appropriate schemes of insurance, which distribute risks and losses over many people and over a longer time, coupled with aid that can compensate

Panel 15.2 Uncertainty in predicting floods (and other environmental variables)

Keith Beven

In its report on the causes of the Mississippi floods in 1993, the US Interagency Floodplain Management Review Committee's major conclusion was that the rainfalls were 'without precedent' (Galloway, 1995). Similarly, in the United Kingdom the Pitt Report described the summer 2007 rainfalls and floods as 'exceptional' and noted widespread demand for better warnings to provide the public more time to prepare and protect their property (Pitt, 2007).

The demand for better warnings appears to pose a relatively simple problem for hydrological science. With some knowledge of the pattern of heavy rainfalls, it should be possible to predict river flows and, during extremes, the likely extent of flooding. Of course, there are also organisational and social problems in conveying flood warnings to the public but here we will concentrate on the scientific problem. It is an example of the type of predictions about environmental variables that are increasingly demanded and extend all the way up to predictions about the future climate based on global atmosphere and ocean circulation models.

In fact, many of these apparently simple science problems turn out to be complex and fraught with uncertainties that are difficult to evaluate. In the case of floods, measurement technique limitations mean that there is uncertainty about the pattern and intensity of rainfall and the relationship between discharge and flood levels during extreme flows. There is uncertainty about how much rainfall will reach a river and when — in part because there is a highly non-linear relationship between the wetness of a catchment before an event and runoff generation processes. Many major floods (examples from the United Kingdom include the summer 2007 floods, the Lynmouth flood in 1952, the Boscastle flood in 2004, the Carlisle flood in 2005 and the Cumbria floods in 2009) were preceded by prior wetting, which increased subsequent runoff. Hydrological models can simulate and predict runoff generation but they can only approximate, thereby introducing further uncertainty.

There are also important modelling uncertainties in predicting the frequency with which a flood of a given magnitude will occur, how that might change in the future as a result of climate variability or change, and the impacts of land management changes on runoff generation. It is therefore unsurprising that uncertainty estimation has been an important research topic in hydrological modelling in the last two decades. This has included analysis of how the nature and magnitude of predictive uncertainties should be communicated to decision-makers and stakeholders (e.g. Faulkner et al., 2007; Beven, 2009).

This research has determined that there is still significant debate about how the effects of relevant uncertainties should be estimated, with the literature revealing a range of strongly held opinions and some interesting debates. The failure to reach more general consensus over this period may appear surprising but there are some fundamental issues involved, which apply much more generally in environmental modelling (see Beven, 2002, 2006a and 2006b).

Disagreement centres on the types of uncertainties involved. Aleatory uncertainties, arising from natural variability, can be distinguished from epistemic uncertainties, which result from the limitations of our knowledge about the system under study. Inherent unpredictability of nature and unrecognised uncertainties ('unknown unknowns') may also influence the errors in model predictions but cannot be treated explicitly because, by definition, they are not accessible for analysis (Sivakumar, 2008).

It is commonly assumed that most sources of uncertainty can be treated as aleatory, which is advantageous because such uncertainties can be treated in terms of probabilities and the full panoply of statistical theory can be used in analysis and prediction. Beven (2006b) argues, however, that this only applies in 'ideal cases'. Most of the uncertainties involved in hydrological and other environmental models have an epistemic as well as an aleatory component. Treating the sources of uncertainty as if they were aleatory in non-ideal cases will produce over-confidence in the model predictions because of the time-variable nature of epistemic uncertainties.

There is no general theory of how to handle epistemic uncertainties and some debate has focused on whether it is always appropriate to estimate uncertainties based on probabilities. Other frameworks, such as the possibilities of fuzzy set theory, allow more flexibility but introduce more subjectivity into the

Panel 15.2 Uncertainty in predicting floods (and other environmental variables) (cont.)

associated assumptions. Probability theory has the attraction of being logically consistent and objective — but if and only if the assumptions about the nature of the errors can be shown to be consistently valid and this is rarely the case. Even in models it can be shown that small departures from the ideal can lead to overconfidence in predictions (e.g. Beven et al., 2008).

In real applications, most sources of uncertainty have both aleatory and epistemic components, but it will often be the epistemic component that dominates. In predicting floods, rain gauges, radar and numerical weather prediction can be used to measure or forecast rainfall over a catchment area and provide inputs to hydrological models of runoff generation. All will be subject to epistemic errors. Numerical weather prediction is useful for identifying potential flood events but does not (yet) give generally reliable rainfall forecasts. Such forecasts are essential for flood warning, especially for flash floods in small basins with short response times, since there is no other way to provide warnings to the public with sufficient lead time. They will, however, be uncertain and not just in aleatory ways.

In larger basins, measurements of rainfall will be sufficient as an input to warning models. However, a rain gauge network may not always provide a good estimate of that input, particularly for localised convective cells or orographic effects, because the spatial pattern of the gauges may not properly represent the spatial pattern of the rainfall. Radar gives relatively good spatial coverage but does not measure rainfall directly and there may be epistemic uncertainties in the corrections and reflectivity-rainfall intensity relationship used, which will vary from event to event.

Similar arguments apply to other types of uncertainties in flood forecasting and frequency estimation.

There is no question that it is better to estimate some form of uncertainty for these predictions than to ignore the uncertainties. But this creates certain challenges. For the scientist, the problem is how best to deal with epistemic uncertainties. For the decision-maker, who depends on model predictions, the problem is how to understand and interpret the uncertainty estimates associated with a prediction — and under what circumstances not to rely on model predictions when making a decision.

Flood forecasting poses additional difficulties. One is the issue of conveying the meaning of flood warnings when the uncertainties in the forecasting process might result in one or a succession of false alarms. Furthermore, as Kundzewicz notes in the present chapter, there is also a need to explain to the public (and even to some decision-makers) that there is a finite possibility that even a new flood defence scheme may be breached by the next flood event (or, as in Carlisle in January 2005, before the new design has been built).

Estimating uncertainty associated with these types of predictions can have important consequences if it alters the resulting decision. Understanding such estimates is easier for users with a clear theoretical foundation in probability (Hall et al., 2007; Todini and Mantovan, 2007; Montanari, 2007) but, as already noted, estimates can be misleading if they lead to overconfidence in the outcomes.

Essentially, science lacks a theory of the true information content of data that is subject to epistemic uncertainties (Beven, 2008). That will take time to develop but in the meantime there are some practical ways of proceeding. One is to involve potential users of model predictions earlier in the prediction process so that decisions can be taken about how to evaluate model performance and handle different sources of uncertainty. The Environment Agency of England and Wales is starting to implement this approach within the framework of 'guidelines for good practice' for incorporating risk and uncertainty into different areas of flood risk management.

This type of stakeholder involvement in the prediction process has been advocated for some time (e.g. Stirling, 1999; EEA, 2001). The guidelines concept provides a framework for agreeing on reasonable assumptions about both aleatory and epistemic uncertainties. It should provide a good basis for assessing the value of different types of model prediction in the decision-making process.

for uninsurable losses, are additional important components of flood preparedness. Flood-risk maps developed for the insurance industry are used to help estimate insurance premiums for properties in the United Kingdom. Post-flood disaster aid, based on voluntary solidarity contributions, national assistance and international help, is essential to restore the livelihoods of survivors.

Despite some encouraging examples, such as in the US after the 1993 flood, the permanent evacuation of floodplains is virtually unthinkable in most countries. This is definitely true for Bangladesh, a densely populated and low-lying country, which ranks as the most flood-prone country on earth. The people of Bangladesh, growing rapidly in number, have to live with regular floods. Most of the country is made up of floodplains and soil fertility depends on regular flood inundation. In 1998, more than two thirds of the country were inundated. New flood embankments, even if affordable, would occupy scarce and highly demanded land. Thus, the options include reinforcing the existing structural defences and enhancing and optimising non-structural measures, including the forecast-warning system. As this example makes clear, optimum strategies for flood protection must be site-specific.

15.3.3 Uncertainty in flood risk assessment

Notwithstanding major research efforts, there is much uncertainty in the hydrological studies that underpin flood risk assessment and management (e.g. in determining a 100-year flood). Various studies (e.g. Beven, 2006a; Hall et al., 2007; Sivakumar, 2008) have judged the uncertainty analysis in hydrological studies to be highly unsatisfactory. Although disagreeing in significant respects, all called for the promotion of uncertainty analysis of measurements and modelled results in hydrological studies; uncertainty analysis should not be an add-on element — an afterthought of little importance. This is easier said than done, however, as there is considerable uncertainty regarding uncertainty estimation.

A good start would be greater rigour and consistency in analysing and reporting uncertainties. One weakness arises from the deficiencies of hydrological models and available observation records for model validation. There is an overwhelming scarcity of homogeneous long-term observation records. The inherent uncertainty in analysing any set of flood flows also stems from the fact that directly measuring the range of extreme flows can be challenging because, for example, rating curves are not available for the high flow range, gauges are destroyed by flood waves or observers are evacuated. Recourse to indirect determination is therefore necessary (Kundzewicz et al., 2010b).

Uncertainty in future projections of river flooding is very high (see Kundzewicz et al., 2010b), and grows the further we look into the future. In the near-term (e.g. the 2020s), climate model uncertainties play the dominant role, while over longer time horizons uncertainties due to greenhouse gas emission scenarios become increasingly significant. Uncertainty in practical flood-related projections is also due to a spatial and temporal scale mismatch between coarse-resolution climate models and the finer scale of a drainage basin. Scale mismatch renders downscaling (disaggregation) necessary. In fact, much more refined data are necessary for the 'point' scale of a locality (e.g. a small riparian town), which is the level at which costly adaptation is undertaken.

15.4 Lessons from floods

Flooding cannot be totally prevented. The occurrence of a flood need not be considered a 'failure' and, conversely, minimisation of losses may constitute a 'success'. The first lesson is that there are always lessons to be learned, from every flood. An example of lessons learned from a single, destructive, flood on the Odra in 1997 is presented in Box 15.1.

Learning a lesson means building awareness and understanding of the reasons for a system's failure or inadequate performance, and identifying weak points using an holistic perspective. Flood forecasting and warning systems fail because links in the chain perform poorly or not at all. The observation system may fail, the forecast may be grossly in error, the warning message may be wrong, the communication of a warning may be deficient and the response may be inadequate. A single weak point in a system, which otherwise contains many excellent components, may render the overall system performance unsatisfactory.

The components in flood forecasting and warning systems must be adequately integrated but responsibility for them may reside with different agencies. This necessitates adequate collaboration and coordination between multiple institutions, which can be challenging. In emergency situations, it may become evident that distribution of roles of

Box 15.1 Lessons learned from the 1997 Odra flood

The dramatic Odra flood in July 1997 occurred after a long flood-free period and revealed the weaknesses of the existing flood preparedness system in Poland, in particular the deficiencies of relevant legislation (Kundzewicz et al., 1999).

The flood occurred during a period of legal transition, as the previous regime's laws were essentially abandoned and many new acts were passed during a short time. The distribution of responsibilities was ambiguous and conflictual, with complicated links between different participants in flood defence activities. The law at the time provided that low-level authorities were not entitled to announce a flood alert or the alarm status. Such decisions had to be issued by the provincial anti-flood committees and were delayed as a result. Local authorities typically resorted to common-sense decisions, without waiting for instructions from above.

The information flow was similarly deficient. Hydrometeorological stations reported to the regional branches of the hydrometeorological service, although also making information available, on request, to local authorities. Some forecasts proved to be of low accuracy.

Responsibilities and cost coverage for the army, police and fire brigades were also not clearly defined. Polish civil defence was geared to act in the event of a war, rather than to deal with a peacetime emergency. In addition, telecommunication support proved vulnerable as some 189 000 telecommunication links were disconnected. Mobile phones provided more reliable communication, but network limitations were also revealed.

Advance warning on the Odra was available for the medium and lower course when the flood occurred in headwaters in Czech Republic and Poland. In principle, the State of Brandenburg in Germany had ten days before the arrival of the floodwater. Even so, detailed forecasts were difficult to obtain due to problems such as the interruption of observations in several gauges and flooding of the flood information office in Wrocław.

Consequently, the need for numerous improvements was recognised, such as building the network of weather radars; automating observations and data transmission; technical upgrading of flood warning centres, including telecommunication facilities (enabling phone, radio and fax to work without mains electricity supply); upgrading and modernising the warning system; enhanced regional, interregional and international flows of flood-related information; and building more suitable forecast models.

Considerable investments were made to improve many of these systems. The nation and the relevant services learned a lesson. When a second flood wave occurred in July 1997 the preparedness and flood management were far better than during the first crest when the nation had largely been taken by surprise.

agencies is unclear and possibly redundant. The institutional framework is a key socio-economic determinant of a nation's vulnerability against natural disasters (Raschky, 2008).

People's experience of flooding may reduce damage in the next flood. Where large floods occur in the same location twice in a short time period (e.g. on the Rhine in Cologne in December 1993 and January 1995), losses during the second flood are typically far lower than those during the first (Munich Re, 1997; Kundzewicz and Takeuchi, 1999). The first flood will provide lessons for diverse groups: riparian homeowners; farmers with fields on the floodplain; professionals in the affected water district; legislators; spatial planning (zoning) officers; and public administrators at the country, province, town and community levels.

Although flood events and human failures provide valuable lessons, memories can fade quickly after a flood. Typically, a destructive flood generates enthusiasm for strengthening flood preparedness systems and heavy expenditure follows. Following a deluge, the relevant authorities elaborate ambitious plans and launch works but lessons are soon forgotten. After some time without flooding, willingness to pay for flood preparedness decreases sharply and projects are downscaled or suspended. When the next deluge comes, it acts as a reminder and starts a new cycle. This vicious turn of events, known as the 'hydro-illogical cycle' (a concept introduced in the drought context by Donald Wilhite in the mid-1980s) is a general principle, valid across different political and economic systems. The return period of a destructive flood is usually much greater than the political horizon of decision-makers and the

electorate, which is determined by terms of office and electoral cycles. Of course, the hydro-illogical cycle is also at odds with the precautionary principle.

In some countries, codifying preparedness in legislation helps overcome the hydro-illogical cycle. A prominent example is the European Union's Floods Directive (Box 15.2).

Interestingly, an important turning point in the development of flood protection strategy can be traced back to the mid-19th century in the US (Williams, 1994) when Congress looked into the problem of the Mississippi floods. The two options considered were:

- using large areas of the Mississippi floodplains as flood storage and overflow areas;
- attempting to control floods by embanking the River Mississippi in a single channel isolated from its floodplain.

Congress selected the latter option and the decision has remained influential on flood protection policy in the US and elsewhere, leading to the transformation of rivers and reduction of wetlands worldwide. In 1936, the US Federal Government assumed primary responsibility for flood damage reduction across the nation and, over the next half a century, embarked on a multibillion dollar programme of structural defences (Galloway, 1999).

Another paradigm shift resulted from the great 1993 US mid-west flood, which proved that structural 'hard' defences cannot guarantee absolute protection. As a result, the US Interagency Floodplain Management Review Committee recommended that the administration should fund acquisition of land and structures at risk from willing sellers in the floodplains, and many vulnerable families have been relocated from risky areas (Galloway, 1999). However, this response is not universal. In most countries, people who suffer in a

Box 15.2 EU Floods Directive

Between 1998 and 2004, Europe suffered over 100 major destructive floods, including the record-breaking August 2002 flood on the Danube, the Elbe and their tributaries. In response to these floods and projections of growing flood risks in Europe, in April 2007 the European Union adopted Directive 2007/60/EC on the assessment and management of flood risks (EU, 2007), commonly known as the Floods Directive. The directive embraces river floods, flash floods, urban floods, sewer floods and coastal floods; its objective is to reduce and manage the risks of floods to human health, the environment, infrastructure and property. It provides that EU Member States shall undertake, for each river basin or other management unit:

- a preliminary flood risk assessment, including a map of the river basin; a description of past floods; a description of flooding processes and their sensitivity to change; a description of development plans; an assessment of the likelihood of future floods based on hydrological data, types of floods and the projected impact of climate change and of land use trends; and a forecast of the estimated consequences of future floods;
- flood hazard maps and flood risk maps (damage maps), for high risk areas, i.e. those that could be flooded with a high probability (a 10-year return period), with a medium probability (a 100-year return period) and with a low probability (extreme events);
- preparation and implementation of flood risk management plans, aimed at achieving the required levels of protection.

Noting the diversity across the EU, the Floods Directive affords Member States flexibility to determine the level of protection required, the measures needed to achieve that level of protection (taking into account the work already done at national and local levels) and the timetables for implementing flood risk management plans.

The directive is probably the most advanced flood protection and preparedness legislation worldwide and implementation should considerably reduce flood risk throughout the 27 EU Member States. Mandatory activities, including assessing, mapping and managing flood risk in the river districts are expected to result in an unprecedented multinational upgrading of preparedness systems. The directive foresees that 'the potential future damage to be expected if no action is taken distinctly outweighs the costs' of implementation.

flood rebuild their houses (possibly more robustly) and their livelihoods in the place devastated by the flood, rather than moving elsewhere. The hazard may not have decreased, however, and floods could recur in that location.

People also take lessons from the failures of past policies. For example, some flood protection infrastructure has been criticised from a sustainable development perspective because it limits options for future generations and introduces disturbances in ecosystems. According to the Environment Agency of England and Wales (1998), sustainable flood defence schemes should protect the present generation from destructive floods but also 'avoid as far as possible committing future generations to inappropriate options for defence'. Renaturalising rivers and flood plains and reconstructing wetlands have been discussed for many years and is now actually likely to come about. Similarly, some large reservoirs, whose construction required the inundation of large areas or the displacement of many people, certainly did not match the principles of sustainable development (Kundzewicz, 1999). Studies on decommissioning reservoirs are now under way and in some cases decommissioning has already taken place, for example in France (Kernansquillec, Maisons-Rouges and St Etienne du Vigan).

Looking back at past developments often reveals that major decisions, such as regarding the construction of a large dam, are based on one-sided arguments with important aspects neglected. This bias can result from a lack of knowledge and understanding at the time that the decision was taken, as well as the evolution of value judgements over time.

15.5 Conclusions: living with floods

Floods are natural events that cannot be avoided. We should protect ourselves against floods up to an agreed safety level, this being a compromise between the desired level of safety and the accepted willingness to pay for protection. Once we accept that no flood protection measures can guarantee complete safety, a general change of paradigm is needed to reduce human vulnerability to floods. The attitude of 'living with floods' and accommodating them in planning seems more sustainable than hopelessly striving to eradicate them (Kundzewicz and Takeuchi, 1999). There must be action plans for events exceeding the design flood (i.e. when defences are bound to fail) and in this context early warning can save lives.

Misconceptions and myths about floods and flood protection are deeply rooted in society — among the general public, politicians and decision-makers. Some people naively believe that floods occur at large and regular time intervals — that terms such as 'return period' and 'recurrence interval' can be taken literally (rather than understood as averages) — and that embankments offer perfect safety.

Each tick of the clock marks the passage of time since the last flood and the countdown to the next. It is therefore important to prepare using a variety of different means, notably:

- rigorous implementation of zoning — using regulations to develop flood hazard areas and leaving floodplains with low-value infrastructure;
- strengthening existing defences;
- building or enhancing flood mitigation monitoring systems;
- forecasting;
- issuing and disseminating warnings;
- evacuation;
- relief and post-flood recovery;
- flood insurance;
- capacity-building (improving flood awareness, understanding and preparedness);
- enhancing a participatory approach, including consultation on the preparedness strategy and the level of flood protection, and household-level flood-proofing and mitigation measurements for both newly built and existing properties.

Only informed stakeholders can make rational decisions and agree on an acceptable flood protection strategy, being aware of both costs and benefits. There may be conflicting interests between those living in floodplains and demanding efficient and very costly protection, and the rest of the nation.

Efficient actions aimed at awareness-raising can reduce flood losses. Many past fatalities could have been avoided with greater awareness. In some developed countries such as the US, most flood fatalities involve vehicles whose drivers underestimate the danger.

Panel 15.3 Dealing with the risk of coastal flooding — experiences from European countries

Pier Vellinga and Jeroen Aerts

Coastal storm surges and floods are the most frequent and costly extreme weather events occurring in Europe, representing 69 % of the overall natural catastrophic losses (CEA, 2007). In 2010, for example, France was the European country hit hardest by the winter storm Xynthia, with 51 casualties and damages of more than EUR 1.5 billion. Many of the country's sea walls, including those around the Isle de Re off the country's west coast, were damaged or washed away (AIR, 2010).

Other low-lying coastal regions in Europe have endured similar experiences. In 1953 the winter storm that hit coastal stretches around the North Sea, especially in the United Kingdom and the Netherlands, killed more than 2 000 people. Areas around Hamburg and Bremen and parts of the Baltic coast are frequently hit by coastal storm surges. And although the shores of the Mediterranean and the Black Sea are generally steep, the river deltas of the Rhone, the Po, the Danube and many other smaller deltas experience floods from time to time. The 'Aqua Alta' in Venice Lagoon is a well known phenomenon.

The risk from coastal flooding is expected to increase in the future. First, climate change and sea-level rise is expected to increase the frequency and severity of flood events. Sea levels on average have already risen by about 10 cm per century over the last two to three centuries and are expected to rise at even higher rates in coming centuries (IPCC, 2007). This trend is exacerbated by land subsidence, which is determined by soil quality and the degree of water extraction in some low-lying coastal areas in Europe. The economic impact of natural catastrophes is also increasing due to the growing number of people living in areas with high risk levels, and increased economic activity in these regions (Bouwer et al., 2007).

History suggests that the human population is usually taken by surprise by coastal floods due to their 'low probability and high impact' character. Vulnerability to such events increases very gradually through slow sea-level rise and socio-economic developments. There is never an acute reason for strengthening the coastal protection system or for elevating settlements until the area and its population are hit by a major flood with significant loss of lives and economic damage.

The records of major coastal flooding episodes in the Netherlands, for example, illustrate that people have been taken by surprise about once every hundred years for the last 1 000 years. Apparently after some 50 years the flood disaster tends to disappear from the collective memory and flood protection measures are insufficiently maintained as a consequence. While the sea level keeps on rising and settlements keep expanding, a new high water event starts a new cycle of disaster and renovation of coastal protection works. The Netherlands and the United Kingdom only began investing in large-scale storm surge barriers after the devastating storm in 1953. The challenge for low-lying countries now is to anticipate climate change and accelerated sea-level rise.

The concept of measures to reduce the risk of flooding varies over time and by region. It ranges from local small-scale embankments to large-scale reclamation works and tidal barriers to lower the probability of coastal flooding. For example, London, large parts of the Netherlands, St. Petersburg in Russia and more recently Venice either have developed or are developing large-scale tidal storm surge barriers. These large engineering projects are expensive but protect population and capital investments up to a certain standard, usually in the order of withstanding the most extreme conditions statistically expected to occur once in a thousand or so years.

On the other hand, the closure of environmentally rich coastal areas such as estuaries through dams and barriers can harm biodiversity and water quality. Hence, flood protection through 'building with nature' has recently gained interest. Examples are periodic beach nourishment and coastal marshland development as ways to protect land and create buffer zones to lower wave impact (Day et al., 2007). Furthermore, coastal zone management strategies in, for example, the United Kingdom and France also aim to reduce the impact of coastal flooding by developing stringent building codes (flood proofing buildings) and zoning regulations (limiting urban expansion).

In France, a system of community-based prevention plans for natural risks addresses floodreducing measures. The possibility of gaining more favourable flood insurance terms provides an incentive for implementing such plans (Letermy, 2009). Innovative examples are found in the cities of Hamburg and

Panel 15.3 Dealing with the risk of coastal flooding — experiences from European countries (cont.)

Rotterdam. These cities have chosen to develop new residential areas on old port facilities located outside the main flood defences and hence prone to flooding but are elevating the buildings to safe levels. In Hamburg even public roads and bridges will be elevated to the height of 7.5 m above sea level to ensure unrestricted access for the fire and emergency services in the event of an extreme storm tide (Aerts et al., 2009).

Future projections of sea-level rise and human exposure to flood risk are inherently uncertain, necessitating new flood management methods and strategies. The 'climate proofing' concept has been developed to deal with sea-level rise and greater uncertainty about extreme weather events (Kabat et al., 2005). For example, levees and storm surge barriers are currently designed according to deterministic principles, using relatively short historic records and extrapolation methods to determine maximum surge heights. Extreme events are rare, however, and data on these events are sparse. Hence, new probabilistic methods are needed that provide engineers with a range of possible scenarios and may support a more robust protection designs.

Other 'climate proofing' measures include broadening levees to form 'superlevees', which can be used as ground for urban development (Vellinga et al., 2009). Such unbreachable dikes were developed in Japan near Tokyo, to protect against the potentially very high seas caused by tsunamis. They are now being considered by many water boards in the Netherlands as a way to deal with higher flood levels. For sandy beaches, the existing practice of beach nourishment (with sand) has become more sophisticated, such that the sand can be placed on the foreshore, creating a buffer against continuously rising seas. Finally, spatial planners, developers and insurers are actively engaged in reconsidering current regulations in order to ensure more flood- and climate-proof development of vulnerable coastal areas (Burby, 2001).

Despite their shortcomings, hard structural flood protection measures, such as dams and levees, will be needed to safeguard existing developments, in particular in urban areas. An effective flood protection system is generally a mix of structural and non-structural measures, with the latter approaches normally conforming better to the spirit of sustainable development.

Mitigating flood risks requires a change from reaction to anticipation. An immediate challenge is to improve flood forecasting at a range of time horizons of concern, from short-term weather forecasting and quantitative precipitation forecasts (useful for flash floods) to longer-term forecasting, useful for large basins. In this we should be encouraged that, thanks to improvements in the advance time and accuracy of forecasts, it has already been possible to reduce the number of flood fatalities in many countries.

Smith and Ward (1998) identify the development of infrastructure on floodplains as the major factor increasing flood risk (in terms of both hazard and vulnerability). Floods constitute a danger to life and property only when humans encroach into flood-prone areas and become vulnerable. This has already happened in many locations in Europe. If endangered locations have already been developed, a remedy is that humans, and infrastructure, move out of harm's way. In many countries the strategy of retreat is unpalatable, however, favoured by neither the broader population nor decision-makers. In some countries, such as Bangladesh, it is simply not an option.

Modern flood risk management comprises pre-flood prevention, risk mitigation measures and preparedness, followed by pre-planned flood management actions during and after an event. The risk-based approach to flood management is based on analysing the probability and consequences of flooding across the full range of severity, and implementing mechanisms to manage all possible events. Modern flood management also looks to the future and flood risk managers should continuously acquire and update evidence about long-term changes in flood risk.

Table 15.1 Early warnings and actions

C. 2000 BC	Levees and dams in China and the Middle-East provide flood protection
1854	Regular flood forecasting in France, following the advance of the telegraph. Italy developed such systems in 1866 and the US did so in 1871
1861	Adoption of a flood protection policy based on levee construction in the US, following a report by the US Army Corps of Engineers (Smith and Ward, 1998). This led to the transformation of seasonal wetlands to productive agricultural land
1931	Destructive summer floods in China cause a huge number of fatalities (although sources vary significantly on the numbers — ranging from 145 000 to 3 700 000)
1944	The Pick-Sloan Flood Control Act, enacted in the second session of the 78th US Congress, authorised a programme of structural defences, dams and levees across the US. It led to the establishment of the Pick-Sloan Missouri Basin Program
1970s	Early use of radar and satellite in flood forecasting
1994	After the 1993 mid-west flood in the US, the Interagency Floodplain Management Review Committee suggested relocating people off the floodplains and reclaiming wetlands (IFMRC, 1994)
1997	Large floods in central Europe affecting the basins of the Odra/Oder (Czech Republic, Poland, Germany) and the Vistula cause 110 fatalities and material damage in the range of billions of dollars — a substantial portion of the GDP of the countries in economic transition
1998	Floods in China cause material damage of USD 30 billion and over 3 600 fatalities
1998	Major flooding occurs in Bangladesh, inundating nearly 70 % of the country
2002	Dramatic floods in Europe (Austria, Bulgaria, Czech Republic, Germany, Hungary, Moldova, Romania, Slovakia, Ukraine) in August 2002 cause total damage in excess of EUR 20 billion
2007	Adoption of the EU Floods Directive

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16 Seed-dressing systemic insecticides and honeybees

Laura Maxim and Jeroen van der Sluijs

In 1994 French beekeepers began to report alarming signs. During summer, many honeybees did not return to the hives. Honeybees gathered close together in small groups on the ground or hovered, disoriented, in front of the hive and displayed abnormal foraging behaviour. These signs were accompanied by winter losses.

Evidence pointed to Bayer's seed-dressing systemic insecticide Gaucho®, which contains the active substance imidacloprid. This chapter presents the historical evolution of evidence on the risks of Gaucho® to honeybees in sunflower and maize seed-dressing in France, and analyses the actions in response to the accumulating evidence regarding these risks.

The social processes that ultimately lead to application of the precautionary principle for the ban of Gaucho® in sunflower and maize seed-dressing are described, with a focus on the ways in which scientific findings were used by stakeholders and decision-makers to influence policy during the controversy.

Public scientists were in a difficult position in this case. The results of their work were central to a social debate with high economic and political stakes. In certain cases their work was not judged according to its scientific merit but based on whether or not it supported the positions of some stakeholders. This situation tested the ability and courage of researchers to withstand pressure and continue working on imidacloprid.

Other European countries also suspended neonicotinoid seed-dressing insecticides. Evidence of the toxicity of neonicotinoids present in the dust emitted during sowing of coated seeds supported such decisions. Most important, the French case highlighted the major weaknesses of regulatory risk assessment and marketing authorisation of pesticides, and particularly neonicotinoids. These insights were recently confirmed by work by the European Food Safety Authority.

From this case study eight lessons are drawn about governance of controversies related to chemical risks. The study is followed by two additional texts. A first panel presents Bayer Crop Science's comments on the analysis in this chapter. A second contains the authors' response to the Bayer comments.

16.1 Introduction

Insecticides come in various forms. Many coat the surface of plants but systemic insecticides work differently, entering a treated plant's sap via the leaves or roots and coming into contact with insects when they feed on the plant. Seed-dressings and soil treatments operate in precisely this way. The active ingredient enters the roots and disperses to the aerial parts of the plant during growth, offering long-lasting protection from aerial and soil pests.

Some systemic insecticides are neonicotinoids, which have been widely used in seed-dressing and soil treatment since the early 1990s but can also be applied by spraying crops. Over the past decade they have become the most widely used class of insecticides worldwide, with total sales of EUR 1.5 billion in 2008 (24 % of the global insecticide market). By 2010, the first neonicotinoid, imidacloprid, was registered in more than 120 countries for foliar and seed treatment (Jeschke and Nauen, 2008; Jeschke et al., 2010).

In some situations, authorised doses of systemic insecticides can affect beneficial insects like honeybees, bumblebees, biological control agents (Smith and Krischik, 1999; Kunkel et al., 2001; Desneux et al., 2007; Rogers et al., 2007; Katsarou et al., 2009; Mommaerts et al., 2009), birds (Berny et al., 1999) and earthworms (Luo et al., 1999; Kreutzweiser et al., 2008; Capowiez et al., 2009). More than 25 000 species of bees exist and are crucial for the survival and evolution of about 80 % of the flowering plant species that depend on animal pollination (FAO, 2011).

The widespread use of systemic insecticides raises serious concerns about their threat to wild pollinators (EPA, 2003; Greatti et al., 2006; Bortolotti et al., 2002; Desneux et al., 2007). Declines in wild pollinators are reported worldwide (Allen-Wardell et al., 1998; Steffan-Dewenter et al., 2005; Biesmeijer et al., 2006), which is particularly worrying since they are essential for 35 % of global crop output (by weight) (Klein et al., 2006). This has lead to growing concern about agriculture's dependence on pollinators and fears of a global pollination crisis (Ghazoul, 2005a and 2005b; Klein, 2008; Aizen and Harder, 2009).

Many factors influence the state of honeybees and pollinators more generally. Land use practices and agrochemicals are regarded as particularly important (Kuldna et al., 2009). This chapter focuses on the risk to honeybees resulting from the seed-dressing systemic insecticide Gaucho®, whose active substance is imidacloprid. Specifically, it examines the vehement controversy in France over the use of Gaucho® and the justifications that ultimately lead to banning its use on sunflower and maize seed-dressing in that country. Another

Box 16.1 Honeybees, wild bees and other pollinators

In Europe, pollination (i.e. the transport of pollen from producing anthers to receiving stigma) is mainly achieved by three means:

- *passive self-pollination* (direct contact between anthers and stigma or transfer through gravity), which is rarely the dominant pollination route;
- *transport by the wind*, which is the dominant pollination route for about 10 % of flowering plants;
- *pollination by animals, particularly insects*, which is the dominant pollination route for the other flowering plant species — 87 of the leading global food crops depend on animal pollination, compared to 28 crops that do not (Klein, 2007).

Worldwide, honeybees have a major role in pollinating:

- *vegetable crops*, such as watermelon, cantaloupe, melon, cucumber, gherkin, pumpkin, squash, gourd, marrow and zucchini;
- *fruit crops,* such as apple, peach, nectarine, kiwi fruit, mango, avocado, plum, pear, sweet cherry, sour cherry, apricot, mirabelle, raspberry, blackberry, cloudberry, dewberry, rowanberry, cranberry, greengage, sloe, carambola, starfruit, durian, loquat, Japanese plum, Japanese medlar, rose hips and dogroses;
- *nut crops*, such as almond, cashew nut, cashew apple and macadamia;
- *edible oil and proteinaceous crops*, such as canola and turnip rape;
- *spices and condiments*, such as coriander, cardamom and fennel (Klein et al., 2007).

Box 16.2 The life of a honeybee

An adult summer worker honeybee lives about four or five weeks. Three days after being laid, the egg becomes a **larva**, which in turn becomes a **nymph** after about six more days. During the following 12 days, the nymph transforms into an adult honeybee.

During its **adult life**, the honeybee fulfils several roles. At first it stays in the hive as a **nurse**, cleaning the hive and nourishing the larvae. After 10–14 days it stores the collected nectar and pollen, ventilates the hive, covers the cells, secretes beeswax and builds new cells. At the end of the period spent inside the hive, it can be a **guard**. After about three weeks inside the hive and until death, the honeybee is a **forager**, and works outside the hive, collecting pollen, nectar, water and propolis. The division of tasks and the age for going from one task to another can vary, depending on the needs of the colony.

Honeybees feed exclusively on pollen, nectar and honey. It is estimated that most of the foraging activity is undertaken within 6 km of the hive, although honeybees can forage up to 12 km from the hive (von Frisch, 1967; Seeley, 1985; Winston, 1987).

Pollen foragers collect pollen on flowers and carry it to the hive on their posterior legs. Nectar foragers transport nectar in their crop and bring it to the colony. It can be consumed immediately or transformed into honey by water evaporation and changes in sugar composition. Pollen and honey are stored in the hive and can be consumed later.

Nectar and pollen are consumed differently by honeybees of different ages:

- Larvae essentially consume jelly, which is secreted from the glands in nurses' heads and also some pollen, depending on their age.
- Nurses consume pollen, essentially to develop their hypopharyngeal and mandibular glands and to produce jelly.
- Adult honeybees consume different quantities of nectar/honey, depending on the tasks they perform. Large amounts of nectar/honey are consumed for wax production, heat production in the hive (brood-attending bees and winter bees) and for foraging (Rortais et al., 2005; Benjamin and McCallum, 2008).

seed-dressing insecticide, Régent TS® (which contains the active substance fipronil) is also addressed, although not extensively as telling its story would require a chapter of its own.

In this chapter we describe and analyse the social processes that lead to the application of the precautionary principle in France. Scientific data played an important role in these processes. We describe the ways in which stakeholders have used scientific findings to influence policy during the controversy. The scientific data considered in this chapter are thus not exhaustive but selected to reflect the French debate.

The French ban on Gaucho® is significant because insecticides containing imidacloprid are among the most used globally (Jeschke et al., 2010) and have a wide range of uses. At its launch, Gaucho® was marketed as a means of reducing aerial pollution because it was supposedly confined to the soil and very small amounts are applied to seeds. For sunflower the application was 0.7 mg/seed, which amounts to 56–70 g of imidacloprid per hectare (Belzunces and Tasei, 1997). For maize the application was 0.98 mg/seed.

Despite these claimed advantages, France banned the insecticide's use in sunflower and maize seed-dressing due to concerns about its risks to honeybees. In this chapter, we present the historical evolution of the evidence regarding the risks of Gaucho® to honeybees in sunflower and maize seed-dressing and analyse the actions taken in response to the accumulating evidence regarding these risks.

Knowledge can vary in its relevance for supporting an action such as banning imidacloprid. Different stakeholders may perceive the relevance differently, with three factors playing a key role:

1. The scientific quality of the knowledge (**substantive quality**), which includes technical aspects (is the measurement accurate?), methodological aspects (is a particular method appropriate for the intended use?) and epistemological aspects (is enough knowledge available?).

Box 16.3 Uses of imidacloprid in France

In July 2010, imidacloprid was authorised in France to treat fruit trees such as apricot, peach, pear, quince, apple and plum trees. It is also present in products for disinfecting storage facilities, shelters for domestic animals, storage and transport material, treatment facilities for waste and transport material. Other uses include insecticidal treatment of rose bushes.

In France, imidacloprid is currently banned for seed-dressing of sunflower and maize but it is still used in seed-dressing for sugar beet, wheat and barley (Ministère de l'Agriculture, 2011). Residues subsisting in the soil might potentially be taken up by the crops cultivated after the seed-treated crop, or by wild plants (Bonmatin et al., 2005).

2. The quality of the research processes that have generated the knowledge and the expert processes that are used to assess its relevance to support an action (**procedural quality**) ([1]). This relates to researchers' and experts' competence, field experience, institutional affiliation, well-being at work, financial dependencies and other kinds of relationships among themselves and with other stakeholders (for instance, whether or not local knowledge is incorporated in the research).

3. The **social quality**, associated to the value judgments influencing the communication and use of scientific information by experts themselves and by stakeholders, in political debates.

In Sections 16.2, 16.3 and 16.4, we present the development of knowledge in these three areas. The first part of this chapter (Section 16.4.3 included) describes in detail the French controversy until the ban of Gaucho® on maize in 2004. Sections 16.4.4 and 16.4.5 are less exhaustive and result essentially from reactions to the different comments made during the reviewing process.

Many scientific and grey references have been produced in the world since 2004 and we could not include them all, in order not to loose focus but also for reasons of space limits. We have included post-2004 references if: 1) they were produced in France and 2) they were produced in European countries where regulatory decisions have been taken to ban imidacloprid.

The analysis yields lessons about the quality and use of knowledge in risk assessment and management ([2]), which are presented in Section 16.5. Conclusions and prospects are presented in Section 16.6.

16.2 Development of scientific understanding of the issue

16.2.1 Technical and epistemological quality of the evidence

1994: early warnings

In France, dressing seeds with Gaucho® was authorised in 1991 for sugar beet, in 1992 for maize and in 1993 for sunflower. Gaucho® was first used in sunflower farming in 1994. After that year, beekeepers started to report alarming clinical signs. After several days of foraging during the sunflower flowering, many honeybees did not return to their hives. Bee behaviour also caused concern: honeybees gathered close together in small groups on the ground or hovered disoriented in front of the hive; foraging behaviour was abnormal; and queens produced increased amounts of brood to compensate for the loss of foragers. In certain cases, dead honeybees were also reported in front of the hives.

In affected apiaries, most hives were impacted. Those apiaries suffered a 40–70 % loss in sunflower honey yield in the years after 1994, relative to the average yield obtained in previous years. Before 1994, the annual yield variation had been ± 10 %. At the end of winter, losses were up to 30–50 % of the hives, compared with the usual 5–10 % (personal communications from 20 beekeepers; Coordination des Apiculteurs, 2001; Alétru, 2003).

([1]) For example, the expert process by which the 'acceptability' of a calculated risk is assessed in official commissions or working groups. Such an assessment determines an action, that is, the use or not of a substance in crop protection.
([2]) For more details on the case, see Maxim and Van der Sluijs, 2007.

In the following years the beekeepers reported the same clinical signs and their specific impacts on honeybees foraging in sunflowers and maize areas (e.g. Belzunces and Tasei, 1997; CNEVA Sophia-Antipolis, 1997; Pham-Delègue et Cluzeau, 1998; Coordination des Apiculteurs, 2001; Alétru, 2003). The intensity of the clinical signs in France fluctuated, both temporally (from year to year) and spatially. They seemed to depend on factors such as the proportion of the different food resources present in the honeybees' environment (CST, 2003).

Appreciable declines in sunflower honey harvest were reported, implying major economic losses. Searching for possible causes, the beekeepers found that Gaucho® had been first used as a seed-dressing in sunflower farming in 1994. They reported honeybee problems increasing concomitantly with the area of Gaucho®-dressed sunflower (Chauvency, 1997; Belzunces and Tasei, 1997; CNEVA Sophia-Antipolis, 1997; Pham-Delègue and Cluzeau, 1998). Consequently, beekeepers asked Bayer (which manufactures Gaucho®) for information about the potential toxicity of the active substance imidacloprid for honeybees (Coordination des Apiculteurs, 2000).

This request was the start of a long series of scientific studies ([3]) involving Bayer-funded scientists, the Ministry of Agriculture, the French Food Safety Agency (AFSSA), beekeepers, and researchers working in public institutes ([4]) (henceforth 'public scientists').

Evolution of knowledge over time

When Gaucho® was launched commercially, the manufacturer considered that it posed no risk to honeybees, provided it was applied as seed-dressing (Bayer, 1992).

Bayer's reaction to the beekeepers demand was to conduct field and semi-field (under-tunnel ([5])) research. According to Bayer these studies showed that Gaucho® posed no risk to honeybees (Belzunces and Tasei, 1997).

However, the clinical signs continued. Bayer's experiments were presented at the Fourth International Conference on Pests in Agriculture, held in Montpellier on 6–8 January 1997, and also during a meeting organised by the Association de Coordination Technique Agricole (ACTA) in October 1997. They were criticised (ACTA, 1997; Belzunces and Tasei, 1997), so public scientists were also asked to research the issue.

Honeybee exposure to imidacloprid: 1993–1999

One of the main issues in assessing exposure to Gaucho® was the precision of measuring very low concentrations of imidacloprid in pollen and nectar. In 1993, the detection limit established by Bayer-funded scientists for measuring the presence of imidacloprid in plants was 10 ppb ([6]) (Placke and Weber, 1993). However, it was later found that much lower detection limits (DL) were needed to identify imidacloprid's presence in pollen and nectar.

The studies undertaken by Bayer during this period either could not detect imidacloprid in pollen and nectar, or detected it but could not quantify it (CST, 2003). In 1999, a study quantified the substance in sunflowers treated with Gaucho® to be 3.3 ppb in pollen and 1.9 ppb in nectar (Stork, 1999).

When public research started (1997–1998), the General Directorate for Food of the Ministry of Agriculture (DGAL) demanded analyses using 'the lowest detection limit possible', but 'without going below 0.01 mg/kg' (10 ppb) ([7]). For the 1998 programme DGAL noted that 'it is not useful to try to work with the lowest detection limits' ([8]). This DL corresponded to the characteristics of the Bayer method (Pflanzenschutz Nachrichten Bayer, 46.1993.2 inverse chromatography in liquid phase and UV detection). Bayer representatives also participated in the committee charged with developing the research protocol.

At the time that the DGAL demanded the analysis, CETIOM (the Technical Center for Oilseed Crops ([9])) had already estimated that detection limits much

([3]) In the following, we have selected the data that played an important role in the debate, rather than uselessly trying to inventory all the data available. The complete list of the results available before 2003 is available in CST (2003).
([4]) In France, scientists working in national research institutes (e.g. INRA, CNRS) and universities are public servants. Their entire salaries and a part of their functioning (sometimes equipment) expenses are funded by the public institution.
([5]) A tunnel is a tent of several meters, which allows air to pass through and isolates the honeybee colony being used for testing from the exterior. The purpose of a tunnel is to ensure that honeybees only feed on the source chosen for the experiment (e.g. plants contaminated with imidacloprid), while simulating field conditions.
([6]) The unit 'ppb' (parts per billion) is used for very low mass concentrations, more precisely 10^{-9} (e.g. 1 ppb = 1 µg/kg).
([7]) In the original French: 'sans toutefois descendre à une valeur inférieure à 0.01 mg/kg'.
([8]) In the original French: 'il n'est pas utile de chercher à travailler avec la limite de détermination la plus basse possible'.
([9]) Centre Technique Interprofessionnel des Oléagineux Métropolitains.

lower than 10 ppb — about 1.4 ppb — were necessary to find imidacloprid in nectar.

Print media learned of the DGAL's recommendation and of Bayers implications in drafting the protocol, raising doubts about the DGAL's impartiality with respect to Bayer and about its willingness to find relevant results (Libération, 1999a).

These first studies of public researchers reported the presence (< 10 ppb) of imidacloprid in sunflower leafs and pollen but did not quantify it (Pham-Delègue and Cluzeau, 1998).

The findings from research 'raised suspicions about the effects of the product, without formally proving its responsibility' ([10]) (Ministère de l'Agriculture, 2001b). Doubts about the harmlessness of Gaucho® led to the application of the precautionary principle. In January 1999 the Minister of Agriculture, Jean Glavany, decided to ban the use of Gaucho® in sunflower seed-dressing (Libération, 1999b).

This ban was renewed in 2001 for two years, again in 2004 for three years and at present, February 2012, it is still in force.

Honeybee exposure to imidacloprid: 2000–2002

Beekeepers continued to report clinical signs of intoxication after Gaucho® use in sunflowers was suspended in 1999. Three explanatory hypotheses were proposed:

- honeybees were still being exposed to the pollen of maize treated with Gaucho® (sunflower and maize are in flower in the same time);
- imidacloprid persists in soil after treatments of other crops (such as sugar beet, wheat and barley) and was taken up by untreated sunflowers grown one or more years after a seed-dressed crop;
- honeybees were affected by the dressing of sunflower seeds with RégentTS®, which had been provisionally authorised in December 1995.

Following the extension of the ban on using Gaucho® on sunflower and the refusal to ban it on maize, in 2001 (Ministère de l'Agriculture, 2001a; Conseil d'Etat, 2002), the Ministry of Agriculture established a Scientific and Technical Committee for the Multifactor Study of the Honeybee Colonies Decline (henceforth the 'CST' ([11])).

Between 2000 and 2002, using different methods and lower detection limits, public scientists identified 2–4 ppb of imidacloprid in seed-dressed sunflower and maize pollen (Bonmatin et al., 2001 and 2002; Bonmatin and Charvet, 2002), 13.3 ppb of imidacloprid in seed-dressed sunflower pollen (Laurent and Scalla, 2001) and 1.6 ppb in seed-dressed sunflower nectar (Lagarde, 2000).

During these years, it was understood that honeybees could collect imidacloprid-contaminated nectar and pollen for up to a month of sunflower and maize flowering. Bees could show the effects of repeated consumption of contaminated pollen and nectar almost immediately or some days or weeks later because pollen and nectar are stored in the hive. Furthermore, different categories of bees could be exposed in different ways and to varying extents. For example, pollen foragers (which differ from nectar foragers) do not consume pollen, merely bringing it to the hive. The pollen is consumed by nurse bees and to a lesser extent by larvae (Rortais et al., 2005).

The exposure of nectar foragers to imidacloprid contained in the nectar they gather can vary depending on the resources available in the hive environment. In addition, foragers take some nectar or honey already stocked in the hive before they leave for foraging. Depending on the distance from the hive where they forage, the honeybees are obliged to consume more or less of the nectar/honey taken from the hive and/or of the nectar collected, for energy for flying and foraging. They can therefore ingest more or less imidacloprid.

In 2002, Bayer publicly declared that the levels of exposure of honeybees to imidacloprid present in pollen and nectar ranged between 0 and 5 ppb (AFSSA, 2002).

Honeybee exposure to imidacloprid: 2003–2006

Based on exposure assessments and using scientific quality criteria to select among the available measurements, CST validated the findings of 3.3 ppb of imidacloprid in the pollen of Gaucho®-treated sunflowers, 3.5 ppb in pollen of Gaucho®-treated maize, and 1.9 ppb in the nectar of Gaucho®-treated sunflowers (CST, 2003).

([10]) In the original French: 'Les résultats ont généré des suspicions sur l'effet du produit, sans pour autant prouver formellement sa responsabilité.'
([11]) Comité Scientifique et Technique de l'Etude Multifactorielle des Troubles des Abeilles.

After seed treatment, imidacloprid transforms in the plant (metabolised) into many derivatives (metabolites), more or less completely. The main metabolites are 5-hydroxy-imidacloprid, 4-hydroxy-imidacloprid, 4-5 hydroxy-imidacloprid, olefin, imidacloprid-guanidine, imidacloprid-urea and 6-chloronicotinic acid.

Although two ([12]) of these metabolites show acute toxicity for honeybees (olefin and 5-hydroxy-imidacloprid), no study measuring metabolites in sunflower nectar or in sunflower and maize pollen, could be validated by the CST. For this reason, this committee recommended the development of detection and quantification limits low enough for their identification and quantification in pollen and nectar.

Lethal and sublethal effects

Pesticides can produce four types of effects on honeybees: acute or chronic lethal effects and acute or chronic sublethal effects.

- **Acute lethal effects** are expressed as the lethal dose (LD) at which 50 % of the exposed honeybees die within 48 hours: abbreviated to 'LD_{50} (48 hours)'.

- **Chronic lethal effects** refer to honeybee mortality that occurs after prolonged exposure (e.g. about 10 days).

In contrast to acute lethal effects, there were no standardised protocols for chronic lethal effects. Therefore, for imidacloprid, they were expressed in three ways:

- LD_{50}: the dose at which 50 % of the exposed honeybees die within 10 days;

- NOEC (No Observed Effect Concentration): the highest concentration of imidacloprid producing no observed effect;

- LOEC (Lowest Observed Effect Concentration): the lowest concentration of imidacloprid producing an observed effect.

Sublethal effects are modifications of factors such as honeybee behaviour, physiology and immune system. They do not directly cause the death of the individual or the collapse of the colony but may become lethal in time and/or may make the colony more sensitive (for example, more prone to diseases), which may lead to its collapse. For instance, an individual with memory, orientation or physiological impairments might fail to return to its hive, dying from hunger or cold. This would not be detected in standard pesticide tests, which focus on acute mortality. In addition, a key aspect in honeybee biology is that the colony behaves as a 'superorganism' ([13]). Hence, sublethal effects affecting individuals performing specific functions can influence the functioning of the whole colony. As was the case for chronic lethal effects, standardised protocols for sublethal effects were lacking.

- **Acute sublethal effects** of imidacloprid and its metabolites were assessed by exposing honeybees only once to the substance (by ingestion or by contact), and observing them for some time (variable from one laboratory to another, from several minutes to four days).

- **Chronic sublethal effects** were assessed by exposing honeybees more than once to the substance during a certain period of time (for example, each 24 hours, for 10 days).

Both acute and chronic sublethal effects are expressed as NOEC and/or LOEC.

Studies of lethal and sublethal effects: 1997–2000

Whereas intoxication by sprayed pesticides is usually confirmed by the numerous dead and moribund honeybees in front of the hives, beekeepers reported disappearance of most foragers in many hives. This lead them to hypothesise that imidacloprid was affecting the general mobility and/or orientation of the honeybees.

From 1999 onwards, **Bayer-funded scientists** also conducted studies on chronic lethal and sublethal effects. They found much lower values of LOEC for imidacloprid than previously reported. Whereas three Bayer scientists (Ambolet, Crevat and Schmidt)

([12]) The other four metabolites do not show any particular toxicity for honeybees.

([13]) Moritz and Southwick (1992) define superorganisms as 'superorganismic units with organisms arranged in at least two non-uniform types and differentiated into sterile and reproductive organisms with different functions' (p. 4). They highlight that superorganisms should not be confounded with social groups because, among other things, 'superorganisms need a sufficient membership so that the number of organisms involved in a task rather than the individual quality of how a task is performed becomes important' (p. 5). These numerous colony members function as a cooperative unit. Superorganisms maintain intraorganismic homeostasis (food storage, nest hygienic) and they are either well armed or highly cryptic. Superorganisms only originate from other superorganisms. For example in the case of bees a large part of a colony with a fertile queen undergoes 'fission' from the initial population and forms a swarm. 'In the end, however, only one feature really counts. It makes absolutely no sense invoking such a definition if natural selection does not act upon the superorganism itself. As long as natural selection is only working on individuals we have no need for such an additional perspective' (p. 6).

had reported a LOEC value of 5 000 ppb at the Fourth International Conference on Pests in Agriculture (6–8 January 1997), the new estimates were just 20 ppb, equivalent to 0.5–1.4 ng per honeybee (Kirchner, 1998, 1999 and 2000).

Other values found in 1999 and 2000 by **Bayer-funded scientists**, for the **highest concentrations which do not produce** sublethal effects (**NOEC**) ranged from 0.25–0.7 ng/honeybee (10 ppb) (Kirchner, 1999, 2000) to 0.94 ng/honeybee, 1.25–3.5 ng/honeybee, 1.5 ng/honeybee, 8.2 ng/honeybee, and 9 ng/honeybee (Schmitzer, 1999; Schmuck and Schöning, 1999; Thomson, 2000; Wilhelmy, 2000; Barth, 2000).

Among the **lowest concentrations at which imidacloprid produces** sublethal effects (**LOEC**), **public researchers** reported: 0.075–0.21 ng/honeybee (3 ppb); 0.15–0.42 ng/honeybee (6 ppb); 0.25–0.7 ng/honeybee (10 ppb), and 0.31–0.87 ng/honeybee (12.5 ppb) (ACTA, 1998; Pham-Delègue, 1998; Pham-Delègue and Cluzeau, 1998; Colin, 2000; Colin and Bonmatin, 2000; Colin et al., 2002).

To enable comparison between the data obtained by Bayer and those obtained by public scientists, we note that, by definition, NOEC is the test concentration **immediately below** the LOEC. The NOEC values corresponding to data produced by public scientists were, by definition, below the LOEC values that they generated and which are presented here.

Having said this, one might find strange that among the values above, the **NOECs** from Bayer are **larger** than most of the **LOEC** obtained by public scientists. However, this strange result can be partially explained by the fact that the values of NOEC of Bayer come from sublethal **acute** intoxication, whereas the two values cited from public scientists are sublethal **chronic** values.

Indeed, the differences between the values above might arise from different sources. For example, as no standard tests existed, the laboratories used differing testing protocols. In addition, various sublethal effects were studied (knockdown effect, locomotion coordination, quantity of syrup ingested, pollen consumption, wax production, parent recognition, memory, visits to the food source, odour recognition, etc.). Of course, the results depend on what, and how, one measures.

Studies of lethal and sublethal effects: 2001–2004

In 2001, **public scientists** identified chronic lethal effects at LD_{50} = 12 pg/honeybee after 10 days of feeding with imidacloprid-containing syrup (0.1 ppb) (Suchail, 2001).

In 2002, **Bayer** declared that 'Bayer's studies established that below 20 ppb, no negative effect can be observed on honeybee colonies' ([14]) (AFSSA, 2002).

Properties of imidacloprid: persistence in soils and presence in untreated crops

In its dossier submitted to the Ministry of Agriculture (Bayer, 1999), **Bayer** quoted half-lives for Gaucho® (DT50) ([15]) of 188 ± 25 days and 249 ± 40 days for two soil types. It should be noted that this exceeds the threshold of three months established in EU Directive 91/414/EEC (Annex VI, Part C, point 2.5.1.1) for conducting detailed ecotoxicological studies:

> 'No authorization shall be granted if the active substance and, where they are of significance from the toxicological, ecotoxicological or environmental point of view, metabolites and breakdown or reaction products, after use of the plant protection product under the proposed conditions of use during tests in the field, persist in soil for more than one year (i.e. DT90 > 1 year and DT50 > 3 months) […] unless it is scientifically demonstrated that under field conditions there is no accumulation in soil at such levels that unacceptable residues in succeeding crops occur and/or that unacceptable phytotoxic effects on succeeding crops occur and/or that there is an unacceptable impact on the environment...'

Gaucho® was authorised in France on the basis of this EU Directive and a French regulation ([16]).

The average levels of imidacloprid found in the soil by **public scientists** were 10.25 ppb during the year that the crop was treated with Gaucho® and 4.4 ppb the following year (Bonmatin et al., 2000).

([14]) In the original French: 'Les études Bayer ont établi que jusqu'à 20 ppb, aucun effet négatif ne pouvait être observé sur des colonies d'abeilles'.
([15]) DT50 is the degradation half-life, or period required for 50 % dissipation/degradation of the initial concentration of substance. DT90 is the time needed for the dissipation/degradation of 90 % of the initial concentration of substance.
([16]) Arrêté du Ministre de l'Agriculture de 6 septembre 1994 portant application du décret no 94-359 du 5 mai 1994 relatif au contrôle des produits phytopharmaceutiques, modifié par l'arrêté du 27 mai 1998.

16.2.2 Methodological quality of the evidence

Method of risk assessment

The risk of sprayed ('classic') pesticides to honeybees were assessed using mortality studies in laboratory conditions, followed by semi-field studies and finally field studies (Halm et al., 2006). The first step in such studies is to calculate a hazard quotient (HQ = the field application rate/oral or contact LD_{50}) (OEPP/EPPO, 2003). Further studies are demanded if the HQ exceeds a certain threshold (Halm et al., 2006).

Bayer used the LD_{50} methodology in its dossier applying for marketing authorisation for Gaucho® (Bayer, 1999). However, the methodology based on LD_{50} is designed to assess the risk of sprayed pesticides and has been shown to be inappropriate for seed-dressing systemic insecticides for several reasons:

- Seed-dressing systemic insecticides are applied on seeds and disperse in the plant during growth. The field application rate of active substance as an exposure parameter is therefore a highly inadequate measure for the true exposure of honeybees (Halm et al., 2006). What is important for the effects of seed-dressing insecticides on honeybees is not the amount applied per hectare, but the amount of imidacloprid (and metabolites) in the pollen and nectar.

- Both acute and chronic effects are important for the colony (given the clinical signs observed), whereas LD_{50} only considers the acute effects on adult honeybees.

- Seed-dressing systemic insecticides can have sublethal effects affecting the performance of the whole colony, not just individuals, because foragers can bring the pesticide inside the hive via pollen and nectar.

- The risks of seed-dressing systemic insecticides vary, depending on the age and role of the honeybees in the colony (Rortais et al., 2005).

Consequently, the risk assessment procedure that the **CST** chose for imidacloprid was based on evaluating the ratio PEC:PNEC. This approach, which is used to assess the environmental risk of industrial chemicals, allows comparisons between the levels of exposure (Predicted Exposure Concentration — PEC) and toxicity (Predicted No Effect Concentration — PNEC), and considers both lethal and various sublethal effects in the short and longer term, for different age groups and casts of honeybees and for different matrices (e.g. honey and pollen) (Halm et al., 2006). Thus, the PEC:PNEC approach results in a probability (risk) that effects found in controlled studies of specific items of toxicity are found in real conditions.

Field and laboratory studies

The **Bayer-funded scientists** and **public scientists** disagreed about the relative relevance of laboratory and field studies ([17]). Bayer held that the results of field experiments would either prove or disprove the risk of the active substance, regardless of whether they conformed to the results of laboratory studies. The public scientists argued that field studies cannot be decisive for deciding on the risk of a pesticide to honeybees.

The principle of an experiment is to vary one factor, keeping all the others constant. This cannot be done in current field experiments with bees, because the combination of abiotic and — especially — biotic factors is never identical in control fields (where the insecticide has not been used) and test fields. Bee

Photo: © istockphoto/Youra Pechkin

([17]) A distinction is made between 'field experiments' and 'monitoring', which measures clinical signs in real conditions.

colonies themselves are not identical, and the food sources available in the environment for honeybees are always diverse.

Furthermore, in field tests, it is impossible to prevent honeybees visiting fields not in the experiment. For example, the distance separating control and test areas is often too small to prevent bees foraging in other fields ([18]). Many differences have been reported in honeybees' mortality, both by beekeepers and during open field experiments (CST, 2003). Therefore, it is probable that observations made in a particular field experiment are not representative of the range of effects that could occur in real conditions. Due to the large variability of factors that cannot be controlled (e.g. soil structure, climate, combination of plants attractive for bees etc.), current field experiments only give information about the particular situation in which they were done.

In the end, it was not a scientific institution but the highest judicial administrative institution in France, the **State Council**, that decided (29 December 1999) that the results of both field experiments and laboratory studies may be legitimately used in risk assessment (Fau, 2000). This is common practice in risk assessment of chemicals, which is based on the PEC:PNEC ratio.

16.3 Processes of generating knowledge and assessing risk

16.3.1 Knowledge producers: public scientists

Public scientists were in a very difficult position in this case. The results of their work were central to a social debate with high economic and political stakes. In certain cases their work was not judged based on scientific merits but whether or not it supported the positions of certain stakeholders. This situation challenged the ability and courage of researchers to continue their work on imidacloprid.

One stated: 'From the beginning of the programme, in January 1998, I personally received a letter from Bayer threatening me with a lawsuit for defamation' ([19]) (AFP, 2003). The letter written by Bayer's lawyers warned of both judicial action and financial reparations (personal letter).

Bayer also wrote a letter to the researcher's hierarchical superior, asking him to use his position to influence the researcher's interventions in the press (personal letter). The superior refused the demand of Bayer but advised his researcher to take extreme care with the press.

Another researcher said: 'I worked for three years on the topic and the management… my managers […], asked me to change topic' ([20]) (Elie and Garaud, 2003).

In 2000, one public scientist acquired European funds to analyse the risk of imidacloprid to honeybees. However, the researcher's hierarchical superior suddenly stopped the programme, even though the researcher had already produced some first results in previous studies on imidacloprid, the funding was confirmed and the work had both social and scientific relevance (personal communication).

We lack information about the experiences of Bayer-funded scientists. During the process of reviewing this chapter a Bayer researcher was directly asked for such information but none was provided.

16.3.2 Official evaluators of evidence of the risk of Gaucho® to honeybees

Commission for Toxic Products (CTP)

In 1993, in the light of Bayer's claims that honeybees were not exposed to imidacloprid applied in seed-dressing, the Commission for Toxic Products (CTP) ([21]) issued an assessment in favour of

([18]) Semi-field (tunnel) studies are also unable to provide a decisive indication of a pesticide's risk to honeybees for several reasons. First, the quantity of food and the time of exposure to the contaminated source are much less important in semi-field experiments than in real conditions. Second, one cannot know if the honeybees really consume the collected pollen and nectar (contaminated for the purpose of the test) or if they continue to consume the reserves already present in the hive at the beginning of the experiment. Third, the foraging distance is very small, and therefore some distance-dependent behavioural effects (for instance, orientation troubles) may not be seen under semi-field experiments but could appear in real conditions, when honeybees have to forage far from the hive.

([19]) In the original French: 'Dès le début du programme, en janvier 1998 j'ai reçu personnellement une lettre de Bayer me menaçant d'un procès en diffamation.'

([20]) In the original French: 'J'ai travaillé trois ans sur le sujet et la direction… ma direction […], m'a demandé de changer de sujet.'

([21]) La Commission d'étude de la toxicité des produits anti-parasitaires à usage agricole et des produits assimilés, des matières fertilisantes et des supports de culture, known as Commission for Toxic Products, was under the aegis of the Ministry of Agriculture. It was composed of experts in toxicology and eco-toxicology. Its remit was to analyse authorisation dossiers from toxicological and eco-toxicological points of view. In 2006, the Commission was replaced by expert groups headed by the French Food Safety Agency AFSSA (called DIVE).

authorising Gaucho®, without consulting its specialist Honeybee Working Group ([22]).

After the emergence of clinical signs in the field and the first evaluation report (Belzunces and Tasei, 1997), the assessment of the CTP (11 December 1997) was ambiguous. It found that in the light of the information available, it was impossible to confirm or deny a causal link between the use of Gaucho® and honey yield losses. The CTP continued to issue ambivalent assessments until December 2002.

From 1997 to 2001, the CTP considered that there was not enough knowledge to pronounce clear conclusions and repeatedly recommended further studies. For example, in 1997: 'The demonstration, made by Bayer that Gaucho® is not involved, is not made in a rigorous and complete manner. On the other hand, the declarations coming from beekeepers are not rigorous and stable enough for saying that Gaucho® is the **only** ([23]) cause of honeybee colonies problems' ([24]) (CTP, 1997).

In 1998 the CTP stated that, 'the data examined do not allow us to conclude to an **unquestionable effect** of imidacloprid and/or of its metabolites on honeybees and honey production. Conversely, it is also not possible **to completely exclude** the effect of imidacloprid and/or its metabolites, given the toxic effect at low doses, which have to do with the concentrations potentially present in the plants at the foraging time' ([25]) (CTP, 1998).

In 2002, the conclusion of the CTP was expressed in unclear language and referred vaguely to all honeybee losses in France instead of focusing on the clinical signs observed in areas of intensive agriculture: 'The risk assessment does not allow us to demonstrate that maize seed-dressing with Gaucho® can be **solely** responsible, at national level, for **all** colony losses, behavioural troubles, honeybee mortalities or general decline in the honey production' ([26]) (CTP, 2002, p. 22).

In all these cases, the CTP conclusions were answering a question that had never been asked, that is, is Gaucho® responsible for all honeybee losses, **everywhere in France**? They thus avoided a clear answer to the question really asked: is Gaucho® responsible for honeybee losses **in intensive sunflower and maize seed-dressed cultures**?

The CPT lacked clear operating procedures and the assessment of the dossiers submitted by companies during the authorisation processes was based on unstructured expert judgement. It did not involve a systematic reflection on the quality of the results presented in these dossiers, based on clear assessment criteria. During their meetings, the workload was such that members of the CTP were often dealing with several dossiers simultaneously and therefore could not have in depth discussions on each of them.

While the CTP issued advice to the Ministry several times during 1997–2002, only one member of the CTP was a bee specialist. The CTP had a Honeybee Working Group but this was not consulted until late in the debate (in 2000). A former member of the CTP argued that they were not consulted earlier because two members were beekeepers and were considered to have an interest in banning Gaucho® (personal communication). Even in the Honeybee Working Group, honeybee scientists were under-represented. Overall, the divergent data coming from different sources, the lack of sufficient expertise on honeybee biology and the absence of enough time and rigorous criteria for evaluating the dossiers, all contributed to producing ambiguous advice.

State Council

In the case of Gaucho®, different stakeholders, persons, and evaluation and decision bodies used varying criteria to judge the quality of the scientific evidence available. Thus, in contrast to the CTP, which was formally charged with assessing the

([22]) The Honeybee Group was a CTP working group set up to report the risks to honeybees of plant protection products (PPP) submitted for authorisation for marketing. It advised on awarding a product the 'honeybee label' indicating that it poses no risk to honeybees when used on flowering plants.

([23]) The underlining in this quote and all subsequent quotes has been added by the authors of the present paper.

([24]) In the original French: 'La démonstration par Bayer que le Gaucho est hors de cause n'est pas établie de façon suffisamment rigoureuse et complète. D'autre part, il n'y a pas assez de rigueur et de stabilité dans les rapports de terrain provenant des apiculteurs pour affirmer que le Gaucho est la seule cause de troubles dont les colonies d'abeilles sont victimes.'

([25]) In the original French: 'Les données examinées ne permettent pas de conclure à un effet indiscutable de l'imidacloprid ou de ses métabolites sur les abeilles et la production de miel. Inversement, il n'est pas possible d'exclure totalement l'effet de l'imidacloprid et de ses métabolites, compte tenu de l'effet toxique à faible doses, doses en rapport avec des concentrations potentiellement présentes dans les plantes à l'époque du butinage.'

([26]) In the original French: 'L'évaluation du risqué réalisée ne permet donc pas de démontrer que le traitement de semences de maïs par la préparation Gaucho puisse être le seul responsable au niveau national de l'ensemble des dépopulations de ruches, des troubles comportementaux, des mortalités d'abeilles et plus globalement de la baisse de production apicole.'

conformity of the existing evidence with the regulatory demands for pesticides risk assessment, the State Council employed legal criteria, assessing conformity with the law.

The first intervention of the State Council was in 1999, immediately after the ban on using Gaucho® on sunflower seeds, when Bayer mounted a legal challenge to the ministerial decision. About that time, several international consortia of seed producers (Monsanto, Novartis, Rhône-Poulenc, Pionneer, Maisadour and Limagrain) rallied behind Bayer and formulated a similar case against the Minister's decision. The beekeepers syndicate UNAF ([27]) co-defended the Minister's decision in court. The State Council decided in favour of the beekeepers and the Minister, judging that the Minister's precautionary decision was based on an appropriate evaluation of the results from the 1998 scientific programme and the conclusions of the CTP, which expressed doubts about the harmlessness of Gaucho® for honeybees.

The State Council was involved again in 2002 and 2004, calling on the Minister to reconsider his decisions refusing to ban Gaucho® in maize seed-dressing (see Section 16.4.2), on the grounds that the Ministry had not rightly evaluated its harmlessness in the way demanded by French legislation ([28]). In its conclusion in 2002, the State Council pointed out that, given the reasons for concern about Gaucho®, the Ministry should have examined all the necessary data to evaluate its effects on honeybees in maize seed-dressing. That is, the Ministry should have asked for quantification of the use of maize pollen by honeybees, as well as of the nature and intensity of the effects on honeybees of maize pollen containing imidacloprid. In 2004, the State Council again stated that the CTP's risk assessment of Gaucho®-treated maize for the Ministry failed to comply with the law as the effects on larvae had not been assessed.

Other cases in court

In 2001, Bayer took three representatives of beekeepers' syndicates to court in their home towns (Châteauroux, Mende and Troyes), accusing them of discrediting Gaucho® (GVA, 2001). In all cases, the courts decided in favour of beekeepers, based on the freedom of the syndicates to play their role in society and to express their opinions publicly. One of the courts explicitly criticised the attempt of Bayer CropScience to intimidate a syndicate leader who was defending the interests of his profession (UNAF, 2004).

An investigation into Gaucho® was launched in a court in Paris, following a charge brought by UNAF in 2001. The investigation continues to stagnate. Since its beginning, two judges have been replaced for different reasons. The judge currently dealing with the case has proceeded with new interrogation of experts and parties involved. In March 2011, the judge was still investigating the available evidence, in order to decide if there will be a trial or not.

16.3.3 Scientific and Technical Committee

Based on the analysis of 338 bibliographical references, the CST concluded that seed-dressing sunflower and maize posed serious risks to honeybee colonies via larvae feeding, pollen consumption by nurses, nectar ingestion by foragers, and honey consumption by honeybees living inside the hive:

> 'Based on our current state of knowledge and on the scenarios we developed to evaluate exposure, and based on the uncertainty factors chosen to evaluate the dangers, the PEC:PNEC ratios determined are of concern. They are in agreement with the field observations reported by numerous beekeepers' areas of intensive corn and sunflower growing, relating to the mortality of foragers (scenario 4), their disappearance, behavioural disturbances and certain winter mortalities (scenario 5). Consequently, the dressing of sunflower seeds with Gaucho® poses significant risks for bees of different ages, with the exception of the pollen ingestion by foragers during the making of pollen balls (scenario 3).
>
> 'Regarding corn seed dressed with Gaucho®, the PEC:PNEC ratio turns out to be, as for the sunflower, of concern in the case of pollen consumption by nurse bees, which would lead to an accrued mortality of these and be one of the explanatory elements for the weakening of bee populations observed

([27]) UNAF (Union Nationale de l'Apiculture Française) is one of the three French beekeeping syndicates, representing about 22 000 beekeepers.
([28]) Arrêté du 6 septembre 1994.

despite the ban on Gaucho® on sunflowers. Finally, given that other factors can contribute to the weakening of bee colonies, research should be continued on the frequency, mechanism and causes of these clinical signs' ([29]) (CST, 2003, p. 11).

Although the interim CST report on the risks of Gaucho® to honeybees was completed in 2002, DGAL (the General Directorate for Food, within the Ministry of Agriculture) did not submit it then to the Management Committee ([30]) of the CST. Just before publication in 2003, the Ministry of Agriculture withdrew its logo. One interpretation of this was that it emphasised the independence of the CST, alternatively it could be seen as demonstrating that the Ministry of Agriculture did not want to show any support for the results. This last interpretation is reinforced by a post-publication letter from the DGAL, in which the Directorate considered that the findings of CST were too precise and asked for more studies.

16.4 Societal debate and the policy responses

16.4.1 Stakeholder strategies

Beekeepers systematically presented and compared the results of studies conducted by Bayer, the Ministry of Agriculture, public research and their own field observations. Their objective was to make the results public in order to show the congruity of their own observations with the scientific results and to mobilise civil society for support. The beekeeping sector was supported by civil society, as the issues were of major concern to the French public. The sector's arguments received good coverage in the national press.

DGAL's public statements were ambiguous. Its lack of transparency undermined trust: for example, when beekeepers' requested the authorisation dossier for Gaucho®, DGAL only released limited information (Clément, 2000). DGAL communicated all the documents requested by beekeepers only after intervention from both the Minister of Agriculture himself and the Commission for Access to Administrative Documents.

There was variance in the public positions of different ministries of the French government and different services within the Ministry of Agriculture. The decisions of the Ministers of Agriculture to suspend the use of Gaucho® in seed-dressings for sunflower (1999, 2001, 2003) and maize (2004) contrasted with DGAL's procrastination.

Bayer had an inappropriate communication strategy on scientific figures, which contributed to increasing mistrust from the other stakeholders. For example, in 2002, Bayer publicly acknowledged exposure 'between 0 and 5 ppb, which is the quantification limit' ([31]) (AFSSA, 2002, p. 32). This statement represented a major step forward in Bayer's communication of scientific figures but was still vague about the information available on imidacloprid. However, Bayer-funded scientists had already obtained precise figures for sunflower, i.e. 3.3 ppb in pollen and 1.9 ppb in nectar (Stork, 1999) ([32]). In addition, between 2000 and 2001 public scientists had also reported quantification limits well below 5 ppb, i.e. 1 ppb for quantifying imidacloprid in pollen and nectar (Lagarde, 2000, Bonmatin et al., 2001) and detection limits of 0.3 ppb for pollen (Bonmatin et al., 2001) and 0.8 for nectar (Lagarde, 2000). These quantification and identification limits, as well as the precise measures of imidacloprid in pollen and nectar, available from public scientists, were ignored by Bayer in its statements on Gaucho® despite being publicly available ([33]).

([29]) In the original French: 'Dans l'état actuel de nos connaissances, selon les scénarios développés pour évaluer l'exposition et selon les facteurs d'incertitude choisis pour évaluer les dangers, les rapports PEC/PNEC obtenus sont préoccupants. Ils sont en accord avec les observations de terrain rapportées par de nombreux apiculteurs en zones de grande culture (maïs, tournesol), concernant la mortalité des butineuses (scénario 4), leur disparition, leurs troubles comportementaux et certaines mortalités d'hiver (scénario 5). En conséquence, l'enrobage de semences de tournesol Gaucho® conduit à un risque significatif pour les abeilles de différents âges, à l'exception de l'ingestion de pollen par les butineuses lors de la confection de pelotes (scénario 3).
'En ce qui concerne l'enrobage Gaucho® de semences de maïs, le rapport PEC/PNEC s'avère, comme pour le tournesol, préoccupant dans le cadre de la consommation de pollen par les nourrices, ce qui pourrait entraîner une mortalité accrue de celles–ci et être un des éléments de l'explication de l'affaiblissement des populations d'abeilles encore observé malgré l'interdiction du Gaucho® sur tournesol. Enfin, étant donné que d'autres facteurs peuvent contribuer à l'affaiblissement des colonies d'abeilles, il convient que les recherches soient poursuivies sur la fréquence, les mécanismes et les causes de ces symptômes.'

([30]) The Management Committee's remit was to supervise the scientific, economic and regulatory aspects of the CST's work and to ensure communication with the Minister of Agriculture, stakeholders and the public.

([31]) In the original French: 'comprise entre 0 et 5 ppb, qui est la limite de quantification'.

([32]) The data obtained by Bayer using radiolabelled imidacloprid have been published in 2001 (Schmuck et al., 2001).

([33]) For instance, Apiservices (2001) presents a synthesis of the available data and was published online on 16 February 2001.

Bayer steadfastly maintained that using Gaucho® in sunflower seed-dressing had no effect on honeybees (Bayer CropScience, 2006). In 2006, the case dossier on the company's website did not mention the CST's conclusion that 'in the actual state of our knowledge […] the PEC:PNEC ratios obtained are worrisome' ([34]), or the findings from French public scientists regarding the risks of Gaucho® for honeybees ([35]).

16.4.2 Policy response to scientific evidence on risk

A dossier prepared by the Ministry of Agriculture (2001c) frames the 1999 decision of the Minister to ban Gaucho® on sunflower in the following terms:

> 'The Ministry of Agriculture has conducted a first series of laboratory studies, as well as field studies in three test departments: Vendée, Indre and Deux-Sèvres. The results yielded suspicions about the effects of the product, without, however, formally proving its responsibility. **Applying the precautionary principle**, the Minister of Agriculture has decided, in January 1999, to temporarily ban the product in sunflower seed-dressing' ([36]).

The Minister of Agriculture's ban on Gaucho® as maize seed-dressing was introduced later. The stakes were higher for Bayer (only 10 % of Gaucho® revenue came from use on sunflower, the area under maize in France being 2.5 times that under sunflower ([37])), for farmers, for beekeepers, for the general public (as articulated by the media) and probably for the Minister himself as a politician. In addition to the economic importance of maize, it is frequently cultivated without rotation. Therefore the pressure from pests (and maize growers) can be higher than for sunflower. Justifying his decision not to ban Gaucho® in maize seed-dressing, the Minister of Agriculture stated to the State Council that maize does not produce nectar and therefore honeybees do not visit this plant for producing honey, apparently unaware that honeybees do, however, visit maize to collect its pollen, which they consume (Conseil d'Etat, 2002).

Although a procedure for the reversal of this authorisation was under way at the State Council, on 21 January 2002 the Ministry of Agriculture renewed the authorisation of Gaucho® on maize for ten more years. Subsequently, the judicial inquiry on Gaucho® was extended to challenge this renewed authorisation (Saunier, 2005). In October 2002 the State Council concluded its re-examination of the scientific evidence and advised the Minister to reconsider his decision. In 2003, the Minister of Agriculture refused again to ban the use of Gaucho® in maize seed-dressing. In September 2003 the CST concluded that imidacloprid in maize seed-dressing posed a serious risk to honeybees (specifically the nurses consuming pollen). Again, in March 2004, the State Council advised the Minister to reconsider their decision but it was not until July 2004 that this use of Gaucho® on maize was banned. The press release communicating the Ministry's decision refers to the CST report, and states that 'the risk for honeybees seems less important than in case of sunflower seed-dressing because exposure occurs only via pollen but is, however, of concern' ([38]) (Ministère de l'Agriculture, 2004).

Prior to this, in a letter published on 21 November 2003, the head of the Bureau for the Regulation of Pesticide Products of the DGAL had revealed various shortcomings of the official risk assessment and management procedure: there were only three public servants to deal with 20 000 applications for authorisation per year; risk assessments were performed jointly with the industry; there was lack of transparency in the procedures; and insufficient attention was paid to the issue of pesticide residues in food during the risk assessment. In consequence,

([34]) In the original French: 'Dans l'état actuel de nos connaissances [...] les rapports PEC/PNEC obtenus sont préoccupants.'

([35]) On the Bayer CropScience France website (www.bayercropscience.fr) in 2006, there was a file entitled 'Honeybees'. In November 2009, on this website, if one searches for 'honeybee' ('abeille'), no document can be found. On the website of Bayer Cropscience World, searching 'honeybees' gives no specific reference to Gaucho®, but searching 'Gaucho' results in some documents on the French case. Among them, the document referring to the ban of Gaucho® on maize still does not mention the conclusions of the CST or of French scientists. In January 2011, seaching for honey + bee + gaucho gives 1 result, referring to the judgement of the court of Chateauroux, whereas searching bee + gaucho gives 14 results, among which 4 refer to honeybees.

([36]) In the original French: 'Le ministère de l'Agriculture et de la Pêche a conduit une première série d'études en laboratoire, comme sur le terrain dans trois départements tests: la Vendée, l'Indre et les Deux-Sèvres. Les résultats ont généré des suspicions sur l'effet du produit, sans pour autant prouver formellement sa responsabilité. En application du principe de précaution, le ministre de l'Agriculture et de la Pêche a décidé en janvier 1999 le retrait provisoire de l'autorisation de mise sur le marché du produit sur traitement de semences de tournesol.'

([37]) Official figures from the website of the Ministry of Agriculture (Agreste, 2011) for the year 2000 put the area used for maize at 1 764 767 ha and for sunflower 728 555 ha.

([38]) In the original French: 'le risque pour les abeilles, s'il apparaît moins important que dans le cas de l'usage pour l'enrobage des graines de tournesol du fait de la seule exposition au pollen, reste préoccupant.'

the Bureau chief concluded, 'it is impossible for the Bureau to accomplish its mission' ([39]).

16.4.3 Costs and benefits of the policy responses

In the last 20 years, the **chemical industry** has been increasingly regulated. Directive 91/414/EEC required the reassessment of active substances contained in plant-protection products already on the EU market. Many active substances have since been withdrawn. Furthermore, some pests have developed resistance to formerly used pesticides.

European manufacturers of agricultural chemicals face higher research and development costs. On average, it costs some USD 50 million to develop a new product. Nevertheless, systemic insecticides represent a highly profitable investment. For example, imidacloprid-based insecticides ([40]) brought Bayer DM 800 million of global sales in 1998 (approximately EUR 409 million) (Bayer, 1998) and EUR 556 million in 2007 (Bayer CropScience, 2008). Furthermore, focusing on these products also represents a networking investment for the industry because partnerships are made with seed producers and distribution chains. We do not have information about the economic consequences for the chemical industry of banning Gaucho® or RégentTS® in France.

The economic situation of the **French beekeeping sector** worsened significantly between 1994 and 2004. In 1994, there were 1 370 220 beehives and 84 800 beekeepers. By 2004, there were 1 360 973 beehives and 68 800 beekeepers (GEM-ONIFLHOR, 2005). Many small producers abandoned beekeeping in the interim. The apparent stability of the number of hives between 1994 and 2004 belies the higher turn-over of colonies to replace those lost. The decrease in the sunflower average honey yield (Belzunces and Tasei, 1997; CNEVA Sophia-Antipolis, 1997; Pham-Delègue et Cluzeau, 1998; Coordination des Apiculteurs, 2001; Alétru, 2003), and the increase in colony mortality forced professional beekeepers to increase the number of hives to compensate for their losses.

The relative contribution of insecticides and other factors (e.g. the international market for honey and honeybee diseases) to the decline of French beekeeping is unclear. France's honey imports per annum rose from 6 000 tonnes in 1993 to 17 000 tonnes in 2004, whereas domestic honey consumption stayed constant at about 40 000 tonnes per annum (GEM-ONIFLHOR, 2005). A study of the cooperative France Miel ([41]) for western France showed that severe losses in the sunflower honey yield started in 1995 and continued over the following years (Figure 16.1).

Data similar to those obtained for western France exist for the cooperative Poitou-Charentes (Figure 16.2) and for the department of Deux-Sèvres, produced by the Agricultural Chamber (Chambre d'Agriculture). In 2005, the important decrease in the production of sunflower honey is also referred to in a national audit report of the beekeeping branch (GEM-ONIFLHOR, 2005).

These data are not exhaustive but they show that the losses of sunflower honey yield were significant, started around 1994 and continued in the following years.

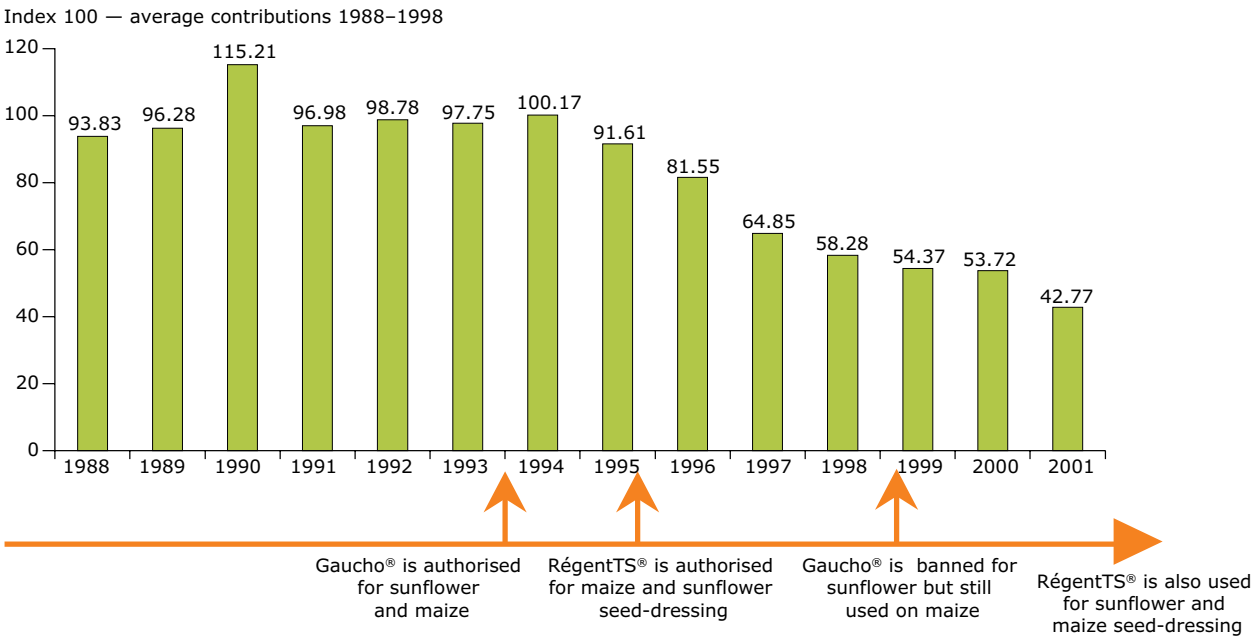
Among the beekeeping sector's expenses, there was also additional outlay on research (funding research to assess the risk of Gaucho® and RégentTS® through European funds for beekeeping) and legal fees (for the different judicial interventions). The financial burden was double because the funds had been intended to support the development of beekeeping. Having been spent on defending beekeepers' stakes in the debate, some could not be used to achieve the development goals.

The beekeepers have not been compensated for their economic losses but after 2003, France was granted financial support from the European Commission to restore honeybee colonies, as general support for beekeeping in a time of economic hardship.

In the **agricultural sector**, the economic repercussions are unclear. A large proportion of French crops (such as sunflower, maize and cereals) were rapidly given seed-dressing protection, even when pest control was rarely needed (for example for sunflowers). The Technical Center for Oilseed Crops (CETIOM) website specifies ([42]) that 'sunflower has a low attractiveness for [click beetle]

([39]) 'Trois fonctionnaires pour traiter 20 000 demandes d'autorisation par an, 'une cogestion de l'évaluation des risques avec les industriels', 'une absence de transparence dans les procédures'. 'En matière d'évaluation des risques, le domaine des résidus de pesticides dans les aliments est insuffisamment couvert.' Enfin, 'Le bureau est dans l'impossibilité de remplir ses missions.' (Le Point, 21 November 2003).
([40]) Gaucho®, Confidor®, Admire® and Provado® in 1998 and Confidor®, Admire®, Gaucho® and Merit® in 2007.
([41]) Additional figures for the evolution of sunflower honey are available in France Miel (2000).
([42]) This information has been already present on this website in 2003.

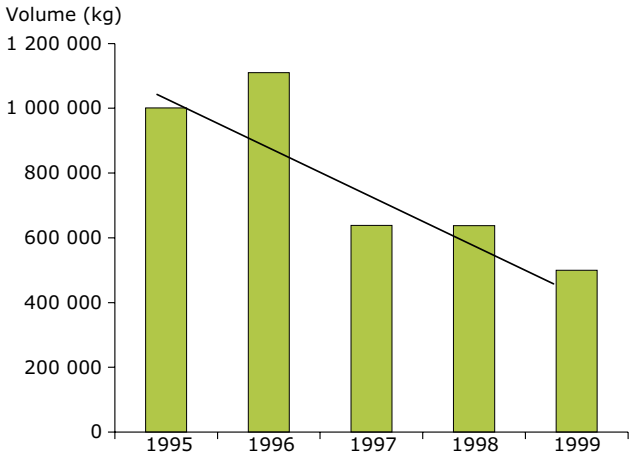
Figure 16.1 Sunflower honey harvest in western France (*)



Note: * The method for obtaining these data was communicated to Laura Maxim by France Miel. The quantities of sunflower honey comprise all the quantities brought to France Miel between 1988 and 1998 by a representative sample of professional beekeepers providing honey to France Miel, from the departments 72 (Sarthe), 49 (Maine-et-Loire), 85 (Vendée), 17 (Charente-Maritime), 33 (Gironde) and 32 (Gers). The vertical axis represents an index 100 — which is the average of the quantities of sunflower honey provided to France Miel between 1988 and 1994. Beekeepers are committed to supply all of their annual harvests to the cooperative. A laboratory further checks the floral origin of the supplied honey. It was not possible to calculate the evolution of the quantity of sunflower honey beyond 2001 because some beekeepers from the sample abandoned beekeeping, left the cooperative, developed other activities in addition to beekeeping or retired. Note that sunflower seeds were also dressed with another insecticide after 1995, RégentTS®.

Source: Laura Maxim.

Figure 16.2 Sunflower honey yearly harvest totals since 1995, for the Cooperative Poitou-Charentes



Source: Coordination des Apiculteurs, 2000.

larvae and the time lag during which the plant is sensitive to these larvae is relatively short' ([43]). Furthermore, for 'most of the areas where sunflower is cultivated in France', the risk is 'low or zero' ([44]) (CETIOM, 2011).

Contrary to the use of curative treatments usually recommended to farmers when pest density was above an economic threshold, the new control method was preventive regardless of the presence and abundance of pests.

Seed-dressing reduces the work needed for crop protection, so it could be economically attractive to farmers. But some farmers said that their productivity was unchanged or diminished, and reported more empty seeds in the flowerheads, suggesting a possible link with the poor pollination associated with Gaucho® (Elie and Garaud, 2003).

([43]) In the original French: 'le tournesol est faiblement attractif pour les larves et la période de sensibilité aux attaques est relativement brève.'

([44]) In the original French: 'Population de taupins nulle à faible, dégâts très peu probables sur tournesol: Majorité des situations où le tournesol est cultivé aujourd'hui en France.'

Mainstream (intensive) farmers' organisations such as the General Association of Maize Producers (AGPM) ([45]) argued that banning seed-dressing insecticides increased pressure from pests, particularly on maize (Beulin et al., 2005; AGPM, 2008).

In 2002 the rapporteur on 'insecticides' in the Committee for Pesticides Authorisation ([46]) stated that, at that time, the two 'really effective' plant protection products that served as alternatives to Gaucho® and were available for certain maize pests were terbufos (which was due to be withdrawn from the EU market in 2003) and RégentTS® (Comité d'homologation, 2002).

In 2005, farmers reported losses of 500 000 tonnes of maize-grain in France (worth EUR 50 million) and some of them linked this figure to the ban on seed-dressing insecticides (Dossier de la protection des sémences, 2005). However, others blamed the productivity drop on the exceptionally hot and dry summer that year. AGPM itself has pointed towards the decrease in maize yield from 2003 due to increasingly drier summers.

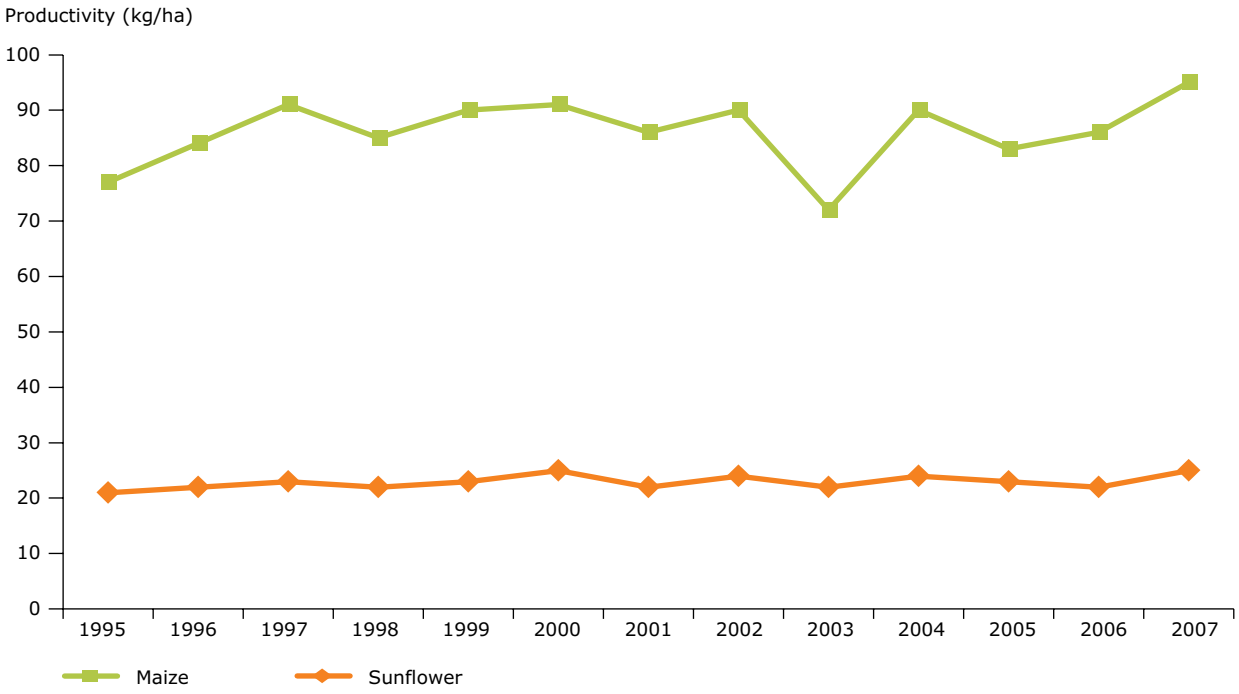
Figure 16.3 shows that the seed-dressing ban is not directly correlated with productivity: 2007 was the best year in over a decade. For maize, production was worst not after 2004, when Gaucho® was banned on this crop and RégentTS® on all uses, but in 2003, when a major heatwave hit Europe.

Beekeepers contended that, because not all maize crops in France were seed dressed, maize could be cultivated without seed-dressing insecticides. Contrastingly, the website of the General Association of Maize Producers (Dossier de la protection des secmences, 2005) reports that there is no authorised alternative treatment to control wireworms.

The losses for agriculture associated to the potential decline in pollination during this period (1994–2004) have not been assessed.

Finally, resistance to insecticides is more likely with the long persistent molecules of seed-dressings (such as imidacloprid, fipronil and thiametoxam) which exert a constant pressure on natural selection, compared to sprays.

Figure 16.3 Trends in maize and sunflower yields in France from 1995 to 2007



Source: Data from AGRESTE, Statistiques agricoles annuelles.

([45]) L'Association Générale des Producteurs de Maïs — also a defender of industrial agriculture, for example through cultivating GMOs and intensive biofuel crops.

([46]) Comité d'homologation — one of the two authorities previously involved in evaluating applications for authorisation of pesticides in France. The other instance was the CTP.

16.4.4 Debate in France: 2004–2011

The figures for bee mortality in France are very diverse and heterogeneous among sources. According to UNAF, since 2003 honeybee colonies have partially recovered in France. UNAF reported that high **summer** mortality has stopped in intensive agriculture areas and the general state of the French hives improved (Clément, 2005; UNAF, 2007 and 2008).

An AFSSA study between 2002 and 2005 on 120 hives reported normal activity of honeybees, and usual winter mortalities (5–10 %) (Aubert et al., 2008).

AFSSA (Faucon and Chauzat, 2008) and some beekeepers (Schiro, 2007) reported high mortality for the **winter** 2005–2006. However, according to EFSA (2008), only 1.2 % of French beekeepers made declarations regarding mortality in 2006 and 0.6 % did so in 2007.

Following the 2006–2007 **winter**, apiaries were reported to be in good condition in early spring 2007 (Clément, 2007).

For the 2007–2008 winter, an inquiry by the National Center for Apicultural Development (CNDA), based on 168 professional beekeepers' answers (representing about 5 % of French hives and 10 % of French professional beekeepers), found an average **winter** loss of colonies for France of around 30 %. That was some 12 % higher than CNDA figures for the two previous winters (De Boyer des Roches et al., 2009).

The reality is that no system exists in France for the accurate and extensive monitoring of honeybees. The national statistics of the French Ministry of Agriculture are recognised to support neither accurate quantification of bee mortality, nor identification of causes. Furthermore, official statistics focus on the survey of bee contagious diseases. The Ministry of Agriculture's data on the influence of diseases on French hives differ markedly from those collected by the AFSSA (2009).

AFSSA has produced several reports after 2004, presenting results from its eco-epidemiological studies, suggesting that honeybee problems had multiple causes, with diseases being important in winter mortalities. They showed that varroa is currently a pressure in French hives, as few drugs against this mite are available (AFSSA, 2009).

The reports AFSSA (2009) and CST (2003) differ in terms of their objectives and, therefore, in their methods. These differences are apparent in their respective bibliographies. Of the 338 bibliographic references considered in the CST report, only five were included in AFSSA (2009). Similarly, 173 of the references available before 2003 and included in AFSSA (2009) report were not included in the CST report.

The majority of the references considered by the CST concern imidacloprid. Contrastingly, 43 % of the documents considered in the AFSSA report concern diseases and viruses and only about 15 % concern ecotoxicological issues, with only 3 % focusing on imidacloprid.

Nevertheless, the AFSSA report describes its analysis as '**An almost exhaustive study** of French and European investigations carried out on the issue of bee morbidity and mortality' (p. 12). It also asserts that 'This information has allowed an almost exhaustive inventory of the causes of bee diseases and particularly bee colony mortality to be drawn up' (p. 101). However, the statistics regarding references demonstrate that almost none of the documents reviewed during the CST were considered by AFSSA. The AFSSA analysis only refers to some of the references available on honeybee losses in France — mainly those referring to diseases. Therefore the AFSSA inventory of sources cannot be considered as being 'almost exhaustive'.

AFSSA (2009) does not assess the influence of Gaucho® and Régent® on honeybees in sunflower and maize areas (e.g. the word Gaucho® is present four times in the main text of the document, twice in naming the precautionary decision of the Ministry and twice in naming the corresponding CST report).

Regarding, generally, the influence of pesticides on honeybees, AFSSA (2009) states that 'The group's deliberations do not confirm the hypothesis of a predominant role attributed to pesticides by beekeeping professionals in French bee colony mortality'. This statement takes an important place, because it is found in the conclusions section. However, this general conclusion lacks precision in several respects that are relevant to the present chapter:

- It is not clear to which 'pesticides' the text refers. Do the authors refer to all pesticides?
- It is not clear to which 'beekeeping professionals' the text refers. Is it beekeepers in maize and sunflower areas or beekeepers in other areas (for example mountain regions)?

- It is not clear which 'French bee mortality' this statement refers to because the time period is not specified. Is it before 2004 (before the ban on imidacloprid in maize seed-dressing and on fipronil in all agricultural uses?) or is it after 2004?

- The method used to draw this conclusion is not clear either. How were the 'group deliberations' organised in order to produce this conclusion? On which bibliographic basis were these conclusions drawn, given that less than 15 % of the documents considered refer directly to pesticides? How were these documents chosen, among all the references available on the effects of pesticides on honeybees, and used to reach this conclusion?

Suchail et al. (2001) investigated the oral acute and chronic toxicity of imidacloprid and its main metabolites (5-hydroxyimidacloprid, 4,5-dihydroxyimidacloprid, desnitroimidacloprid, 6-chloronicotinic acid, olefin, and urea derivative) in *Apis mellifera*. Regarding two metabolites (urea and 6-chloronicotinic acid), their results were contested in a study published by a Bayer-funded scientist (Schmuck, 2004). This study could not find any increased treatment-related mortality or behavioural abnormalities following chronic exposure of honeybees to these two metabolites, at 0.0001, 0.001, and 0.010 mg/L 50 % sucrose solution.

Schmuck (2004) did not address the parent molecule, imidacloprid, in an experimental way but through a literature analysis. The author argued that comparison with other studies should be considered sufficient to reject the results found by Suchail (2001), based on the argument that Suchail's results are lower than others. This comparative literature survey neither analysed the sources of the differences between the results, nor examined comparatively the protocols used by the various researchers to understand the sources of these differences.

Post-2003 studies also found that exposure to imidacloprid is also possible through aerial pollution, through foraging on wild flowers coated with imidacloprid-containing dust as a result of sowing-related activities (Greatti et al., 2006) and through consumption by honeybees of leaf guttation drops of corn plants germinated from imidacloprid-coated seeds (Girolami et al., 2009).

Public scientists in France found that the persistence of imidacloprid resulted in its presence in untreated crops cultivated after seed-treated crops. Bonmatin et al. (2005) found 1–2 ppb imidacloprid in flowerheads of untreated sunflowers grown a year after seed-dressed sunflowers. Imidacloprid was still detectable two years after treatment (detection limit = 0.1 ppb). In pollen, imidacloprid was detected one year after treatment (detection limit = 0.3 ppb).

Immunodepression caused by sublethal exposure to insecticides may favour lethal diseases (Glinski and Kauko, 2000; ISIS, 2011). Indeed, beekeepers formulated this hypothesis and launched a call for research (Alétru, 2003). Results of a survey initiated in France showed that the most frequently found pesticide residue in pollen samples was imidacloprid (in 49.4 % of the samples), followed by one of its metabolites, 6-chloronicotinic acid (in 44.4 % of the samples). At least one of these two molecules was present in 69 % of the samples (Chauzat et al., 2006).

Alaux et al. (2009) found that honeybees that were both infected with the pathogen Nosema and exposed to imidacloprid at concentrations encountered in the environment showed the highest mortality rate comparing to honeybees infected with Nosema alone or treated with imidacloprid alone. Although imidacloprid contamination in the hive is usually found at sublethal doses, infection with Nosema increases the energy demands of bees and therefore their food intake. By this means bees could be exposed to lethal doses. Alaux et al. (2009) found that in the long term the synergy between Nosema and imidacloprid induced the immunosupression of an enzyme essential in sterilising larval food, leading to higher susceptibility of the colony to pathogens.

Authorisation has been requested since 2004 for two other seed-dressing insecticides in France. Poncho® (with the active substance clothianidin), produced by Bayer, has not been authorised for maize. Cruiser® (with the active substance thiametoxam), produced by Syngenta, has been authorised and honeybees were monitored in three regions in 2008 and six in 2009. In June 2009, the Minister of Agriculture decided not to renew the marketing authorisation of Cruiser® until autumn 2009. In December 2009, Cruiser® was reauthorised for use on maize for 2010.

Relationships between beekeepers and the Ministry of Agriculture seem to have improved. The decisions of the Ministers of Agriculture to ban Gaucho® on sunflower and maize significantly calmed the controversy and a Technical Beekeeping Institute has been created.

16.4.5 Assessment of Gaucho® at the European level

In the framework of Directive 91/414/EEC, imidacloprid has been assessed at European level for inclusion on the list of active substances allowed for marketing in the European Union. The rapporteur Member State for imidacloprid was Germany, which submitted a Draft Assessment Report (DAR) to the EFSA in 2005 (Rapporteur Member State, Germany, 2006). In 2008, imidacloprid was included on the list of active substances allowed for marketing in the EU ([47]).

Several studies produced in France, relating to the risk of Gaucho® to honeybees were not considered in the DAR. Notably missing were relevant studies on the exposure of honeybees to contaminated pollen and nectar (e.g. none of Jean-Marc Bonmatin's studies was included). In addition, the DAR report accorded only limited importance to sublethal effects, although there were at the core of the investigations in France because of their potential to create lethal effects in field conditions. Finally, the risk assessment methodology was not adapted to seed-dressing formulations.

Several NGOs (Stichting Natuur en Milieu, PAN-Europe, Inter Environment Wallonie, Nature et Progres and Mouvement pour le Droit et le Respect des Générations Futures (MDRGF)), analysed the DAR in a letter sent to the European Commissioner for Health. They articulated several criticisms of the DAR: the absence of necessary tests for each bee category (e.g. larval tests); underestimation of the nectar consumption per bee, meaning that the non-effect concentration was set too high; validation of studies without any validation criteria; discrediting of reports non-favourable to imidacloprid but thorough validation of reports favourable to the thesis that there were no risks to honeybees; flawed consumption tests and colony sizes too small to test egg-laying; insufficient measurement of sowing dust effects; and no consideration of synergic effects between the active substance and bee pathogens (Kindemba, 2009).

16.5 Lessons on the governance of controversies

The lessons developed in the present chapter are based on the case study of Gaucho® but may be relevant for governance of the controversy about systemic insecticide risks in general, in France and in Europe.

The most important factor fuelling the debate in France was increasing mutual mistrust between the parties involved, arising, in part, from a failure to generate and ensure access to information. This reinforces one of the lessons from the first volume of *Late lessons from early warnings* (EEA, 2001), namely the need to 'Provide adequate long-term environmental and health monitoring and research into early warnings'.

Initially, various local/regional government services confirmed the clinical signs described by beekeepers (CNEVA, 1997; AFSSA, 2001; Chambre d'Agriculture de la Vendée, FDSEA de la Vendée and FDSEA des Deux-Sèvres in Alétru, 2003). However, beekeepers have stated that on several occasions they could not access raw field data held centrally by the Ministry of Agriculture. Thereafter, beekeepers viewed further initiatives of the DGAL with suspicion, criticised the 'paralysis by analysis', the diversion of the 'official' research towards too 'complex' subjects and their exclusion from creating the research protocols. The Ministry of Agriculture did, however, finance two post-doctoral projects for two years, which made an important contribution to the work of the CST.

Another important lesson from the first volume of *Late lessons from early warnings* is the need to 'Ensure the use of "lay" and local knowledge, as well as relevant specialist expertise in the appraisal' (EEA, 2001) to ensure a correct understanding of the problem and to deal with conflicting social processes.

The first volume highlighted the importance of rigorous monitoring to identify early warnings and the need to provide sufficient funding to achieve that goal. We could add that the experience of honeybee colony decline in France shows that **bodies performing monitoring studies should have the trust and acceptance of the field actors directly concerned** (in our case, beekeepers and farmers). From the first alert, particular attention should have been given to the professional beekeepers, who have daily experience and good knowledge of the land and of the insects they breed. Where key actors are not properly engaged, the monitoring process becomes discredited and ineffective. For example, the actors directly concerned may cease to participate or the monitoring protocols may be poorly designed, leading to a focus on non-essential features of the

([47]) France maintains its ban on sunflower and maize seed-dressing.

problem. Furthermore, extensive local observations from such actors can help understand variability in clinical signs and the reasons that different circumstances produce varying exposures and effects.

Ensuring that relevant specialist expertise is involved is also of key importance to increase trust and the quality of information. As the current case exemplifies (see Section 16.3.2 above), there is a need to ensure that specialists involved in risk assessments are selected based on competence and transparent procedures. Furthermore, the risk assessment process should involve the relevant disciplines and the experts should have the relevant research experience (i.e. articles on the topic, published in peer-reviewed journals). For example, members of the official commissions assessing the evidence in risk assessment of honeybees must include more honeybee specialists than, for example, plant specialists. Where a causal pattern is being researched, balance should be ensured among the different fields of specialisation (such as honeybee diseases, toxicology and climate) because specialists in, for example, diseases are more prone to produce conclusions on diseases than on ecotoxicological aspects.

Governance of controversies about chemical risks must therefore be guided by a continuous focus on promoting mutual trust between the stakeholders, including scientists and policymakers.

With that goal in mind, **eight new lessons can be drawn from the present case study**.

First, governance must focus on identifying potential properties of new chemicals and anticipating surprises that may arise from them. It is unwise to assume that methods used to assess the risks of existing technologies are also appropriate for assessing risks from new technologies ([48]). In the present case, even though the nature of the risk posed by systemic pesticides was different from the one associated with sprayed insecticides, the same assessment tools (LD_{50} and HQ) were used for authorisation, without any assessment of their adequacy for new patterns of exposure and effects. The lesson learned is: **when dealing with new technologies, verify whether the methods already in use for risk assessment are relevant, given the specific new properties and characteristics of new risks**.

A second lesson deals with the adequacy of the present standardised tests regarding the assessment of pesticide risks to honeybees. The lesson is: **develop new tests to assess sublethal effects of pesticides, their chronic effects and their effects on the colony**.

The laboratory studies measuring imidacloprid's sublethal effects or chronic lethal effects showed a range of different results. One important reason for this diversity is the lack of standardised protocols for such studies, resulting in each laboratory using different approaches. From one study to another, several factors can be a source of variability (the subspecies of honeybees used, their age, the temperature, the fasting time, etc.). Each of these parameters can induce differences in the results. For example, it has been shown that there is considerable genetic variation between colonies regarding the immune responsiveness of colony members (Evans and Pettis, 2005). Alaux et al. (2009) also found differences between the responses of colonies to their experiment, despite the fact that these colonies came from the same location and were exposed to the same environment. They suggested that genetic background and colony history (pathogens, food sources) can produce these differences.

The differences between existing protocols are producing results that are difficult to compare. To address sublethal and chronic lethal effects of pesticides on honeybees, new official directives using standardised protocols are therefore needed.

Today, field experiments play a decisive role in determining the risks of a substance. However, the complexity of environmental factors and of bee colonies themselves means that the same conditions can never be reproduced. A particular combination of such factors arising in a field experiment cannot be considered representative of some kind of 'average' environmental conditions to which honeybees or other organisms could be exposed.

After 2004 a group of honeybee experts appointed (but not funded) by the French Ministry of Agriculture was tasked to develop new tests for honeybees for inclusion in risk assessment practice. This group had proposed several draft tests to the Commission for Biological Essays, charged with validating methods for risk assessment in France.

In Europe, until 2010, honeybee tests followed the European and Mediterranean Plant Protection Organisation (EPPO) 2001 norms (OEPP/EPPO, 2001). The International Commission on Plant-Bee

([48]) This is a very old lesson, developed in detail in the analysis of DDT by Dunlap (1978).

Relations (ICPBR) proposed a modified honeybee risk assessment scheme for systemic pesticides and changed the test guidelines for semi-field and field studies. Both have been submitted to EPPO for consideration (Thompson, 2010). The modified risk assessment scheme has been adopted as EPPO norm in 2010 (OEPP/EPPO, 2010a, b).

However, the process of revising this norm failed to significantly change the risk assessment pattern. The 2010 norm still does not consider sublethal and chronic effects properly. Furthermore, standardised laboratory tests are still missing for chronic and sublethal effects. Therefore, the European Commission has mandated the European Food Safety Authority (EFSA) to create a working group to assess the current risk assessment scheme.

The third lesson is not to underestimate the resources needed to implement policies. The case of Gaucho® revealed the French administration's difficulties managing the authorisation of new pesticides. Policymakers need to **ensure adequate personnel (in number and competence) and financial resources to design efficient regulatory procedures for risk governance and thus reinforce their ability to manage risks effectively**.

The fourth lesson is that **the independence and competence of the experts on the issue at hand must be assured, as well as complete transparency of the research process**. This lesson refers to researchers working both in private and in publicly funded structures.

Publically funded researchers can be also at risk of conflicts of interest. First, the low funding of public research can mean that some laboratories are obliged to find external sources of funding (including pesticide-producing companies). Second, some public researchers may also be consultants for the chemicals industry (e.g. addressing the effects of certain substances on honeybees or other subjects such as the development of anti-mite products against *Varroa jacobsoni* for companies which are also producing insecticides used in crops visited by honeybees).

Conflicts of interest can be financial, with the funding potentially influencing a researcher's work in favour of the funder. They can also be intellectual, where the prior commitment of a scientist to a particular world view prevents him or her seeing other perspectives. However, even if no scientist is 'completely free' of subjectivity, some strive to be as impartial as possible. All the conditions for them to be able to do so must be institutionally insured. Furthermore, building a clear framework for their expertise, which reduces the possibility of selective use of information, of avoiding responsibility or of ambiguous statements, could reinforce the legitimacy of expertise and diminish its potential for generating controversies.

Research policies and funding should be balanced between two core goals: science explicitly targeting the development of knowledge with commercial purposes (resources for the 'knowledge economy'); and science targeting the development of socially valuable knowledge (resources for the 'knowledge society'), such as knowledge on health and environmental risks. The first kind of science can draw largely on private funding. The second type of knowledge requires publicly managed funding and a particular status for the researchers involved, ensuring the 'highest possible level' of independence from vested interests and institutional pressure. Research developed in public structures can complement the evidence on chemical risks produced by the industry pursuant to existing regulatory frameworks.

In addition, the contractual relationship between industry sponsors and public or private researchers of risk could provide for a legal guarantee that, for example, findings will be published regardless of their content.

Industry dossiers that support the authorisation of chemicals must be transparent. External parties should be allowed to scrutinise the dossiers and the original studies, contributing to content and to the overall quality of the dossier. The capacity of different stakeholders to provide comments should be balanced, thereby preventing the most powerful stakeholder from capturing the process with repeated comments. Complete information on the assessment of health and environmental risks should be easily available to both scientists and NGOs, and opportunities to comment should be created and stimulated. One option could be Substance Information Review Forums, similar to the Substance Information Exchange Forums organised in the framework of the REACH Regulation. To create real opportunities for review, the original studies on which risk assessments are based should be available through a cost-free database. Such a library could be also useful for cases where doubts arise about the risks of a substance after is has been authorised.

All researchers, private or public, publishing or involved in regulatory risk assessments should communicate their conflicts of interest. This is

already the case in many situations but these declarations should also be readily available to the public (e.g. on the internet). Researchers should not be involved in evaluating the risk of pesticides produced by the company financing them or their laboratories.

The fifth lesson is: **be aware that the social quality of the scientific information you communicate in the debate determines your public trustworthiness**. The present case study showed major deficiencies in the communication of scientific information by Bayer and by certain administrative services of the French State, contributing to the distrust of other stakeholders and intensification of the debate. We have six recommendations for the social quality of information communicated in a contested policy process:

- be reliable — base your arguments on all available scientific knowledge;
- be robust — answer criticism instead of ignoring it;
- be complete — do not ignore the information produced by other stakeholders, especially those contradicting your own views;
- have a discourse relevant for the issue under debate (e.g. regarding the particular clinical signs or the geographical area evoked), instead of referring to general issues only distantly related to the problem addressed;
- be logical, do not contradict yourself except if you change your views and you explicitly recognise this;
- ensure the legitimacy of your sources (make appeal to competent researchers, who do not have conflicts of interests) (for further details, see Maxim and van der Sluijs, 2007).

The sixth lesson is that **structures responsible for assessing the scientific adequacy of applications for marketing authorisation should develop clear and standardised scientific quality criteria to enable existing studies to be evaluated and compared**.

All the existing literature, including scientific papers, should be taken into account in risk assessments and the scientific quality of the data submitted by the industry should somehow be assessed. An important issue is the balance between the burden of proof (i.e. who has the responsibility to produce evidence for decision-making on risks) and its credibility. The selection of valid studies (e.g. for obtaining marketing authorisation) should be based on uniform and clear criteria of scientific quality, not on some unjustified 'expert appreciation' of their relevance. Lack of precise criteria for evaluating the quality of a study can lead to arbitrary or subjectively justified exclusion of certain studies from the risk assessment process. This exclusion can potentially have a decisive influence on the final result.

In addition to existing practices for the quality of the laboratory work, criteria for evaluating the scientific quality of studies should be established. Good Laboratory Practice (GLP) standards ensure a framework in which laboratory studies are controllably planned, performed, monitored, recorded, reported and archived. However, the GLP certification only provides guarantees about the transparency and the traceability of the laboratory work. It does not guarantee the scientific quality of the study. For non-standardised tests, GLP does not warrant, for example, that the protocol chosen for a study adequately takes into account the biology and the behaviour of the studied organism or that the results are correctly interpreted. However, whereas new patterns of risk need to be assessed, novel tests that are not yet standardised are increasingly needed.

The seventh lesson deals with multicausality: **prioritise the potential causal factors and address them separately before assessing potential correlation or synergies among them**. Honeybee losses can be influenced by many factors but this should not become an excuse for not dealing with particular clinical signs and particular causes. Action should not be hampered because several potential causes are involved. On the contrary, potential causes have to be prioritised before being addressed. The different causes could play different roles, e.g. some might be 'primary' (i.e. influencing the expression of other causes), whereas others may be 'secondary' (e.g. immunodepression due to pesticides could favour diseases, as was shown for imidacloprid and Nosema) (see also Maxim and Van der Sluijs, 2010).

The discourse on multicausality is only apparently contradictory with the discourse on the risk of Gaucho® to honeybees. Thus, the fact that many factors influence honeybees **all over the country** does not contradict the fact that Gaucho® posed a risk to honeybees **in Gaucho®-treated extensive sunflower and maize areas**. It is obvious that some

causes can mainly act in some geographical areas and other factors can be present everywhere in a country. Certain factors could act at particular moments of the year (e.g. during the summer), whereas others could act throughout the year.

In choosing which factor to focus research on first, considerations such as feasibility, potential to reduce the final effects, and co-benefits (e.g. reduction of social conflict) need to be taken into account. Investment in research, to improve understanding of synergistic effects between low doses of systemic insecticides and other factors like diseases, seems important for addressing losses of bee colonies.

The eight lesson is: **build the regulatory background needed to protect early-warning scientists**. The case of Gaucho® raises questions about science's role in democracy and about the resources scientists receive from society. There are many critics of science but how many also address society's obligations towards scientists? How much freedom of thought and responsible action are science professionals institutionally given in such conflicting cases? How does society recognise and provide legal protection to early warning scientists?

Although the impacts of pesticides are important and have high social relevance, generalised social conflict associated with this issue is likely to discourage scientists from working on the subject.

In the European 'knowledge society', democratic production of knowledge should benefit from institutional structures favouring scientific accountability (based on sound peer review and validation) and the freedom of scientists to pursue their work independently on socially sensitive issues. If science is to continue to inform decision-making, open discussion and criticism, respectfully expressed, is to be encouraged. Misuse of scientific results to support predetermined conclusions, and actions that provoke anxiety and psychological pressure are unacceptable (see also Gleick, 2007).

16.6 Conclusions and prospects

Imidacloprid seems to be a substance particularly 'fit for the precautionary principle'. The effects on living beings are highly variable, both for honeybees (the lowest oral LD_{50} is 21 times lower than the largest LD_{50}, a factor of 40 separates the lowest and largest contact LD_{50}s and a factor of 1 000 separates the LOECs for chronic toxicity) and for other organisms, for example wild bees (Tasei et al., 2000; Morandin and Winston, 2003; Desneux et al., 2007; Colla and Packer, 2008; Mommaerts et al., 2009). Calculated half-lives of imidacloprid range from 83 days to 1–2 years.

Imidacloprid's persistence in soil is affected by various factors, including temperature, soil composition and whether the field is cropped or not (Canadian Council of Ministers of the Environment, 2007). It is thus plausible to say that the risks of imidacloprid are dependent on a specific assembly of environmental factors, such as temperature, humidity and soil composition. Furthermore, more than one study failed to find a dose-effect relationship between imidacloprid and chronic effects (Suchail, 2001; Schmuck, 2004). Given this variability, it seems likely that some of the effects of Gaucho® are **uncontrollable**.

The present chapter focused on the **social** consequences of this diversity of ecotoxicological effects. It is interesting to find that a diverse ecotoxicological portfolio allows each stakeholder to identify their own 'scientific arguments' and use them for defending opposite positions in the debate.

Declining honeybee colonies have been reported in several European countries (e.g. Belgium, Italy, Portugal, Germany, the Netherlands and the United Kingdom) and have sometimes been related to seed-dressing insecticides (CARI, 2003; Panella, 2001; Ministério da Agricultura, do Desenvolvimento Rural e das Pescas, 2000; COLOSS, 2009). The European Parliament has officially acknowledged the issue since December 2001, when a resolution dealing with the production and marketing of honey was adopted (European Parliament, 2001). It states that: 'extremely serious damage has been caused to bee populations in several Member States by systemic insecticides with extremely long residual activity periods used in arable seed coatings, which have led to the mass poisoning of colonies.'

The precautionary principle has been applied in other European countries for seed-dressing insecticides. Imidacloprid, clothianidin, thiametoxam and fipronil have been temporarily banned in Italy, on oilseed rape, sunflower and maize seed-dressing. A research programme (APENET) has been started to improve understanding of relationships between these active substances and the honeybee losses found in this country. APENET found that after the ban, the number of reports of high mortality during spring

decreased from 185 cases in 2008 to two cases in 2009 (Il punto coldiretti, 2009). The ministry decided on 14 September 2009 to extend the ban until 20 September 2010 (Ministero della Salute, 2009) and then until the 30 June 2011 (Ministero della Salute, 2010). Italian researchers found a clear indication that honeybees were killed by the dust emitted during sowing neonicotinoid-coated maize in conditions of high humidity (Marzaro et al., 2011).

In Slovenia, clothianidin, thiametoxam and imidacloprid in oilseed rape and corn seed treatment have been successively banned, reapproved and then banned again between 2008 and 2011.

In Germany, eight insecticidal seed treatment products with the active substances clotianidin, thiametoxam and imidacloprid were temporarily banned on maize in May 2008 and the bans were renewed for February 2009 (BVL, 2009). In January 2011, certain formulations of the three active substances were suspended, whereas others were authorised in agricultural uses (BVL, 2011). Germany lifted the suspensions except for the use of the neonicotinoid clothianidin in corn seed-treatment (EPA, 2011).

Since 2006, American apiaries have reported 'Colony Collapse Disorder', where colonies are suddenly lost (MAAREC, 2011). Because the clinical signs of disappearing adult honeybees recalled the clinical signs found by French beekeepers, the popular and scientific media — rightly or wrongly — drew parallels with honeybee colony decline in France. Clearly, before any conclusions are drawn, the specific characteristics ('fingerprints') of the clinical signs and their spatial and temporal patterns must be properly compared.

There is growing evidence in some European countries of parallel declines in pollinators and pollinated plants (Biesmeijer et al., 2006; Vaissière, 2005). In some cases, such as China's Sichuan province (Newsweek, 2008), honeybee declines have forced farmers to pollinate fruit trees by hand. Can Europe afford this?

Domestic honeybees are managed by humans and represent a source of revenues. Much less is known about other species. The role of the honeybee as a bioindicator for the state of the environment was highlighted during the debate in France. A study published in the journal *Nature* (The Honeybee Genome Sequencing Consortium, 2006) found that honeybees tend to respond faster than other insects to environmental pollution. It seems that the size of the major detoxifying gene families is smaller in the honeybee, which makes it unusually sensitive to certain pesticides; honeybee losses can be interpreted as an 'alarm bell' of harm to other entomofauna and indirectly to plants, birds and other species.

Our case study highlights the importance of ensuring scientists' independence (which is never absolute but varies significantly). Knowledge of risks can be limited by a number of factors: funding constraints, which necessitate the need for private sector resources; a dearth of research positions in toxicology and eco-toxicology; or assessing the quality of the research by institutional rather than scientific criteria.

Social concerns are essential to establishing a relevant research agenda. As pollinators, honeybees have an ecologic impact on the survival of plants in the wild. But they have important impacts on people, most notably the economic value of free pollination of many fruits and vegetables.

Table 16.1 Early warnings and actions

1991	First authorisation of Gaucho® in France, for sugar beet seed-dressing. Adoption of Council Directive 91/414/EEC
1993	Authorisation of Gaucho® for sunflower seed-dressing
1994	First use of Gaucho® in sunflower seed-dressing First clinical signs observed by beekeepers, during sunflower nectar flow. Analysing all the potential factors involved, beekeepers suspect Gaucho® of harm to their apiaries
1995–1997	Bayer conducts several studies on the risk of Gaucho® for honeybees. All report absence of harm. Greater declines in honeybee colonies are reported. At the same time, the areas growing Gaucho® seed-dressed sunflower are also rapidly increasing
1997	During an important meeting with representatives of Bayer and the Ministry of Agriculture, beekeepers publicly point to Gaucho® as cause for observed massive honeybees' losses. The first report of the Commission for Toxic Products is published. It recommends further research
1998	The first research programme involving publicly funded researchers detects imidacloprid in sunflower nectar and pollen. RégentTS® is suspected of contributing to the clinical signs in honeybees. On 17 December, more than 1 000 beekeepers demonstrate in Paris, in front of the Eiffel Tower, demanding a ban on Gaucho®. In the apiaries affected, sunflower honey yields 30–70 % below normal potential are reported
1999	In January, the Ministry of Agriculture decides to ban Gaucho® in sunflower seed-dressing for two years, applying the precautionary principle. The conflict shifts to court, as Bayer challenged the ministerial decision in the administrative court of Paris (March 1999). The UNAF defends the Minister's decision in court
2000	In response to new scientific findings detecting imidacloprid in maize pollen and confirming high persistency in soils, beekeepers demand to ban imidacloprid for all uses
2002–2003	Intoxication episodes severely affect several thousand hives; residues of fipronil are found in dead honeybees
2004	The Minister of Agriculture temporarily bans Gaucho® in maize seed-dressing and RégentTS® for all agricultural uses
2005–2007	French beekeepers report cessation of high summer mortality. Colony recovery is gradual but winter losses vary annually
2009	Scientific publication proving synergic effects between imidacloprid and Nosema
2010	UNEP publishes report on global honeybee colony disorders and other threats to insect pollinators (UNEP, 2010)
2011	French/German beekeepers ask EEA to consider bees as sentinel species for their ecosystems (EEA, 2011)

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Panel 16.1 The Bayer CropScience view on Maxim and van der Sluijs 'Seed-dressing systemic insecticides and honeybees

Dr Richard Schmuck, Head of the Department of Environmental Safety of Bayer CropScience

The authors' efforts to analyse the challenge for democratic governance of controversies on chemical risks are commendable in their aims. There are, however, shortcomings in the focus they chose. Democratic governance is a complex matter. It requires looking at the root causes of societal and political reactions and to separate them from emotional and intellectual forces involved. Moreover, policymakers are often under pressure to take rapid decisions: thus as long as causal patterns are far from clear, all potential ones should at least be addressed.

The publication focuses on chemical governance in response to bee colony losses in France. The insecticidal seed treatment Gaucho® is taken *a priori* by the authors as THE key cause of these losses. This approach can not arrive at a balanced conclusion since it fades out numerous scientific papers that cover the multiple factors contributing to bee losses (such as bee diseases, habitat loss and with that loss of bee feeding-grounds, changing agro–ecosystems, including due to economic and trade reasons, or unfavourable climatic conditions that add stress on honey bee health). The authors also omit to consider literature (Rivière-Wekstein, 2006) that covers the sum of the socio-political, economic and other drivers that led to the suspension of Gaucho® in France. This would, however, have been an essential source when undertaking this research, especially in the context of governance.

Bee losses were first attributed to imidacloprid in France during the 1990s. They were not related to specific product incidents. Rather the product market introduction coincided with a time when bee health issues had increased. Later, an accident with another neonicotionoid insecticide occurred in Germany which was attributed to an inappropriate quality of the seed treatment process. This was very regrettable, although lessons were learned and resulted in enhanced mitigation measures to prevent reoccurrence. Due to both these situations much research — partly pioneering new testing designs was undertaken. As a consequence more is known today about bee safety of the neonicotinoids.

For some years now, the majority of researchers have highlighted the multi-factorial nature of bee colony losses. A series of long-term, large-scale monitoring programmes confirm these findings. They have been conducted in Belgium, France, Germany, the US and other countries. In these programmes, exposure to pesticides was measured as well as colony health and safety. None of them have found a correlation between colony losses and exposure to neonicotinoid seed-dressing products (Chauzat et al., 2009, 2010; Nguyen et al., 2009; Genersch et al., 2010).

Bayer CropScience is committed to finding solutions to enhance honeybee health, e.g. by providing Varroa mite management products including potential new treatments, and bee safety, e.g. by ensuring the sustainable use of its pesticides through research and promotion of 'bee-responsible' farming practices. When evaluating new pesticides (this costs about EUR 250 million per compound) prior to market release we follow legal requirements and the spirit of precaution in a way that is as practical and responsible as possible; we also acknowledge that perceptions will vary among stakeholders of what constitutes an acceptable level of precaution, depending on their knowledge, perspectives and interests. The positive tension between innovation and precaution we see, continues to drive both technological progress and the move towards enhanced pesticide regulation — to the benefit of agriculture, the consumer and the environment. This is what was generated through the Gaucho® case, especially in the context of bee safety. Suspending products may be helpful in some instances. It does however bear the risk of stopping innovation if it is not handled carefully, thus being made reversible — should new data confirm the lack of plausibility of earlier decisions.

From field observation of aphids, we were already able to deduce, before the first registration of Gaucho®, that bees would not be affected by systemic residues in treated sunflowers. Laboratory tests had shown that aphids are ten times more sensitive to Gaucho® than bees. Despite treatment of seeds with Gaucho®, aphids were observed in the field re-invading sunflower plants before blooming, so it was logical to conclude that there would no longer be effects on bees either at the time of blooming. Since its registration in the early 90s, Gaucho® has met all post-registration re-evaluation requirements and NO evidence of a causative link between Gaucho® use and bee colony losses could be found. (e.g. Faucon and Chauzat, 2008; Nguyen et al., 2009). In addition, large-scale monitoring programmes run under field conditions during the

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post-authorisation period confirmed the original findings of 1998 (no causative link to Gaucho®) of the ACTA monitoring programme (Association de Coordination Technique Agricole).

Gaucho® continues to be registered for use in sunflower crops in various countries, including Argentina, Australia, Bulgaria and Croatia. In none of these countries have bee colony losses been reported in connection with sunflower growing (Neumann and Carreck, 2010; Ivanova and Petrov, 2010; Tlak Gajger et al., 2010). During the years following the suspension of Gaucho® in France, bee colonies have continued to suffer losses (e.g. Faucon and Chauzat, 2008; AFSSA, 2009; Chauzat et al., 2010b). According to a statement made in November 2007 by the then French Minister of Agriculture, Michel Barnier to the National Assembly bee losses were also observed in regions where Gaucho® had not been applied.

We are thankful for the opportunity to share our view here with various stakeholders. Further information on the subject can be found in Bayer's 2011 publication on 'Honey bee care: Challenges and solutions' http://www.bayercropscience.com/bcsweb/cropprotection.nsf/id/EN_Bee_Health_Crop_Protection_2010/$file/Honey_bee_care.pdf.

See the full comprehensive review, including additional references: http://www.eea.europa.eu/publications/late-lessons-2/bees-insecticides-debate.

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Panel 16.2 Response to the Bayer Cropscience (Richard Schmuck) comments on the chapter

Laura Maxim, Jeroen van der Sluijs

Mr Schmuck insists on how complex and uncertain things are and on how policymakers are taking decisions under pressure. However, the decision to ban Gaucho® was taken in France about five years after the first clinical signs in bees and two years after the public boom of the controversy — for sunflower. The corresponding delay for maize was ten, respectively seven, years. The word 'rapid' does not seem adequate to us for these time frames.

Further in the text, these same policymakers (Mr Barnier) are subsequently quoted in Mr Schmuck's text as legitimate and reliable sources. Should one understand that policymakers 'act under pressure' when they apply the precautionary principle as they did in banning Gaucho®, and that they are 'good policymakers' when they see reality as being too complex to take a decision but actually decide to maintain the status quo?

The speech of Mr Barnier is, by the way, perfectly reasonable, stating that honeybees' losses are not all due to only one factor (indeed, nobody ever claimed that one factor causes all honeybee losses!). He also says that several factors influence honeybees, and that all these factors do not act at the same time and at the same place, which are truisms. The fact that honeybee losses can be due to Gaucho® is not at all contrary to the fact that honeybee losses can also be due to diseases or lack of food, just as human beings can die of many causes, such as car accidents, diseases or cancer. This is not an argument for not trying to limit car accidents or treat cancer, just as the fact that many factors can influence honeybees is not an argument for not dealing with Gaucho®.

Multicausality cannot become an argument for avoiding dealing with specific causes, or for avoiding establishing priorities among causes and addressing them. There is clear value in prioritising those causes that are easier to control. For example, it is much more difficult to address climate change than to limit the use of a specific pesticide.

The phrase 'The insecticidal seed treatment Gaucho® is taken *a priori* by the authors as THE key cause of these losses' is a blunt misrepresentation of our text, Mr Schmuck then arguing against this misrepresentation. If read carefully, our text is precise: 'In this chapter, we present the historical evolution of the evidence regarding the risks of Gaucho® for honeybees in sunflower and maize seed-dressing, and analyse the actions in response to the accumulating evidence regarding these risks.' Our subject is not all honeybee losses, in France or in the world, in all times. We address honeybee losses 'in sunflower and maize areas', from the start of the controversy in 1994, to the political decisions to ban Gaucho® in sunflower and maize seed-dressing, in 1999 and 2004, and analyse the developments in science and society that ultimately lead to these decisions. As we have also specified in our chapter, 'many factors can play a role in the state of honeybees and pollinators more generally'.

We disagree with Mr Schmuck that the book of Gil Rivière-Wekstein can be considered an 'essential source'. Its author is the director of a firm providing consultancy for companies, who has produced papers on diverse subjects not related to honeybees such as USA Elections 2004: eleven democrat candidates facing George W. Bush and Enron, the crush of an empire.

More generally and beyond this particular reference, the length of our paper did not allow us to include extensive reference to several insightful and relevant books written in France on the subject of Gaucho® by journalists, policymakers or NGOs, including:

- Cicolella, André and Benoît-Browaeys, Dorothée, 2005. Alerts on health: experts and citizens face to private interests ([49]).
- Nicolino, Fabrice and Veillerette, François, 2007. Pesticides: revelations about a French scandal ([50]).

([49]) Alertes santé : experts et citoyens face aux intérêts privés.
([50]) Pesticides : revelations sur un scandale français.

Panel 16.2 Response to the Bayer Cropscience (Richard Schmuck) comments on the chapter (cont.)

Massive bee-poisoning events from dust emissions during sowing of maize coated with neonicotinoids such as the one in 2008 in Germany are not incidents or accidents but have continued to happen since in many countries. The Italian moratorium on seed dressing with neonicotinoids lead to a reduction of the number of such reported poisoning incidents from 185 beekeepers (6 328 hives) per year to 3 beekeepers per year, these 3 remaining cases could all be linked to illegal use of neonicotinoid seed dressing (APENET) ([51]).

The loss of 2 500 bee colonies during maize sowing in the Pomurje region in Slovenia in April 2011 demonstrates that the prescribed mitigation measures are still insufficient (Drofenik, 2011).

A series of recent field trials by Girolami's group (Marzaro et al., 2011; Girolami et al., 2012; in press) has demonstrated that even when all mitigation measures are implemented such as deflectors and improved coatings, the pneumatic maize sowing machines still produce a ellipsoidal toxic cloud of dust particles of 3 meter high and 20 meter wide that is acute lethal to honeybees that cross this cloud on their flight. A single flight though that dust cloud showed to provide an average dose of 300 ng imidacloprid per honeybee.

The use of 'Gaucho®' in sunflower crops in countries such as Argentina and Australia cannot be compared to its previous use in France. The concentration of imidacloprid presently used in the 'Gaucho®' product is much lower than it was in France in the 1990s. The two situations are therefore not comparable, since that lower doses of imidacloprid lead to lower exposure of bees, and might have more long-term than short-term effects. As well, it can be hypothesised that national characteristics such as soil, climate, relative attractiveness of the plants for honeybees etc. could significantly influence the imidacloprid uptake from soils and its availability to honeybees.

It seems that Mr Schmuck used extrapolation from aphids to honeybees for being 'able to deduce, before the first registration of Gaucho®, that bees would not be affected by systemic residues in treated sunflowers'. He does not specify if this extrapolation was based on scientific publications or on some sort of 'expert judgment'. So we have searched in the Web of Science — Current Contents database (including 8 500 major journals and 9 000 web sources) with the key words (in topic): aphid AND honeybee (variant: honey bee) (+ AND extrapolation). Only two relevant records were found (Matsuda, 2009 and Guez, 2003), which did not exist at the time when the extrapolation had apparently been done before the registration of Gaucho®. These publications rather support evidence against this extrapolation.

Moreover, several important differences between honeybees and aphids raise doubts about the relevancy of such an extrapolation:

- looking at aphids behaviour on sunflower plants only considers short-term effects but ignores the long-term effects. Indeed, honeybees store pollen and nectar in the colony and can consume them on the long run. The honeybees could repeatedly ingest the contaminant on the long term, leading to chronic effects.
- different ages of individuals in a honeybee colony vary in their sensitivity to insecticides. Even if foragers (collecting pollen and nectar in the fields) are not affected, other honeybees in the colony could be intoxicated (nurses, larvae)
- all the aspects related to the complex social organisation of honeybees are missing in aphids
- observing aphids cannot account for synergic effects of neonicotinoids on the honeybees colonies, as those highlighted by Cummins (2007), Alaux et al. (2009), Videau et al. (2011) and Pettis et al. (2012) for imidacloprid and the pathogen Nosema.

We are astonished that the effects in aphids were assumed to be similar to the effects in honeybees. Such extrapolative assumption would indicate lack of selectivity of imidacloprid on target and non-target species and should have, on the contrary, raised worries about the potential effects on honeybees.

([51]) http://www.bijensterfte.nl/sites/default/files/Piotr_Medrzycki_-_Apimondia_2009.pdf and http://pub.jki.bund.de/index.php/JKA/article/view/146/131.

Panel 16.2 Response to the Bayer Cropscience (Richard Schmuck) comments on the chapter (cont.)

Several other sources cited by Mr Schmuck merit consideration. First, it is normal that different signs and potential causes will be identified depending on the protocol used and the specific situation studied. Ivanova and Petrov (2010) and Tlak Gajger et al. (2010) employed surveys that did not address summer mortalities but winter colony losses. In both papers, the causal investigation used only beekeepers' opinions but did not undertake chemical analysis. The Bulgarian survey looked at 1.3 % of beekeepers, the Croatian one at 3.6 %. One of the two papers, Ivanova and Petrov (2010), refers to sunflower, mentioning: 'untypical behaviour of honeybees in some regions of north Bulgaria manifested by avoiding flowering sunflower was also reported'. No indication is given about how this behaviour had been measured or observed, for example whether it was apparent in diminishing sunflower honey production or behavioural signs. The paper mentions that 'the problem appeared to be more serious for areas with cultivated fields and grasslands due to crop protection activities, such as the north-central and north-eastern parts of Bulgaria….'

Neumann and Carreck (2010) is another undue reference for addressing honeybees' intoxication on sunflower crops, as sunflower is not referred to at all. The paper notes, however, that 'These interactions are particularly worrying, as sub-lethal effects of one driver could make another one more lethal; for example a combination of pesticides and pathogens' (p. 3).

Another paper by Bacandritsos et al. (2010), which was not cited in Mr Schmuck's response, refers to summer losses in Greece. This paper reports results of chemical analysis of honeybee tissues showing that 60 % of the samples analysed contained imidacloprid, in an average concentration of 27 ng/g tissue. A high level of virus and N. ceranae infection accompanied this contamination. Also, the study by Krupke et al. (2012) shows a link between clothianidin coated maize and bee mortality in spring in the same area.

Some of the authors quoted by Mr Schmuck have recently published papers on pesticide loads in France (Chauzat et al., 2010). Imidacloprid was found to be widely available to honeybees. The average levels of imidacloprid found in pollen is 0.9 ppb (with a maximum of 5.7 ppb). These results are in line with results published four years earlier by Chauzat et al. (2006), who found that the most frequently found pesticide residue was imidacloprid (identified in 49.4 % of the samples), followed by one of its metabolites, 6-chloronicotinic acid (in 44.4 % of the samples). At least one of these two molecules was present in 69 % of the samples. Statistical tests also showed no variance in concentrations between sampling locations, meaning that imidacloprid is present *everywhere* in the 5 sites considered, and that it is present in pollen loads *throughout the year*, with a maximum presence during July–August but comparable concentrations during spring and autumn.

The presence of imidacloprid in pollens all through the year, even long after the treatment moment, shows that honeybees are exposed all through the year, and not only during the agricultural season. This could also be an indication that imidacloprid is so persistent that it might be uptaken in non-treated crops or wild plants. Indeed, imidacloprid is currently banned in France for seed-dressing of sunflower and maize but it is still used in seed-dressing for sugar beet, wheat and barley. It is also authorised to treat fruit trees such as apricot, peach, pear, quince, apple and plum trees, in products for disinfecting storage facilities, shelters for domestic animals etc.

In conclusion, our chapter responds to one of the main objectives of the present report, which is to describe and analyse cases of application of the precautionary principle and reflect on what can be learned from these cases. The partial French ban of Gaucho® in sunflower and maize seed-dressing is one such explicit application of the precautionary principle.

See the full answer at: http://www.eea.europa.eu/publications/late-lessons-2/bees-insecticides-debate.

Panel 16.2 Response to the Bayer Cropscience (Richard Schmuck) comments on the chapter (cont.)

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17 Ecosystems and managing the dynamics of change

Jacqueline McGlade and Sybille van den Hove

A decade after Rachel Carson's *Silent Spring* was published, describing the toxic legacy of the twentieth century, Annie Dillard in her Pulitzer prize winning book *Pilgrim at Tinker Creek*, opened up a different way of looking at the world. It presaged a twenty first century in which the global economy would be based on a more thorough understanding of nature, its functioning and material wealth. Wholly descriptive, yet increasingly relevant, her book captured the very essence of what this chapter is about: that amongst the observations which routinely help to predict the evolution of the natural world are the seeds of surprise — surprise of the unusual and surprise as a portent of future change. Our systemic failure to anticipate such surprises forms the core of this chapter. A series of case studies from fisheries, forests, savannah and aquatic systems are used to underline how early warnings about changes in these natural systems emerged but were not used.

The chapter highlights how the division of knowledge into political, disciplinary and geographic silos has led to the 'recurring nightmares' of short-term interests outcompeting long-term vision; situations where competition replaces co-operation; fragmentation of values and interest; fragmentation of authority and responsibility; and fragmentation of information and knowledge leading to inadequate solutions or even additional problems. In addition, the lack of institutional fit has often confounded the effectiveness of the stewardship of ecosystem services, and led to unexpected surprises, excessive rent seeking and high transaction costs.

Using counterfactual thinking (i.e. the dependence of *whether*, *when* and *how* one event occurs on *whether, when* and *how* another event occurs and the possible alteration of events), built around the four interconnected concepts of *planetary boundaries, tipping points, panarchy* and *resilience*, the chapter provides an analytical lens through which to explore why many of the warning signals were not seen. The chapter concludes by suggesting why ecosystems are likely to be even more at risk in the future and why we will need to observe and interpret the dynamics of both nature and institutions ever more closely if we are to avoid sudden irreversible ecological changes.

17.1 Introduction

> 'The road we have been traveling is deceptively easy, a smooth superhighway on which we progress with great speed, but at its end lies disaster. The other fork of the road — the one 'less travelled by' — offers our last, our only chance to reach a destination that assures the preservation of our earth' (Carson, 1962).

A decade after Rachel Carson called the world's attention to the dangers of industrial chemicals in her book *Silent Spring* (Carson, 1962), another writer, Annie Dillard (1974) took her readers on a yearlong investigation into nature's beauty and complexity in her Pulitzer prize winning story *Pilgrim at Tinker Creek*. Quintessentially descriptive, the book shows how close observation of nature and its inherent surprises — both of the unusual and as a portent of things to come — is vital for achieving an understanding of the resilience of ecosystems and the resources within them. Charles Keeling, dubbed the father of climate change science, followed this same approach throughout his lifetime's work on measuring the levels of carbon dioxide in the atmosphere.

Detailed observation of past forms of nature is also vital for anticipating surprises. As R. G. Collingwood (1939) argued in his autobiography, history provides something 'altogether different from [scientific] rules, namely insight'. The historian is like a woodsman compared to an ignorant traveller who might say 'Nothing here but trees and grass' whereas the woodsman says 'Look, there is a tiger in that grass'.

Memory is also an important element in determining current ecosystem structure and function (Hendry and McGlade, 1995). For example, the history and age of an individual tree determine its susceptibility to physiological shock, native disease and parasites; this generally rises with age, leading to an increased probability of accelerated death in elderly stands. However, the history of each position within a forest also has an influences on the current stand, as the state of the soil, the height of the water table, the level of nutrients are affected by the species that have grown there over previous centuries.

By combining insights such as these with detailed observations from comparative analyses of ecosystems and heuristics from the natural and social sciences, scientists have begun to build a more general theory of the dynamics of socio-ecological change across a broad range of ecosystems (Walker et al., 2006); they include lakes and wetlands (Carpenter and Brock, 2004), rangelands (Janssen et al., 2004), forests (Bodin et al., 2006) and coral reefs (Hughes et al., 2003). These developments have also highlighted just how limited many more classical scientific approaches really are for dealing with real-world situations (i.e. developing hypotheses and testing them with simple causal models validated with controlled experiments or statistical sampling). As the case studies in this chapter show, the continued dependence of many resource managers on these more traditional approaches has contributed to the catastrophic decline of some resources.

The chapter looks at how scientific evidence and advice are generated and used in policies for managing natural resources and ecosystems. Through case studies of key events, resources, important actors and institutions and the lens of planetary dynamics and resilience of socio-ecological systems, the chapter explores the reasons why the evidence was sometimes flawed, how and why scientific advice influenced or was ignored during the process of decision-making, and looks at some prospects for the future.

17.2 Data, knowledge and counterfactual thinking

Field ecologists have traditionally adopted a diversity-oriented approach to gathering data and creating knowledge. Their assessments are often based on detailed case studies using measurements of many system-specific attributes with configurational complexity (McGlade, 2003). Conversely, resource managers, have historically adopted a variable-oriented approach based on the measurement of a small number of attributes relating to global patterns emerging from surveys of a large number of cases. The two approaches represent the ends of an inverse relationship between the number of cases and variables. They represent a fundamentally different way of developing counterfactual thinking (i.e. the dependence of whether, when and how one event occurs on whether, when and how another event occurs and the possible alteration of events) and their misapplication has contributed to the catastrophic demise of some the world's key ecosystems and resources.

This section contains two case studies(Box 17.1 and Panel 17.1): the first demonstrates how a well-structured diversity-oriented approach, using

close observation at carefully selected sites and correct counterfactual thinking, produced a data series which influenced the global community's thinking about climate change. In contrast, the second shows how a variable-oriented approach based on flawed counterfactual thinking and a poorly described polythetic scheme, led to the catastrophic demise of an international fishery. This second case study shows how false inferences were used to suppress early warnings leading to an unanticipated, sudden collapse and irreversible demise and highlights how ill-suited the models and observations were in relation to the complexity of the socio-ecological system; and the consequences of separating knowledge about the resource into disciplinary, community and geographic silos.

17.2.1 Complex causality and configurations — context matters

The diversity-oriented approach uses information about cross-scale interconnections amongst many parts of the system to produce a detailed representation of a particular ecosystem. Causation is viewed as conjunctural, or combinatorial and heterogeneous and there is no assumption that the same causal factors operate in the same way in all contexts or in all instances. Diversity-oriented analyses tend not to provide insights into causal generalisations, but rather into the validity of specific processes. This approach builds links between the detail of specific ecosystem analyses and the broad view of ecology via an understanding of complex causality and the identification of specific necessary and sufficient conditions for a particular set of interactions to influence the overall system (Hogg et al., 1989). It works best when causation is complex, where no single condition is either necessary or sufficient or when causes are sufficient only in combination. Identification of the necessary conditions for change and their detection are extremely important steps in ecosystem assessment and can have very powerful policy implications.

Few variable-oriented studies are framed in such terms. Instead, the variable-oriented approach takes a small number of dependent variables across many instances in order to identify a parsimonious set of causal variables. Causation is dealt with through simplifying assumptions about chains of association between independent variables, reflecting the inferential framework of many resource managers. The theoretical basis is an additive linear model, which relies on the fact that it is possible to assess the independent effect of each causal variable, net of the effects of all others. The assumption is that for a particular outcome, the necessary conditions need only be presence or absence.

Typically, variable-oriented analyses focus on statistical similarities and differences and inductively derive a small number of groupings where within-group differences are minimised and between-group differences maximised. These schemes are polythetic, i.e. the cases that are grouped together can differ substantially from each other for one or more attribute as long as they are similar for the majority of attributes selected by the researcher. By contrast in diversity-oriented analyses, context matters and cases are examined as configurations in which as many as possible relevant aspects as possible are looked at in the form of combinations. Such analyses concentrate on the specific features of individual cases, identifying those that are most relevant, whilst considering how those features cohere with each other as distinct types.

Polythetic schemes, typical of the variable-oriented approach widely used in resource management, violate the core principles of the configurational or diversity-oriented approach used for studying resilience and the dynamics of socio-ecological systems. The question is whether the approach adopted can make a difference in terms of being able to better understand or anticipate surprises and change.

A good example of a configurational, diversity-oriented approach with strong counterfactual thinking is the work of the climate scientist, Charles Keeling (Box 17.1). Whilst there are some sceptics who maintain that the cause of global warming is evidenced in measurements of solar radiative output, the vast majority of policymakers and scientists now agree that the root cause, i.e. human activity, can be seen in the measurements of carbon dioxide. To a large extent, this view is the result of the Keeling's work. Having built up a picture of the causal linkages between greenhouse gas emissions and human activities, he carefully chose sites where he then took precise measurements of carbon dioxide at rapid intervals over more than four decades. What he was able to show was the inexorable increase in CO_2 over that time. The Keeling Curve (see Figure 14.1) is now one of least disputed pieces of evidence of climate change. Keeling adhered to the idea that close observation of a natural phenomenon — the 'breathing of the planet' — was an essential part of understanding the dynamics of global changing.

Box 17.1 The Keeling Curve — how close observation revealed the secret of climate change

Fifty-five years ago, the young American scientist Charles Keeling began one of the most important projects in the study of climate change, recording in immense detail the changing levels of carbon dioxide in the atmosphere. Staring out in January 1958, Keeling set up his equipment on the northern slope of world's largest volcano, Mauna Loa and started a lifelong experiment that would change our view of humans on the planet.

The real story had begun much earlier, when Keeling was only 27, and had told colleagues that all the existing measurements of carbon dioxide were wrong or misleading. Recognising that no one else was really interested in taking consistent, continuous measurements of the levels of carbon dioxide in the atmosphere, he decided to take on the task himself. He had studied chemistry, but his great love was being close to nature. So he jumped at the chance to combine these two passions in a post at the California Institute of Technology.

Keeling had by then developed his own protocols and started taking measurements of CO_2 every three hours in different areas, including the roof of Caltech. He did not mind that it was not the most exciting science; collecting samples gave him the chance to do what he loved — packing up his car and family and heading off into the wilderness, camping in forests and national parks, far away from any urban areas.

He kept meticulous records of all his measurements in a series of notebooks, and it was from these that he got his first clue as to how carbon dioxide in the atmosphere was changing — work that would later see him dubbed 'the father of climate change science'.

Scientists already knew that CO_2 levels fluctuated according to the seasons and location, but they did not know why or whether there was a global base level. Keeling wanted to use his new measuring techniques to find out if there was. He and colleagues began getting measurements from carefully selected sites all around the world, including Antarctica, with the intention of making comparisons between them.

What Keeling understood from his own counterfactual thinking was that the measurement of CO_2 in the atmosphere was vital to the development of an understanding of humanity's effects on the planet. He also realised that persistence and attention to detail were essential to the success of the experiment, so whilst other scientists might have moved on to discover new phenomena, Keeling decided that he could not give up — he had to stay with it. In this sense, the science itself forced him to behave unusually as a scientist

By 1956 he had accepted a post at the Scripps Institute of Oceanography; realising that he needed to measure CO_2 over the course of years not months he knew had to find the ideal spot to run the experiment. The site he chose was a former US military site on the slopes of the world's largest volcano Mauna Loa in Hawaii. In the middle of a huge ocean, it was away from contamination and any sources of CO_2 which would have interfered with the measurements. Given that Keeling had to pick an initial site to represent the whole of the world, Mauna Loa observatory was probably the best choice he could have made.

In this ideal environment Keeling started his project, taking samples of air and making CO_2 measurements for the next 40 years. Each day he would venture outside and, after holding his breath, fill a specially designed flask with the incoming ocean breeze. The air would be taken back to the lab to measure its carbon dioxide content.

The result was one of the most famous graphs in science, and would become known as the Keeling Curve. It showed a jagged edge with an amazing regularity and a steep relentless rise of carbon dioxide in the Earth's atmosphere, showing the world's inability to absorb the excess carbon dioxide that human activities were producing.

Placing a temperature curve on top of this curve gave Keeling the foreboding in the 1970s of what was to come. The clean curve of the increase in carbon dioxide spoke to the magnitude of the forces at work, and a picture of all of humanity's exhausts superimposed on the 'breathing' of the planet.

What Keeling discovered is one of the few undisputed pieces of evidence in climate science. Several times he faced cuts to his funding, but always found ways to carry on. His analyser, which was installed in March 1958, collected carbon dioxide data in its original configuration until it was decommissioned in January 2006; even the original strip chart recorder operated from 1958 until 2006. Charles Keeling died in 2004 and today his son Ralph continues the work.

17.2.2 A tale of two cods

The widespread use of variable-oriented approaches in resource management has thrown up a number of problems, especially a general lack of anticipation about sudden collapses. In fisheries, a simple equilibrium model became paradigmatic during the 1960s; it was based on determining the Maximum Sustainable Yield (MSY) under different extraction rates and constant rates of birth, growth and death. The model was related to the larger literature of optimal control techniques and the calculus of variations, which had been successfully applied in theoretical physics, aeronautics, chemistry and management (Hotelling, 1931; Pontryagin et al., 1962), and then spread to economics and resource policy (Dasgupta, 1982; Clark and Kirkwood, 1986). Concerns were raised by some about the utility of MSY models (Larkin, 1977), but these early warning signals were ignored.

It was only when the northern cod (*Gadus morhua*) off Newfoundland collapsed in 1986 (Panel 17.1) that questions began to be raised about its effectiveness. The story of what happened in Newfoundland exposed fundamental flaws in the inferences being made about why the cod population was decreasing, about the roles of the scientists and fishermen in the collection of data, the development of advice and the delays in actions taken by the government. However, the comparison with what happened in Norway is just as interesting. The immediate reaction by the Norwegian government to the collapse of the Barents Sea cod was to impose a moratorium and to invest in more research. The outcomes of the two government actions could not have been made clearer when three years later the Barents Sea cod spawning biomass was bigger than it had been in twenty-five years, whilst the potential collapse of Canadian fish stock was still being covered up.

What is also interesting from the perspective of *Late Lessons* was the reaction by Norway's Fisheries Minister, Oddrum Pettersen, who said that although the warning signs were there, the knowledge to understand them was missing. As a consequence the government took precautionary actions through the moratorium and invested in research to increase knowledge about the linkages between species of fish, especially cod and capelin, and mammals in the Barents Sea. This led Norwegian scientists to develop new counterfactual thinking about the collapse of the cod stock. They believed that the large year-classes of two and three-year old cod had eaten over a million tonnes of capelin at the same time as there was overfishing of the same capelin stock. The result was a sudden collapse of the capelin, which led to the cod eating each other; the seal population, which fed on capelin, also turned to feeding on cod. At the same time a change in ocean temperatures triggered collapses in stocks in the coastal waters of Russia, Iceland, Sweden, Finland and the Faeroes and Lofoten islands.

Meanwhile in Canada, the government scientists insisted that there was no proven connection between fishing on spawning stocks and the survival of the 0-year class. Senior officials maintained that there was no evidence that fishing on spawning grounds in any way harmed the stock. In Norway such fishing was banned on the basis that although it was difficult to find the relation between recruitment and spawning stock, the scientists were convinced that there was such a relation. The Norwegians had understood that no evidence of harm is not the same as evidence of no harm.

17.2.3 Post moratorium

What lessons can be learnt from the demise of the northern cod, especially as the majority of the world's commercial fisheries are over-exploited and many resources are managed using similar models and approaches?

Fisheries management is like a black-box; it is very difficult to see how things are calculated or how things work. In the case of the Canadian moratorium, the Minister of Fisheries, John Crosbie, blamed the collapse on three main factors:

- overestimation of the stock leading to the setting of total allowable catches that were too high;
- foreign overfishing;
- devastating ecological factors.

The effects of ecological factors became myth-like, but in fact as Finlayson and McCay (1998) point out, there were some very obvious problems with these assertions which showed that the counterfactual thinking behind the assessment was deeply flawed.

First of all the stock was treated as one unit whereas it was known to be comprised of distinct populations with different migratory behaviour and patterns; not including this variability may have contributed to the overestimation of biomass (deYoung and Rose, 1993; Finlayson, 1994).

Panel 17.1 The last hunters

Jacqueline McGlade

A view from inside

In 1980, as a newly recruited scientist in the Department of Fisheries and Oceans (DFO), in the Canadian federal government, I was given the responsibility for assessing the size of the stocks of pollock (*Pollachius virens*) off the eastern coast of Canada and determining the size of the quotas. Pollock was one of the less valuable stocks, but nevertheless thousands of tonnes were landed each year. At the time, DFO was the largest employer of biologists in the public service and the second largest of research scientists and technicians; it was heavily decentralised with more than 2 200 personnel and nearly one third of the departmental budget. When the 200 nautical mile limit was declared, the offshore area accounted for one third of Canada's territory.

My task involved estimating the size of the spawning biomass, determining the distribution of potential yield in terms of catch per unit of effort by all the fleets across all age-classes. I was given a small team, a computer, historical data sets and a model, derived from the equilibrium model of Beverton and Holt, known as a Virtual Population Model, plus a few weeks of ship-time on a research vessel in the middle of the winter to complete the annual recruitment survey, an inshore programme for tagging juveniles and a genetics laboratory to determine stock structures. Estimates of catches and effort from the dockside and fleets would arrive at the Bedford Institute of Oceanography in Nova Scotia and we would quality check the data, enter the various numbers, and eventually age-biomass tables would be calculated and graphs produced for different levels of fishing mortality: the target of choice was $F_{0.1}$. — the level of fishing mortality at which the increase in yield to be obtained by adding one unit of fishing effort is 10 % of the increase in yield to be obtained by adding one unit to a lightly exploited stock.

When we went out tagging, we would talk to the fishermen about what they were observing but this was not a common practice, nor was it a regular part of the assessment for most of the stocks. Once a year, the scientists from the department responsible for groundfish would meet under the auspices of CAFSAC (Canadian Atlantic Fisheries Scientific Advisory Committee) and go over the analyses for each stock to set annual predictions of stock abundance on which to establish the total annual allowable catches and harvesting rules. I used to say that you had to leave your ego at the door, because you would often be sent out again and again to redo the analysis using new combinations of recruitment, fishing effort and mortality rates: this was the reason why it was called 'tuning'.

My colleagues had similar experiences to me, but there was always the worry especially with some of the more valuable stocks that the models were too simple to capture the complexity of the real-life situation and the mechanics of running them on the available computers were not straightforward. There was also the issue of the quality of the data: they were often out of date and even though we had an observer programme to check what was going on at sea, there was no guarantee that the fishermen were accurately recording the locations or the size of their catches. Successive ministers would say that science was the foundation of everything, and that fisheries management required a sound knowledge of the fish stocks.

Canada's northern cod

Many official reports, articles and books have been written about the collapse of the northern cod (*Gadus morhua*) in the 1980s (see especially Finlayson, 1994; Harris, 1998, Steele et al., 1992). The question is: why, with such open support and well funded research, did DFO scientists not anticipate the problem?

From the fisherman's perspective, there were signs in the 1980s that the condition of the inshore cod was deteriorating. The industry asked Memorial University biologists to review the1986 cod assessment for Newfoundland waters. Their conclusion was that the DFO assessment had seriously overestimated the size of the stock. The authors also postulated a connection between the large offshore landings and the poor inshore catches. The surprise was that they had used the same data and come out with startlingly different conclusions.

In the 1986 CAFSAC Advisory Document there were inconsistencies between the projected increases in biomass and the fact that the total allowable catches had been at least twice as high as they should have been over the previous eight years. The document suggested that something was very wrong. When the research survey results came in, pointing to an enormous abundance of cod, scientists should have realised that there was no biological means for the stock to have increased as much when there were still

Panel 17.1 The last hunters (cont.)

so few fish inshore. There was, however, one potential explanation for the increase: in the 1960s, another biologist Wilfrid Templeman had warned that if the dense schools of cod which gathered to spawn in the deep warmer waters were overfished, they would continue to concentrate but in a smaller areas. Thus catch rates might continue to increase even as the stock was collapsing. Unfortunately, DFO accepted the data as they stood.

The next year, in 1987, another external panel of experts was commissioned to write a report on the cod; this time they were given access to the DFO data and also looked at the anecdotal evidence of fishermen. The report concluded that DFO had got its figures tragically wrong (Alverson, 1987). The Chairman, Lee Alverson said that the problem had been caused by errors in interpretation of some of the survey information, compounded by a reliance on a faulty mathematical model. He said that the error had been magnified because it had taken several years to find and admit to the problem and by then the stock was already on a downturn. When asked who was to blame he pointed to the government who owned and managed the resource on behalf of all Canadians and were reticent in making effective and timely decisions. He also pointed out how little the DFO scientists knew about the biology of the species and the ecosystem in which it lived.

It was at this point that the DFO scientists came up with the idea that the absent cod inshore were trapped in warmer water, avoiding the cold intermediate layer, rather than being fished out.

Alverson's report was the first time that the government's concerns about the health of the stock were made public, yet the politicians and senior staff in Ottawa remained convinced that the ocean would continue to provide fish and raised the allowable catch level for 1988. This was a clear indication that any concerns about the health of the stock were put far behind socio-economic considerations.

In December 1988, DFO scientists in a dramatic reversal of advice proposed a fifty per cent cut in the quota for 1989.The Federal and Newfoundland Ministers knew that this would lead to thousands being out of work and bankruptcies everywhere. They decided that the consequences would be too devastating, supporting their decision by saying that the scientists had been wrong before. Moreover, there was resistance amongst some senior DFO scientists to admit that any mistakes had been made. The assistant deputy minister later published the official line: 'It appeared that the sudden, unexpected decline in northern cod during 1991 was the result not of high fishing mortality, but rather abnormal environmental conditions … which, through mechanisms not yet understood, may have led to an abrupt increase in natural mortality in the early 1980s' (Parsons, 1993).

Despite the increasing evidence that the unthinkable was happening to the cod stock, the politicians asked for more evidence. In 1989 the Northern Cod Review Panel, led by Leslie Harris, began its work. Meanwhile the inshore fishermen took the federal government to court to stop destructive fishing practices on the spawning grounds. They lost and DFO officials maintained the line that there was no evidence that fishing on spawning grounds in any way harmed the stock. By now Ottawa was already subsidising Newfoundland to the level of 2.56 billion Canadian dollars (CAD). The release of the Harris report in 1990 showed how dire the situation had become: it concluded that the reduction in quotas in 1990 would not enough to reverse the trend of a declining spawning stock but would rather contribute to a further decline (Harris, 1990).

On the point of how had the collapse come about, Harris pointed to the disastrous advice given to managers and politicians by the DFO scientific branch. He stated that the scientists 'lulled by false data signals and, to some extent, overconfident of the validity of their predictions, failed to recognise the statistical inadequacies in their bulk biomass model and failed to properly acknowledge and recognise the high risk involved with state-of-stock advice based on relatively short and unreliable data series … it is possible that if there had not been such a strong emotional and intellectual commitment to the notion that the $F_{0.1}$ strategy was working, the open and increasing scepticism of inshore fishermen might have been recognised as a warning flag demanding more careful attention to areas of recognised weakness in the assessment process' (Harris, 1990).

Harris recommended that the assessments be peer reviewed by those not involved in DFO. He warned that the models had become more important than the study of the species themselves; he said that what was needed was nothing short of a massive research effort to understand the life in the oceans. Ottawa

Panel 17.1 Case study: The last hunters (cont.)

accepted nearly all the recommendations made by Harris, but reducing the total allowable catch on cod was not approved. In 1992 the minister closed the northern cod fishery, saying it had collapsed due to unusual ecological and environmental conditions.

The collapse of the northern cod stock was one of the most catastrophic failures in fisheries and an ecological disaster. The social and economic consequences have been enormous and many communities remain devastated. DFO now admits that it had evidence as early as 1986 and that 'the model used to determine the status of most of the key groundfish stocks has consistently overstated their abundance and understated the level of mortality' (Auditor General of Canada 1997).

Barents Sea cod

Meanwhile on the other side of the Atlantic Ocean, in Norway, the1989 autumn survey results showed that cod stocks in the Barents Sea were at their lowest for over a hundred years. Scientists and fishermen had already been worried that the fish were too small and earlier estimates of abundance too high. Cod quotas were slashed and the capelin fishery also closed. Fishermen warned that the fish they were catching appeared to be starving. 'When scientists told the Norwegian politicians that there had to be severe quota cuts, the politicians acted immediately and backed the cuts despite a firestorm of criticism from their constituents. Oslo also immediately implemented policies to reduce the number of cod fishermen and vessels' (Harris, 1998).

In January 1990 the government imposed a moratorium. Fishermen's incomes dropped by up to 40 per cent and in the end the Norwegian government spent more than EUR 50 million to remove capacity from the fleet. However, the prompt action by the government meant that by 1991 signs of a recovery were seen and in 1992 the spawning biomass of the stock was larger than it had been for 25 years.

Second, key variables, such as recruitment and natural mortality, were treated as constants in the models used. This in combination with problems in the periods used to derive averages used to generate the constants also resulted in overestimates (Finlayson, 1994).

Thirdly, data from the fishing industry used in stock assessments, in combination with research vessel survey data, were seriously distorted by the practice of discarding undersized fish. There was also a bias towards the use of offshore versus inshore landings as an index of abundance to 'tune' the stock assessment model. Inshore fisheries landings were not systematically used in the assessments because of difficulties obtaining consistent measures of 'catch per unit effort' and otherwise dealing with messy and often anecdotal data. Therefore evidence of decline in the abundance and size of inshore migrating fish was apparently missed (Steele et al., 1992; Neis, 1992), contributing to DFO's inclination to dismiss the concerns of inshore fishers.

Why was the research on basic cod biology not being carried out? One obvious reason was the career structure of fisheries scientists who were assessed on their publications in peer reviewed journals. The number of papers published on northern cod, one of the most important resources in eastern Canada fell from more than 10 per year to 2 annually over a twenty year period, in contrast to the increase in papers seen in the Norwegian setting, where research was being actively encouraged.

Another problem however was the hubris amongst senior government officials in denying that there was anything wrong. This was a projection of the government's own crisis around its institutional authority and epistemological legitimacy. For example, in the February 1988 issues of *Fo'c'sle*, aimed at fishermen and the general public, the DFO Newfoundland office published an article entitled '*The Science of Cod'*. In the introductory statement the Director General says:

> 'It is reassuring that the conclusions of the Task Group [the Alverson Report, 1987] and CAFSAC about northern cod are quite similar with respect to the present stock size and the causes for the decline in the inshore fishery since 1982. The credibility of DFO scientific advice was not questioned. The northern cod stock continues to increase, but perhaps not as fast as projected several years ago'.

Finlayson and McCay (1998) also asked why it was that scientists who knew or suspected that there were problems with the stock assessment did not

speak up. It is clear from the inside that some DFO scientists had misgivings about the quality of the scientific advice given about cod, but as in any civil service they were not allowed to speak publicly about the issues once it had become policy. It was also the case, however, that many assessment scientists had little contact with the fishing industry or actual fish, dealing rather with 'paper fish'. There was also a tendency when scientists were presenting their assessments to the relevant advisory body that they would minimise the problems associated with data reliability, uncertainty, the models and data-sets, issues of stock structures or even admitting to the possibility of unknown unknowns! ([1]).

17.2.4 Knowledge systems

The fisheries case studies serve to underline the fact that simple variable-oriented analyses are no match for the complexity of real socio-ecological systems. So why have these approaches not been replaced, especially given that it has long been recognised that the majority of the world's fisheries are over-exploited (Pauly et al., 2002; FAO, 2010)? One reason is perhaps the lack of consensus about which approaches could replace them in order to understand complex systems and manage resources more effectively. This partly stems from the low pedigree of knowledge about the causality linking many of the processes and elements in socio-ecological systems (Table 17.1).

The division of knowledge into political, disciplinary and geographic silos can lead to Yaffee's (1997) 'recurring nightmares' of short-term interests outcompeting long-term vision; situations where competition replaces co-operation because of conflicts in management; fragmentation of values and interest; fragmentation of authority and responsibility; and fragmentation of information and knowledge leading to inadequate solutions or even additional problems. In situations where strong counterfactual thinking is needed, for example in developing early warnings, the presence of silos of knowledge can become a real hindrance.

The fact that ecosystem and resource management is highly interdisciplinary, involving fields of varying states of maturity and with very different heuristic and social practices is also a challenge. Those involved in planning and policy development often find themselves having to use inputs from areas of expertise with which they are potentially unfamiliar, making it difficult to apply the same level of judgement as in their own core field. The result can be a dilution of quality control in the information gathering process and a weaker quality assurance of results. It is unsurprising that planning and management institutions have been unable to respond to crises or change, as in many instances, the organisations are suffering from a chaotic mixture of information, analysis and interpretation with no paradigmatic structure in which to incorporate all the various forms of scientific, interdisciplinary, and indigenous knowledge (McGlade, 2001).

In the pre-modern environment, knowledge was rich and adapted to the requirements of living locally. Individuals today are just as knowledgeable but they receive information from an enormous number of sources, some technical, some cultural. In this way we can see a form of second-order science emerging in which individuals must rely on other peer groups and experts to be able to evaluate the information within their own domains of expertise.

Table 17.1 Pedigree of knowledge

Pedigree	Theoretical paradigm	Data	Peer acceptance	Colleague consensus
4	Established	Experimental	Total	All but cranks
3	Theoretical model	Historical/field	High	All but rebels
2	Computer model	Calculated	Low	Competing schools
1	Statistical procedures	Educated guess	Low	Embryonic field
0	Definitions	Random guess	None	No opinion
∞	Unknown unknowns	Unknown	Unknown	Unknown

Source: McGlade, 2002.

([1]) This phrase, cited by many military experts, was made infamous by Donald Rumsfeld (2002) in his press briefing on weapons of mass destruction in Iraq, where he said '[T]here are known knowns; there are things we know that we know. There are known unknowns; that is to say there are things that, we now know we don't know. But there are also unknown unknowns — there are things we do not know we don't know.' 12 February 2002.

This type of interaction is especially important in ecosystem and resource management, because direct scientific evidence is likely to be missing but there is often a wealth of local and lay knowledge to be gained through the close observation of and proximity to nature, as Annie Dillard experienced during her year spent next to Tinker Creek. In this sense the concept of an expert as part of the system of governance has to be broadened to include those who have particular knowledge about a system but who do not necessarily walk the corridors of power and/or of science. It is interesting in this regard to note that the newly established Intergovernmental Platform on Biodiversity and Ecosystem Services (IPBES) explicitly recognises the contribution of indigenous and local knowledge to the conservation and sustainable use of biodiversity and ecosystems, yet it is still struggling to find operational ways to include such knowledge into its work.

17.3 Planetary dynamics and ecosystem change

This section looks at ecosystem change through the lens of four interconnected concepts arising from the scientific field of non-linear dynamical systems behaviour: **planetary boundaries** (Rockström et al., 2009); **tipping points** (Lenton et al., 2008; Schellnhuber, 2009), **panarchy** (Gundersen and Holling, 2001) and **resilience** (Walker and Salt, 2006). Based on information drawn from socio-ecological systems around the world, we explore whether or not these concepts could help communities and managers anticipate sudden change or the collapse of a resource and provide a practical basis for sustainable management of our relationship to ecosystems.

17.3.1 Navigating the Anthropocene

The dynamical behaviour of the planet's natural systems is now changing more rapidly than at any time previously during the previous 10 000 years of the Holocene. Evidence of the scale, magnitude and significance of these changes has been sufficient for geologists to conclude that an epoch-scale boundary has been crossed and that we are now in a new epoch — the 'Anthropocene' (Steffen et al., 2011; Zalasiewicz et al., 2011). Living in the Anthropocene will require us to deal with ongoing and rapid or sudden onset threats such as oil spills, chemical and nuclear accidents, earthquakes, landslides, tsunamis, volcanic eruptions, severe weather, storms and cyclones, floods, wildfires and epidemics, and slow-onset threats such as air quality, droughts and desertification, food security and epidemics and climate variability (UNEP, 2012).

The 1980s and 1990s saw the emergence of the theories of chaos, non-linear dynamics and many other highly sophisticated mathematics as a source to explain the complexity of ecosystems (May 1982; McGlade 1999). At the same time, knowledge about the planet's own dynamics was growing: from debates about the impact of the Milankovitch cycles on climate to the idea that the 'flap of a butterfly's wing' could cause changes thousands of kilometres away.

The analytical basis of ecosystems science was also growing but the sophistication of the tools and computational methods meant that few field biologists could really make use of the ideas beyond concepts and definitions. Instead, the advances were largely taken forward by climate scientists, meteorologists, oceanographers and biogeochemists under the aegis of the Intergovernmental Panel on Climate Change. The models of global change which were developed, however, generated scenarios of the likely magnitude of global temperature increases, sea-level rise, melting of the ice caps, glaciers and sea ice, droughts and tropical storms which would have direct consequences for ecosystems.

It was with this information, that a network of theoreticians and mathematical ecologists began to expand their ideas on four major concepts: *planetary boundaries* (Rockström et al., 2009); *tipping points* or *elements*, (Lenton et al, 2008; Schellnhuber, 2009), *panarchy* and *resilience* (Holling, 1996; McGlade, 1999).

Rockström and colleagues have proposed nine hard global biophysical limits, or planetary boundaries, for human development — land-use change, biodiversity loss, nitrogen and phosphorous levels, freshwater use, ocean acidification, climate change, ozone depletion, aerosol loading, and chemical pollution. Each has its own metric, for example greenhouse gas emissions, concentrations of various pollutants in air and water, and aragonite concentrations in the ocean. At present, none of these limits can be entirely dismissed either by firmly ruling out a possible anthropogenic triggering of irregular dynamics or confirmed by providing relevant estimates for activation or reaction times. Nor can the response times of the various sub-elements be estimated beyond a certain resolution e.g. yearly in the case of aerosol loading and loss of summer sea ice or millennia in the case of ocean acidification. However, the widespread lack of in situ observations to validate the models underpinning these limits and the inbuilt latency of the planetary system itself, mean that there

will be many decades of tantalising ignorance about whether or not any of these boundaries *per se* have been crossed.

Instead it is more likely that the effects of the tipping elements described by Schellnhuber, Lenton and co-workers, will come to define future surprises. We are experiencing some of them already — Arctic sea-ice loss; boreal forest dieback; melting of Greenland ice sheet; instability of the west Antarctic ice sheet; Atlantic deep water formation and permafrost and tundra loss. Others are potentially yet to come — climatic change-induced ozone hole; greening of the Sahara; chaotic multi-stability of the Indian monsoon; changes in the amplitude or frequency of the El Niño Southern Oscillation (ENSO); dieback of the Amazon rain forest; west African monsoon shift; and changes in Antarctic bottom water formation. The causality and inter-linkages between these potential tipping elements raises both long- and short-term questions. For example, will increasing levels of greenhouse gases lead to a permanent change in the ocean current system including the north Atlantic Gulf Stream and the El Niño regime that could ultimately suppress the Quaternary glacial 'cycles', while drastically altering the number of extreme weather events such as droughts, storms, cyclones and tornadoes?

Tipping elements pose one of the toughest challenges for contemporary science, because key emergent properties (and consequently early warning signals) are likely to arise on a range of spatial and temporal scales and be observed by scientists across many disciplinary silos, which are themselves populated by elites and people with their own paradigms and language. Global changes in climate, ocean acidification and even possibly ozone depletion may cause thresholds on a planetary scale to be crossed that alter or reconfigure the functioning of some ecosystems, leading to abrupt transitions and potential irreversible changes on a local scale. Identifying thresholds based on a generic model of tipping points is an exercise in futility; instead we will need to adopt an approach based on cascading thresholds, where early warnings and signals of change are linked to observations of key processes on a local and regional scale.

17.3.2 Anticipating surprises — adaptive cycles and panarchy

Over the past fifteen years, Buzz Holling, Brian Walker, Carl Folke, Terry Hughes, Steve Carpenter and colleagues have been exploring socio-ecological systems around the world (www.resalliance.org). The idea has been to create an empirical and theoretical base on which to understand abrupt change in managed resources and to develop a general theory with heuristics and principles to better understand resilience (Holling, 1973; Gunderson and Holling, 2002; Walker et al., 2006).

The concept of resilience in ecosystems was introduced by Holling in his classic paper on non-linear dynamic models that captured the relationship between stability and resilience in ecosystems (Holling, 1973). Whilst some ecologists considered resilience to be a measure of how quickly a system returns to an equilibrium state after a disturbance (what is now known as engineering resilience), Holling kept to the notion that ecological resilience was the measure of how far an ecosystem could be perturbed without experiencing a regime shift (Hogg et al., 1989; Holling, 1996; McGlade, 1999).

There are many examples where ecological resilience has been described and its loss recorded (Table 17.2). In most instances, the dynamics of the adaptive cycles are the product of the interlinkages between the ecosystem and people, and it is generally these, sometimes hidden, cycles that managers are actually coping with. As the diversity of the case studies shows, the scale of the management challenge is enormous. However, one aspect that is of particular importance is the anticipation of surprise or abrupt changes, and the rapid shift to a new regime. In some literature, the term 'alternative state' is used: this is a misnomer. Complex ecological and socio-ecological systems are better expressed as configurations of states with the same controls at work, i.e. the same feedbacks, but where the configuration describes the kinds and strengths of feedbacks and where the different internal controls on functions represent alternate regimes with thresholds between them. Striking examples of this are the desertified regions of the Sahel and the emergence of permanent summer algal blooms in the Baltic Sea.

As part of the development of a more general theoretical basis for managing socio-ecological systems, Walker and colleagues (Walker at al., 2006) proposed five heuristics: two describing the dynamics across scales — adaptive cycles and panarchy, and three describing the properties of the system — resilience, adaptability and transformability. Adaptive cycles in ecosystems generally follow a path known as 'ecological succession', involving growth (r) where resources are plentiful, and conservation (k). Most socio-ecological structures are not scale invariant but are built on combinations of slow and fast

Table 17.2 Case studies of socio-ecological systems

Location of case study (researcher; cited in Walker et al., 2006)	Socio-ecological characteristic	System change	Vulnerabilities	Resilience
Causse Méjan, France (Etienne & Bousquet)	Ecosystem diversity is totally dependent on grazing.	Pine trees from neighbouring forest stands are invading the steppic grasslands. Agriculture has destroyed many flatlands.	New social groups, including forest owners, secondary residents.	Keeping alive the Causse culture and traditions of environmentally friendly farming through sharing labour and knowledge and the co-evolution of habitat and farming.
Caribbean coral reefs (Hughes, 2003)	Coral reefs have been on a trajectory of serious decline. In the 1950s a single species of sea-urchin was keeping macro-algal blooms in check. In the 9170s a disease outbreak led to the catastrophic loss of urchins, precipitating blooms that persist today.	Collapse of many reefs due to overharvesting, pollution, disease and climate change. Loss of key habitat forming *Acropora* species.	Long-term trajectory of a shift from fish- to echinoid-dominated destructive herbivory.	Reefs exhibit numerous alternate states, but the resilience of these is unknown. Experiments with No Take Areas and protection of hotspots may help locally, but are unlikely to stem region-wide loss of resilience.
Dry spiny forests, southern Madagasar (Elmqvist)	High degree of endemism; inhabited by the People of the Thorn Bush who protect dense forest patches through strong informal institutions.	Fragmentation and loss of forest due to insecure land rights.	Tensions between Christianity ad customary institutions, government policies and local informal arrangements.	Strong social capital and the large capacity of spiny forests to regenerate.
Everglades, Florida (Gunderson, 2001)	Internationally recognised wetland, which was historically partitioned into agricultural, recreational and conservation areas. Area is now maintained through canals, pumps and levees.	Ecological crises brought on by changes in water quality and quantity caused by the volume and timing of flooding.	Institutional reformation and realignment, plus the need for large-scale, expensive, technologically based solutions. Conflicts over water use amongst institutions and actors.	Example of a perversely resilient social system based on conflict and a formal closed network of government agencies and policies.
Gorongosa National Park, Mozambique (Lynan)	Park was home to large herbivore and carnivore populations but these were decimated in the war of Independence in the 1980s. Now home to some 500 bird species and 10 000 people.	The loss of major species.	There are no schools, clinics or facilities for the people living in the park who provide local protection to the ecosystem. No local enforcement of existing conservation policies in the buffer zone.	Remains one of the prime protected areas in southern Africa.
Goulburn-Broken Catchment, Australia (Ryan)	Sub-catchment of the Murray River. Climate temperate with sparse vegetated plains. Originally occupied by Aboriginal people but subsequently populated by Europeans after the discovery of gold. Today heavily agricultural.	Irrigation infrastructure and clearing of more than 70 % of the native vegetation cover have substantially altered the hydrological balance.	Climatic variation causing changes in vegetation and groundwater recharge. Substantial land-use change, with dry-land areas delivering significant salt and nutrient loads to the waterways. Increasing demand for non-consumptive water and conflicts amongst property rights.	Property rights and downstream accountability in place. Costs of maintaining the regime mounting, resource base degrading, regional economy more brittle. System more vulnerable to shocks and disturbance (Anderies et al. 2006).
Northern Highland Lakes District, Wisconsin (Petersen & Carpenter)	Pristine wilderness with management focused on protection and promotion as a wilderness tourist destination.	Lakeshore development for tourism and second homes. Invasive species including rainbow smelt, rusty crayfish and Eurasian milfoil have reduced the quality of fishing and boating. Proliferation of suburban life.	Stakeholders with many divergent views. Natural resource management has been slow to adjust to ecological and social change. Invasive species and eutrophication.	Multiple states and thresholds are known relating to eutrophication, collapse of fisheries, trophic cascades, woody habitat and inertia of long-lived predator and tree populations. Non-reversible threshold may be caused by species invasions and a shift from old-growth timber harvesting to pulpwood rotation.

Source: Adapted from Walker et al., 2006. Detailed descriptions of each case study can be found at www.resalliance.org.

processes; panarchy is the term that describes how these different types of processes operate across time and space scales. Disturbances can lead to another connected regime in which resources that have been historically bound-up are released (Ω) and the fundamental structure collapses; this is followed by a phase of re-organisation (α) in which novel structures can take hold leading to another growth phase in a new cycle. There are many examples of disturbances causing shifts in this way, including forest fires (Dublin et al., 1990), forest pest outbreaks (Ludwig et al., 1978), algal blooms in eutrophied aquatic systems (Carpenter and Brock, 2004) and droughts.

17.4 Socio-ecological systems — institutional fit and resilience

In this section we look at socio-ecological systems from the perspective of institutional fit and resilience as sources of anticipation and adaptive capacity. As Elinor Ostrom (2005), Carl Folke and colleagues (Folke et al., 2007) have pointed out, the lack of institutional fit can confound the effectiveness of stewardship of ecosystem services and resource management, and can lead to unexpected surprises, excessive rent seeking and high transaction costs (Kofinas, 2009).

Despite innovations in institutional arrangements and a greater awareness of the importance of the need for more effective forms of governance, the loss of trust in bureaucracies has been growing. Deeply embedded differences in attitude towards conserving ecosystems versus exploiting resources have led to highly politicised public debates around false dichotomies, such as choosing between protecting the environment and employment or energy, or diversionary arguments such as the tragedy of the commons. In the case of the collapse of the northern cod, the commons were neither open-access or unregulated, but the use of this discourse meant that the only solution sought was downsizing of the fleets, rather than a closer examination of the complexity of the causes of the problem, such as flawed scientific advice, vested interests and government priorities.

The key question is what happens when there is a real crisis, brought about by sudden change in a resource or ecosystem? Do those institutions with most to lose become destabilised or do they attempt to renegotiate their power relations? Do those with most to gain seize the opportunity for restructuring?

In Newfoundland it has been the social structure of the fishery that has collapsed even though the inshore fishermen potentially had the most to gain in the aftermath. The resource scientists and managers on the other hand have only made modest changes despite being at the core of the problem. This might suggest that modern science is much stronger and more deeply embedded as a social and political authority than generally assumed. It means that it will take more than the collapse of a resource or a shift in an ecosystem to displace the existing form of authority that has been built on a certain control of science. It also raises questions about how to build up institutional fit and resilience and develop effective science-policy interfaces.

17.4.1 Institutional fit and governance

Institutional infrastructure, along with governance and leadership, heavily influence our capacity to manage complex systems and cope with abrupt change. It has been the lack of institutional fit that has often confounded the effectiveness of the stewardship of ecosystems and the systems they provide, and led to unexpected surprises, excessive rent seeking and high transaction costs. The causes of a lack of institutional fit are many and can stem from mere folly (Tuchman, 1984), complexity, uncertainty about roles, a lack of ownership and property rights, institutional frailty and vested interests.

An example of the consequences of the confounding effects of a poor institutional fit can be seen in the 1997 legal case of Nunavut Inuit concerning the Canadian Fisheries Minister's decision to increase the turbot quota against the advice of the NAFO scientific council and then to assign the additional tonnage to his own constituents rather than to the Inuit of the Nunavut region or Denmark ([2]). It was said in an internal memo to the Fisheries Minister that the Canadian government could be seen as hypocritical by the international community because it exhorts others to share the burden of conservation but was unwilling to do likewise.

Judge Douglas Campbell set aside the Minister's decision and referred the matter back for

([2]) Nunavut Tunngavik Inc. v. Canada (Minister of Fisheries and Oceans) (C.A.), [1998] 4 F.C. 405. 13 July 1998 (http://reports.fja.gc.ca/eng/1998/1998fc22910.html).

reconsideration of the quota. The Minister appealed, stating that he possessed:

> 'absolute discretion… to issue leases and licenses for fisheries or fishing. The rationale for such discretion is that Canada's fisheries are a common property resource belonging to all the people of Canada and licensing is a tool to manage fisheries which is given to the Minister whose duty it is to manage, conserve and develop that resource in the public interest. … The actual exercise of such discretionary power is influenced by numerous fluctuating policy concerns which go beyond the necessary issue of conservation and protection of fish to include cultural, political, scientific, technical and socio-economic considerations or policies.'

The Court of Judicial Review rejected the appeal for reasons that the Minister had not acted lawfully, but it made clear that the Court was 'not to become an academy of science to arbitrate conflicting scientific predictions, or to act as a kind of legislative upper chamber to weigh expressions of public concern and determine which ones should be respected… [it] is concerned with the legality of the ministerial decision resulting from an exercise of discretion, not its opportunity, wisdom or soundness'. There was clearly a lack of institutional fit between the legality of the defined role of the Minister and a legal framework in which the Minister's actions could be judged on the basis of evidence of fairness and long-term sustainability of the resource.

Over the past two decades, a number of important institutions and initiatives have been created to bridge the science-political divide and support international agreements on managing and protecting our global resources. These range from the UN Convention on Biological Diversity and the UN Conference on Straddling Fish Stocks and Highly Migratory Species to initiatives such as the Millennium Ecosystem Assessment, IPBES (International Platform on Biodiversity and Ecosystem), TEEB (The Economics of Ecosystems and Biodiversity) and ABS (Access and Benefit Sharing). These are primarily aimed at reducing the likely impacts of a growing human population and climate change on ecosystems and ensuring the sustainable use and equitable distribution of natural resources. However, as we show in the case study on European Union fisheries, even with highly cohesive, well-resourced institutions the consequences of a poor institutional fit remain one of the largest obstacle to the resilience of our fisheries (Panel 17.2).

There are a number of structures of governance; including the minimal state, corporate governance; new public management; good governance; sociocybernetic systems and self-organising networks (McGlade, 2001). This last type involves complex sets of organisations drawn from the public and private sector and is particularly interesting in relation to the governance of resources. The key to understanding their importance comes from the observation that integrated networks can resist government steering; they develop their own policies and mould their environment. This leads to interdependencies between organisations in order to exchange information and negotiate shared resources and a significant degree of autonomy. In the end, this form of governance can hollow out the state through privatisation and by limiting the scope of public intervention. A manifestation of this type of governance is swarms of amorphous groups that link together to tackle single issues such as dolphin-friendly tuna fishing and anti-sealing and whaling. In managing resources it is necessary to understand that governance is becoming increasingly operative, where lines of authority are less formal, legitimacy is more ambiguous and where people are choosing when and where they want to engage in collective action.

The majority of fisheries are operated through instrumental actions, i.e. where technical rules are developed and implemented. However, in many of the case studies listed in Table 17.2, the communities manage the resources through consensual actions and norms, such as religion, deity or faith, rather than legal ones. The effectiveness of this type of action and user participation is that in times of crisis, participants learn more quickly and show a greater capacity to adapt and even transform. For example, after the initial water-table crisis in the Goulburn Broken Catchment in the 1970s, conflicts gave way to networks that connected people and interests to deal with issues of flooding, waterlogging and drainage (Anderies et al., 2006). Leaders emerged to form committees to represent the concerns of the various networks throughout the catchment. They pooled existing knowledge, identified gaps and invested in research and effectively lobbied government agencies for support. Despite all this, government leaders opted for adaptation rather than transformation.

By contrast, the ecological crises in the Florida Everglades (Gunderson, 2001) which had originally given rise to a network dominated by government agencies and formal policies, gradually led to a network of government and non-governmental

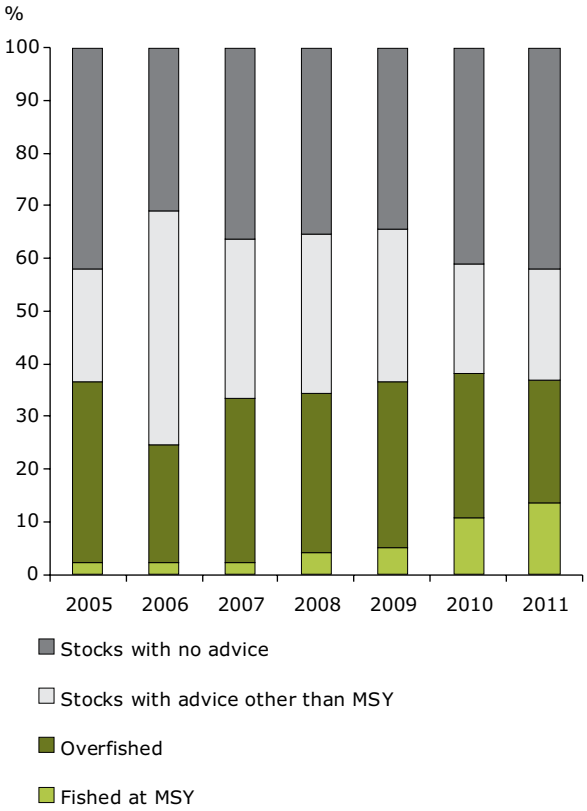
Panel 17.2 Knowledge-based management of EU fisheries — how much is scientific evidence being used?

Constança Belchior and Johnny Reker

Despite being managed under one of the most complex and expensive science-based management systems in the world, since 1983, the condition of Europe's fish stocks has continued to worsen (O'Leary et al., 2011; EU, 2011). The 2002 and 2012 reforms of the EU Common Fisheries Policy (CFP) aimed to deal with the failure to achieve the core objective of ecological, economic and social sustainability, where 72 % of all assessed EU fish stocks were estimated to be overexploited, and over 20% fished beyond safe biological limits, i.e. with a greater risk of collapse. (In the north-east Atlantic the number of stocks known to be overfished fell from 94 % to 63 % from 2004 to 2010, compared to 82% in the Mediterranean) (EC, 2010, 2011a).

One problem is that data of sufficient quality to support scientific advice on MSY and overfishing is missing for approximately two-thirds of the stocks for which quotas (Total Allowable Catches) are set in the north-east Atlantic (EC, 2011a) (Figure 17.1). This figure was intended to show fishing opportunities, but inconsistencies in the data on different stock parameters (e.g. number of stocks with no or insufficient data, or for which an excess TAC was set) point to the underlying difficulty of producing coherent assessments. For example, data quality and availability is so poor in the Mediterranean, that in 2010, only 16 out of 102 candidate species could be assessed (EC, 2010).Part of the problem is that Member States have not provided the relevant scientific data despite there being a legal responsibility to do so (EC, 2011a), introducing greater uncertainty into the scientific advice, and thus further undermining its credibility (Piet et al., 2010).

Figure 17.1 Trends in status and advice setting for north-east Atlantic fish stocks between 2005 and 2011



Source: EEA, based on EC, 2011a.

There have been many analyses of why EU fisheries management has not been successful (e.g. Sissenwine and Symes, 2007; Khalilian et al., 2010; EC, 2009; EU, 2011). The main conclusion, alongside the lack of scientific knowledge and ineffective management options to restore fish stocks and fisheries to profitable and equitable conditions, is the very nature of the decision-making process (Villasante et al., 2010; Piet et al., 2010; O'Leary et al., 2011). Overall, scientific advice has been largely overruled when setting fishing opportunities for EU fish stocks; between 1987 and 2006, the TACs only matched scientific advice in 8% of the assessed stocks (Piet et al. 2010), and were consistently set well above the scientifically advised level by an average of 47 % since 2003 (EC, 2011a).

The actual impacts of such mismatches remains uncertain (O'Leary et al., 2011), but it is likely to be significant given the cumulative impacts of overfishing and increased capacity on the integrity of the wider marine ecosystem (Anticamara et al., 2011). For example, it has been estimated that the recovery time for benthic habitats in areas in the Greater North Sea where there was low natural disturbance, was between 7.5–15 years following only one pass of a beam trawl (OSPAR, 2010). In German waters some areas have experienced up to 4 000 hours of beam trawling (Pedersen, 2009). Fisheries are thus a significant contributor to pressures on European marine biodiversity where only 2 % of the species and 10 % of the habitats reported under the Habitats Directive are considered to be in favourable conservation status (HELCOM, 2010; EEA, 2010).

Panel 17.2 Knowledge-based management of EU fisheries — how much is scientific evidence being used? (cont.)

As a response to the current situation, an ecosystem-based approach to management has become one of the CFP's objectives under the EU Marine Strategy Framework Directive. The intention is to implement more holistic, integrated management strategies to achieve EU ambitions on securing healthy and productive marine ecosystems, including halting the loss of biodiversity, ensuring sustainable economic growth and improving resource efficiency.

The ecosystem approach sets out a framework for understanding the socio-ecological system, where the hidden long-term costs or externalities and subsidies are accounted for, in order that options that generate more societal value can be prioritised (e.g. ISU, 2012; Crilly and Esteban, 2011). In a recent study on the potential benefits of restoring 43 European fish stocks to their maximum sustainable yield from current levels (Crilly, 2012), the authors found that it could generate 3.53 million tonnes of additional landings, and an additional value of EUR 3 188 billion annually. This is more than five times the annual fisheries subsidies paid to EU Member States), and could in turn support the creation of more than 80 000 jobs in the sector in the EU.

Thus it seems that there is sufficient available knowledge to underpin informed decision-making to support an ecosystem approach to fisheries, but also one that prioritises solutions that will benefit society the most. At a time where the EU already depends on substantial imports to meet more than 65 % of total EU consumption of seafood (EC, 2011a) and where food security is becoming a global growing concern, managing fish stocks sustainably provides a competitive advantage to the EU which should not be overlooked by individual or national interests. However, as previously discussed, this is unlikely to happen as long as decision-making in the CFP allows for short-term economic interests to compete with and outcompete long-term sustainable and precautionary scientific advice at the very beginning.

The question remains: has Europe learned from past experiences? The short answer is yes, but we are still not reacting to our knowledge fast enough. Fisheries are still not being managed sustainably and the majority of European fish stocks are still overfished. Furthermore, there are considerable gaps in our knowledge regarding the status of fish stocks, yet on average TACs are still set well above scientific recommendations showing a disregard for scientific advice and also for the precautionary approach. From a societal perspective, further evidence also shows that overfishing also means the EU is getting much less out of its fish stocks than if they were restored and sustainably managed. This situation is mirrored at a global level, where the 'sunken billions' in world fisheries due to excess fishing capacity have been estimated at 50 billion US dollars annually (World Bank, 2009).

The new CFP proposal (EC, 2011b) features ambitious measures from the European Commission, namely the commitment to establish management measures 'in accordance with the best available scientific advice' and no longer just 'based on scientific advice'. Also, it proposes to give more power and responsibilities to the actual stakeholders, making them more accountable for the resource they are being allowed to exploit, alongside other measures which aim to better integrate the precautionary and ecosystem approaches into the CFP. Overall, it sets out a more flexible mechanism that should allow it to cope better with the inherent diversity in both EU fisheries and the changing marine environment.

It is questionable, however, whether a management system in which scientific evidence is consistently being undermined, either by lack of compliance by Member States in delivering sound fisheries data, or by disregarding it due to narrow political interests and negotiations, will ever be able to deliver its objective of long-term sustainability. This is a point recognised by the European Parliament in its review of the proposal for the new CFP regulation (EP, 2012). Therefore one of the greatest challenges in managing EU fisheries and specifically the EU 2012 CFP reform remains the level of respect for scientific advice as a fixed boundary condition for natural capital when negotiating political agreements.

A socio-ecological management system solidly grounded in science is undoubtedly a more objective way to manage natural resources following established criteria, whilst also coping and adjusting to uncertainties. Together with the precautionary approach, it could help to set out a long-term transparent management system for fisheries, unlike the vested political decision-making system that prevails in the CFP today. Governance arrangements in and around EU fisheries will need to respect scientific advice and ensure the compliance of national data obligations to support it, as well as allowing for more transparent and inclusive decision-making that favours a wider sectorial and public engagement. This could be through broader representative constituencies and greater societal benefits as opposed to the current practice that favours the exhaustion of natural capital whilst leading the fisheries sector towards a deteriorating future.

groups which opted for transformation. New institutions, technological solutions were created on the back of significant levels of investment. As many of the cases indicate, two of the most critical factors for adapting to change and transformation are institutional fit and leadership.

17.5 Future prospects

This final section looks at some of the key lessons that emerge from the various case studies and reflects on how they might be used to improve resource management and ecosystem stewardship in the future. The six major lessons that resource managers and those living in a particular socio-ecological system need to consider to ensure that sudden, abrupt changes do not lead to catastrophic collapse are as follows:

- Close observation of ecosystems and natural phenomena.
- Development of a diversity-oriented approach to resource management that reflects the complex causality of the real-world context.
- Widening the sources of information and knowledge about the dynamics of socio-ecological systems.
- Reducing delays between early warnings and actions.
- Developing a deeper understanding of the full adaptive cycle of the ecosystem and resource base being managed.
- Building up the learning, leadership and innovative capacities in the institutional and societal context to enable transformation rather than only adaptation. As seen in so many of the case studies there is a need for greater participation and transparency regarding vested interests.

The evidence used to develop management advice will also need to be far more explicit about the dynamics of processes across different time and space scales and uncertainty. Resource managers and the community at large will need to develop the skills and capacities to create consensus — and where not possible compromises (van den Hove, 2006) — about how to handle uncertainty and which diagnostic criteria and metrics will be used to elicit action in the case of early warning signals (Table 17.3). For example, thresholds in water use, size of patches of forest clearance, wildfire management and the extent of agistement have all been shown to be critical activities in determining the resilience of the socio-ecological systems examined.

Table 17.3 Examples of early warning and possible outcomes and responses

Type of early warning	Possible outcome	Examples	Possible solutions
Spatial	Potential rapid spread via multiple unknown pathways	Bird flu; various fungal diseases, invasive species	Establish broad jurisdictional authority to monitor spread and develop potential policy actions; develop in situ monitoring, and multi-scale and multi-interaction models
Temporal	Potential spread of problem on different time scales linked to ecological and physiological processes leading to collapse and a different regime	Drought, over-exploitation of key resources over time, invasive species	Develop an understanding of the adaptive cycle, multiple pathway and time-dependent models and ensure appropriate in situ monitoring of human and ecological systems
Demographic	Potential long-term impacts on the health of the ecosystem and human population	Age-related diseases	Develop more intense monitoring of entire adaptive cycle and long-term monitoring of age-related processes
Threshold behaviour	Potential for issue/events to create socio-ecological regime shifts with significant long-term economic and/or ecological impacts including irreversibility	Sustained over-harvesting of fish stocks leading to collapse of keystone species; runoff from nitrogen fertilizer leading to eutrophication	Develop integrated assessments with scenario analyses that include the potential to identify long-term physiological and ecological shifts
Cascading effects	Potential that problem effects cannot be buffered or can be amplified between domains leading to significant socio-ecological impacts	Reduction in the polar ice cap opens up northern sea routes to shipping; creating new forms of land use change and local harvesting of resources	Develop multi-jurisdictional approach to manage changes; develop integrated assessments and scenario analyses to understand the multi-dimensional dynamics and resilience of the socio-ecological systems; establish new monitoring systems

The fundamental assumption that the existing institutional landscape is fit for purpose should also be examined carefully. As Hobbes (in *Leviathan*, 1651) and Machiavelli (in *The Prince* ca. 1514) well understood, user participation and the frameworks of power are the most important elements to understand when mapping out the rights of the community. In ecosystem and resource management there are a number of regimes including: laissez-faire; market regulation; communal governance; state governance and international governance (generalising from McCay, 1993). As shown in each case study, property rights and the authority to constrain exploitation are at the heart of the matter and inevitably come under intense pressure during a crisis. Ensuring the resilience of socio-ecological systems requires an explicit understanding of the rights and responsibilities during periods of transformation.

A final observation is that many interventions in resource management are made on the basis of a belief that these would have predictable outcomes. The assumption has been that all interactions can be adequately understood and that all future states are contained within the present structure of the socio-ecological system. The hubris of this type of thinking parallels that of the financial world in which a constrained set of tools and those using them (known as 'quants') created short-term indebtedness, mispricing of securities and a false protection against unknowable uncertainties. Ultimately, the two worlds of finance and resources became intertwined via market volatility and the mispricing of commodities, and led to the catastrophic consequences of the economic crisis all over the world (McGlade, 2009).

We must avoid repeating the mistakes of the past, as these will ultimately result in the collapse of ecosystems and social crisis. Instead, we should acknowledge that resilience in nature contains the seeds not only of surprise but also of transformation.

Box 17.2 Definitions

Adaptive management
Adaptive approaches to management are defined as those that recognise uncertainty and encourage innovation while fostering resilience (after Chapin et al., 2009). It is often considered as an approach based on learning by doing and implemented through careful and regular observation of socio-ecological conditions, drawing on these observations to improve the understanding of the system's behaviour, evaluation of the implications of emergent conditions and various options for intervention and action and responding in ways that support the resilience of the socio-ecological system.

Configurational complexity
Characteristic of diversity-oriented analyses, where context matters. Cases are examined as configurations in which all relevant aspects are looked at in the form of combinations. Such analyses concentrate on the specific features of individual cases, identifying those that are most relevant, whilst considering how those features cohere with each other as distinct types (McGlade, 2003)

Counterfactual thinking
The dependence of *whether*, *when* and *how* one event occurs on *whether*, *when* and *how* another event occurs and the possible *alteration* of events.

Diversity-oriented approach
Analyses of socio-ecological systems based on detailed case studies using measurements of many system-specific attributes with configurational complexity (McGlade, 2003).

Earth System
The Earth System is defined by Schellnhuber (1999) as the conglomerate formed by human civilization and its planetary matrix, i.e. all parts of the Earth that interact with the members and manifestations of our species.

Institutional fit
This refers to the linkages between ecosystems and socioeconomic and cultural systems in their local, regional, national, continental, and global contexts. The use of the word 'fit' in English refers to a match of sizes, e.g. if the shoe fits, then it is a good match for the foot. Social and ecological systems and processes have sizes too: they have spatial and temporal dimensions which interact and depend on each other within a specific geographical space. The degree to which these match is meant by 'institutional fit.'

Box 17.2 Definitions (cont.)

Panarchy
Describes the way in which nested evolving hierarchical systems with multiple interrelated elements interact on different time and space scales (Gundersen and Holling, 2001). Panarchy is the structure where natural systems (e.g. fish stocks) and of humans (e.g. capitalism), as well as combined human-natural systems (e.g. institutions that govern fisheries resource use), are interlinked in continual adaptive cycles of growth, accumulation, restructuring, and renewal. These transformational cycles can occur on scales ranging from a drop of water to the biosphere, over periods from days to geologic periods. Understanding these cycles and their scales can help identify leverage points to foster resilience and sustainability within the overall system.

Polythetic scheme
Characteristic of a variable-oriented approach in which the cases that are grouped together can differ substantially from each other for one or more attribute as long as they are similar for the majority of attributes selected by the researcher (McGlade, 2003).

Regime shift
An abrupt large-scale transition to a new state or stability domain characterised by a very different structure and feedbacks (Chapin et al., 2009).

Resilience
The capacity of a social-ecological system to absorb a spectrum of shocks or perturbations and to sustain and develop its fundamental function, structure, identity, and feedbacks as a result of recovery or reorganisation (Walker and Salt, 2006; Chapin et al., 2009).

Tipping point and tipping elements
Tipping points are popularly understood as a situation where at a particular moment in time, a small change can have large, long-term consequences for a system, i.e. popularly understood as 'little things can make a big difference' (after Gladwell, 2000). Lenton et al. (2009) offer a more formal definition for the earth system, introducing the term 'tipping element' to describe subsystems of the Earth system that are at least sub-continental in scale and can be switched — under certain circumstances — into a qualitatively different state by small perturbations. The tipping point is the corresponding critical point — in forcing and a feature of the system — at which the future state of the system is qualitatively altered. The term tipping point has been used to describe a variety of phenomena, including the appearance of a positive feedback, reversible phase transitions, phase transitions with hysteresis effects, and bifurcations where the transition is smooth but the future path of the system depends on the noise at a critical point.

Variable-oriented approach
Analyses of systems based on the measurement of a small number of attributes relating to global patterns emerging from surveys of a large number of cases (McGlade, 2003).

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Part C Emerging issues

Contents — Part C

18 Late lessons from Chernobyl, early warnings from Fukushima

Paul Dorfman, Aleksandra Fucic and Stephen Thomas

The nuclear accident at Fukushima in Japan occurred almost exactly 25 years after the Chernobyl nuclear accident in 1986. Analysis of each provides valuable late and early lessons that could prove helpful to decision-makers and the public as plans are made to meet the energy demands of the coming decades while responding to the growing environmental costs of climate change and the need to ensure energy security in a politically unstable world.

This chapter explores some key aspects of the Chernobyl and Fukushima accidents, the radiation releases, their effects and their implications for any construction of new nuclear plants in Europe. There are also lessons to be learned about nuclear construction costs, liabilities, future investments and risk assessment of foreseeable and unexpected events that affect people and the environment.

Since health consequences may start to arise from the Fukushima accident and be documented over the next 5–40 years, a key lesson to be learned concerns the multifactorial nature of the event. In planning future radiation protection, preventive measures and bio-monitoring of exposed populations, it will be of great importance to integrate the available data on both cancer and non-cancer diseases following overexposure to ionising radiation; adopt a complex approach to interpreting data, considering the impacts of age, gender and geographical dispersion of affected individuals; and integrate the evaluation of latency periods between exposure and disease diagnosis development for each cancer type.

Given the degree of uncertainty and complexity attached to even the most tightly framed and rigorous nuclear risk assessment, attempts to weight the magnitude of accident by the expected probability of occurrence have proven problematic, since these essentially theoretical calculations can only be based on sets of pre-conditioning assumptions. This is not an arcane philosophical point but rather a very practical issue with significant implications for the proper management of nuclear risk. With its failure to plan for the cascade of unexpected beyond design-base accidents, the regulatory emphasis on risk-based probabilistic assessment has proven very limited. An urgent reappraisal of this approach and its real-life application seems overdue.

Whatever one's view of the risks and benefits of nuclear energy, it is clear that the possibility of catastrophic accidents and consequent economic liabilities must be factored into the policy and regulatory decision-making process. In the context of current collective knowledge on nuclear risks, planned pan-European liability regimes will need significant re-evaluation.

18.1 Introduction

The chapter on climate change has demonstrated the need to plan for a low-carbon energy future, and an ambitious long-term target of 80–95 % reductions in greenhouse gases by 2050 has been set by the European Union (EU) (EU, 2011). Although some scenarios suggest that future energy demands could be met without nuclear electricity production ([1]) (IPPC, 2011; SRU, 2011b), others suggest greater reliance on new nuclear capacity in Europe ([2]), as well as Asia (Yi-chong, 2011).

At present, nuclear energy is used in 30 countries and Taiwan, producing roughly 13 % of the world's commercial electricity, and currently 14 countries and Taiwan are in the process of planning the building of new nuclear capacity. There are 435 nuclear power reactors in operation around the world — at the peak of nuclear generation in 2002 there were 444 — of which 189 are in pan-Europe and the Russian Federation, comprising about one third of the world's 146 civil reactors, with France alone generating close to half of the EU's nuclear production from 58 plants (Schneider et al., 2011).

With mounting public concern and policy recognition over the speed and pace of low carbon energy transition needed to mitigate climate change, nuclear power has been reframed as a response to the threat of global warming. Proponents conclude that nuclear provides a secure supply of low carbon base-load energy, safe in operation and powered by a reliable source of uranium supplies (IAEA, 2000; EDF, 2012; NIA, 2012; WNA, 2012). However, at the heart of the question of nuclear power are differing views on how to apply foresight, precaution and responsibility in the context of the possibility of accidents.

18.2 Chernobyl

On the 26th April 1986 an explosion at the Chernobyl Nuclear Power Plant No. 4 in Northern Ukraine resulted in widespread cross-boundary atmospheric pollution by fission-product radioisotopes. Following what is understood to have been a misconceived reactor experiment, a positive void coefficient caused reactivity excursion, resulting in a steam explosion that destroyed the plant. Over the six days of open containment 30–60 % of the Chernobyl reactor core's fission products were released to the atmosphere, 6.7 tonnes of material from the core. This material was projected high into the atmosphere, spreading radioactive isotopes over more than 200 000 square kilometres (km^2) of Europe (UNDP, 2002). In response, the authorities evacuated and subsequently relocated around 115 000 people from areas surrounding the reactor; after 1986, a further 220 000 people from Belarus, the Russian Federation and Ukraine were re-settled (UNSCEAR, 2008).

Each day some 3 500 workers enter the 30 kilometre exclusion zone, established by the Ukraine, to monitor, clean and guard the site, where remediation work is likely to continue until 2065 — although less than half the resources needed to fund the remediation have been raised, and the completion date has slipped by a decade. The work includes managing the long-term storage of waste from Reactor 4, and more than 20 000 spent fuel canisters from the site's other reactors. Significant quantities of radioactive waste continue to be generated — partly due to ongoing flooding in some areas of the waste-storage buildings and Reactor 4's turbine hall, forcing the pumped discharge and on-site storage of around 300 000 litres of radioactively contaminated water per month (Peplow, 2011).

18.2.1 Post-Chernobyl meta-analyses

Whilst it is outside the remit of this discussion to rehearse in detail the very broad literature on radiation risk epidemiology, it is sufficient to note that the precise estimation of acute and long-term health effects as a result of the Chernobyl accident remains problematic and subject to ongoing critique. This is because epidemiological evidence on health impacts is contradictory and conflicting. The link between radiation and the aetiology of cancer and leukaemia is well established — but the debate continues about the risks of those diseases, in particular childhood cancer and leukaemia, from Chernobyl releases and in the vicinity of other operational nuclear installations elsewhere (Box 18.1).

It is therefore unsurprising to see significant differences in the understanding and interpretation

([1]) The German governments Energiekonzept involves a reduction in primary energy consumption by 50 % between 2008 and 2050, a reduction in electricity consumption of 25 %, and a reduction in carbon emissions by 80 % (SRU, 2011a).

([2]) Planning for the same carbon target as the German government, the UK government's National Policy Statement on Energy envisages a doubling of electricity demand by 2050 and a potential trebling of total installed capacity (DECC, 2011). As a result, the policy foresees the construction of a series of new nuclear plants in the United Kingdom.

Box 18.1 Low level radiation epidemiology

There are significant uncertainties associated with the choice of differing models used to interpolate radiation risk between populations with different background disease rates; for the projection of risk over time; for the extrapolation of risks following primarily a single external high dose and a high dose-rate in contrast to cumulative low dose and low dose-rate exposures (ARCH, 2010). Despite this, the analysis of incidence and distribution of disease (epidemiology) remains fundamental to radiation-risk determination and standard setting. Epidemiological investigations ranging from the Japanese atomic bomb life span survivor studies to more numerically and temporally limited studies have provided a weight of evidence about the effects of ionizing radiation on humans. Whilst a range of studies suggests no causal or associative link between routine discharges from operating nuclear plants (Jablon et al., 1991; Yoshimoto et al, 2004; Evrard et al., 2006; COMARE, 2011), this important debate is ongoing.

One of the most significant data sets in this debate comprises a national case-control study, funded and published by the Federal Office for Radiation Protection on behalf of the German Federal Ministry for the Environment and conducted by the German Childhood Cancer Registry on childhood cancer near nuclear installations. This study investigated childhood leukaemia and cancer incidence near nuclear plants from 1980 to 2003, providing evidence of a significant increase in childhood leukaemia and cancer risk near to nuclear plants in Germany (Kaatsch et al., 2007; Kaatsch et al., 2008a; Kaatsch et al., 2008b; Spix et al., 2008). The German Federal Office for Radiation Protection formally confirmed these findings, stating that 'in the vicinity of nuclear power plants, an increased risk of 60 % was observed for all types of childhood cancer, and for childhood leukaemia the risk doubled equaling a risk increase of approximately 100 %' (BfS, 2008). In response, the UK scientific advisory body Committee on Medical Aspects of Radiation in the Environment (COMARE) 14th Report (2011) critiqued the German study, and discounted the findings, noting that COMARE's primary analysis of the latest British data had revealed no significant evidence of an association between risk of childhood leukaemia and living in proximity to a UK nuclear facility (COMARE, 2011). The Committee also pointed to the role of unidentified viral infections rather than radiation exposure in the aetiology of childhood leukaemia near nuclear power plant (Kinlen, 2011).

Subsequently, in early 2012, a further nation-wide case-controlled investigation by Institut Nationale de la Santé et de la Recherche Medicale (INSERM) on behalf of France's nuclear safety research body, Institut de Radioprotection et de Sûreté Nucléaire (IRSN), demonstrated a statistically significant doubling of the incidence of leukaemia near to nuclear plants in France between 2002 and 2007 (Sermage-Faure et al., 2012). However, neither a causal link nor an association between gaseous discharges and ill health were established.

of Chernobyl health effects. The problem may be exacerbated by the nature of previous studies, which have been described as forming a patchwork rather than a comprehensive, structured attempt to delineate the overall health consequences of the accident (ARCH, 2010). Nevertheless, despite differences in the types of exposure, doses, dose rates and applied methodologies, data on the health consequences of the Chernobyl accident add to knowledge collected from atomic bomb victims and from populations over-exposed during nuclear accidents and nuclear weapons testing. Integration of the available data on related health risks gives added value in preparing radiation protection protocols and in the management of subsequent nuclear accidents, such as Fukushima.

Focusing only on Belarus, Ukraine and the Russian Federation, and no other exposed countries and populations, the International Atomic Energy Authority (IAEA) convened the Chernobyl Forum (2005) that predicted a potential total mortality of about 4 000. Discounting the significantly raised childhood thyroid cancer incidence ([3]), the United Nations Scientific Committee on the Effects of Atomic Radiation (UNSCEAR, 2008) found no evidence of increases in overall cancer incidence or mortality rates or in rates of non-malignant

([3]) In Belarus, the Russian Federation and Ukraine nearly 5 000 cases of thyroid cancer have now been diagnosed to date among children who were aged up to 18 years at the time of the accident (WHO, 2006).

disorders that could be related to radiation exposure. Both of these estimates were subject to critical analysis by Yablokov et al. (2006), who suggested a higher death toll as a consequence of the Chernobyl fall-out. Based on Belarus' national cancer statistics, the study predicted approximately 270 000 cancer incidences — of which 93 000 would prove fatal. A follow-up meta-analysis, which included Belarus, Russia and Ukraine, suggested further increased predicted premature deaths as a result of the radioactivity released (Yablokov et al., 2007).

It is worth noting that UNSCEAR (2008) decided not to use models to project absolute numbers of effects in populations exposed to low radiation doses from the Chernobyl accident, because of unacceptable uncertainties in the predictions. Given that UNSCEAR (1993) and IAEA (1996) estimate a total world-wide collective dose of 600 000 person-Sieverts over 50 years from Chernobyl fallout, and the standard risk estimate from the International Commission on Radiological Protection (ICRP, 2005) is 0.057 fatal cancers per Sievert, this suggests an estimate of about 34 000 fatal cancers over that time period (Ramana, 2009). Given the widely accepted linear no-threshold radiation risk model may overstate or understate risks by a factor of two (BIER VII, 2006) — then estimates for post-Chernobyl cancer mortality extrapolation may range from 17 000 to 68 000 over 50 years.

These differences in meta-analysis estimates also obtain around post-Chernobyl leukemia aetiology: Whilst UNSCEAR (2008) suggests that the incidence of leukaemia in the general population, one of the main concerns owing to the shorter time expected between exposure and occurrence compared with solid cancers, does not appear to be elevated, the UK government scientific advisory Committee Examining Radiation Risks of Internal Emitters (CERRIE, 2004) concluded that, in the judgment of a large majority of committee members, it is likely that radioactive fallout from the Chernobyl accident resulted in an increased risk of infant leukaemia in the exposed populations.

In addition, there were immediate deaths of emergency workers and firefighters resulting from acute radiation exposure. Treatment of these people also placed hospital staff and funeral workers at risk of radiation over-exposure (Box 18.2).

18.2.2 Post-Chernobyl cancer risk

The most susceptible populations for thyroid disease development after nuclear overexposure are pre- and post-natally exposed children, young people and women (Shimizu, 1991; Nagataki and Nystrom, 2002; McCarthy, 1997, Prysyazhnyuk, 2007). As both external and internal exposure to ionizing radiation can cause thyroid cancer, similar incidences were detected amongst those exposed in Hiroshima, Nagasaki, and following the Chernobyl accident, with a much higher prevalence in children than adults (Larsen et al., 1982; Pacini et al., 1999). Increased levels of anti-thyroid antibodies, hyper- or

Box 18.2 Acute medical care of Chernobyl radiation casualties

'By May 5, 10 days after the accident, 172 individuals, 47 of them fire fighters, had been admitted Hospital #6 with the most severe form of radiation sickness. All had visible burns, were in severe pain and had little chance of survival. It should be remembered that all medical staff entering the rooms of irradiated patients were also exposed to intensive radiation from victims whom they were supposed to treat. We should express deep gratitude to all personnel, from the reception area, sterile rooms, specialized offices and laboratorie, to dosimeter controllers for their tireless service and sacrifice. As experienced radio-biologists, we understood that some of our patients would not survive — they had received radiation doses of more than 1 000 rad, which resulted in large and deep radiation burns and the penetration of their bodies by significant amounts of radioactive material. Therefore, we planned for their funerals, including the selection of appropriate location(s) and estimates of the necessary depth of tombs to avoid increases in the radiation level above the tomb. We needed to equip vehicles that would transport the dead bodies with strong protection layers quickly so as not to harm the drivers and to avoid radiation pollution between the hospital and the cemetery' (Grigoriev, 2012).

Despite these challenging circumstances it is important to note that, thanks to round-the-clock care over many months by a dedicated team of doctors, and through a wide range of holistic treatments, the lives of many patients with acute radiation sickness were saved (Grigoriev, personal communication, 2012).

hypothyroidism and thyroid cancer have different latency periods after exposure, even at relatively low doses of less than 1 Sv (Nagataki, 1994), and the data from the Chernobyl and atomic bomb victims should be of significance in bio-monitoring exposed subjects following the Fukushima accident.

In recent years, an increased incidence of leukaemia has been described among clean-up workers and the population aged 0–5 years at the time of the Chernobyl accident (Noschenko et al., 2010; Romanenko et al., 2008). Such a trend may continue as the latency period for leukaemia can exceed more than 40 years, as shown for myelodisplastic syndrome (pre-leukaemia) and the related increased risk for acute myeloid leukaemia after the Hiroshima and Nagasaki A-bomb detonations (Iwanaga et al., 2011).

Lactating women may be more susceptible to ionizing radiation, as breast tissue bio-accumulates iodine as part of the physiological process of its accumulation in breast milk. These levels of accumulated radioiodine in breast milk may also increase the risk of thyroid cancer in newborns (Bland et al., 1969; Tazebay et al., 2000; Hatch et al., 2005). This information may prove necessary and significant for breastfeeding sub-populations in cases of increased radioiodine levels. Similar results were shown for breast cancer incidence after Hiroshima and Nagasaki, as the highest dose-specific excess relative risk was among women exposed prior to the age of 20 years (Land et al., 2003), with the latency period for breast cancer development at approximately 10 years for both those affected by the atomic bombs and Chernobyl (Tokunaga, 1979; Pukkala et al., 2006), with raised incidence of breast cancer found among young and pre-menopausal women exposed during the Chernobyl accident.

In order to improve preventive measures following over-exposure to ionizing radiation, it is imperative that the latency period between exposure and disease development be re-evaluated for each cancer type; as the currently approved 10-year latency period of international radiation protection agencies does not seem in accord with data reported for certain solid cancers, with a 4-year latency period reported post-Chernobyl (UNSCEAR, 2008; Ivanov et al., 2009). The question of latency in cancer induction is further complicated through radiation biology discoveries about the underlying complex cellular response mechanisms by which radiation interacts with living organisms (Box 18.3).

18.2.3 Post-Chernobyl non-cancer health consequences

Evaluation of health risks relating to accidental overexposure to ionizing radiation is usually limited to estimations of increased cancer incidence; however, current knowledge of complex interactions of ionizing radiation and living systems demonstrates that in addition to increasing cancer risk, exposure to radiation may disturb a number of other biological pathways. For example, analyses of the Japanese A-bomb survivor Life Span Studies mortality data (1950–1997) show a statistically significant dose-response pattern for death from diseases other than cancer, and these excesses do not seem limited to any particular disease (Preston et al., 2003; Yamada et al., 2004). Disturbance of pathways by ionizing radiation may be modified by age, gender, psychological status of a person (stress) or diet, all of which impact on the final increase of health risk and its duration.

Correspondingly, the Chernobyl nuclear accident also caused non-cancerous diseases, such as cardiovascular and immunological disorders, and cataracts (Hatch et al., 2005; Cardis, 2011). In children exposed to long-term low doses after the Chernobyl nuclear accident, a significant increase of cardiovascular diseases was reported, followed by decreased physical status (Kostenko, 2005). A significant increase in cardiovascular disorders was also recorded among adults (Bebeshko et al., 2007; Eglite et al., 2009), which was compatible with atomic bomb survivor data (Zubovksi and Tararukhina, 1999; Shimizu et al., 2010).

Immunological disturbances have been reported for both clean-up workers and the environmentally exposed population affected by the Chernobyl accident. In children, marked immune disturbances were detected after Chernobyl, with significant differences between directly exposed children and children born to irradiated parents (Baleva et al., 2011). In children residing in the zone 30–90 km from the Chernobyl site, immunological disturbances arising more than 20 years after the nuclear accident are still clinically presenting (Sajjadieh et al., 2009). Additionally, immunological disorders are combined with inflammations and an increased risk of cardiovascular disease in both those exposed to radiation following atomic bomb and the Chernobyl accident (Kusunogi et al., 1999; Hayashi et al., 2003; Kusunoki et al., 2010; Timoshevskiĭ et al., 2011). It has also been suggested that data regarding cataracts in subjects participating in the clean-up and building of sarcophagi in Chernobyl may fail to support the ICRP 60 risk guideline assumption of a

Box 18.3 Genomic instability and the bystander effect

The theoretical underpinning of the biological effects of ionizing radiation is based on sophisticated variants of target theory, such as track structure theory. Target theory stipulates that the biological targets damaged in the cell are relevant to the endpoint: for example, damage to a tumour suppressor gene might lead to cancer. Target theory holds for single locus hereditary disease but there were problems in applying it to somatic cell endpoints such as cancer. However, in 1992 evidence inconsistent with target theory emerged in the form of two effects, genomic instability (Khadim et al., 1992) and the bystander effect (Nagasawa and Little, 1992). Such effects are collectively known as non-targeted effects because the target is large enough to encompass the whole nucleus of the cell, and radiation does not directly affect the damaged cell. Genomic instability is characterised by the acquisition, *de novo*, of various kinds of damage, mostly to DNA, up to several cell generations after the exposure. Damage associated with genomic instability may not be directly caused by the radiation but is a secondary response of the cell to radiation insult. The bystander effect occurs in cells that experienced no radiation events, but are neighbours of cells that have.

These phenomena pose a set of significant research questions for the understanding of the underlying mechanisms involved, and could imply the need for a re-appraisal of the target theory approach, and the emergence of a new theoretical framework for the biological bases of the effects of radiation. Perhaps the most worrying aspect from the public health perspective is the potential for trans-generationally inherited genomic instability. A number of mechanistic hypotheses have been proposed to explain genomic instability (ARCH, 2011), and Baverstock and Karotki (2011) have suggested a further explanatory conceptual framework.

Whilst two European Commission projects, RISC-RAD (http://riscrad.org/) and NOTE (http://www.note-ip.org), specifically directed at obtaining a better understanding of genomic instability, have reported — so far no replacement for the underpinning framework based on target theory has emerged. This may be because, as usual with radiation biology, the picture is complex, especially in distinguishing between the interpretation of results from *in vitro* and *in vivo* studies. Yet more recent work indicates that additional mechanisms may also be important for the understanding of the impact of genomic instability and bystander effects on radiation protection regulation: Mukherjee et al. (2012) suggest that radiation-induced chromosomal instability may also result from inflammatory processes having the potential to contribute secondary damage expressed as non-targeted and delayed radiation effects. Lorimore et al. (2011) conclude that complex multi-cellular interactions resulting from bystander effects may influence carcinogenic susceptibility, with inflammatory processes responsible for mediating and sustaining the durable effects of ionizing radiation. Given that the genotype of each individual is a key determinant of carcogenic susceptibility, then genotype-directed tissue responses may be important determinants of understanding the specific consequence of radiation exposure in different individuals (ibid). One potentially significant implication of these finding is that differing people may have differing responses and susceptibilities to radiation insult.

5-Gy threshold for detectable opacities, but rather point to a dose-effect threshold of under 1 Gy (Worgul et al., 2007; Chumak et al., 2007).

One of the most at risk groups is infants and children (Box 18.4).

Although increased levels of stress and depression have been found in children and teenagers born to exposed parents (Panchenko et al., 2005); in general, post-Chernobyl psychological disturbances, stress, depression and suicides in children and adults have been poorly described. The significance of psychological impacts on survival rates after exposure may prove important, as there has been increased suicide rates among clean-up workers (Rahu et al., 1997).

18.3 Fukushima Dai-ichi

On 11 March 2011, the Japanese Great Easter Earthquake, involving 5 to 10 metres of slip motion on fault zones more than 100 kilometres in length along the Japanese Trench Subduction Zone, struck the east coast of Japan triggering the shut down of 10 operating nuclear power plants. At the time of the earthquake, Fukushima Dai-ichi units 1, 2, and 3 were operating at full power (Marshall and Reardon, 2011). The plants, designed to withstand a maximum 8.2 earthquake on the logarithmic Richter scale, received a seismic shock 9–15 times higher than the design limit (Park, 2011). At the time of the accident, the radiological inventory at risk within the 6 reactor cores comprised 487 tonnes of uranium, of which 95 tonnes include 6 %

Box 18.4 Infants and children: susceptible sub-populations

Children are generally more susceptible to ionizing radiation and other environmental pollutants, and may suffer from life-long health consequences, some of which may be pre-natally determined (EEA, 1999; BCPT, 2008; Fucic et al., 2008). Pathological changes in reproductive function, peri-natal illnesses and mortality were reported several years after the Chernobyl nuclear accident. The birth rate was additionally influenced by migration of the population, use of contraceptives, stress and induced abortions (Kulakov et al., 1993), and a peak in Down Syndrome cases was observed in newborns born in 1987, one year after the Chernobyl nuclear accident (Zatsepin, 2007). New DNA mutations in children born after the accident to irradiated parents and living in non-contaminated territories confirm the long-term health risks in the exposed population (Aghajanyan and Suskov, 2009; Weinberg et al., 1997). Additionally, trans-placental exposure to radioisotopes may significantly increase the rate of spontaneous miscarriages without clinical symptoms in mothers or difference in level of genome damage between women exposed to external and internal radiation by radioisotopes (Fucic et al., 2008).

plutonium from the MOX assemblies ([4]). There were a further 1 838 tonnes of stored spent fuel on the site, including 1 097 tonnes in the central pool store (Large, 2011a).

At the Fukushima Dai-ichi No. 1 plant, site emergency diesel generators provided on-site power to the reactor cooling pumps and other essential services of the three operating nuclear plants, as well as cooling for the six-reactor unit spent fuel ponds, and also for the central spent fuel store (Brumfiel and Cyranoski, 2011a). On-site power supplies continued in operation for just over one hour until the entire site was swamped by a 15 metre tsunami with the total wave height amplified by the backwash as the tsunami wave was contained and reflected by the heavily terraced western section of the site. This part of the site contained four reactors, three of which had been fully operational at the time of the earthquake, resulting in the failure in two or three of the nuclear power plants robust sealed containment structures as water poured into the plants (Large, 2011b) ([5]) (Box 18.5).

The collapse of the Japanese electricity distribution grid resulted in the shut-down of individual nuclear power plant's electricity systems, resulting in loss of essential reactor fuel cooling and crucial instrumentation and control systems. This loss of offsite power and onsite AC power combined with the rapid discharge of DC batteries led to a complete station blackout which disabled the emergency core cooling systems which, in turn, disabled the monitoring of critical parameters such as reactor water levels and open critical

Box 18.5 Japanese earthquakes and tsunamis

Minoura et al. (2001) conclude that traces of large-scale invasion tsunami recorded in the coastal sequences of the Sendai plain show an approximate 1 000-year re-occurrence interval, noting that more than 1 100 years have passed since the historic Jgan tsunami and, given the reoccurrence interval, the possibility of a large tsunami striking the Sendai plain was high. Their findings indicated that a tsunami similar to Jgan would inundate the present coastal plain for about 2.5 to 3 km inland. More recently, post-Fukushima, the University of Tokyo's Earthquake Research Institute concluded that risk of a large-scale earthquake in the region has risen considerably since the Great East Japan Earthquake of 2011. This implies that, since neither practical nor theoretical models can properly determine the dynamics of imminent large earthquakes, much greater emphasis may need to be placed on natural hazards for nuclear risk assessment (Park, 2011).

([4]) MOX (mixed oxide) is a form of nuclear fuel designed for use in breeder reactors, consisting of a blend of uranium and plutonium oxides.

([5]) According to the Japanese Commission tasked with reviewing the disaster, the tsunami that struck the plant was twice as high as the highest wave predicted by previous risk assessments, and the assumption made by Tokyo Electric Power Company (TEPCO) that the plant's cooling system would continue to function after the tsunami struck worsened the disaster (The Investigation Committee, 2011).

safety valves, cascading to significant fuel and containment overheating and damage (Buongiorno, 2011). As Tokyo Electric Power Company (TEPCO) was unable to restore either on or off-site power; the entire Fukushima Dai-ichi nuclear complex went into, and remained, in station blackout.

The blackout meant that no safety systems remained intact, just passive design features and defense in depth layers — representing a beyond design base accident. In Unit 1, steam was bubbled through the suppression pools, further increasing water temperature, and water leaving the core was not replaced. As the water dropped below the top of the fuel, the temperature in the fuel and cladding began to rise rapidly, causing fuel degradation. The zirconium in the cladding oxidized, releasing hydrogen into the containment dry-well, and after a short time, pressure levels in the containment were at or above the design pressure, raising risk of containment rupture. In response, operators manually opened valves to release steam from containment into the reactor building, and the vented steam containing hydrogen violently and exothermally ignited, destroying the reactor building, allowing gaseous fission products to escape, and exposing elements of the spent fuel to open containment.

Units 3 and 4 soon experienced similar beyond design-based cascading conditions. At this point, elevated radiation levels of several fission products including Caesium 137 and I-131 were detected at the reactor buildings, and the plant boundary; providing the first indication that some fuel in the reactor had already melted (Butler, 2011). The presence of hydrogen and these volatile fission products in the released steam suggested that the temperature had severely damaged the fuel cladding inside the reactor pressure vessel (Bonin and Slugen, 2011).

Backup generators and batteries arrived some hours later, restoring partial power to plant, but these were insufficient to power any of the cooling pumps; instead smaller ad hoc fire pumps were used to pump boranated seawater into the reactor core and containment.

Within a few hours the reactor cores of the three operating units were subject to varying degrees of meltdown. The molten fuel had slumped to the bottom of the reactor pressure vessels, the reactor pressure vessels themselves had failed and, in various degrees, the primary containment of the pressure suppression system had failed. What remained of the reactor instrumentation clearly indicated an ongoing and deteriorating situation — with thermal activity within the reactor buildings resulting in sharp perturbations in containment pressure and radiation levels, particularly within what remained of the primary containment. Doubts about the effectiveness of water injection, and increasing concerns about the volumes of highly contaminated water have been linked to TEPCO's necessary emergency seawater cooling strategy, which also involved unconventional cooling efforts with helicopter and water cannons over the period of a week.

18.3.1 Fukushima Dai-ichi radiation releases: cross boundary pollution

The multiple meltdown of reactors at the Fukushima Daiichi nuclear plant released more radiation than any accident since Chernobyl. Japanese regulatory officials initially assessed the accident as Level 4 on the International Nuclear Event Scale (INES), with the risk level successively rising to 5 and eventually to the maximum of 7 — a rating equal to the Chernobyl disaster. Of primary concern were fission products, readily absorbed by the human body, and the actinides, which act as heavy metal poisons. Caesium 137 (Cs-137) represents the most significant long-term hazard since it is readily taken up in human metabolic, environmental, and agricultural systems.

Early measurements reported from the United States, more than 7 000 km from Fukushima, confirmed maximum concentrations of radioxenon (Xe-133) in excess of 40 becquerel per cubic metre (Bq/m^3) — more than 40 000 in excess of normal expected average concentration (Bowyer et al., 2011). High activity concentrations of several man-made radionuclides (I-131, I-132, Te-132, Cs-134 and Cs-137) were detected along the Iberian Peninsula from 28 March to 7 April 2011, deduced through back-trajectories analysis, and verified by activity concentrations (Lozano et al., 2011). Other elevated levels were recorded in air sampling, rainfall and sheep's milk at Thessaloniki, Greece (Manolopoulou et al., 2011). In April and May 2011, fallout radionuclides (Cs-134, Cs-137, I-131) were detected in environmental samples in Krasnoyarsk, Russian central Asia. Similar maximum levels of I-131 and Cs-137/Cs-134 and I-131/Cs-137 ratios in water samples collected in Russia and Greece suggested the high-velocity global movement of radioactive contamination from the Fukushima nuclear accident (Bolsunovsky and Dementyev, 2011); as did results from the Russian rapid response Typhoon monitoring system (Box 18.6).

Box 18.6 Typhoon monitoring system

For hazardous facilities located close to larger cities, early stage accident detection, monitoring and warning systems are critical — as they allow for better impact prediction and mitigation of human and environmental consequences. During the Fukushima accident, Typhoon, the early monitoring network associated with the Russian Early Warning and Emergency Response System (REWERS), carried out operational analysis and forecasting for this large-scale radioactive emergency. The monitoring was achieved through a network of observational stations, with radiometric laboratories providing the measurement data for environmental samples. The first Fukushima air mass transfer dispersion calculations made by Typhoon's experts were carried out on the evening of 11 March and on 12 March 2011 — the radiation monitoring network of Roshydromet in the Russian far east was set to rapid measurement mode to obtain radionuclide dose rate measurements every hour. Throughout the accident period at Fukushima, Typhoon cooperated with the IAEA and the World Meteorological Institute in performing calculations and assessments of trans-boundary emissions (Shershakov, 2011).

18.3.2 Post-Fukushima Dai-ichi radiation releases: Japan

The very high population density near the damaged reactors and spent fuel dispersions implies increased risk for local communities. The regulators conducted an initial evacuation of 100 000 people from around Fukushima, and after some hesitation, Japan's Nuclear Safety Commission established a new 20 km evacuation zone, with a further 90 000 people evacuated. Because damaged plant monitoring proved unreliable — on at least four occasions TEPCO retracted findings on the amount and composition of radionuclides in areas in and around the plant, or on reactor parameters — it has been suggested that more complete analyses of reactor-event scenarios and release fractions can be derived from outside Japan (Nature, Editorial, 2011a).

The radiation releases dispersed according to the wind direction and weight of the particles. The radionuclides of interest were I-131, primarily linked to thyroid cancer; Cs-134 and Cs-137, primarily linked to bladder and liver cancer; and strontium, primarily linked to bone disorder and leukaemia. Significantly, there is confirmed isotopic evidence for the release of plutonium into the atmosphere and deposition on the ground in northwest and south of the Fukushima nuclear site (Zheng, 2012).

In September 2011, Japan's Nuclear and Industrial Safety Agency (NISA) estimated that the Fukushima Daiichi plant had released 15 000 terabecquerels Cs-137 to air. Other estimates vary. However, it may well be too early to accurately estimate or determine the scale of the damage and radiological releases (Cyranoski and Brumfiel, 2011). A meta-analysis comprising radionuclide measurement data and atmospheric dispersion modeling (Stohl et al., 2011), reported in Nature (Brumfiel, 2011), suggested that the disaster at Fukushima Daiichi may have released far more radiation than Japanese regulatory estimates; concluding that the emissions started earlier, lasted longer, and were therefore higher than earlier official estimates assume. The study noted that:

> 'While at first sight it seemed fortunate that westerly winds prevailed most of the time during the accident, a different picture emerges from our detailed analysis. Exactly during and following the period of the strongest Cs-137 emissions on 14 and 15 March as well as after another period with strong emissions on 19 March, the radioactive plume was advected over Eastern Honshu Island, where precipitation deposited a large fraction of Cs-137 on land surfaces. The plume was also dispersed quickly over the entire Northern Hemisphere, first reaching North America on 15 March and Europe on 22 March. In general, simulated and observed concentrations of Xe-133 and Cs-137 both at Japanese as well as at remote sites were in good quantitative agreement with each other. Altogether, we estimate that 6.4 TBq of Cs-137, or 19 % of the total fallout until 20 April, were deposited over Japanese land areas, while most of the rest fell over the North Pacific Ocean. Only 0.7 TBq, or 2 % of the total fallout were deposited on land areas other than Japan' (Stohl et al., 2011, p. 28 322).

In other words, Fukushima releases may have contained an estimated 3.5 × 1 016 Bq Cs-137 — roughly twice the official government figure, with almost one fifth falling on the Japanese mainland. This means that the Fukushima release can be

estimated to equal to 40 % of the Cs-137 release from Chernobyl.

By November 2011, the air radiation level in Ibaraki Prefecture was about 0.14 microsievert per hour, equivalent to an annual dose of about 1 millisievert, the safety limit for exposure under normal standards (Ishizuka, 2011). On 14 December 2011, the Japanese Science Ministry assessed caesium fallout in Fukushima Prefecture in the four months after the March 11 disaster at 6.83 MBq/m^2 — 94 % of which was concentrated in March, an indication of the severity of radiation discharge shortly after the onset of the accident (Asahi Shimbun, 2011).

Fallout attaches strongly, through ion exchange, to soil — in particular to clay soils common throughout Fukushima. From there the radiocaesium will move slowly into plants, at a rate, and level of risk, that remains unclear. Cs-137 strongly contaminated the soil in large areas of eastern and northeastern Japan, whereas western Japan was relatively sheltered by mountain ranges. The soils around the Fukushima nuclear site and neighboring prefectures have been extensively contaminated with depositions of more than 100 000 and 10 000 megabecquerel per square kilometre (MBq/km^2), respectively (Yasunaria et al., 2011).

Correspondingly, it was reported that Fukushima Prefecture survey conducted in June and July 2011 found 33 Cs-137 hot-spots in excess of 1.48 MBq/m^2, the level set by the Soviet Union for forced resettlement after the Chernobyl accident. A further 132 locations had combined Cs-137/134 of more than 0.555 MBq/m^2, the level at which the Soviet authorities called for voluntary evacuation and imposed a ban on farming (Obe, 2011). Further reports suggest that radiation pollution is widely dispersed in Japan, with the Japanese Science Ministry confirming that Cs-134 and Cs-137 fallout was present in all prefectures, with the highest combined cumulative density of Cs-134 and Cs-137 found in Hitachinaka, Ibaraki Prefecture, at 0.0408 MBq/m^2, followed by 0.0226 MBq/m^2 in Yamagata, the capital of Yamagata Prefecture, and 0.0174 MBq/m^2 in Tokyo's Shinjuku Ward (Ishizuka, 2011). Further reports indicated that the Japanese Environment Ministry estimated the contaminated zones at circa 2 400 km^2 over Fukushima and four nearby prefectures, with Cs-134 and Cs-137 the dominant contaminants, mainly contained in the topsoil layer. By definition, shorter-lived isotopes decayed promptly (Reuters, 2011).

The Fukushima accident contaminated large areas of farmland and forests, albeit not as severely or extensively as at Chernobyl. But lacking land for resettlement and facing public outrage over the accident, the Japanese government has embarked on an unprecedented decontamination effort. The Japanese Ministry of the Environment estimates disposals of 15–31 million m^3 of contaminated soil and debris by the time the decontamination projects finish (Bird, 2012). The total remediation programme may cover about 500 km^2 where radiation dose levels are above 20 millisieverts per year (mSv/year), and about 1 300 km^2 where radiation dose levels are between 5 mSv/year and 20 mSv/year (IAEA, 2011a). In order to cope with this level of contamination, and in contradiction to international radiation protection standards, Japanese regulators have raised dose constraints to 20 mSv/year — thereby subjecting schoolchildren to exposures normally only tolerated by adult nuclear workers.

Over the time of the accident, the amount of highly contaminated water on the site rose from 10 000 to 100 000 tonnes, presenting storage capacity difficulties (Reardon, 2011). The French Institute for Radiological Protection and Nuclear Safety estimated that between March and mid July, the amount of radioactive Cs-137 discharged into the Pacific from the Fukushima Daiichi plant amounted to 27.1 million megabecquerels — the greatest amount known to have been released to water from a single accident (Brumfiel and Cyranoski, 2011b).

18.3.3 Fukushima Dai-ichi aftermath

The Japanese government established an independent Investigation Committee on the Accident at the Fukushima Nuclear Power Stations of Tokyo Electric Power Company on June 7, 2011. The Committee's December 2011 Interim Report strongly criticised both central government and TEPCO, noting that both seemed unequal to the task of making decisions in order to stem radiation leaks as the situation at the coastal plant worsened in the days and weeks following the disaster. The Interim Report also noted that Japan's response to the crisis was flawed by poor communication and delays in releasing data on dangerous radiation leaks at the facility, and was critical of the regulatory authorities' 'inappropriate preparation' of nuclear disaster emergency planning (Investigation Committee, 2011).

In a commentary published in *Nature*, committee members Tomoyuki Taira and Yukio Hatoyama, both also members of the House of Representatives in the Japanese Diet, with Hatoyama having served

as Prime Minister of Japan from 2009 until 2010, noted that their investigation had

> 'shown that key pieces of evidence remain incomplete… Particularly important is finding out whether the worst-case scenario occurred: that is, whether self-sustaining nuclear reactions were re-ignited in the core (re-criticality), creating more fission products and heat damage; whether the explosions that rocked the plant days after the earthquake were nuclear in origin, releasing radioactive metals from damaged fuel rods; and whether molten fuel has broken through the reactor's base, threatening environmental contamination' (Tomoyuki and Hatoyama, 2011).

These internal critiques were compounded by others, questioning the relative independence of Japanese regulators:

> 'The Japanese government's main sources for scientific information for Fukushima were the industry ministry's Nuclear and Industrial Safety Agency and the Nuclear Safety Commission. Although these bodies might have expertise in nuclear reactor physics, they also have ties to the nuclear industry that create a conflict of interest. And they were not an effective and prompt source for quick decisions on decontamination or health risks' (Nature, Editorial, 2011b).

Despite these ongoing difficulties, on 16 December 2012, the Japanese Prime Minister, Yoshihiko Noda, declared that the Fukushima nuclear plant had entered the state of cold shutdown; with cold shutdown confirmed by IAEA in their Status Report (IAEA, 2011b) ([6]). However, whilst the reactor temperatures had fallen, there still remained uncertainty about a series of ongoing problems, including the state and level of the nuclear fuel, particularly after confirmation that molten fuel may have eaten through three-quarters of the concrete under unit 1 and damaged the bases of two of the other reactors (TEPCO, 2012). A revised TEPCO timetable suggests that decommissioning, including melted reactor fuel, fuel rod removal, and repair of containment vessels, will take up to 40 years (ibid).

Extrapolating from monthly trade ministry data, the average Japanese nuclear power plant utilisation rate fell to 15.2 % in December 2011 from 67.9 % a year earlier (Reuters, 2012) and, following a further reactor shut-down in January 2012, to 10.3 % (Japan Times, 2012). With almost all of Japan's 54 reactors either offline in early 2012, or scheduled for shutdown, the issue of structural safety looms over any discussion about restarting them. Japan, traditionally a pro-nuclear country, derived about 30 % of its electricity from nuclear plants in 2010 — however opposition has been emerging as an important political issue, and the country's nuclear industry has been repositioning itself for a significantly less attractive market, halting plans to build 14 further reactors by 2030 (Crooks, 2011).

Although post-Fukushima plans for bio-monitoring and epidemiological assessment are still not finalised, it is clear that there will need to be a significant assessment of a wide range of environmental risk factors. Because some of the evacuees have started to settle across the country, long-term follow-up of the victims will need to account for geographic dispersion (Sugihara and Suda, 2011).

The final Report of the National Diet of Japan noted the severity of the future decontamination challenges that Japan faces, and strongly criticised the underlying organisational, institutional and legal framework that resulted in the 'regulatory capture' of safety systems. The Independent Investigation Commission also concluded that the Fukushima accident was a man-made disaster, pointing to the key role of human agency in radiation risk controversies, see Box 18.7.

18.3.4 Post-Fukushima nuclear policy impact

Before the Fukushima accident, most planned nuclear power plant projects were in Asia and Eastern Europe, extending a trend from earlier years, including a dispersion of proposed new reactors around the Pacific seismic region. Between 2009 and April 2011 construction started on nine units; and where projects are going ahead, they do so with strong government support, including implicit or explicit public subsidy (Box 18.8).

Since the Fukushima accident, the number of operating reactors fell from 441 at the beginning of 2011 to 435 in early 2012, with a total net installed

([6]) 'Cold shutdown' normally refers to a state in which a reactor has become subcritical, with the temperature having been brought to a stable level below 95 °C through the operation of normal systems.

Box 18.7 The Fukushima Nuclear Accident Independent Investigation Commission (NAIIC, 2012)

'The earthquake and tsunami of 11 March 2011 were natural disasters of a magnitude that shocked the entire world. Although triggered by these cataclysmic events, the subsequent accident at the Fukushima Daiichi Nuclear Power Plant cannot be regarded as a natural disaster. It was a profoundly manmade disaster.'

'The Commission recognizes that the residents in the affected area are still struggling from the effects of the accident. They continue to face grave concerns, including the health effects of radiation exposure, displacement, the dissolution of families, disruption of their lives and lifestyles and the contamination of vast areas of the environment. There is no foreseeable end to the decontamination and restoration activities that are essential for rebuilding communities. The Commission concludes that the government and the regulators are not fully committed to protecting public health and safety; that they have not acted to protect the health of the residents and to restore their welfare.'

capacity of just more than 368 gigawatts (GW), representing a decrease in installed nuclear capacity of around 10 GW or 3 %. Similarly, construction starts fell from 15 in 2010 to just 2 in 2011. New nuclear plant construction is progressing in Brazil, China, India, and Russia. Iran has recently completed its first reactor. New-build orders have been placed in the United Arab Emirates and the United States, with a planned call for tender in South Africa. Ordering continues in China, India, Korea and Russia.

In Europe, Finland and France are completing their new Generation III European Pressurized Reactor (EPR) at Olkiluoto and Flammanville (Box 18.9), with the Finnish parliament and regulators having granted permits for construction of the country's sixth and seventh commercial reactors to Teollisuuden Voima (TVO) and Fennovoima (a subsidiary of E.ON), with a further reactor to be built at Olkiluoto by TVO. In October 2011, Fennovoima announced that it had chosen Pyhäjoki, in northern Finland, as a site for further nuclear expansion, with construction expected to start in 2015. Elsewhere, the United Kingdom's government, excluding Scotland, has in principle approved the concept of a new generation of up to eight nuclear power plants, subject to reactor generic design approvals; Bulgaria has begun detailed planning for a reactor at Belene; Romania has issued a planned call for tender; Poland's state utility, PGE, has shortlisted three sites as possible locations for their first nuclear power plant; and the Czech Republic is progressing with planning new-build — despite downsizing the proposed Temelin site tender from five to two reactors and Austria's strong objection to the expansion of the Temelin plant, which is situated near the border of the two countries.

Although Sweden formerly had a nuclear phase-out policy aiming to end nuclear power generation by 2010, on 5 February 2009, the Swedish Government announced an agreement allowing for the replacement of existing reactors. However, the

Box 18.8 Nuclear costs

A key challenge for nuclear power has been the high cost of construction (Davis, 2011). Nuclear new builds are high value and high risk construction projects with a marked tendency for significant delay and delay claims, cost growth and investor risk (KPMG, 2011). Based on the experiences of 52 United States investor-owned utilities that built nuclear power plants in 1960–2011, the Texas Institute (2011) concluded that building nuclear power plants provide significant economic risks involving a 70 % certainty that a power utility would see borrowing costs rise due to the downgrading of credit rating once construction began, with plant construction marred by significant cost overruns and electricity tariff increases. Nuclear plants, which are among the largest and most complex engineering projects in the world, also carry high technical and regulatory risks, with World Nuclear Association figures showing very significant cost overruns for most projects, implying that utilities may only be able to pay for new plants if governments guarantee their income (Thomas, 2010a). Thus, costs and risks associated with nuclear construction may mean that plants may only be built with implicit and explicit public subsidy, including long-term power purchase agreements (Professional Engineering, 2011).

Box 18.9 European Union Nuclear New-build Experience

The Olkiluoto 3 EPR in Finland was originally planned to go online early in 2009, but is now predicted to start generating in late 2014 (Thomas, 2010c). The new 1.6 GW AREVA designed EPR is conceived as first of type, with Siemens responsible for steam turbines and electricity generators. Originally priced at EUR 3 billion, the project is now estimated at EUR 5.7 billion and rising. The fixed price turn-key contract is subject to an ongoing dispute between the French manufacturer AREVA and TVO with the former claiming compensation of EUR 1 billion for alleged failures, and the latter demanding EUR 2.4 billion in compensation for delays (Thomas, 2010b). Similarly, in France, EDF confirmed the EPR Flamanville project was running late and increased its estimate of the cost. Originally scheduled to start operating in 2012, it is hoped that the reactor may be operational by 2016. Originally priced at EUR 3.3 billion, the reactor completion is currently estimated at EUR 6 billion (Thomas, 2011).

Fukushima disaster may have reversed prior public support of nuclear power, with a BBC World Service — Globescan (2011) poll showing that 64 % of Swedes opposed new reactors while 27 % supported them. Similarly, whilst Spain has no plans for expansion or closure, public opposition to new nuclear build remains very high at 55 %. The United Kingdom is more favourable towards the use of nuclear energy than any other European country, with 37 % in favour of building new nuclear infrastructure (ibid).

Given that Germany uses around 20 % of all EU electricity, the government's March 2011 decision to close 7 of its 18 reactors, followed in June by the German Parliament vote to phase out nuclear power by 2022 and to invest in renewables, energy efficiency, grid network infrastructure, and plan for trans-boundary pumped-storage hydroelectricity (PSH), may prove significant for European energy policy as a whole. In June 2011, Italian voters also passed a referendum to cancel plans for new reactors, with over 94 % of the electorate voting in favour of the construction ban. Because 55 % of the eligible voters participated, the vote is binding. Elsewhere, six months after the Fukushima plant catastrophe, strong Swiss public opposition to nuclear led to a decision not to replace the country's five reactors when they come to the end of their operation in 2034. Belgium also confirmed a nuclear phase-out, with no firm date set for end of operation, whilst the only Dutch reactor at Borssele will remain open until 2033 if it can comply with the highest safety standards. It is also worth noting that, at a ministerial meeting in Vienna; ministers and heads of delegations of Austria, Greece, Ireland, Latvia, Liechtenstein, Luxembourg, Malta and Portugal, observed by ministers from Cyprus, Denmark and Estonia, concluded that nuclear power was not compatible with the concept of sustainable development, suggesting that nuclear power does not provide a viable option in combating climate change (Vienna Declaration, 2011).

Before Fukushima, the IAEA had predicted that around the world nuclear plants would add 360 GW of generating capacity by 2035, the equivalent of over 200 new reactors. Post-Fukushima, it has halved this forecast, partly due to diminishing public acceptance of nuclear energy, but also to the increased costs of nuclear security improvements and of insurance premiums for accident-related damages (Leveque, 2011). France has set radical safety standards for the industry. However the required plant upgrades are both technically difficult and expensive, with the French nuclear authority, ASN, estimating the cost of necessary improvements at the country's 58 nuclear reactors at around EUR 10 billion (Nature, Editorial, 2012).

Western European Nuclear Regulators Association (WENRA) 'Stress Tests' comprised a targeted reassessment of the safety margins of nuclear power plants in the light of Fukushima, including extreme natural events which challenge plant-safety functions, leading to severe accident (WENRA Task Force, 2011). However, since the European Nuclear Safety Regulators Group (ENSREG, 2011) decided that security issues were outside WENRA's remit, post-Fukushima stress tests of EU's 143 nuclear power reactors did not include accident and incident from an aeroplane strike or terrorist attack. The exclusion of these security issues seems unfortunate given that, for example, all UK civil nuclear infrastructures are uniquely implicated in all four high priority tier-one threats identified in the UK National Security Strategy (HM Govt., 2010).

Despite further new-build plans in e.g. Finland, France and the United Kingdom; the general post-Fukushima situation in the EU implies that the limited construction of nuclear new-build since 2000, and potentially in the coming decade, combined with the ageing of nuclear power

plants and the finalisation of nuclear phase-out in Germany and other European countries, will lead to a relative decreasing share of electricity production sourced from EU nuclear energy after 2020. The emphasis is likely to shift towards maximizing output of existing reactors through extension, up-grade and retrofit (Leveque, 2011; Coenen and López, 2010).

The energy futures landscape within Europe is one of major national differences between state and market, choices and trade-offs over supply-side, demand-side, transmission and load-balancing infrastructure (Schiellerup and Atanasiu, 2011). Although EU Member States diverge in terms of cultural and industrial landscapes, public opinion, technological structures, institutions, regulatory practice and energy mixes (Box 18.10), the European energy policy offers a fairly open and flexible framework in which some Member States could develop collective action on energy issues. The development of sustainable and affordable low carbon energy remains a growing economic sector with huge potential for job creation (Andoura, 2010).

18.4 Nuclear liability

The risk to people, the environment and to the future of nuclear energy as a consequence of a major incident is significant. The cost of the Chernobyl accident can only be roughly estimated, but a variety of government estimates from the 1990s put the cost of the accident, over two decades, at hundreds of billions of dollars.

More recent events at Fukushima tend to support the conclusion that reactor accidents may prove the single largest financial risk facing the nuclear industry, far outweighing the combined effect of market, credit, and operational risks. Perhaps unsurprisingly, liability estimates vary with ongoing events. Japanese replacement power costs in 2011 alone have been estimated at EUR 6.5 billion (JPY 700 billion), with decommissioning costs for the six reactors are estimated at EUR 9 billion (JPY 1 trillion). On 20 May, 2011, TEPCO reported a net loss for the fiscal year ending in March 2011 of EUR 11.5 billion (JPY 1.25 trillion), the largest corporate loss in Japanese history outside the financial sector. By mid 2011, Bank of America Merrill

Box 18.10 Cultural and policy diversity in energy governance

Finland: The Finnish discussion culture can be summarised as one in which decisions are preceded by an open public and policy debate, but once the decision has been made, according to the rules and regulations in force, there should no longer be room for complaints and further debate. Provided that proper procedures have been followed, changing course would mean loss of face and identity. Correspondingly, nuclear power has acquired the reputation of being the cheapest, safest, and most reliable source of electricity generation. This is primarily because there have been no serious nuclear accidents in Finland, and their reactors maintain a high reliability and load factor. These advantages are coupled with arrangements under the Mankala Principle, whereby large industrial corporations such as forest and heavy industry — as shareholders in nuclear power companies — can buy electricity at cost price (Lehtonen, 2010a; Lehtonen, 2010b).

Germany: Decisions on nuclear power cannot be separated from prior energy policy choices, and Germany has demonstrated a very strong, historic commitment to renewables, with renewable electricity production doubling between 1998 and 2003 and again between 2003 and 2008. By 2010 renewables contributed 17 % of total electricity production, and there are plans to increase this to at least 35 % by 2020 (BMU, 2011). Innovative German practice includes the first implementation of a fixed price feed-in-tariff, and huge purchases of solar photo voltaics (PV), which have driven down the world price of modules. Energy futures have also devolved to the local level, with communities securing political agreements under which the *Bundesländer* (federal states) are enabled to set goals and locations for renewable generation. This ensures that local energy resources and financial subsidies — paid for by customers (through feed-in tariffs) or taxpayers (through cheap loans provided by the government development bank (KfW)) — benefit not only the energy companies but also the local people, with profits and employment kept in the region. Germany's non-nuclear energy policy is framed in the context of national pride and scientific-technological achievement, twinned with economic expansion: 'As the largest industrialized (European) nation, we can achieve a transformation toward efficient and renewable energy, with all the opportunities that brings for exports, and the development of new technologies and jobs' (Chancellor Angela Merkel, in German, 2011).

Lynch reported that compensation claims could total EUR 93–102 billion (JPY 10–11 trillion) over the next two years, with liabilities far exceeding the current market cap (Maloney, 2011). By September 2011, Fukushima liabilities stood at anywhere between EUR 76–152 billion, with the Japanese Centre for Economic Research estimating clean-up remediation at EUR 190 billion over the next 10 years (Kobayashi, 2011).

Currently, individual European nuclear accident liabilities are capped at EUR 169 million for operators. However, the Paris Convention on Nuclear Third Party Liability and Brussels Convention (2011) ([7]) aims to raise this to ensure that victims of a nuclear incident are compensated for resulting damage. Under the proposals, nuclear operators would be liable for the first EUR 700 million for any accident, with the national government having the option of adding a maximum of a further EUR 500 million towards the company's liabilities. Collectively, other signatory states could contribute a further EUR 300 million, potentially bringing the total available to EUR 1 500 million for any one accident.

Yet actuarial analysis suggests that even this level of cover may fail to account for liability in case of major accident. Versicherungsforen Leipzig GmbH (2011), a company that specialises in actuarial calculations, concluded that these costs were not adequately internalised, suggesting that full insurance against nuclear disasters would increase the price of nuclear electricity by up to EUR 2.36 per kilowatt hour (kWh) — a sum that may weaken the economic case for nuclear power compared to other low-carbon sources.

Both the required liability (EUR 6.09 trillion), based on an estimate of the average maximum damage and corresponding variance, and the resulting insurance premium, are significantly higher than the financial resources currently legally required of nuclear power plant operators. Versicherungsforen Leipzig's study estimated that future damage and liability insurance costs would exceed the financial resources that nuclear power plant licensees are currently required to maintain by several orders of magnitude. In this context, nuclear disasters seem uninsurable, due to a combination of methodological difficulties in estimating the probability of occurrence of damage, insufficient size of the risk pool, and the extent of potential maximum damage (ibid).

To the extent that liability rules provide incentives for prevention, the financial limit on the liability of an operator may lead to under-deterrence — since, as a result of the financial cap on liability, the potential complementary function of liability rules in providing additional deterrence may be lost. The financial limit, and the resulting nuclear subsidy, may also distort competition by unduly favoring nuclear energy compared to other energy sources (Faure and Fiore, 2009).

The issue of nuclear waste liability has also been subject to intense and prolonged debate, especially in the context of high burn-up fuel proposed for Generation III reactors (Box 18.11).

Box 18.11 High burn-up fuel

Following the liberalisation of the EU energy market, it was realized that a decrease in nuclear costs could be achieved if reactor power could be optimized by using more uranium as reactor fuel and keeping the fuel rods in longer. This means that generation III reactor high burn-up spent fuel will be significantly more radioactive than conventional spent fuel. Five years after discharge, each square metre of spent fuel in the proposed EPR cooling ponds may generate up to 17 kW of heat compared with 11 kW from more conventional spent fuel pool. And the high density of spent fuel racks from the proposed Westinghouse AP1000 reactor implies that 24–36 kW of heat may need to be removed from each square metre. Safety could depend on the effective and continuous removal of the significant thermal power of high burn-up spent fuel, potentially requiring additional pumps, back-up electricity supplies and back-up water supplies: all systems potentially vulnerable to mechanical failure or deliberate disruption. It is also likely that densely packed high burn-up spent fuel may require additional neutron absorbers, and greater radiation shielding during encapsulation and storage (Richards, 2009).

([7]) Note, not all EU Member States are signatories. Belgium, Denmark, Finland, France, Germany, Greece, Italy, the Netherlands, Norway, Portugal, Slovenia, Spain, Sweden, the United Kingdom and Turkey are signatories to the Paris Convention on Nuclear Third Party Liability and Brussels Convention.

18.5 Nuclear risk: probabilistic risk assessment and beyond design-based accidents

Key to the analysis of nuclear safety is the analytical concept of probabilistic risk assessment (PRA) or probabilistic safety analysis (PSA). Whilst PRA calculations are not taken as absolute, but rather as significant indicators of plant weaknesses, they do underpin the concept of acceptable risks and tolerable consequences under fault conditions. In this context, the risk of an accident must be acceptable, and the radiological consequences tolerable, with more frequently occurring incidents countered by greater resilience through enhanced safety systems grounded in robust engineered structures. However, PRA has proven structurally limited in its ability to conceive and capture the outcomes and consequences of a nuclear accident resulting from a cascading series of events, as described in the Fukushima disaster and all previous major nuclear accidents. This implies that relatively simplified chain-of-event fault-tree models may not be sufficient to account for the indirect, non-linear, and feedback relationships common for accidents in complex systems. Here, modeled common-cause, common-mode, and dependent failures have proved problematic; partly due to data limitation (since major failures occur infrequently), and because failure mechanisms are often plant specific (Ramana, 2009).

Most PRAs assume failure likelihood can be captured through identical, independent log-normal failure distributions. Since strong independence assumptions employed in PRAs assume that reactor safety systems are duplicated and reliable, core damage frequency estimates are typically very low. Because of this, there may be good reason to question the conceptual and theoretical completeness, and empirical and practical reliability of PRA models. This is partly because PRA is prone to under-counting accident scenarios — since risk is estimated for enumerated reactor states, failure to account for unknown and serially cascading beyond design-base accident scenarios leaves an un-measurable model error in the core damage frequency estimate (Maloney, 2011).

Before the Fukushima accident, for example, the Japanese Nuclear Regulatory Commission Guidance (NSC, 2006), updated in early 2011, concluded that 'robust sealed containment structures would prevent damage from a tsunami… and no radiological hazard would be likely'. Whereas after the accident, the Chairman and President of the European Nuclear Society High Scientific Council stressed that 'the magnitude of the tsunami that struck Japan was beyond the design value to which the reactors were supposed to withstand' (Bonin and Slugen, 2011). These pre- and post-facto statements suggest that, although reactor design can prove relatively robust against specific accidents and specific modes, safety cannot be guaranteed for cascading beyond design-base accidents. In the case of Fukushima, because the cascade from earthquake, through tsunami, to reactor and spent fuel fault condition was discounted, no account was taken for the need to respond to the failure of three nuclear reactors and spent fuel ponds.

Pre-Fukushima probability estimates of a major nuclear accident were around 1:100 000 for the 440 reactors in operation over the next 20–25 years. Since Fukushima, estimated probabilities of major nuclear accidents have increased significantly. However, estimation of core melt and containment failure may still prove problematic. Chernobyl and Fukushima together comprise catastrophic meltdown in four nuclear reactors over the past few decades, implying that that the probability of a major accident in the current worldwide fleet over the next 20–25 years is around 1:5 000. Thus, whereas earlier estimates assumed a probability of one major nuclear accident over a 100-year period, reoccurrence of these events can be expected once every 20 years (Goldemberg, 2011). This reassessment of nuclear risk has been particularly apparent in Germany, where Chancellor Angela Merkel concluded that Fukushima 'has forever changed the way we define risk' (Schwägerl, 2011); an analysis echoed by Norbert Röttgen, Germany's Environment Minister, who noted that Fukushima 'has swapped a mathematical definition of nuclear energy's residual risk with a terrible real-life experience… we can no longer put forward the argument of a tiny risk of 10–7, as we have seen that it can get real in a high-tech society like Japan' (ibid).

Importantly, the governmental German Advisory Council on the Environment also concurred with this critique, suggesting that: 'The widespread view that the extent of the damage due even to major incidents can be adequately determined and limited in order to be weighed up… is becoming considerably less persuasive… The fact that the accident was triggered by a process which the nuclear reactor was not designed to withstand… casts a light on the limitations of technological risk assessment… based on assumptions, and that reality can prove these assumptions wrong' (SRU, 2011b, p.11).

Levels of reliability required for a complex interactive and tightly coupled nuclear power plant are very great (Perrow, 1984), with the range of

operating reactors having differing sets of designs and configurations. Because of their complexity and the physical conditions during reactor operation, the understanding of the reactor design and operation is always partial. Additionally, as system components and external events can interact in unanticipated ways, it is not possible to predict all possible failure modes. It follows that numerical estimates of probabilities of significant accidents remain deeply uncertain. As the Fukushima Investigation Committee concluded (2011, p. 22): 'The accidents present us (with) crucial lessons on how we should be prepared for… incidents beyond assumptions'.

18.6 Conclusion

Because it is likely that post-Fukushima health consequences may start to arise and be documented over the next 5–40 years, a key lesson to be learned concerns the multi-factorial nature of this event. It can be expected that a number of chemical agents were released and, hence, the final biological effect may depend on the consequential complex radiochemical environment. Thus, in planning future radiation protection, preventive measures and bio-monitoring of exposed populations, it is of great importance to:

- integrate the available data on both cancer and non-cancer diseases following overexposure to ionizing radiation;
- take a complex approach in the interpretation of data — considering the impacts of age, gender, and geographical dispersion of affected individuals, and the psychological, educational and social status of victims; and
- integrate the evaluation of latency periods between exposure and disease diagnosis development for each cancer type.

Bunn, the former adviser to the US Office of Science and Technology Policy, and Heinonen, the former Deputy Director General of the IAEA, also conclude that there is a need for more stringent nuclear safety standards, and propose six areas for improvement involving substantial cost and time investment:

- operators must plan for events beyond design bases;
- more stringent standards for protecting nuclear facilities against terrorist sabotage;
- a stronger international emergency response;
- international reviews of security and safety;
- binding international standards on safety and security; and
- international co-operation to ensure regulatory effectiveness (Bunn and Heinonen, 2011).

In addition, there is also the need to defend and adapt the coastal sites of nuclear plants to the hazards of rising sea levels, storm surges, flooding and the possibility of eventual nuclear site islanding (IME, 2009; Kopytko and Perkins, 2011). It should also be understood that it is very unlikely that current major accident liability regimes will prove adequate, and a significant re-adjustment may be essential.

This wide-ranging set of recommendations constitutes a significant step forward in radiation protection philosophy. However, there seem to be no resounding new revelations over the vulnerability of nuclear power to unforeseen natural disasters like earthquakes and tsunamis, or through human or engineering based fault conditions, including accidental or deliberate harm. Accidents are by nature, accidental, and the cost of ignoring this common-sense axiom can prove radiologically catastrophic (Stirling, 2011).

Whilst the imaginative use of foresight and precaution are key to the management of nuclear risks, a further paradox lies at the heart of the debate: Whereas fundamental radiation protection science is characterised by very real uncertainty, indeterminacy and contingency, the regulation and operation of nuclear facilities is based on the language of certainty. The nearer one gets to the fundamental science and engineering of complex technological systems, the greater the uncertainty and complexity; yet the nearer one gets to regulation and operation, the greater the certainty and simplicity. Since somewhere along this continuum, uncertainty has been translated into certainty, and risk has been translated into 'safety', the question remains: when, how, and why does this transformation happen?

Given the degree of uncertainty and complexity attached to even the most tightly framed and rigorous nuclear risk assessment, attempts to weight the magnitude of accident by the expected probability of occurrence has proven problematic, since these essentially theoretical calculations can only be based on sets of pre-conditioning assumptions. This is not an arcane philosophical point, but rather a very practical issue with

significant implications for the proper management of nuclear risk. With its failure to plan for the cascade of unexpected beyond design-base accidents, the regulatory emphasis on risk-based probabilistic assessment has proven very limited. An urgent re-appraisal of this approach, and its real-life application seems overdue.

Whatever one's view of the risks and benefits of nuclear energy, it is clear that the possibility of catastrophic accidents must be factored into the policy and regulatory decision-making process. In the context of current collective knowledge on nuclear risks, both the regulation of operating nuclear reactors and the design-base for any proposed reactor will need significant re-evaluation.

Given the size of the long-term investments that are now needed across the options of nuclear, carbon based fuels, renewables, energy efficiency and conservation, grid network infrastructure development and load balancing; it is clear that European public needs to play a key role in taking these critical, social, environmental and economic decisions ([8]). Here, public values and interests are central, and the role of public dialogue and the participatory practices that enable it are core to the building of mutual understanding between European states, governments, industry and people. If carried out in a truly involving way, the integration of public, policy, and expert scientific knowledge allows for greater accountability, transparency, and much better take-up of necessary change and improved long-term likelihood of problem resolution. This conclusion mirrors those from many chapters in this publication — from leaded petrol to nanotechnology: that wider public engagement in choosing strategic innovation pathways is essential.

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19 Hungry for innovation: pathways from GM crops to agroecology

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Innovation's potential to deliver food security and solve other agriculture-related problems is high on the agenda of virtually all nations. This chapter looks at two different examples of food and agricultural innovation: genetically modified (GM) crops and agroecological methods, which illustrate how different innovation strategies affect future agricultural and social options.

GM crops are well suited to high-input monoculture agricultural systems that are highly productive but largely unsustainable in their reliance on external, non-renewable inputs. Intellectual property rights granted for GM crops often close down, rather than open up further innovation potential, and stifle investment into a broader diversity of innovations allowing a greater distribution of their benefits.

Science-based agroecological methods are participatory in nature and designed to fit within the dynamics underpinning the multifunctional role of agriculture in producing food, enhancing biodiversity and ecosystem services, and providing security to communities. They are better suited to agricultural systems that aim to deliver sustainable food security than high external input approaches. They do, however, require a broader range of incentives and supportive frameworks to succeed. Both approaches raise the issue of the governance of innovation within agriculture and more generally within societies.

The chapter explores the consequences of a 'top-down transfer of technology' approach in addressing the needs of poor farmers. Here innovation is often framed in terms of economic growth in a competitive global economy, a focus that may conflict with efforts to reduce or reverse environmental damage caused by existing models of agriculture, or even deter investment into socially responsible innovation.

Another option explored is a 'bottom-up' approach, using and building upon resources already available: local people, their knowledge, needs, aspirations and indigenous natural resources. The bottom-up approach may also involve the public as a key actor in decisions about the design of food systems, particularly as it relates to food quality, health, and social and environmental sustainability.

Options are presented for how best to answer consumer calls for food quality, sustainability and social equity in a wide sense, while responding to health and environmental concerns and securing livelihoods in local small-scale agriculture. If we fail to address the governance of innovation in food, fibre and fuel production now, then current indications are that we will design agriculture to fail.

19.1 Introduction

Would it not be a loss to humanity if society's science and policy institutions delivered wonderfully sophisticated technological tools for agricultural innovation, but yet were out of touch with the needs for food security, poverty alleviation and ecological sustainability? In agriculture, as in other industries, research and development is guided by innovation policies. Within these policies, the incentive systems set at the highest levels of policymaking largely determine who is innovative and what innovative products will look like. They also favor those who will most benefit. Under the current innovation policies for industrial agriculture, continuous increases in wealth, sufficient food production to more than feed the current population, and ongoing investment in particular kinds of research and technology fail nearly a billion people who are undernourished or hungry, well above Millennium Development Goals (FAO, 2010, 2011a). Has modern agriculture, despite good intentions, been unwittingly designed to fail?

A confluence of issues surround agriculture and its existing problems: Ongoing societal and trade issues, food price volatility (FAO, 2008), inefficient energy utilisation, harvesting/storage and production systems (Nellemann, 2009) as well as retail/consumer level waste (Gustavsson, 2011) to name a few. These challenges are building on decades of environmental degradation from high-external input farming, and centuries of environmental damage from inefficiencies within traditional farming that have exacerbated social inequities (IAASTD, 2009a). The extent of these environmental and social consequences of current agricultural practices in food-wealthy and food-poor countries alike means that food production must be rethought in order to achieve greater resilience and sustainability within these systems. The new goal for agricultural innovations is a transition towards social, economic, and environmental sustainability that can support needed production levels (De Schutter, 2010; EU-SCAR, 2011; UNEP, 2011).

Scientific and technological advances within agriculture have the potential to alleviate hunger and increase food security, particularly where food productivity and sustainability are solely limited by simple technical issues or their availability, rather than by institutional or societal constraints (Heinemann, in press). Science and technology have the capacity to produce valuable outcomes from investments in research and development. However, the efficacy of innovation is more than merely invention; it must also meet real needs and be effectively accessed, supported and adopted by farmers who, like retailers, consumers and community members must share in the benefits.

Agriculture is multifunctional (IAASTD, 2009a). It provides food, fibres and fuel for local and international needs, income for producers who purchase education, health and consumer goods, calories and nutrients for families, and cultural and social identity. Through its practice skills are transferred and developed, biodiversity and greenhouse gas emissions are changed — depending on how agriculture is practiced (Hoffman, 2011; IAASTD, 2009c). However, food production remains local. Local needs must be met through both technological and non-technological advances which can be adapted to fit local conditions through ongoing innovation (Altieri, 2011b; Vanloqueren, 2009).

In the global context, the policy focus on agricultural development and food production is shifting from 'how much' through to 'how long' to just 'how'. Some see the problem as not enough production to feed the world. Others note that we have a global food surplus, but the lack of good infrastructure, conflicts and appropriate tools for local farmers cause food shortages and insecurity in many places (MEA, 2005).

Even other commentators see farmers no longer as producers of food, but more accurately of biomass, as part of an economic system that can vary the usage of this biomass as human food, animal feed, biomaterial or biofuels (Pengue, 2005a). Competition among different markets (for energy, industrial products, food production or animal fodder) is creating further constraints on food availability in some parts of the world. Moreover, with the predominant food production practices, there are also concerns that current demands on yields require an unsustainable level of environmentally damaging external inputs of agrochemicals and supply of exogenous energy. For example, industrial agricultural practices on average require 10 calories of exogenous energy (used for everything from petrochemical production, extraction, transport etc.) for every 1 calorie of food produced (Giampietro, 1993; UNEP, 2011). Growing populations, competing demands for crop biofuels and demand for meat will continue to intensify these pressures on agricultural food production. This insight draws us full circle: food security will follow not only from producing more food, but how we produce and consume it (IAASTD, 2009c).

The role of innovation to end food insecurity and solve other problems caused by, and for, agricultural is high on the agenda of virtually all nation states. More and more frequently, governments are framing innovation as a means for economic competitiveness by using the promise of returns on intellectual property (IP) as incentive for both public and private innovators (Heinemann, 2009). As a result, those that innovate by inventing technologies — mainly products — that can be commodified in a form that meets the criteria for IP instruments, e.g. patents or patent-like plant variety protections, are incentivised by the prospect of financial rewards. Moreover, the problems identified for solution will tend to be those that can be packaged and sold — usually to the largest/wealthiest/most lucrative market and largely bypass the poor (Spielman, 2007). This was perhaps the most evident early warning of the so called 'Green Revolution', where supplying technological product packages of seed and agrochemical inputs for monocultures on large tracts of land in some developing countries would increase yields and production for cash crops (e.g. in Asia but not Africa), but would prove to be incompatible with the cultural and social structures surrounding farming practices in many places that it was implemented (e.g. Africa). Indeed, its successes for decreasing hunger and malnutrition was a useful stop-gap solution, yet has not shown to be a sustainable approach for contributing to local food security or diet diversity for resource-poor small tract farmers or generate sufficient surplus income for many to be a path out of poverty (IAASTD, 2009b). Meeting these needs for a healthy and diverse diet would require the development of locally adapted varieties that are tailored to local environments, agricultural practices and needs for a range of nutrient dense foods from local food crops (Reynolds, 2006). 'Although the world food system provides an adequate supply of protein and energy for over 85 % of people, only two-thirds have access to sufficient dietary micronutrients. The supply of many nutrients in the diets of the poor has decreased due to a reduction in diet diversity resulting from increased monoculture of staple food crops (rice, wheat and maize) and the loss of a range of nutrient dense food crops from local food systems.' (IAASTD, 2009d).

Those who might invest in research or invent solutions that are not derived from a technology or technological process leading to a product that can be licensed under existing IP instruments are often left out of the innovation development and support system. Instead of a view of agricultural innovation focused on seed products from genetic improvement or developing external inputs, the neglected innovations are often locally adaptable practices and services related to complex and dynamic ecological processes that do not lend themselves to commodification—at least not in the way current IP instruments require—but are transferable knowledge that can undergo further innovation at the local level by the end user. A good example of this is the 'push-pull' systems developed at the ICIPE in Kenya (Cook, 2006; Hassanali, 2008).

For this case study on innovation, we have chosen to contrast genetically modified (GM) crops and agroecological methods as two examples of innovation outputs and strategies that have very different outcomes in the way we produced food. We illustrate how these contrasting innovation strategies shape, and in some cases limit, future social options. The former is driven by production goals and short-term profit maximisation incentives, where the predominant types of GM crops developed thus far are economically profitable within a system of high-input industrialised monoculture that is largely unsustainable in its reliance on external, non-renewable inputs. In such systems, economies of scale allow the farmer to outweigh the higher costs of production of such farming practices ([1]). The latter innovation strategy, based on an understanding of co-evolution and dynamics at ecological and social levels of agriculture, is better suited to agricultural systems that are in transition to sufficient production and socio-ecological sustainability, and requires a broader range of incentives and shelters to succeed (Tilman, 2002). That is, agroecological systems may be better suited than the current practice with GM crops to answer the call from affluent consumers for food quality, sustainability and social equity in a wide sense, responding to health and environmental concerns as well as securing livelihood in local small-scale agriculture. These issues may be crucial for the future of diverse agricultural practices needed to address improvements to the resilience and sustainability of agricultural systems. If we fail to address the governance of innovation in food and fibre production now, then current indications are that we will surely design agriculture to fail.

([1]) While hypothetically not all GM crops would necessarily require high-input or monoculture farming methods, their development to date has focused on 'technology traits' amenable to agricultural practices focused on high-input and monoculture production methods.

19.2 Innovation: what kinds and for whom?

Agriculture has not escaped the wave of new policies behind the banner of 'innovation'. The European Commission (EC) is running the 'Innovation Union' campaign (EC, 2011). The explicit claim is that innovation 'speeds up and improves the way we conceive, develop, produce and access new products, industrial processes and services. It is the key not only to creating more jobs, building a greener society and improving our quality of life, but also to maintaining our competitiveness on the global market.' The EC further endorses innovation as a means for stimulating economic growth investment in knowledge generation where 'innovative ideas that can be turned into new marketable products and services help create growth and quality jobs' (EU-Council, 2011). Similar initiatives and campaigns will be found in most developed and developing countries (Kiers, 2008) ([2]).

How innovation is conceived shapes how it is promoted, and who benefits from the promotion. The EC sees 'expensive patenting, market fragmentation, slow standard-setting and skills shortages' as barriers to innovation because they 'prevent ideas getting quickly to market' (van den Hove, 2011). This preoccupation with how efficiently technology products flow from knowledge holders to technology users is what Altieri (2002) called the 'top-down transfer-of-technology approach' in the context of addressing the needs of poor farmers. Here innovation is often framed in terms of economic growth in a competitive global economy, a focus that may conflict with efforts to reduce or reverse environmental damage caused by existing models of agriculture, or even disincentivise investment into socially responsible innovation (Tilman, 2002). This is an aspect deserving of representation in European innovation discourses, policies, and actions (van den Hove, 2012).

Kiers et al. (Kiers, 2008) argue for a more comprehensive approach to innovation: '[i]nnovation is more than invention. Success is not based on technological performance in isolation, but rather how technology builds knowledge, networks and capacity…innovation demands sophisticated integration with local partners'. This emphasis on the appropriateness of the technology for the target user is what Altieri (2002) called 'a 'bottom-up' approach, using and building upon the resources already available: local people, their knowledge and their autochthonous natural resources. It must also seriously take into consideration, through participatory approaches, the needs, aspirations and circumstances of smallholders'. The bottom-up approach also may involve the public as a key actor in decisions in the design of food systems, particularly as it relates to food quality, health and environmental sustainability.

Either pathway could lead to policy decisions to drive efficiencies in food production, lower food costs through increased supply, and become a means out of poverty. Where these pathways differ is in *who is considered the critical innovator and thus who should primarily benefit from innovation policies*. The key innovator in the top-down approach is usually a specialist technology producer, such as an agroindustrial company that builds technologies optimised for a specific type of farming system that shape the agroecosystems in which they are to be applied. For example, the use of herbicide tolerant GM plants coupled with the application of a specific herbicide creates a type of farming suited towards low agrobiodiversity and high capital inputs (e.g. multi-row spraying equipment) to maximise efficiency, and demands a scale investment and specialised farmer. However, this approach is incompatible with the available resources and needs of the subsistence and small farmer (see Box 19.1), the key innovator in the bottom-up approach and the target of strategies to feed the world through local production (IAASTD, 2009a). Bottom-up approaches place emphasis on the ability of the small-scale farmer to innovate to address critical local needs.

Will the predominant top-down approaches to agricultural innovation— and the science policies and legal instruments which support them — be better pathways to achieving the Millennium Development Goals, namely, to sustainably feed the world nutritious and desirable food, and through the production of this food, provide pathways out of poverty for the poor? Or might there be alternative strategies better suited to meeting these needs?

Our focus here will be whether top-down innovation produces the necessary benefits to small-scale farmers as well as income- and food-insecure countries as has been claimed. And in this attempt to create a consistent set of common regulatory and market incentives

([2]) For example, New Zealand defines it this way: 'Innovation is defined as the introduction of any new or significantly improved goods, services, processes, or marketing methods' (see Statistics-NZ, 2012).

Box 19.1 Herbicide tolerant GM crops: a technology for developing country agriculture?

Starting in the 1990s, the agroecosystems adopting herbicide tolerant GM crops simplified weed management through a near exclusive reliance on a single agrochemical product ('Roundup'), with its active ingredient glyphosate. The Roundup and Roundup-tolerant GM crop package promises lower labour costs through a simplified weed management strategy. It is also compatible with no-till practices that can reduce soil erosion (Duke, 2008).

These advantages are, however, disappearing (Service, 2007; Pengue, 2005b;Benbrook, 2012). Extensive and continuous use of glyphosate with the introduction of GM crops (Powles, 2008) has led a rapid evolution of glyphosate-resistant weeds (Binimelis, 2009; Duke, 2008; Heap, 2012; Heinemann, 2008; NRC, 2010). This has a negative overall effect on sustainability, where minimising the use of external inputs such as agrochemicals is key. Since glyphosate tolerance can be overcome by using more glyphosate, farmers have entered into a treadmill where overuse of a single product leads to tolerance and tolerance is overcome with more product, leading to ever higher levels of tolerance in weeds and an increase in the number of species that display tolerance (Binimelis, 2009; Duke, 2008; NRC, 2010). In some cases, farmers are returning to tilling and using other (and possibly more toxic) herbicides (Binimelis, 2009; Duke, 2005; Heinemann, 2008b; Mortensen, 2012). Further, indications of harm stemming from the widespread and intensive use of glyphosate for the environment and human health has been documented in the scientific literature and remains a concern (Greenpeace, 2009; Séralini 2012).

The herbicide-GM crop package is not compatible with how most people farm, and especially with small and subsistence farming practices. The package is most economical when herbicide can be sprayed in great quantities using mechanised delivery (e.g. airplanes) or expensive, multi-row sprayers and this would not be possible in a mixed cropping landscape (Binimelis, 2009).

Moreover, this top-down solution to the problem of weeds threatens long-term retention of alternative weed control skills. 'Although seed and chemical companies can generate enormous revenues through the packaged sales of herbicides and trans- genic seeds, the [integrative weed management] approaches… are based on knowledge-intensive practices, not on saleable products, and lack a powerful market mechanism to push them along' (Mortensen, 2012). The farming system is 'deskilling' and losing the know-how to implement other pest management approaches (Binimelis, 2009). A second problem with this package is that it is encouraging the expansion of damaging agricultural practices. For example mixed agriculture/animal husbandry instead would require animal production further out into marginal lands or necessitate clearing new lands and accelerating rates of deforestation (Morello, 2007).

A bottom-up innovation for addressing weed problems is integrative weed management (IWM). The advantages of this system are that it uses, maintains and improves local knowledge of weed dynamics and ecology to develop multiple weed management approaches (Liebman, 2001) and is affordable to poor farmers. 'IWM integrates tactics, such as crop rotation, cover crops, competitive crop cultivars, the judicious use of tillage, and targeted herbicide application, to reduce weed populations and selection pressures that drive the evolution of resistant weeds' (Mortensen, 2012). IWM improves agrobiodiversity conservation, soil-quality, on farm energy efficiency — all of which enhance a more multifunctional system of agriculture that produce important environmental services (Boody, 2005). Farmers benefit from the same high yields and profits (Anderson, 2010; Liebman et al., 2008; Pimentel, 2005). Further, the soil-building under IWM helps to achieve conservation goals and improves soil quality even above no-till approaches based on herbicides (Venterea, 2006). This does not cause resistance problems of the magnitude seen with simplified chemical controls (Davis, 2007).

'Stacking additional herbicide tolerance genes into existing plants is not an alternative to IWM or other pest management strategies. They are likely to undermine sustainable agriculture further because 'the new traits will encourage continued neglect of public research and extension in integrated weed management' (Mortensen, 2012).

The transfer of herbicide tolerant GM crops to poor farmers, which has demonstrated not to be a sustainable approach for addressing the needs of developed country agriculture, appears to be another example of a top-down approach that has not, and will not produce the beneficial outcomes for the poor farmer (Heinemann, 2008b). However, there are already viable bottom-up approaches; all that is lacking is the political will and institutional capacity to make them available.

Box 19.1 Herbicide tolerant GM crops: a technology for developing country agriculture? (cont.)

Finally, the adoption of these crops is not leading to uniform or sustainable increases in income for farmers (Botta, 2011). The highest yielding varieties of GM crops are so because of ongoing and intensive genotype improvement through traditional breeding, rather than through the development of genetically engineered traits (Gurian-Sherman, 2009). Even in the most mature GM agroecosystems, such as cotton plantations in the US south, GM-farmers have not enjoyed a net economic benefit for adopting these plants compared to other high yield varieties (Jost, 2008). The high rent of patent-protected seeds is an upfront cost to farmers who may not realise a benefit from the trait each year, or would have to purchase other inputs, such as expensive agrochemicals, to gain any benefit. Here again, especially for poor farmers, those initial costs can be too high (Delmer, 2005).

(itself a top-down approach) if it in tandem will be suited to promoting the kind of innovation needed in countries with conditions favouring small-scale farms as well as those that are poor and food insecure. Building on the late lessons from prior top-down innovations in agriculture, we find that the promise of this approach to deliver the expected benefits will continue to be elusive when the pace and scale of innovations are prioritised over considerations for the intertwined institutional, governance and societal issues. Critically, innovation pathways that do not include such considerations may condition innovation directions, diversity and distribution away from the very kinds of innovation that are best adapted to meet local needs (STEPS, 2010). With this in mind, the lure of short-term wealth production from predominantly productivist frameworks for innovation must be re-balanced with those that prioritise long-term goals for sustainability — including financial sustainability and nutritional goals of small and subsistence farmers. This means supporting not just innovations which create new technology, but also those that create social good by addressing the non-technological, social, institutional, organisational and behavioural aspects along with new technology (van den Hove, 2012).

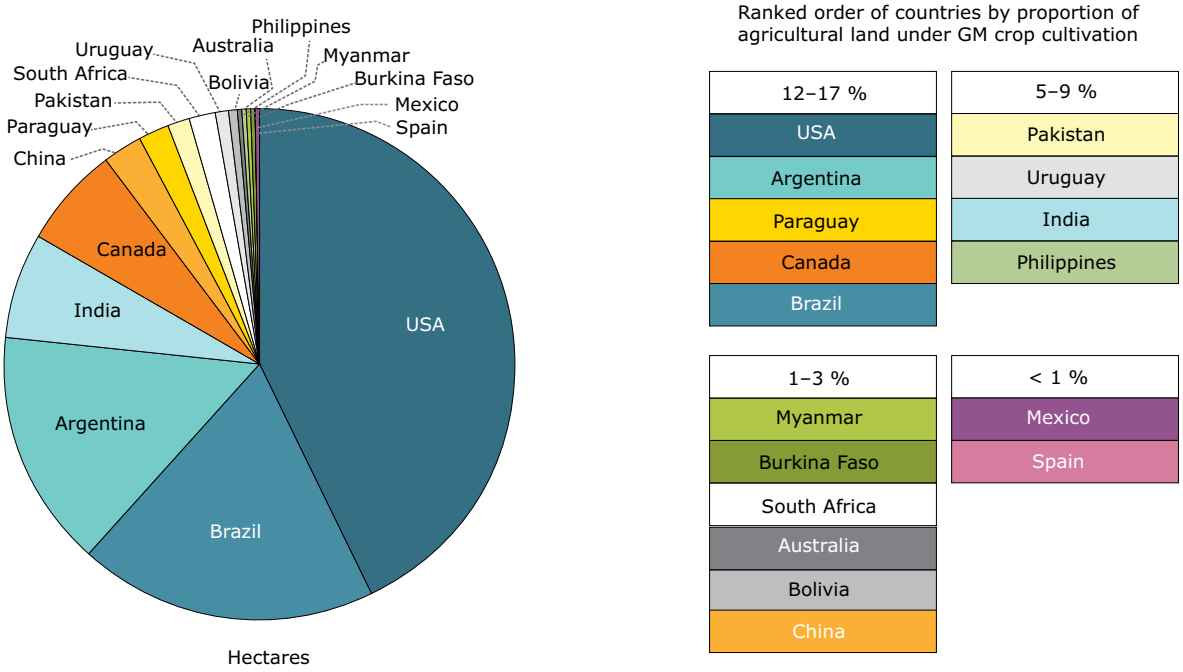
There is increasing evidence that the top-down approach to innovation will not achieve the expected stimulus to innovation (Baldwin, 2011), where an approach reliant on private incentives (primarily through IP protections) may actually have a negative effect on the progress in certain fields, including biotechnology (Murray, 2007).

19.3 GM crops as a top-down path out of poverty and hunger

The use of genetic engineering to produce commercially viable GM agricultural products is so far and for the foreseeable future restricted to crop plants (Heinemann, 2009). The crops are predominantly cotton, maize, rapeseed (canola) and soybeans ([3]) (James, 2011). Despite more than 30 years of research and development and nearly 20 years of commercialisation of GM crops, surprisingly only two traits have been significant in the marketplace — herbicide tolerance and insecticide production. And they are grown at scale only in a small number of countries. Industry-derived figures (James, 2011) report a large number of global hectares under GM cultivation, but when examined by country indicate an uneven global commitment to GM crops. The five countries USA, Brazil, Argentina, India and Canada account for 91 % of the global GM crop production, with the next five largest GM-cultivating countries accounting for another 8 %, leaving a total of 1 % of all GM acreage produced annually among just seven other countries. The proportion of agricultural land with GM varied from < 1 % to 17 % per country (Figure 19.1). These 17 so-called GM 'mega-countries' combined had 159 million hectares under GM cultivation in 2011 — seemingly a large figure, but in reality is just 3 % of the world's agricultural land (Figure 19.2). Some crop types have been converted entirely (or effectively entirely) to GM production in some countries. For example, nearly 100 % of the soybean crop in Argentina and the US is GM, sugarbeet in the US, and cotton in India at the present time is almost exclusively GM.

([3]) However GM papaya, sugar beet and possibly alfalfa are grown commercially in the US, with tomato and peppers reported in China yet at very low levels.

Figure 19.1 Ranked commitments to GM by the 17 largest producing countries



Note: Left: Countries range from a high of 69 million (USA) to < 50 000 hectares. Lowest level shown in graph is Spain at an industry estimated 100 000 hectares.

Right: Countries range from a high of 17 % (USA, Argentina) to under 1 % conversion from conventional to GM plants in commercial production. The rankings by proportion differ from the rankings by absolute number of hectares showing significantly different commitments to GM for primary production.

Source: GM hectares data taken from the industry source ISAAA (James, 2011). Agricultural land values taken from FAOSTAT (FAOSTAT, 2012).

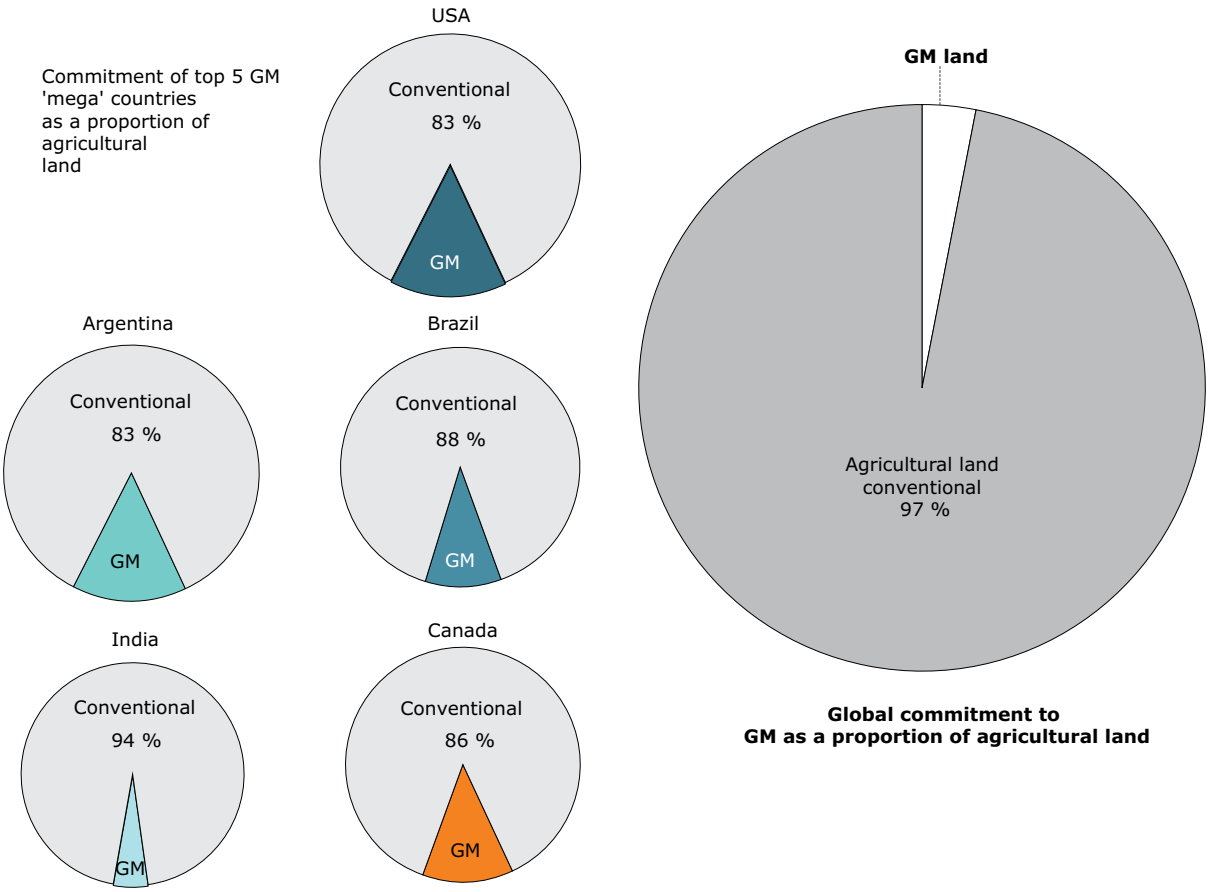
Why this patchy and limited global adoption of GM? There are several reasons. First, significant markets of high-income consumers have rejected GM (Gaskell, 2010). Given that the types of crops being commercialised, and the types of traits on offer, provide no direct benefit to consumers and may be introducing unintended adverse effects (see Box 19.2), in some places there exists skepticism on claims of net benefit. The main argument for adoption is the indirect benefits, financial and management-related, that GM crops offer to certain kinds of farmers (Heinemann, 2009).

Among the GM-adopting farmers are usually large-scale commodity growers that cultivate monocultures (e.g. soybeans in Argentina) or are in two-crop rotations (e.g. maize/soy in the US Midwest). The US and other OECD countries produce plenty of food or have the income to purchase it. While their agricultural systems deliver what they need, the OECD agroecosystems rely on heavy taxpayer subsidies to remain viable (Kiers, 2008).

It is perhaps no surprise that GM crops, the paradigmatic examples of top-down products, are most commonly crops that benefit from subsidies, such as maize, soy and cotton in the US (Pechlaner, 2010). These subsidies lead to the second reason for patchy adoption, where their use in developed countries undermines the market for these crops in developing countries. 'The average support to agricultural producers in the major developed countries as percentage of gross value of farm receipts was at 30 % for the period 2003–2005, representing an amount of almost USD 1 billion per day (OECD, 2006). These developed-country agricultural policies cost developing countries about USD 17 billion per year — a cost equivalent to five times the recent levels of ODA [official development assistance] to agriculture' (Hoffman, 2011).

The incentive brought by subsidies give a third reason for patchy adoption. The high rent of GM seeds and associated management inputs, such as proprietary agrochemicals, and other high costs of high external farming, confines these tools for agriculture to countries that redistribute wealth to farming for export, whether rich or poor (Delmer, 2005). Such capital and management intensive

Figure 19.2 Proportion of land in GM production



Note: Left: Charts indicate the proportion of total agricultural land per country in GM cultivation. The 5 countries shown have the highest absolute number of hectares in GM.

Right: Global value of GM production as a function of global agricultural land.

Source: GM hectares taken from the industry source ISAAA (James, 2011). Agricultural land values taken from FAOSTAT (FAOSTAT, 2012).

agricultural practices simply are not well adapted to use by small and subsistence farmers (see Box 19.1).

Poor countries that adopt this export lead are in danger of being caught on a loss leading treadmill where they produce agricultural goods at a net social loss and must continue to bear this debt as agriculture becomes a leading source of export income (Heinemann, in press; Pengue, 2005b). GM crops have not migrated to countries that have yet to commit to this strategy or are avoiding it, because the upfront costs are too high (Delmer, 2005).

19.3.1 Top-down incentives homogenise tool building

Too often the 'how to feed the world debate' (possibly a shorthand for the Millennium Development Goals) is presented as if it were an either/or choice between genetic engineering and agroecological science (Marris, 2008; Vanloqueren, 2009). Advocates for or against these technologies often are distinguished by their beliefs on whether it is genes or the environment that is the right substrate to manipulate to improve agriculture.

This dichotomy is in essence artificial, because few when pressed would argue against the relevance of both genotype and environment for meeting agricultural production and sustainability goals. However, there is an underlying truth to this division. The emphasis on genetics, or seed-based tools (Lal, 2009), is an unavoidable outcome of how innovation in the top-down model works. Modifying genotypes and capturing them as IP through plant variety protection and patent instruments is a far easier means of capturing financial benefits than

attempting to commodify management-based innovations, such as cover crops, rotation schedules and composting, farmer-initiated training and education and small scale marketing and credit programs. When a singular, centralised and highly specialised approach to agricultural development is followed, such as through genetic engineering, it can stifle other approaches that might produce even more desirable outcomes.

The size of the market available to genotype-manipulated tools may also be larger than for management-based approaches ([4]). Provided that the agroecosystem can be homogenised through the use of external inputs (e.g. fertilisers, agrochemicals), then a small number of varieties based on a proprietary genotype can be sold to a large number of farmers. In contrast, management-based techniques are knowledge- rather than product-intensive and must be customised to the location and often the circumstances of the farmer (e.g. whether irrigated or non-irrigated land, mixed or monocropping, combined crop and livestock production) and thus require more investment relative to the size of the market. Yet the benefits of these investments to promote and sustain management-based agricultural improvements are better distributed because they are not concentrated back to a seed producer. However, these asymmetries in investment incentives mean that management-based approaches do not receive the same levels of support and investment as do approaches that are easily recaptured in the marketplace.

To some degree, however, the environment does offer commercial opportunities through top-down innovation yet even then it comes from selling farmers tools that homogenise the environment to support proprietary genotypes. These tools are usually in the form of external inputs such as fertilisers and agrichemicals. The success of the green revolution was its ability to convert very different lands into similar agroecosystems using external fertilisers and other inputs to achieve high yields, but at great long term environmental costs, fossil fuel consumption and greenhouse gas emissions (Giampietro, 1993; Pretty, 2011; UNEP, 2011). Indeed, the unsustainability of the green revolution shows it will not be the model for future agriculture.

The editor of Nature magazine summed up the duality of genotypic and environmental sources of technology for addressing future needs in agriculture when he said: 'A second green… revolution will require a wholesale realignment of priorities in agricultural research. There is an urgent need for new crop varieties that offer higher yields but use less water, fertilisers or other inputs — created, for example, through long-neglected research on modifying roots — and for crops that are more resistant to drought, heat, submersion and pests. Equally crucial is lower-tech research into basics such as crop rotation, mixed farming of animals and plants on smallholder farms, soil management and curbing waste. (Between one-quarter and one-third of the food produced worldwide is lost or spoiled.)' (Editor, 2010).

That is, the tools and knowledge needed to transform agriculture towards a more sustainable path are not sufficiently prioritised in research and development. The failure of current top-down approaches to deliver on promises of a wide range of trait innovations needed by farmers, for example those that are tolerant to various environmental stresses (i.e. salt tolerance, water stress tolerance) requires a fundamental shift in agricultural innovation priorities towards improvements in genotype and environmental management approaches.

19.3.2 Effects on the knowledge pipeline

At the start of the 21st century public sector spending on agricultural research and development was just under twice the amount spent by the private sector (IAASTD, 2009b). Developing countries invested the majority of public funding at around USD 12 billion per year while high-income countries invested only around USD 10 billion. To see the investment imbalance another way, consider that the Consultative Group on International Agriculture Research, the world's largest international public sector research body, has an annual budget of only 12 % of the combined research and development budgets of the world's 6 largest breeding and genetic engineering companies (Spielman, 2007). Private funding in agricultural research is largely focused on innovations that will allow a high return on that investment to shareholders.

These statistics require deeper analysis to be fully understood. First, the shift in responsibility for agricultural research and development from

([4]) While both classical breeding and genetic engineering are different ways to create plant varieties, the latter creates novelty through the use of modern biotechnology (involving the in vitro manipulation of nucleic acids or fusions across the taxonomic boundary).

public research institutions to the private sector is unequivocal in high-income countries. This shift has profound effects on what comes from innovation. Second, high income countries have cited the need for increasing their economic competitiveness through instituted 'industry-driven' priorities into the research and development spending that they still do, thereby further leveraging the public contribution toward (often privately held) top-down innovation. This compromises the unique function and capacities that public funding supports pro-poor agriculture (Spielman, 2007), which may lack sufficient financial incentives to attract investment from the private sector (Tilman, 2002). Third, much of the existing public funding has direct or indirect ties to industry. Direct ties can take the form of private-public partnerships at universities and indirect ties include preferential relationships with institutions that maintain long-term industry-friendly cooperation (Knight, 2003; Lotter, 2009b; Seabrook, 2011).

Top-down innovation is guided by patent and patent-like plant variety protection (PVP) instruments, many newly applied to agriculture only in the last decades of the 20th century (Heinemann, 2009). Patents 'provide more control since (PVP) certificates have a research exemption allowing others to use the new variety for research purposes' (Fernandez-Cornejo, 2006; Mascarenhas, 2006).

The general argument for this approach is that patent and patent-like IP rights instruments on biotechnology create net social benefits, by encouraging and then capturing wealth for developers whether they be private or public (Pray, 2007). The main limitation here is that such an approach ignores significant effects on the innovation pipeline (Heinemann, 2006b; Kleinman, 2003; Krimsky, 2004; Shorett, 2003b; Wright, 2000) which shift innovation priorities towards economic policies and financial incentives. Leading international institutions have dismissed prevailing IP instruments as agents of constructive economic or food security change in developing countries at least at their stage of development (WHO, 2005; WorldBank, 2007). Furthermore, they impede practices that uphold and improve both food security and sovereignty. For example, seed savings and exchanges have become incompatible with these more severe IP instruments as shown in the conversion of behaviour in the US, and would, if adopted by developing countries, undermine what is now seen as an important source of bottom-up innovation: farmer by farmer breeding and adaptation of germplasm (Bellon, 2011; Borowiak, 2004; Mascarenhas, 2006; WHO, 2005).

The patenting of germplasm is concentrating IP rights-based control of the seed supply under a very small number of multinational corporations (Adi, 2006; Barlett, 2008; Sagar, 2000; Howard, 2009). The consolidation of the seed industry also has resulted in lower competitiveness (Pinstrup-Andersen, 1999) as the 'concentration of the top four' (CR4) seed companies breached a critical threshold (WorldBank, 2007). For example, the UK Parliament now says that:

'The use of patents on genes is controversial. There are concerns that in countries where GM technology is widespread in agriculture, seed companies may have reduced incentives to develop conventional varieties, as the market for these varieties is reduced, and they tend to have weaker IP rights than the patents usually used with GM crops. In the US, this is the case for soy, with conventional breeding now mainly left to universities and to small seed producers who focus on niche markets. The presence of patents may also limit public-sector research in some areas' (POST, 2011).

Is the answer to empower public institutions to secure IP instead? If the goal is to stimulate innovation across the board, history to date indicates that it does not seem to be so. Intriguingly, the flow of IP to the private sector has been fuelled by an unprecedented accumulation of IP claims in biotechnology made by public sector institutions whose behaviour is consistent with top-down innovation models despite their historic public-good role (Graff, 2003). This creates a feedback loop in which the best-funded researchers are those with top-down innovation interests, and they in turn out-compete other researchers — and their possible innovations — from future funding. This loop can decrease bottom-up innovation, even products that would provide much greater benefit. The downstream effects are stifling of public-good knowledge commons, upon which the modern agroecosystems of North America and Europe were initially built, and neglect of the needs of poor and subsistence farmers who are key to feeding the world.

'[F]or scientific knowledge subject to both Open Science and private property institutional regimes, the granting of IP [rights] is associated with a statistically significant but modest decline in knowledge accumulation as measured by forward citations (in academic publications)…Overall, we are able to reject the null hypothesis that IP [rights] have no impact on the diffusion of scientific knowledge… These patterns provide a novel perspective on the economic consequences of the privatisation of the

Box 19.2 GM crops: a late lesson case in the making?

The benefits and harms of GM crops are still being verified, despite there being science-based calls for greater scrutiny concerning the release of genetically engineered organisms from early on in the US FDA ([5]) (Drucker, 2012) and elsewhere (Traavik, 1999). The literature is accumulating indicators both of inflated benefit claims and of evidence of adverse effects (Bøhn, 2008; Botta, 2011; Hilbeck, 2012; Jost, 2008; Mesnage, 2012; Rosi-Marshall, 2007; Service, 2007). The benefits that may have been overstated are the reduction in pesticide use (Service, 2007), the reduced use of more toxic pesticides (Mesnage, 2012; Séralini, 2009), higher yields (Gurian-Sherman, 2009) and farmer income (Jost, 2008).

While GM crops are not found at scale in many places (see Figure 19.1), because they dominate as commodity crops they can be present at low levels in many types of food and feed, fibres and industrial products. Thus, exposure is global even if production is mainly in a few countries.

At what point is there sufficient evidence to be concerned and take action about the effects of GM crops on human health and the environment? How strong is the evidence of safety vs. risks?

The outcomes of many risk assessment studies equate the conclusions of 'no evidence of harm' to be synonymous with safety. The troubling outcome is that the safety of GM crops is presumed when there is a lack of evidence of harm, as if this were equivalent to evidence of lack of harm, when it clearly is not. Hence many of the safety conclusions arising in risk assessments stating 'no evidence of harm' are assumptions-based, rather than evidence-based, reasoning (Spök, 2004). Critically, when this lower standard of safety assurance is followed, as is the case with the mainstream risk assessment approaches today, important effects may be missed.

Of course, it is plausible that there simply are no effects to be found. Yet, what is the likelihood that the existing risk assessment approaches would capture an adverse effect caused by a particular GM plant? Are there particular challenges to detecting biologically important but difficult to detect effects? If so, what regulatory approaches can help avoid or overcome these challenges?

Emerging from the experience with biosafety research and risk assessment is a number of obstacles and limitations in policy or methodology that can limit or underestimate the detection of potential harms that may be present.

Obstacles to conducting biosafety research
Biosafety research and the safety investigations required for regulatory approval are the two main means for identifying potential adverse effects. However, a number of obstacles may limit or prevent the observation adverse effects in research, if they were indeed occurring:

- Industry contracts with researchers and farmers restrict access to material for safety testing. For example, 26 scientists released a public statement criticising that confidentiality and material transfer agreements made conducting any independent research on GM foods virtually impossible (Pollack, 2009).

- GM innovation research and development is outpacing biosafety research necessary to evaluate for safety. When it comes to research funding for biotechnology (including genetic engineering research), biosafety-related research has been lagging behind. From 1992 to 2002 the USDA disbursed USD 1.8 billion for biotechnology research, yet only approximately 1 % (USD 18 million) of this went to risk-related research (Mellon, 2003).

- Safety interested scientists face tough career choices. Researchers who have published scientific evidence unfavourable to the interests of GM crop developers have experienced personal and professional attacks on their work (Delborne, 2008; Editor, 1999; Waltz, 2009a, 2009b), and in some cases leading to threats or loss of research funding and dismissal (Lotter, 2009a, 2009b).

([5]) FDA Memos. FDA Memos 1991, 1992a and 1992b above are 3 of 24 internal FDA documents obtained through a FOIA (Freedom of Information Act request by the Alliance for Bio-Integrity, see http://www.bio-integrity.org/list.html).

Box 19.2 GM crops: a late lesson case in the making? (cont.)

Risk assessment: barriers to detecting adverse effects
The release of a GM crop into the environment, or for use in feed or food, is preceded in many countries by a pre-market risk assessment. The principles, concepts and methodologies of assessment vary, but most countries use international guidance (e.g. OECD/Codex Alimentarius, Cartagena Protocol on Biosafety) as a basis of their systems. Scientific and other information may also inform the risk assessment or secondary evaluation by expert committees.

Policies can undermine the effectiveness of risk assessment (Pavone, 2011) by allowing risk standards which increase the likelihood that adverse effects, if occurring, would not be identified during the appraisal.

Key examples:

- Many jurisdictions require scientific testing to be done by the developer and supplied to the regulator, who often lacks any capacity to perform independent testing. This lack of independence in the testing sets up the situation of bias in the studies outcomes as a result of 'the funding effect' — where results tend to correlate with the wishes of the funder (Krimsky, 2004). Various research efforts have found that the funding effect reaches well into the public research community and especially into biotechnology (Diels, 2011; Heinemann, 2006a; Shorett, 2003a).

- Often there is a provision to keep secret information that the developer claims is of proprietary value. When regulators agree to keep some information in the risk assessment confidential, review or reproduce the study by independent scientists is prevented (Fontanarosa, 2005). Transparency is a fundamental principle of good science reporting and practice but lacking in many risk assessments (AHTEG, 2012).

- Risk research conducted for the purposes of a risk assessment by the developer often lacks sufficient methodologies to allow statistical rigor that would yield meaningful results. Risk studies with low sample numbers lack statistical power, and bias the outcome towards no observation of differences/ effects between treatment groups (for examples, see Marvier, 2002). Further, they might not have been designed to test for potential hazards that the regulator has not asked the developer to test, or to the sensitivity that the regulator might find valuable (Séralini, 2009) or which have long lag time frames (Marvier, 2007).

- The regulator's policies on what to test will also affect what might be found. This approach may miss unintended changes to other gene products or metabolites or the effects of cooking and processing. For instance, applicants are often allowed to use a transgenic protein 'surrogate' (derived from a source other than the transgenic organism for which environmental release or consumption is being sought) in the place of the actual transgenic protein in safety testing from which regulatory approval is sought. Often the protein used in safety testing is that produced in bacteria, which is not going to be released into the environment or used as food — leaving the actual protein produced by the GM plant untested for safety. Since there can be significant biological differences in how the transgenic protein is produced in different hosts (e.g. in plants vs. bacteria), any differences would not be possible to detect (Freese, 2004).

- Currently, no regulatory framework requires mandatory toxicity or allergenicity testing from the consumption (or inhalation, see Kroghsbo 2008) of GM crops or their products. Commonly, only 90-day (usually rat) feeding trials are conducted and conclusions of long-term risk are based on these short-term tests, despite their critical deficiencies in revealing sub-chronic and chronic effects (Séralini, 2009; Spiroux de Vendomois, 2010). Research has indicated the importance of life-time studies for health affects where indications of adverse health impacts only manifested after 120 days (Séralini, 2012).

- A common practice in risk assessment is a comparative approach: the new GM plant is compared to a similar plant to see if there is any evidence of additional potential to cause harm. In actual practice, however, developers will often further include 'reference lines' (usually genetically less similar and grown under different environmental conditions) in the comparison which will expand background variation where any potential signals to be drowned in statistical noise and thusly concluded as 'within the range of biological variation' (Antoniou 2012; Dolezel and Gaugitsch 2009).

Box 19.2 GM crops: a late lesson case in the making? (cont.)

- Ongoing risk assessment may not be benefitting as much as it could from new information, because of a general lack of comprehensive post-release monitoring efforts. As pre-market risk assessments are based on information acquired over short term and/or small scale investigations, they are not designed to capture effects that may occur when exposure is on a larger scale, or for longer time periods, or result from unanticipated interactions with other GM plants post release. While monitoring is mandated in some jurisdictions there is very little information on its effectiveness and no uniformity in design or methodology (Züghart, 2008, 2011; AHTEG, 2012; Heinemann, 2012).

Can the precautionary principle make scientific risk assessments more scientific?
The precautionary principle has been legitimised as an important objective in GMO legislation (e.g. European Union, Cartagena Protocol on Biosafety). Nonetheless, it thus far has mainly been considered as a risk management tool and not part of the scientific risk assessment. While critics of the precautionary principle consider it easily misused as a barrier to trade and the cause of more regulation, this misrepresents how precaution may be appropriately applied. Importantly, precaution has a role to play in the scientific risk assessment itself in two fundamental ways. First, applying precaution within risk assessment practice also means applying more robust scientific standards — that is, the need for precaution and the need for scientific rigor are not incompatible but complementary (Groth, 2000). Second, particularly when testing hypotheses, value judgements within science practice (Funtowicz, 2003; Rudner, 1953) may be informed by precaution, including levels of evidence, directions of error (Brosi, 2009; Lemons, 1997), and by acknowledging and communicating what we know, do not know, and cannot know with existing methodologies (Aslaksen, 2006; Myhr, 2002). The formal acknowledgment of uncertainties and the choice of error type from the risk assessment and their communication to decision-makers are key components of rigorous science-based risk assessment.

Conclusion: avoiding old lessons from earlier late lessons
The critical late lesson that may be emerging from GM crops is not the evidence of harm — the early indications of harm are just emerging — but the persistence of the same institutional patterns that led to the old late lessons already learned from asbestos, benzene and BSE (Harremoes, 2001). In these cases, weak risk assessment standards were implemented that prevented identifying the harm and taking precautionary action. To avoid this old lesson, the appropriate application of the precautionary approach to risk standards would help ensure we are not repeating the same error with GM crops, and thus avoid a late lessons case in the making.

scientific commons. Rather than simply serving to facilitate a 'market for ideas,' IP may indeed restrict the diffusion of scientific research and the ability of future researchers to 'stand on the shoulders of giants,' at least for research of the type published in *Nature Biotechnology*' (Murray, 2007).

This has been a brief review of the predominant top-down innovation models that characterise the main policy developments of wealthier and food rich nations (Heinemann, 2009). We have found that if this framework of innovation for agricultural development is followed, the outcome is likely contrary to the stated objectives to create a global food production capacity that delivers on calories and nutrients to all. It will fail in the long run to produce food security because it does not have the necessary incentives to create resilient and sustainable production systems. If the demands on agriculture are reasonably expanded to include delivery of culturally diverse foods, produced locally by those most in need, and which serves as a path out of poverty, then the top-down innovation models of today are the wrong pathways to achieve it.

In coming to these stark realisations, we do not argue that top-down innovation is irrelevant at all times and in all countries. Indeed, the right mix of innovation is essential. Likewise, seed-based versus environmental approaches both have value in all agroecosystems at all times. The question is more complex. When industries or private providers become out of balance in scale, power or access to information, then one can smother the other. At the heart of it, most farmers are private sector, even if they are feeding themselves with the products of their labour and capital. But there is a difference between the economic scale of the large US farming unit and the farmer, especially the one most prone to hunger, and the one searching for long-term

agroecosystem sustainability. Similarly, there is a difference in scale between the university and the multinational corporation, and between both and the farmer. When public institutions must act in a way that is consistent with how companies must act, then the imbalance between farmer and knowledge access grows.

19.4 The bottom-up path towards sustainable farming

A core quality of bottom-up approaches is that they can generate, harness and exchange information and innovation in a multitude of ways that bring users of innovations into the process so that local adaptation and shaping of technologies fit the ecological, socio-cultural and technical dimensions of the system (STEPS, 2010; Wagner, 2007).

Bottom-up innovation is demonstrating its potential to build not just sustainable farming systems, but also sustainable communities through the support of local food production and local markets (Altieri, 2011a; UNEP-UNCTAD, 2008). Discussions on increasing agricultural sustainability tend to put the emphasis on biodiversity, soil and water management and ecological principles to improve productivity and energy efficiency (including reductions in greenhouse gas emissions). This is a specialty of the science of agroecology. Instead of engineering nature to fit into our desired technological system, agroecological innovations fashion our technological solutions to fit nature (Schumacher, 1973) by applying ecological concepts and principles to the design and management of agroecosystems (Altieri, 1995). Agroecology strives to increase the sustainability of agriculture by minimising the use of agrochemical and energy inputs and instead leverage ecological synergisms and interactions between biological components of the agroecosystem to produce their own productivity, crop protection and soil fertility. This type of production system has also been captured as a means for transitioning to more sustainable agricultural practices under the banner of 'green agriculture' (UNEP, 2011).

While this science also values the importance of conventional breeding and genotype optimisation, it tends to address yield problems using management solutions, often through a modification of agricultural practices that remove, rather than adapt to, the problem (Lal, 2009). Biodiversity is important to create greater system resiliency within the agricultural environment (Enjalbert, 2011; Ensor, 2009; Li et al., 2009). Enhancing on-farm biodiversity and soil organic matter can make agriculture more resilient to climate change (drought, flooding, severe weather, and temperature change) and enhance ecosystem services (Hajjar, 2008). In a recent survey, of agricultural productivity after hurricane Mitch in Central America revealed that farms that engaged in agroecological practices such as intercropping, cover crops and agroforestry incurred less damage than neighbouring conventional monoculture farms (Altieri, 2011a). Hence, increasing the adaptive potential of agricultural systems will be vital in the face of global climate change (Bellon, 2011).

We have chosen to use agroecological science (including compatible organic certification schemes) as an example of an outcome of bottom-up innovation because this science is delivering excellent results in the farming systems most in need of innovation (Altieri, 2011b; De Schutter, 2010; FAO, 2011b; Pretty, 2011; UNEP-UNCTAD, 2008 (Khan et al., 2008)). The main feature of the bottom-up approach is that it decentralises solution providers and their solutions, thereby facilitating the transfer of products, services or information that allows continued innovation at the hands, skills and knowledge of the local user. In contrast to top-down approaches, the real innovation potential does not stop with the farmer, but often starts there. In addition, consumer concerns and desires for food quality, health and environmental concerns are facilitated by initiating discussions over agricultural innovations as a bottom-up approach (SCAR, 2012).

It is important to distinguish between traditional farming approaches and agroecological science. The former can, yet in different ways be as destructive to the environment, and unsustainable, as any high external input industrial 'modern' farm (IAASTD, 2009a). While in general agroecological science utilises a 'low tech' toolbox, it is far more sophisticated, knowledge intensive, and integrative both on environmental and institutional levels than simple kitsets of seeds, fertilisers and agrochemicals that characterise industrial farming operations. That is, this approach creates a strong need for farmer support through extension services and farmer-lead educational initiatives, calling for broad participation across a range of scientific disciplines and policy actors.

19.4.1 Bottom-up incentives homogenise productivity and resilience rather than tools

Rather than sell farmers packages of tools that bring in improved seed and convert their soils to near replicas of those for which elite varieties of

plants have been optimised, agroecological science facilitates local development of soil conservation practices and supports farmer seed exchanges for breeding of local varieties or local elite varieties (Badstue, 2007; Jarvis et al., 2008). These practices support agrobiodiversity, which contributes to sustained productivity by creating resilience to unpredictable changes at the local level, such as to resource availability, or changes to climate, all the while making the farm less likely to attract pests (Bellon, 2011; Jarvis, 2000). Here the emphasis is on the farmer rather than the breeder, where they are different (Reynolds, 2006).

The focus on farmers is a viable alternative to the focus on genotypes. As the UN FAO have argued, '75 % of the additional food we need over the next decades could be met by bringing the production levels of the world's low-yield farmers up to 80 % of what high-yield farmers get from comparable land' (Molden, 2007). This suggests that the future of sustainable, low impact agriculture is one in which products and methods are developed at landscape rather than global or even national levels. In this way we agree that 'there is a need to invest in science and practice which gives farmers a combination of the best possible seeds and breeds and their management in local ecological contexts' (Pretty, 2011).

19.4.2 Bottom-up innovations are participatory

Bottom-up approaches often include participatory activities built on open collaborative models, with the aim to address problems that are relevant to the local ecological and sociocultural context through experimentation and education (Baldwin, 2011; Ceccarelli, 2006; Toomey, 1999; Witcombe, 1996). Even where the incentive systems are tuned towards generating IP, such as in plant breeding, the choice of relevant instrument can encourage ongoing innovation through participatory innovation development.

For example, legal instruments such as patent-like PVP and patents restrict farmer use of this legally protected germplasm from breeder innovation unless they negotiate permission for use from the license holder. Poor and subsistence farmers who may most benefit from their own local innovation are unlikely to have access to either public or private patent holders who reside in urban centres far away, often out of country (Howard, 2009). In contrast, PVPs which recognise breeder's rights allow farmers and others to continue development including making locally adapted varieties for sale or for exchange (Figure 19.3). PVP allows a wave of innovation to extend from an initial variety and contributes to the speed of technology transfer within an institutional context that supports agricultural sustainability (Gyawali, 2007; Steinberg, 2001). Thus breeding innovation that is centrally controlled by contracts between the license holder and selected breeders can bottleneck technology transfer. This phenomenon has been associated with the 'yield gap' experienced by GM varieties because of the use of patents to control these products (Fernandez-Cornejo, 2006).

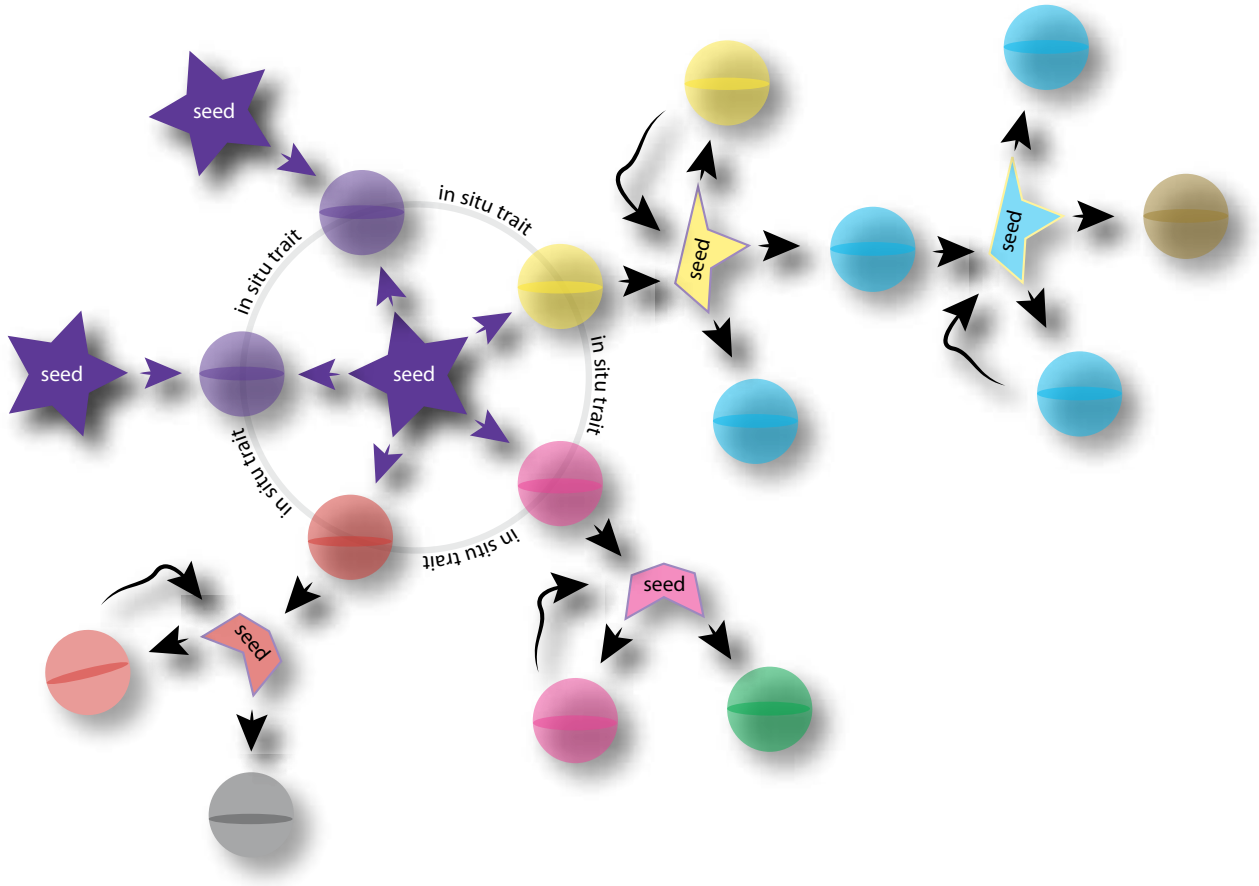
The knowledge required to select and save seed, and the infrastructure for exchanges, are also social resources that if (or when) lost may be difficult to re-establish (Howard, 2009). In a future of climate change, decentralisation of public breeding and in situ conservation are likely to be fundamental to the survival of billions of people (Bellon, 2011; Ceccarelli, 2006; McIntyre, 2011).

'Farmers (including pastoralists and agro-pastoralists) should not simply be seen as maximisers of food and agricultural commodity production, but also as managers of the food and agricultural commodity-producing eco-systems' (Hoffman, 2011). That role requires farmers to have freedom to innovate as well as the confidence of governments in the value of that innovation.

Participatory research that leads to new innovations in agriculture often starts from a point of co-inquiry, whereby farmers and scientist work as partners and bring their own, complementary knowledge, experience and insights to developing innovations that are relevant to the needs of farmers. That is, participatory research treats farmers as experts with their own scientific knowledge and experience that is complementary to more formalised training expertise. In participatory breeding initiatives, traits of value to local farmers might be identified and often are different than those valued by national and international breeders: 'Professional breeders, often working in relative isolation from farmers, have sometimes been unaware of the multitude of preferences — beyond yield, and resistance to diseases and pests — of their target farmers. Ease of harvest and storage, taste and cooking qualities, how fast a crop matures, and the suitability of crop residues as livestock feed are just a few of the dozens of plant traits of interest to small-scale farmers…' (Toomey, 1999).

Another example of participatory innovation models, the farmer field schools, have been instrumental in designing new ways to decrease

Figure 19.3 Participatory IP instruments



Note: When farmers and breeders can continue to innovate on seed or propagule stock, the benefits of elite varieties are more quickly adapted to local conditions and other desirable traits and may inspire new breeder income. Consider seed with a novel genotype (purple star) being sold to farmers who find a variety of phenotypes after planting (pink, yellow, orange circles) due to local gene x environment interactions. Some of these new phenotypes may be desirable and could inspire the farmer or professional breeder to capture the new variety for ongoing sale. Other farmers may wish to return to the original seed stock (purple stars to the left). The new varieties may be purchased by other farmers or the same farmer and additional breeding may bring new and some desirable traits (blue, brown, blue, green and black circles).

insecticide use in studies from Indonesia, Bangladesh and Vietnam, and increases in crop yield in China, India and Pakistan (Van den Berg, 2007). These programmes teach farmers how to problem solve and experiment independently through interactive learning, which will help adapt technologies to their specific environmental and management needs (Vasquez-Caicedo, 2000).

19.4.3 Bottom-up approaches deliver the right kind of innovation to the right kind of users

Agroecological bottom-up innovations are relevant and work. By focusing on locally adapted and developed integrative innovation over remotely developed standardised innovation they can help create sustainable farming systems that deliver more food, nutrition and wealth to the farmers and their communities that are needed to feed the world. There is mounting evidence that the scale-up of these approaches may offer, beyond improvements to crop productivity, enhanced environmental benefits, e.g. reductions in chemical inputs and soil erosion, improved water conservation and soil organic matter content, and higher levels of biodiversity (Pimentel, 2005). Further, bottom-up approaches offer a means to tackle issues related to land degradation to restore soil fertility (de Jager, 2005).

The world's largest meta analysis comparing science-lead industrial and agroecological (organic) farming systems found that the latter could match

the former in the common metric of yield (Badgley, 2007). Critically, this intensification of farming systems through agroecological science achieved the same or superior yields with a concomitant reduction of external inputs, including a much lower dependence on agrichemicals and fossil fuel-derived fertilisers. Finally, this study also provided evidence to suggest that mature agroecological conversions (those in excess of five years old) consistently out produced industrial operations. This study exposed the reason for other studies reporting that agroecological farms are less productive: it takes about five years of intensive work to rehabilitate soils converted from traditional or industrial farming management to agroecological and past studies lumped young and mature conversions together.

International projects to initiate organic and sustainable agriculture have shown excellent overall results. UNEP-UNCTAD reported an average crop yield increase of 116% for organic and near-organic projects involving more than 1.9 million African farmers on roughly 2 million hectares of cultivated land within the 114 cases analysed. The benefits were not just in yield — improvements in natural, social and economic capital associated within these farming systems led to an array of benefits that have increased food security. The report authors concluded: 'Organic agriculture can increase agricultural productivity and can raise incomes with low-cost, locally available and appropriate technologies, without causing environmental damage. Furthermore, evidence shows that organic agriculture can build up natural resources, strengthen communities and improve human capacity, thus improving food security by addressing many different causal factors simultaneously' (UNEP-UNCTAD, 2008), and can be more economically profitable than conventional farming (Edwards, 2008; Nemes, 2009).

Another synthesis study investigated the increases in productivity since the implementation of 286 sustainable agriculture initiatives from the FAO, which covered 37 million hectares in 57 countries (Pretty, 2008). They found increased productivity on 12.6 million farms with an average crop increase of 79 %, and a rise in key environmental services.

A commissioned report from the Foresight Global Food and Farming Futures Project of the UK government (Foresight, 2011) appraised 40 sustainable intensification projects developed in the 2000s, from 20 countries in Africa. The projects were developed based on a range of bottom-up approaches to agriculture, including participatory plant breeding, integrated pest management, agro-forestry and agroecological soil conservation measures. The results speak for themselves: by 2010 the projects had led to a range of documented benefits and improvements to 12.75 million hectares for the 10.39 million farmers and their families, including a doubling of crop yields, on average (2.13-fold increase) spanning a 3–10 year period (Pretty, 2011).

Results from bottom-up approaches are also evidenced in the global North. In Wisconsin, USA, a 12-year study on productivity of organic vs. conventional cropping systems found that diverse, low-input systems can be as productive per unit of land as that of conventional ones (Posner, 2009). A 30-year study by the Rodale Institute in the US compared organic and conventional agricultural methods and found yields, economic viability, energy efficiency and human health indexes improved with organic farming (Rodale, 2011).

Scaling up these successes will require policies that stimulate investment into key sectors that support bottom-up approaches. In one modeling study (UNEP, 2011), the outcomes of targeted 'green' investments over a 40 year period are compared to the same amount of financial investment into conventional and traditional 'business as usual' agriculture of today. Overall, the green investments lead to numerous comparative benefits, including increased yield, soil quality, greater water efficiency and land use, increased GDP growth and employment, and reduced CO_2 emissions and energy consumption. Therefore the potential scale-up for agroecological based bottom-up approaches appear to be immense.

19.5 Case example: Contrasting top-down and bottom-up innovation solutions to water stress

Consider the anticipated application of top-down innovation to address the challenges of agricultural water stress. Agriculture is already the largest user of water among human activities and lack of access to water is an increasing problem (Hoffman, 2011; Marris, 2008). Climate change is expected to further exacerbate the problem (Schiermeier, 2008). The most likely top-down product for addressing this problem will be genotypic changes to germplasm to enhance traits that confer drought tolerance. Already progress is being made in some crops through classical breeding (CIMMYT, 2012; Heinemann, 2009), especially augmented through

marker-assisted selection ([6]). Yet similar genotypic approaches using genetic engineering have not been as successful. As drought tolerance depends on the action of multiple genes, drought tolerant varieties require changes in multiple genes all at once, rather than adding genes singularly (as with genetic engineering). Developing adapted varieties will require more responsive breeding and development than can be offered through the extensive process for creating a commercially viable genetically engineered drought tolerant product (Gurian-Sherman, 2009; Heinemann, 2008a, in press). Further, plants with ever more extreme adaptation of genotypes will likely continue to exacerbate the depletion of the water table. Nevertheless, any seed (or propagule)-based product that is better adapted to drought stress would be amenable to prevailing IP instruments such as plant variety protection (PVP), patent-like plant variety protection, or patents and therefore it is no surprise that genotype innovation receives so much emphasis, especially from industry.

In contrast, bottom-up environmentally based management solutions, some of which have been in practice for decades, tend to raise latent water levels and retention capacities in soil as well as improve the genetics of crop plants (Heinemann, 2008a; Lotter, 2003; Pimentel, 2005; Scialabba, 2007). Environmental management using locally-adapted drought tolerant varieties, cover crops, polycropping, rotating in fallow years, compost and soil conservation to raise organic matter levels, agroforestry and building small dams all raise water levels (Altieri, 2002; Lal, 2006). The resiliency of this kind of system is equally affected: In fact, it may not be possible to feed the world in 2050 unless soil quality and water retention capacity are raised regardless of how efficient plants can become at extracting water (Hoffman, 2011). 'If soils are not restored, crops will fail even if rains do not; hunger will perpetuate even with emphasis on biotechnology and genetically modified crops' (Lal, 2008). Many of these improvements would be considered innovations by our bottom-up definition (Kiers, 2008), but by their nature could not be easily described or protected by patents or similar IP instruments in order to facilitate the knowledge transfer to the commercial sector, and thus are not innovations in the currently practiced top-down model. By following the top-down approach, the private sector will offer solutions to a problem that either possibly cannot be solved using technologies that are described under prevailing IP instruments or which will only shift the problem in time or space, addicting us to finding and producing even more extreme genotypes through genetic modification.

19.6 Conclusions

We have attempted to contrast two pathways to innovation and their relative opportunities and costs for agricultural development. We find limitations to top-down innovation because of largely productivist objectives. These tend to shut down rather than open up innovation and options, particularly those for addressing social welfare issues. Further, science and its role as a public good become conditioned within certain notions of progress (Callo, 1994). This framework will only continue to create technological lock-ins and path dependence to specific research choices at the expense of others (Stirling, 2007).

We find that both top-down and bottom-up approaches will have their roles to play, but getting them in the right mix, order and framing is critical to ensure their benefits and risks are more evenly distributed if we are to produce the kinds of innovations capable of achieving the Millennium Development Goals. This will require rebalancing innovation towards the public good, further requiring that innovation frameworks focus not only on scientific and technological developments, but also on the interlinked institutional, organisational and social changes. In terms of agriculture, taking these issues seriously means operationalising the outcomes from the IAASTD (2009a) and SCAR (2012) reports. The recent recommendations on research, innovation and agricultural knowledge coming from the European Commission's Standing Committee on Agricultural Research (SCAR) call for 'increased support be provided for research on the economic and social dimensions of these new technologies and farming practices. Approaches that promise building blocks towards low-input high-output systems, integrate historical knowledge and agro ecological principles that use nature's capacity should receive the highest priority for funding' (SCAR, 2012). To achieve this, a public sector free from political incentives for top-down innovation is an essential capacity. However, the small business and the farmer, while still private sector and benefiting from proprietary knowledge, will be an essential source of creativity, problem solving and income for their communities.

([6]) Marker-assisted selection is a breeding technique that uses biotechnological tools to concentrate particular traits within the existing plant by traditional breeding. This allows for a more efficient breeding process for achieving varieties with specific traits of interest. It does not involve the use of in vitro modified nucleic acids as with genetic engineering.

Further, scientists are not passive members of the scientific enterprise, but a powerful force from within that influences the techno-sciences and the options available to society to benefit from scientific research. The modern techno-science culture took shape just after WWII in an unusual convergence of thinking across the East-West geopolitical divide. Nuclear power in the United States and space travel in the Soviet Union become exemplars of a new form of conceiving and doing science, and witness a deep transformation in its ethos and political economy. The convergence of internal culture, economic and political power was and is an irresistible force. Scientists today cannot shirk from their role and their responsibility on how science is done and governed, as practitioners and frequently as participants, entrepreneurs and citizens.

Lastly, top-down innovations will be most effective when scientific knowledge from specialised fields within biology, chemistry, ecology, genetics, soil microbiology, etc. converge with bottom-up approaches to innovate locally optimised solutions. In this way, the benefits of advanced scientific knowledge will naturally become be much more diverse and widely distributed.

We have made the case that the future of agriculture and global food security is one that requires a truly long-term vision, attendant to the environmental and social costs of production, and with an emphasis on the small and subsistence farmer. Long term, there will be enough food if agriculture both intensifies and remains local. We have found that if the bottom-up approach is followed, the transfer of knowledge and further innovation potential is augmented, and success far more likely, than the outcomes witnessed to date from the prevailing top-down approach, where the innovation potential downstream is severely limited. Conversely, the proceeds of bottom-up innovation disproportionately flow to adopters rather than the providers. By their very distributive and participatory nature, bottom-up innovation strategies do not tend to concentrate power, financial or political, into providers which otherwise are easily displaced by wealthier and more powerful champions of top-down policies.

If the policy demands on agriculture are reasonably expanded to include delivery of culturally and nutritionally diverse foods, produced locally by those most in need, and which serve as a path out of poverty and malnutrition, then the bottom-up innovation models are the responsible innovation models, and require investment and support (De Schutter, 2011).

On the one hand, we have explored a path directed by top-down innovation models. As a type of black-box technology that is protected by particularly restrictive IP instruments (patents and patent-like PVPs), so-called 'biotech' crops (GM and similar) and their co-technologies are expensive to buy, destroy local seed savings and exchange practices, and prevent further farmer tinkering and improvement of innovations. When working as advertised, we find that top-down innovation as promoted by the large market economies, directed at advancements in agriculture (which ironically is maintained by extra-market subsidies), undermines the stated national and international goals of poverty reduction, sustainability, and increases food insecurity. They contribute to a feedback loop that continues to concentrate wealth and power into a smaller number of companies and large farms (Botta, 2011; Spielman, 2007; USDA, 2009; World Bank, 2007). Top-down providers are invariably attracted to the largest markets (real or subsidised), the most uniform agroecosystems, and the highest volume farmer. They therefore will always serve last those who are foremost needed to feed the world in the future: the presently small and subsistence farmer on < 2 hectare plots of land where highly diverse and intermixed crops and livestock production work best to meet local needs.

On the other hand, bottom-up approaches emphasise the contextual role of innovation, even when the product is technology (van den Hove, 2012). Bottom-up innovation is the kind that provides useful tools, methods and knowledge that can be adapted to and by the farmer and farming system. Products that depend on ecosystem, cultural and financial homogenisation damage biodiversity and ecosystems, but also cultural identities as they eliminate the need for local knowledge (in the short term) and shift communities away from traditional foods and ethnobiological knowledge. Obstacles to taking bottom-up approaches need to be addressed and overcome by policy makers seeking to create a sustainable agricultural system (De Schutter, 2009, 2011).

If there is a solution to the global mal-distribution of access to sufficient quantities of nutritious foods, how do we find it? In the process, how do we build agriculture into a pathway out of poverty without also raising greenhouse gasses and increasing soil erosion? How can we support agricultural systems that are resilient and sustainable? A commitment and investment of public resources as incentives to promote strategies for agricultural and ecological sustainability will require a radical shift on how we think about and perform innovations in the future,

where 'business as usual' in agriculture is no longer an option. As Einstein said, 'The solution will not come the same kind of thinking that created the problem'…

Innovations in agricultural food production have been deeply part of the human experience for over 10 000 years. They will continue to be central to how we feed the world. The agricultural innovations of the future will have to be more 'hands on' and local if we are to meet our goals of food security, poverty alleviation and environmental sustainability (Benessia, 2012). For as long as the problems needing products are framed as technological rather than social, behavioural or political, then innovation will be directed toward technological products (van den Hove, 2012). The technological 'solutions' are often just responding to symptoms of the underlying cause of existing socio-ecological solutions. As the late Nobel Laureate Joshua Lederberg said: 'Our imperfect solutions aggravate every problem.' (Lederberg, 1970).

We find the '3D Agenda' of the STEPS Centre (2010), cognisant of the ways which the directions, distribution and diversity of innovations affect their use, to be a compelling model for the future thinking of innovation in agricultural development.

As we have discussed, where the directions of innovation that follow top-down approaches — highly specialised, centralised and capital intensive — tend to shape innovation towards technological lock-ins. Economic and political forces that promote these innovation trajectories then become hard to reverse, or crowd out alternative approaches, such as agroecology. In contrast, bottom-up approaches facilitate participation of the user to shape the directions that innovation will take. The innovation direction further moulds the potential distribution of benefits, costs and hazards brought by the adoption of the innovation pathway. Often top down approaches leverage legal instruments of knowledge control that close down access to knowledge or further innovation, defines who indeed innovation is for, who can access it, based on who can afford to pay for it. An important consequence here is that top-down approaches marginalise those for whom innovations are more critically needed to increase the productivity and sustainability of agriculture. Lastly, these two aspects of innovation — direction and distribution — further determine the diversity of innovation possible, not only the scientific and technical aspects of innovation, but the social, organisational and innovations that support it. Diversity in innovation buffers against lock-ins and creates the potential for local adaptation within the ecological and economic contexts for which they are designed. This means a more integrative focus of the agroecosystem, beyond the genotype approaches towards augmenting biodiversity within agro-environments to develop sustainable and resilient agroenvironments as protection against future uncertainties.

19.7 Lessons learned

In 1961, outgoing President of the US Dwight D. Eisenhower warned society to be vigilant of the large, concentrated interests in technology when he said: 'The prospect of domination of the nation's scholars by Federal employment, project allocations, and the power of money is ever present — and is gravely to be regarded. Yet, in holding scientific research and discovery in respect, as we should, we must also be alert to the equal and opposite danger that public policy could itself become the captive of a scientific technological elite' (Wikisource, 2012).

The early warning, or perhaps late lesson, to be heeded here is that if one follows the top-down, usually technologically oriented, approaches to innovation,the desired outcomes for addressing food insecurity will not be achieved. Top-down approaches will most likely fail to deliver on the large promises of food security and alleviation of poverty, mainly because these approaches contribute to a feedback cycle that concentrates resources, knowledge, and influence as witnessed in the seed and agrichemicals sector (Adi, 2006; De Schutter, 2009; Fernandez-Cornejo, 2006; Howard, 2009). Through this power, top-down providers can artificially homogenise both the conception of the problem to be solved and the solutions — such as GM crop plants — they propose. All too often questioning the *rationality* of the approach gets lost in the background of the unquestioning discussion over the *use* of the approach (Pavone, 2011 and see discussion in Boxes 19.1 an 19.2). Perhaps greater reflection and social deliberation into why and for whom agricultural innovations should be produced is needed if we are truly going to follow more sustainable pathways in the production of food and fibre.

In the path ahead, societies will have to make more conscientious choices of how to define and shape innovation to produce solutions that are appropriate for meeting global challenges related to agriculture. Bottom-up approaches are proving capable of getting sustainable, participatory and locally adapted solutions into the hands of those that need them most (Altieri, 2011a;

De Schutter, 2011), but are incapable of flourishing where invention is limited to what can be easily described by prevailing IP instruments. Change the directions, distribution and diversity of innovation, and you change the world.

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20 Invasive alien species: a growing but neglected threat?

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Biological invasions are one of the five major causes of biodiversity loss as global human travel and trade have moved, and continue to move, thousands of species between and across continents. Some species of alien origin have a high probability of unrestrained growth which can ultimately lead to environmental damage.

An alien species — animal, plant or microorganism — is one that has been introduced, as a result of human activity, either accidentally or deliberately, to an area it could not have reached on its own. A common definition of the term 'invasive' focuses on its (negative) impact, while other definitions consider only rate of spread and exclude considerations of impact.

Despite the growing amount of legislation being adopted at the global scale, biological invasions continue to grow at a rapid rate, with no indication yet of any saturation effect. Decision-making in this area is very challenging. The overall complexity of the problem, its interdisciplinarity, the scientific uncertainties and the large number of stakeholders that need to be informed and involved, together demand governance actions that are difficult to see emerging at the regional scale (as in the EU), let alone globally.

It is widely agreed that preventing biological invasions or tackling them at a very early stage is the most efficient and cost-effective approach. Harmless species can be confused with harmful invasive species, however, leading to a waste of resources. Even more seriously, harmful invaders can be mistaken for innocuous species — so-called 'invaders in disguise' — and no appropriate action may be taken to counter the threats they pose.

Even with a very good risk assessment system, new outbreaks of invasive alien species could still occur, necessitating a system of rapid early warning and effective eradication response. The decision on where to draw the line on the acceptable environmental risks versus the introduction of new species or new communities that may carry invasive alien species then becomes a value judgement.

There is lively debate within the scientific community regarding the most appropriate strategies for managing invasive alien species. Governments and institutions charged with making decisions have access to considerable knowledge on the topic, but the lack of rules of interactions between multiple parties regularly thwarts effective decision-making.

20.1 Introduction

Biological invasions are one of the five major causes of biodiversity loss, alongside habitat destruction, over-exploitation, climate change and pollution (Millennium Ecosystem Assessment, 2005). Global human travel and trade have moved, and continue to move, thousands of species between and across continents (McNeely, 2001). Only a small proportion of alien species become established, some of these spread, and a small subset produce major ecological, economic or social effects (generally termed 'impacts'). Ecological impacts include local extinction or a reduction in the diversity of native species, and various types of ecosystem-level changes such as modifications of nutrient cycling or water quality. As an example, in an analysis of 680 recent animal extinctions worldwide, causes were compiled for about 25 % of these. Ninety-one (54 %) included invasive species among the causes of extinction, and in 34 cases they were the only known cause (Clavero and Garcia-Barthou, 2005). For example, feral cats on islands are responsible for at least 14 % of global bird, mammal, and reptile extinctions in recent times (Medina et al., 2011). All types of organism, from micro-organisms, including microbes and diseases, to mega-herbivores, can become invasive, and all can cause impacts on biodiversity and ecosystem functioning. All types of ecosystem are affected: terrestrial, freshwater and marine.

Biological invasions are receiving increased attention in many countries, some of which have already set in place comprehensive legislation or national strategies to deal with various aspects of invasions, in particular concerning their management (e.g. Australia, Great Britain, Mexico, New Zealand, South Africa and USA) (Pyšek and Richardson, 2010). As regards the management of invasive alien species (IAS), it is widely agreed that preventing biological invasions or tackling them at a very early stage is the most efficient and cost-effective approach. For example, the cost of eradicating weeds can increase at least 40 times if action is not taken promptly (Harris and Timmins, 2009), and in most cases eradication quickly becomes unfeasible (Genovesi, 2007). Preventive management calls for a precautionary approach, because prompt response often does not permit full assessment of the risks connected to a newly detected invasion (Genovesi et al., 2010). Despite widespread agreement on these principles, the full range of problems associated with IAS still lacks political recognition and too few government-coordinated actions are in place, or are effective, in most parts of the world, including in the European Union.

There is nevertheless a lively debate within the scientific community regarding the most appropriate strategies to adopt for managing invasive alien species. Aspects of this debate offer important pointers to dimensions that need to be better studied and the measures needed to make the phenomenon of biological invasion better understood by all stakeholders. Invasive alien species represent a growing threat, in particular in a globalised world, as they are introduced and spread by people (McNeely, 2001). This is more a human-driven environmental problem than a strictly biological one. Inherent uncertainties remain about what species will be introduced and which will become invasive. Consequently, making decisions is very challenging. The overall complexity of the problem, its interdisciplinarity, the scientific uncertainties, and the large number of stakeholders that need to be informed and involved, together demand governance actions that are difficult to see emerging at the regional scale (as in the EU), let alone at the global scale. Lessons already learnt in different parts of the world need to be considered when seeking to improve management regimes for IAS in different environments and at different scales.

20.2 The difficulty of defining invasive alien species

The terminology applied to organisms involved in biological invasions is complex, often confusing, and there is no universally accepted definition of IAS (Riley, 2005; Falk-Petersen et al., 2006; Richardson et al., 2011a); all this has serious practical consequences. The term 'alien' (exotic, foreign, non-indigenous, non-native) requires a geographical, biogeographical or ecological context to have a useful meaning — an alien species is one which has been introduced as a result of human assistance, either accidentally or deliberately, to an area it could not have reached on its own. The area in question has to be specified since a species 'may be alien to any definable area, e.g. continents, islands, bio- or eco-regions, or any political entity (e.g. countries, states, provinces)' (Lambdon et al., 2008). The terms alien and invasive both have political overtones. The Convention on Biological Diversity (CBD) requires its Parties, through Article 8(h) to 'prevent the introduction of, control or eradicate those alien species which threaten ecosystems, habitats and species' and uses the term 'invasive alien species' to refer to such species and defines these as 'alien species whose introduction and/or spread threaten biological diversity'. The term 'invasive' is therefore defined by the CBD in terms of (negative) impact, while other definitions

employ ecological and biogeographical criteria, i.e. invasive species are defined as alien species that sustain self-replacing populations, often in very large numbers at considerable distances from the site of introduction such as in natural areas, and explicitly exclude considerations of impact (see Richardson et al., 2011a; Blackburn et al., 2011 and references therein). Other definitions also include economic impacts, for example on agriculture or the use of amenities, and social impacts such as on human health.

In general, the biogeographical concept is more widely used in the academic world, whereas the impact concept is widely used by decision makers (Ricciardi and Cohen, 2006). Such terminological and conceptual problems have contributed to difficulties in developing a coherent and effective political response to biological invasions.

The amount of information on IAS has grown steadily (Gurevitch et al., 2011) in the last 20 years. Since 2000, when the International Union for the Conservation of Nature (IUCN) Invasive Species Specialist Group (ISSG) established the Global Invasive Species Database (http://www.issg.org/database/welcome/, the first web-based, freely accessible database on invasive species), many tools have been created ([1]). However, partly for the reasons discussed above, accurate and comprehensive information on global or regional numbers of invasive alien species is still difficult to obtain and statistics that are available are often ambiguous and difficult to interpret (e.g. see discussion in Richardson and Rejmánek, 2011). Even taxonomic reference works such as *Floras and Faunas* are notoriously bad at distinguishing between native and alien species (Lambdon et al., 2008). The need for accurate identification is an essential prerequisite for detection of IAS, and many cases of misidentification are coming to light. For example, harmless species can be confused with harmful invasive species, leading to a waste of resources and, even more serious, harmful invaders can be mistaken for innocuous species, so-called 'invaders in disguise' (Verloove, 2010), and no appropriate action taken to counter the threats they pose.

Europe is fortunate in having generally good information about invasive alien species, with many countries having prepared lists, although much more critical evaluation is needed in many cases and under-recording remains a problem. An overview is provided by the DAISIE database (http://www.europe-aliens.org/) and its List of Species Alien in Europe although there are still significant gaps in coverage and distribution and many problems of accurate identification remain to be resolved. For example, even well-known plant invaders such as *Heracleum mantegazzianum* and *Fallopia japonica* are frequently confused with related species, and the invasive hybrids often referred to as *Rhododendron ponticum* have now been named *R.× superponticum* (Cullen, 2011). In other taxa such as the genus *Opuntia* it is often unclear which species are involved in particular invasions, with experts disagreeing, for example, about whether *O. maxima* and *O. ficus-indica* are separate species.

However outside Europe, very few countries have comprehensive, regularly updated lists of alien or invasive alien species. For example, the McGeoch et al. (2010) review of available data on invasive alien species for a set of 57 countries found that the number of invasive alien species varied from 9 to 222, reflecting as much a lack of information as real differences of incidence. Furthermore, because of the dynamic nature of biological invasions, the lists that do exist need regular revision. An example of the difficulties of interpretation is the much-cited paper by Pimentel et al. (2005) which estimates that 50 000 alien species have entered the US. This figure is, however, misleading unless broken down. In the case of plants, the figure of 25 000 alien species (compared with a native flora of about 17 500 species) includes agricultural and horticultural crops, timber and ornamental trees, garden plants, and weeds! In addition, although several countries had compiled lists of alien or invasive alien species by the late 1990s, there is general lack of coordination and harmonisation between these lists. Aggregation of lists developed using different criteria and definitions is a complex task which makes the interpretation of data and the planning of common action difficult and laborious.

20.3 Emergence of awareness of an old problem

The effects of IAS have been known for a very long time. As early as 77AD, Pliny the Elder wrote in his *Naturalis Historia* (The Natural History) that the invasion of rabbits in the Balearic Islands, Spain, was a very severe problem requiring effective control (see Scalera and Zaghi, 2004). In the 19th century,

([1]) See http://www.cbd.int/doc/meetings/sbstta/sbstta-15/information/sbstta-15-inf-14-en.pdf for a very partial overview of main global data providers.

Charles Darwin noted the invasive behaviour of some alien species during his explorations on the *Beagle*. Indeed, Darwin's musing on invasive alien species contributed to the development of his theory of the 'survival of the fittest' (Darwin, 1859). In most cases, however, alien species at that time were regarded as curiosities, rather than a significant threat to global or even regional biodiversity. Concerns regarding the impacts of alien species on native vegetation, particularly on islands (Kiehn, 2011; Kueffer et al., 2010), started to be voiced in the 19th century (Inderjit et al., 2005; Cadotte, 2006). For example, J D Hooker wrote in 1864: 'Among the most interesting phenomena connected with the distribution of plants, are those that concern the rapidity with which some species of one country will, when introduced into another, rapidly displace the aborigines and replace them' (Hooker, 1864). It was not, however, until the 20th century, especially in the second half, that they began to be recognised as a rapidly growing threat to global biodiversity.

A key figure in the history of invasion biology was the British zoologist and ecologist Charles S. Elton (1900–1991) who not only made seminal contributions to modern population biology and community ecology but also set the scene for the emergence of invasion ecology as a separate discipline. His influential monograph *The Ecology of Invasions by Animals and Plants*, published in 1958, set out his concerns about the escalating impacts of IAS on natural ecosystems and the need to conserve species diversity from their adverse impacts. Elton's landmark publication is seen by many as a starting point for the understanding of invasion biology as a distinct field of study, and has been very widely cited (Richardson and Pyšek, 2008), although Kueffer and Hirsch Hadorn (2008) note that the European tradition of research on biological invasions is actually older and is rooted in floristic studies of adventive species in the 19th and early 20th centuries which already considered the role of humans as agents in biotic invasions.

The circumstances in the mid-20th century when Elton formulated his ideas were very different from those of today. The book *Fifty years of Invasion Ecology. The legacy of Charles Elton* documents the radical changes in the extent and nature of invasions since the 1950s and in the ways in which humans perceive and consider managing alien species (Richardson, 2011a). In Europe, in particular, these concepts were slow to manifest themselves widely; for many biologists and conservationists, biological invasions were still perceived as happening 'somewhere else' (rabbits in Australia, water hyacinth in African lakes and waterways, etc). It was not until the last two decades of the 20th century that the significance of biological invasions and the threats they pose to native biological diversity became widely acknowledged at both global and national levels.

An international research programme on the Ecology of Biological Invasions ran in the 1980s under the auspices of the Scientific Committee on Problems of the Environment (SCOPE) (see Drake et al., 1989). This initiative ('SCOPE I') had a strong conservation focus ([2]), and was important in shaping the research agenda on IAS in its framing of the problem and in the core questions that the programme set out to examine. SCOPE I was a global research programme, and collated case studies and syntheses from around the world, thereby providing clear evidence of the global scale of the problem.

Another landmark was the Convention on Biological Diversity (CBD) which entered into force at the end of 1993. IAS was established as a cross-cutting issue and the CBD adopted a set of Guiding Principles for the Prevention, Introduction and Mitigation of Impacts of Alien Species that Threaten Ecosystems, Habitats or Species (COP decision VI/23).

A second SCOPE research programme ('SCOPE II') on IAS was launched in 1997. This was more inter/transdisciplinary than SCOPE I, and considered economic valuation, stakeholder participation, pathway analysis and management (Mooney et al., 2005). SCOPE II was run under the auspices of a consortium of scientific organisations including SCOPE, IUCN, and CABI which developed the Global Invasive Species Programme (GISP), with the explicit objective of providing new tools for understanding and coping with IAS. The report *Invasive Alien Species: a Toolkit of Best Prevention and Management Practices* (Wittenberg and Cock, 2001) gives a good synthesis of the concepts current in the 2000s on biological invasions. In 2011 GISP was closed down, for financial reasons.

In Europe, research on IAS was limited and uncoordinated until the late 1980s. Ambitious research programmes, focussing on risk analysis, inventories and the management of IAS, were launched in the early 2000s, including the EU

([2]) The outcomes of SCOPE 1 were published in a special issue of the journal Biological Conservation, volume 44, parts 1 and 2, published in 1988.

programme 'Delivering Invasive Alien Species Inventories for Europe' (DAISIE; http://www.europe-aliens.org) and 'Assessing Large Scale Risks for Biodiversity with Tested Methods' (ALARM; http://www.alarmproject.net/alarm) to cite only two important European initiatives.

The amount of information on IAS that was accumulating and the need to make it widely available to an audience of managers and scientists led to the development of national, regional and international databases and information systems, web portals and clearing house mechanisms such as the Global Invasive Species Information Network (GISIN) ([3]), the Global Invasive Species Database ([4]), the Invasive Species Compendium (ISC), the Inter-American IABIN Invasives Information Network (I3N) ([5]) for the Americas and NOBANIS ([6]) for North Europe and the Baltic.

20.4 A new discipline with its own approaches and research agenda

The global approach of the SCOPE I project in the 1980s consolidated the recognition of the study of biological invasions as a new scientific discipline. Kueffer and Hirsch Hadorn (2008) reviewed and analysed the state of research on biological invasions, and distinguished different approaches. The research topics have been further divided to make the distinctions clearer, but all these elements have coexisted over time.

The **classical model** of biological invasions that emerged from the SCOPE 1 programme in the 1980s examined case studies of invasions to attempt to answer three main questions: the traits that determine whether or not a species is an invader, why some habitats are more vulnerable to invasion than others, and how management systems using this knowledge can be developed (Drake et al., 1989; Williamson, 1996). During this phase, research on invasions was restricted mainly to population and community ecology, and was based mostly on biogeographic comparisons of invasions, the underlying assumption being that the alien origin of species was important for explaining their behaviour. Despite many studies, and advances on many fronts, no single/common list of traits emerged that distinguish invasive from non-invasive species. The most informative criterion that emerged is that a species becoming invasive elsewhere (assuming that it has had the opportunity to do so), is a powerful predictor of whether that species will become invasive, although this criterion must be used with great caution in a world of rapid global change (Kueffer, 2010).

Invasions were then considered according to the different phases characterising their successive ecological and evolutionary processes. '**Phase transition models**' break biological invasions down into at least the following steps: entry of a species into a new area, establishment after a possible lag phase during which the population size of the species remains small, and spread. Although the idea is older (Usher, 1986), considering invasions as a sequence of distinct phases has become a central piece of biological invasion theory since around 2000 (Richardson et al., 2000; Kolar and Lodge, 2001) and has since guided much synthetic thinking in the field (e.g. Dietz and Edwards, 2006; Blackburn et al., 2011). The development of risk-assessment systems also emerged (e.g. Pheloung et al., 1999). Risk-assessment schemes seek to identify alien species (including those not yet introduced into a territory) that are likely to become invasive, as a basis for preventive measures or prioritised management action. The phase transition model also represents a conceptual basis for a multi-stage management approach involving prevention of entry at borders as a priority, plus early detection and eradication as key responses when prevention fails, or sustained containment and mitigation of impacts as the last option if the former steps fail (Wittenberg and Cock, 2001). Such a model also facilitates taking into account climate and global change.

As a result of SCOPE II and GISP, the **study of pathways of introduction** became an active research area, integrating natural and human sciences, since human activities are the central cause of movement of species (e.g. global trade and travel by rail, road, sea and air, wars, shipping movements and ballast waters, trade in animals and plants, intentional introductions for economic reasons or by tourists, accidental introductions) (McNeely, 2001; Ruiz and Carlton, 2003). A landscape-scale perspective on biological invasions was largely neglected, focusing initially on spatial models of spread, and

([3]) GISIN website: http://www.gisin.org.
([4]) GISD website: http://www.issg.org/database/welcome.
([5]) IABIN website: http://i3n.iabin.net.
([6]) NOBANIS website: www.nobanis.org.

did not became prominent until around 2000 (With, 2002). Such types of study also included the role of land-use change in invasions (Vilà and Ibañez, 2011).

There is now increasing acceptance that biological and social factors interact in complex ways to initiate and sustain different facets of biological invasions (Kueffer and Hirsch Hadorn, 2008), and several studies have in particular highlighted the role of economic factors in the introduction and spread of invasive species (e.g. Kueffer et al., 2010; Pyšek et al., 2010; Essl et al., 2011; Jeschke and Genovesi, 2011). Lately, research on the impact of invasive alien species on ecosystem resilience and ecosystem services has been gaining importance (EFSA, 2011).

Indeed the advances in understanding the mechanisms and the correlates of invasions have had a significant influence on awareness of the issues, and on the development of innovative and more effective response strategies. For example, the recent engagement of European institutions ([7]) to adopt more stringent measures to deal with IAS may also have been helped by an assessment showing that, in addition to the ecological impact, the economic costs of invasive alien species in the region exceed EUR 12.5 billion/year (Kettunen et al., 2009). Furthermore, several assessments have shown the efficacy of eradication of invasives for the recovery of native species affected by IAS at a global scale, with eleven birds, five mammals and one amphibian species having improved their conservation status as a result of the successful removal of IAS (McGeoch et al., 2010). These results contributed to the increased implementation of this management option, with more than 1 100 campaigns being carried out in the world (Genovesi, 2011). However, although some eradications are being undertaken in Europe (e.g. *Carpobrotus* spp. in Menorca or Ruddy Duck *Oxyura jamaicensis* in the United Kingdom, France and Spain), they are uncommon.

20.5 A wealth of initiatives worldwide

Many initiatives focussing on IAS, dealing with legislation, management and communication, have emerged from international organisations, non-governmental organisations, governments and universities across the world. The case of the EU is detailed in Box 20.1. Some are listed below to illustrate their diversity (the listing is in no way exhaustive):

International treaties and agreements

As Riley (2005) notes, at least 42 treaties dealing with environmental issues, the marine environment and international quarantine refer to the regulation of IAS in the world. As regards terrestrial IAS, one of the major treaties is the International Plant Protection Convention (IPPC), setting international standards for phytosanitary measures (although it only covers non-marine invertebrates and plants). The IPPC initially focused mainly on the protection of cultivated plants, but extended its scope in 1999 to include issues relating to wild plants and the environment. The CBD also recognises the need to address invasive alien species in Article 8(h). In 2004, the two Conventions signed a Memorandum of Understanding to avoid duplication of efforts on IAS (Tanaka and Larson, 2006). This required a revision of the glossaries and procedures of the two Conventions for dealing with the analysis of environmental impacts associated with IAS. These organisations have counterparts at the regional scale, and countries are obliged to implement legislation on IAS.

Governments

Governments and parliaments play a major role in preventing the entry and controlling the spread of IAS, in particular through the adoption and enforcement of legislation (both national and international), conducting or financing the eradication of some IAS through appropriate agencies, and promoting research and public awareness of the issue. Within countries, responsibility for the topic is usually divided between ministries of the environment and of agriculture (including farming, forestry, hunting and fisheries, although some aspects may fall within the ministries of health, energy, infrastructure and transport, etc.), with the ministries of agriculture also being responsible for plant and animal health and the associated legislation. Although the environmental and agricultural sectors cooperate at the international level, the mandates are not always clear at the national level. This reflects the fact that pest management (under the plant and animal health regimes) has a longer history than control of invasions, as well as the multiple impacts that IAS may have and the difficulty of categorising these.

Many countries have implemented dedicated legal instruments that relate to the entry and control of IAS (e.g. Australia, New Zealand, USA, South Africa, the United Kingdom), and as a result the number of legal tools has increased steadily in recent decades (McGeoch et al., 2010). For

([7]) See European Commission Environment website: http://ec.europa.eu/environment/nature/invasivealien/index_en.htm).

Box 20.1 Varying European approaches for dealing with IAS

The current situation in Europe is that despite many studies to assess the impacts of IAS, and possible solutions (e.g. Miller et al., 2006), no comprehensive regulation or legislative framework for the EU is yet in place. Partly as a result of the lack of coordinated action, Europe houses a very large number of alien species (around 11 000 according to DAISIE http://www.europe-aliens.org), of which about 10 % (1 094) have ecological impacts and 12 % (1 347) have economic impacts (Vilà et al., 2010). Moreover, many of the invasive alien species of plants and animals that countries spend millions of Euros in managing and controlling can still be freely purchased in some outlets. For instance, the water hyacinth (*Eichhornia crassipes*), which caused spectacular invasions in Portugal, Italy and along 75 km of a Spanish river — which took a few months and 18 million Euros to control (Cifuentes *et al*., 2007) — can still be bought and traded freely in the EU. Another example is the American grey squirrel (*Sciurus carolinensis*) which is known to have replaced the native European red squirrel (*Sciurus vulgaris*) in most of Britain and yet was released in the wild in Italy at three sites, in 1948, 1966 and 1994. Even though the Bern Convention (see below) requested the government of Italy to eradicate the introduced population 'without further delay' and prohibit the trade in the species in 1999, and appropriate plans were made, twelve years later it is still legally offered for sale in pet shops, while the invasive population continues to grow in the absence of any efforts to control or eradicate it (Standing Committee to the Bern Convention, 2011).

Europe has a complex, fragmented and continually developing network of legislative instruments and regulations aimed at prohibiting the introduction and spread of alien species that pose a threat to native biodiversity (Miller et al., 2006). The European and Mediterranean Plant Protection Organization (EPPO) establishes regional standards on phytosanitary measures, and the Convention on the Conservation of European Wildlife and Natural Habitats, generally known as the Bern Convention (1979), commits its contracting parties to a strict control of the introduction of alien species (article 11) and since 1993 has established a working group aimed at supporting states in the implementation of their obligations concerning IAS (see Brunel et al., 2009 for further details). These plant health and environment organisations work closely together, and have, for example, jointly published the *European Code of Conduct on Horticulture and Invasive Alien Plants* (Heywood and Brunel, 2009).

European states have developed national legislation on IAS but often in an un-coordinated manner. For example, Norway has adopted comprehensive and coordinated legislation on invasive species, Germany and Austria are developing a list of regulated species (Essl et al., 2011), the United Kingdom is working on a similar list, Spain adopted legislation in November 2011 which includes a list of regulated species, and Switzerland adopted similar legislation in September 2008. However, given that the regulation of trade in the EU lies within the European Commission, all these efforts will only have limited effectiveness until there is a legal tool that can be applied across the EU. No coordinated legal instrument is yet in place despite the many studies undertaken on the topic, but the European Commission is preparing a dedicated legislative instrument to be ready by the end of 2012 (see European Commission, COM, 2011). However, there will always remain matters that are more appropriately regulated on a national basis because of climatic or other country-specific contexts.

One of the reasons for the lack of a coordinated European approach is that neither of the European legal instruments on nature conservation that deal with IAS — the Bern Convention, covering 45 European States, and the Habitats Directive, applied in all the EU-27 Member States — are very specific on the topic of IAS. They were formulated in 1979 and 1992 respectively, before IAS became a major concern of governments. The Bern Convention simply asks governments to '**strictly control the introduction of non-native species**' and the Habitats Directive requires Member States to '**ensure that the deliberate introduction into the wild of any species which is not native to their territory is regulated … and, if they consider it necessary, prohibit such introduction**', without giving much information on how to deal with the IAS issue as a whole i.e. dealing with the prevention of new entries, pathways, unintentional introductions, containment or eradication of introduced species, early detection and rapid response systems, etc. Although the Bern Convention's 'European Strategy on Invasive Alien Species' (2003) and the European Commission's technical documents produced during the preparation of the EU Strategy on Invasive Alien Species (2011) do contain sufficient guidance for precise government action, they are not legally-binding documents and their application has been patchy. Within the framework of a revision of the Plant Health regime, European national plant protection organisations have identified the inclusion of invasive alien plants having detrimental effects on biodiversity as one of their first concerns (Agra CEAS Consulting et al., 2010).

Europe, no coordinated legal instruments are yet in place, despite the many studies undertaken on the topic, but the EU has committed to presenting a draft dedicated legal tool by the end of 2012, and an assessment of the different legal options was published in December 2011 ([8]).

Countries with national strategies on IAS include Canada (Gouvernement du Canada, Environnement Canada, 2004), South Africa, for the Cape Floristic region (CAPE Partnership Program, 2009), Mexico (Comité Asesor Nacional sobre Especies Invasoras, 2010), the Bahamas, (see Pyšek and Richardson, 2010), and a number of European countries (see Box 20.1).

A few governments have also established large interdisciplinary programmes for dealing with invasive species 2011).

Non-governmental organisations

Non-governmental organisations cooperate in the management of IAS through the preparation of strategic documents and gathering of information, or directly by managing sites to conserve native species and restore ecosystems. The Invasive Species Specialist Group (ISSG) of the International Union for the Conservation of Nature (IUCN) is one of the oldest organisations active in this field ([9]). ISSG has long worked with all the main global initiatives, including SCOPE and the Convention of Biological Diversity, providing technical support for improving the ability to prevent and mitigate the impacts of invasive species on biological diversity.

Other major institutions active in the field include CABI, Birdlife, The Nature Conservancy, Wildlife Conservation Society, and Island Conservation (whose mission is specifically to prevent extinctions by removing invasive species from islands). Across the world, at the national and local scale, thousands of associations or foundations are also involved in controlling IAS, for example in nature reserves.

Universities

Many universities and research institutes across the world are engaged in research on IAS, within the disciplines of biological science, weed science, agronomy, and more recently social science. Dedicated research centres and networks have been created in several parts of the world. Networks of scientists are also very active and organise conferences (e.g. NEOBIOTA, see http://cis.danbif.dk/neobiota2010 or EMAPI, Ecology and Management of Alien Plant Invasions).

Thus, despite the growing amount of legislation being adopted at the global scale, invasions continue to grow at a rapid rate, with no indication yet of any saturation effect (Butchart et al., 2010). In addition to the more than 42 international treaties dealing with environmental issues referring to the regulation of IAS (Riley, 2005), there is much reliance on voluntary codes of conduct which by definition lack sanctions for non-compliance, the latest in Europe being the European Code on Pets and Invasive Alien Species (Davenport and Collins, 2011). None of this is helped by the inherent difficulties of defining and tackling IAS and the consequent continuing confusion and debate over terminology and the lack of an agreed core definition of IAS. It is therefore not surprising that the scientific community recurrently undergoes soul-searching over these issues.

20.6 Obstacles to a common understanding

The issue of the extent to which IAS adversely affect the natural environment has long been a subject of controversy, not just between stakeholders with different interests (e.g. conservationists versus horticulturists/foresters) but also within the scientific community. Dissenting voices periodically challenge the extent to which IAS represent a major threat to biodiversity, and the measures that should be taken (see for example the exchange between Sagoff, 2005 and Simberloff, 2005).

The obstacles to reaching a common agreement about the threats posed and measures needed are reflected in the scientific debates on the topic. Although debates and discussion are inherent to the development of any discipline, too much focus on these controversies can have a deleterious effect. A more extensive discussion of the valuation of invasive alien plants can be found in Larson (2007), Kueffer and Hirsch Hadorn (2008), Hattingh (2011) and Rotherham et al. (2011). Some of the key issues that are a cause of conflicting expert views are reviewed in the next section.

([8]) Document available at http://ec.europa.eu/environment/nature/invasivealien/index_en.htm.
([9]) Founded in 1993, it was the first thematic (as opposed to taxonomic) specialist group of the IUCN SSC to be created. ISSG is a voluntary global network of about 1 000 scientists and practitioners working to mitigate the impacts of biological invasions.

Dissenting voices about the 'pros' and 'cons' of managing IAS

As already noted, IAS are broadly defined according to the negative impacts they cause (cf. the CBD definition and definitions extending to economic impacts). The very definition of IAS along these lines is therefore somewhat of a hybrid, mixing biological elements (a species), the effects on the environment that we are able to detect, and human perceptions of its economic, environmental or social impacts. Assessment of these impacts, specially when considering those on the environment (which in some cases are not easy to quantify or qualify, not to mention the dynamic nature of the environment), are subject to multiple interpretations. The assessments are particularly difficult in the context of a precautionary management approach that builds on an ability to predict potential future impacts. It is widely acknowledged that some IAS can have major impacts and that in these cases it would, in principle, be ideal to prevent these invasions before they happen. However, there are divergences in our perception of how common problematic alien invaders are and whether the alien origin of a species is a reliable heuristic for predicting problematic spread. Davis et al. (2011) question whether conservation money is efficiently spent on preventing the introduction of any new alien species until such species are proved innocuous, as a strict interpretation of the precautionary principle would require. In effect, they highlight the opportunity costs of a strict prevention of introduction of alien species, including the opportunity costs of losing the benefits that some alien species might provide.

The IUCN Invasive Species Specialist Group (ISSG) (2011) responded to these points by explaining that the escalating loss of biological diversity is the motivation for invasive management action on alien species. They also recalled that alien species may not manifest invasiveness till decades after their introduction, and draw attention to species that may only have a subtle immediate impact but which eventually affect entire ecosystems, for example through their effect on soil properties. In addition, invasions and impacts appear to be context-dependent. This is particularly true for plants: for example, while an alien species of cinnamon (*Cinnamomum verum*) has been considered as potentially beneficial for restoring novel mid-elevation forests in the Seychelles, it is a major invader in nearby montane cloud forests (Kueffer et al., 2010). The ISSG (2011) argues that, irrespective of how common problematic invasions of alien species are, prevention is needed because of the huge impacts of the invasions that do happen.

Based on such a perspective, the cost of inaction has been estimated at up to USD 1.4 trillion per year, representing about 5 % of global GDP (Pimentel et al., 2005). Examples are also available for countries: USD 138 billion per year for the US, USD 14.45 billion for China (figure for 2000, representing 1.36 % of Chinese GDP) and over EUR 12 billion per year in Europe. While the cost of inaction in Europe is EUR 12 billion per year, the cost of action is estimated at EUR 40–190 million per year, depending on the possible policy options (Kettunen et al., 2009). The management of IAS is therefore, according to this perspective, considered a very cost-effective investment.

It is not, however, obvious how to decide on priorities and what actions should be taken to address the benefits or harm to native biodiversity, human health, ecological services and economies that species might pose when such benefits and harm cannot be predicted. The solution may come from a pragmatic approach that involves prevention or mitigation of the worst impacts of invasives through a combination of preventive measures, early detection and rapid response to new incursions, with permanent management as only the last option.

The lack of acceptance by society of some management actions

Measures to manage IAS may also be subject to criticism, in particular when they involve the killing of animals, or the use of biological control agents or phytosanitary products (i.e. herbicides or pesticides) (see Boxes 20.2 and 20.3). Opponents of the management of invasive alien plants may also oppose the use of herbicides or pesticides, which they perceive as a bigger threat than the actual impacts of the invasives.

Native vs. alien: a polemical topic to explain to the public

A misunderstanding that is pervasive when talking about IAS lies in not differentiating between invasive species and alien species, as already mentioned above, and using this to justify interventions against alien species in general. While conservation biologists and ecologists refer to the threats from alien species because of evidence that indicates that some of them entail particular ecological and economic risks, some social scientists such as Larson (2007) and Warren (2007) have pointed out the problematic social and cultural connotations of such 'prejudice' against

Box 20.2 The grey squirrel and the ruddy duck: too cute to be killed

A good example of protest by animal welfare groups is the case of the grey squirrel (*Sciurus carolinensis*) in Italy. The two officers in charge of the eradication of grey squirrel were brought to court and charged with cruelty toward animals and illegal methods of capture, despite consultations with animal welfare groups and exercising caution in killing the animals. The legal case delayed the enforcement of any action, ruining the whole eradication campaign, and the grey squirrel is now expected to spread across Europe, with huge impacts on biodiversity as well as the economy of the entire region (Bertolino and Genovesi, 2003; Bertolino et al., 2008).

Another relevant case is the control of the American ruddy duck (*Oxyura jamaicensis*) which escaped from captivity in the United Kingdom and, after reaching a population of several thousand, spread throughout Europe and started to hybridise with the endangered native white-headed duck (*Oxyura leucocephala*). In Spain it threatened the very intense efforts of the conservation authorities to prevent the extinction of the native species. Selective shooting of ruddy ducks and hybrids soon started in Spain, but this was only a temporary measure. Realising that the long-term solution for the Spanish populations of white-headed duck could only come from the eradication of the ruddy duck in the United Kingdom, a European eradication plan was proposed by the Bern Convention and its eradication financed by the UK government and the European Union from 1997. The problem was that shooting attractive ruddy-ducks caused a public and vociferous outcry in that bird-loving country, until the support of the Royal Society of the Protection of Birds for the controls was decisive in getting the project started. That courageous decision cost the society the loss of probably a few thousand members, but by December 2011 the number of birds in the United Kingdom had been reduced to a few hundred and there are good chances of eradicating the species from the wild in Europe by 2015 (Standing Committee to the Bern Convention, 2011; Consulting et al., 2010).

species of non-native origin. Some consider that environmentalists, conservationists and gardeners are 'xenophobic' when dealing with IAS.

Invasive species may indeed be flagged in the press with pejorative names such as 'the yellow peril' for water primroses (*Ludwigia grandiflora* and *L. peploides*) in the south of France. But from a scientific point of view, the focus on alien species is not xenophobic but has a scientific basis (Simberloff and 141 scientists, 2001). The focus lies on alien species not because they are considered unwanted *per se*, but because they show that some species of alien origin have a higher probability of unrestrained growth which can ultimately lead to environmental damage. One reason why some alien species differ ecologically from native species is that they are not subject to the control of natural enemies (diseases, pests, herbivores) that are not present in the newly colonised area.

An even greater difficulty in defining what is 'natural'

The debate on native versus alien goes beyond the species level and touches on the definition of ecosystems and on what conservationists or society decide to protect. The definition of an 'alien' species in an era of accelerated global change is also a challenge. Davis et al. (2011) call for management approaches that recognise that the 'natural' ecosystems of the past have changed forever due to drivers such as climate change, nitrogen eutrophication, increased urbanisation and other land-use changes. They argue that most human and natural communities now contain both long-term residents and new arrivals, and that ecosystems with combinations of species that never existed before are emerging as a consequence of climatic and other global change ('novel ecosystems' *sensu* Hobbs et al., 2006; 'no-analogue ecosystems' *sensu* Williams and Jackson 2007).

These arguments only represent a part of the emerging challenges in the struggle against invasions (Kueffer, 2010). For example, the increasing use of novel alien crops such as those used for biofuel and biomass present a risk of favouring new invasions (Genovesi, 2010; Sheppard et al., 2011); and synthetic biology may in the near future produce still more fundamentally novel species. To overcome the effects of climate change, some authors have proposed translocating native species to areas outside their natural ranges (so called assisted migration (McLachlan et al., 2007) or assisted colonisation (Hunter, 2007; Hoegh-Guldberg et al., 2008): see Seddon et al., 2009; Stanley-Price, 2010), with the possible risk of causing further impact on native species, as in the case of the proposed translocation of the Iberian lynx into the British Isles (Thomas, 2011; Vilà and Hulme, 2011).

Box 20.3 Fear of biological control agents

Biological control is a management method that triggers reluctance in decision makers and the public, though generally supported by scientists if proper and conclusive research has first been carried out. Such caution prevents this efficient technique from being used when IAS are widespread. The mistrust of biological control agents springs from the fear that the agent may not prove specific enough and end up attacking non-target native species, thus aggravating the problem instead of solving it. The public also finds it odd and risky to introduce a new non-native species into a complex ecosystem, particularly in a psychological context of negative feelings towards alien species. Often scientists are not fully trusted either. The use of the lepidopteran *Cactoblastis cactorum* (Pyralidae) to manage the invasive *Opuntia* species that threatens endemic plants in rocky habitats is a typical example that is used to oppose biological control. While the introduction of the Lepidopteran had proved successful in managing millions of hectares of invasive *Opuntia* species in Australia, South Africa and then in Hawaii and the Caribbean Islands, *Cactoblastis cactorum* was then accidentally introduced in Florida where it threatened a native *Opuntia* species (Sforza, 2006). In this case, the potential for accidental spread of the species in areas where it could be detrimental had not been assessed accurately.

Another well-known example of the introduction of a biological control agent that itself became invasive is that of the cane toad (*Rhinella marina*) which was introduced in Queensland (Australia) to control insects that feed on sugarcane and other crops. Cane toads became naturalised and spread, and have detrimental impacts as they feed on many terrestrial animals and compete with native amphibians for food and shelter (Global Invasive Species Database http://www.issg.org/database/species/ecology.asp?fr=1&si=113). In this case, the potential adverse impacts of the species on native fauna had not been assessed accurately.

Even if successful, the method may be susceptible to criticism. The recent release of *Cibdela janthina* in Reunion Island in 2009 to combat the highly invasive plant *Rubus alceifolius* (Le Bourgeois and Della Mussia, 2009) triggered intense debate in the media. Apiculturists and fruit producers feared that the biological control agent would outcompete bees, jeopardising fruit production on the island. The issue even reached the French Senate (JO Sénat, 21/05/2009). After undertaking additional studies and dialogue with stakeholders, it finally appeared that *Cibdela janthina* had no impact on bees, and was efficient at controlling the targeted plant. Many other biological control programmes have proved successful, and the selection of an agent is nowadays carefully studied through formal risk assessment protocols (the same as those used for IAS) that greatly reduce the chance of unexpected behaviour of released species.

At a European level, legislation on the introduction of biological agents is quite stringent, while legislation against the introduction of any other species, including acknowledged invasive ones is non-existent.

In the case of the control of the water hyacinth (*Eichhornia crassipes*) in Spain, mentioned above, the authorities ruled out the introduction of a biological control agent, used successfully in Africa, because of the complex European legislative framework impeding the release of agents.

It should be noted, however, that after extensive research and discussion, the biological control agent *Aphalara itadori* was released in the United Kingdom to control the highly invasive Japanese knotweed (*Fallopia japonica*) whose management and control costs more than GBP 150 million a year. This represents the first classical biological control release against an invasive alien plant in Europe. CABI had carried extensive testing on this insect over the past five years to verify that it can be safely released into the environment. A public consultation was launched: 20 respondents were against the release, 42 in favour (CABI, 2010).

20.7 The limits of governance on the complex issue of IAS

The interdisciplinary nature of the skills required for dealing with IAS is a challenge and can slow action and cooperation. An IAS may, for example, have both environmental and agricultural impacts as well as providing other agricultural benefits. This raises the question of which legislative framework should be in charge. At a macro scale such as the EU, various principles, terminologies and legislative frameworks need to be aligned before any decision can be taken, complicating and slowing the effective application of legislation and management measures. This has been of particular concern in the case of ragweed (*Ambrosia artemisiifolia*). The pollen of this plant is very allergenic, and the species is also a weed in crops,

particularly of sunflower. Discussions on which department — health or agriculture — should deal with the problem has much delayed measures to control the species.

Managing an invasive alien species is difficult not only because of its intrinsic biological characteristics and technical difficulties, but also because of the very many stakeholders that need to be involved for coordinated action. Classical environmental management tools (i.e. habitat protection, liability for environmental damage or mediation in environmental conflicts) prove of little use for IAS. Indeed, before becoming invasive, a species may remain unnoticed in an area for several decades, the so-called 'lag phase'. This can makes the application of a liability approach very difficult, as the traceability of who introduced a species may be lost with time. Environmental mediation that would permit a consensus between conflicting interests about the introduction of a particular species is handicapped by uncertainty in the potential invasive behaviour of an introduced species, as the decision on whether or not to introduce a species needs to be taken far in advance of the species becoming effectively invasive. For example, the potential impacts had not been assessed accurately before introducing the signal crayfish (*Pacifastacus leniusculus*) into Europe. When the Scandinavian fisheries of European crayfish (*Astacus astacus*) were damaged by a crayfish plague, signal crayfish, originating from North America, were introduced to Norway and Finland for recreational and commercial crayfish capture. It turned out that signal crayfish was not only the carrier of the crayfish disease, but it also became invasive, threatening the European crayfish as well as macro-invertebrates, benthic fish and aquatic plants. The species has spread widely and is now out of control (Global Invasive Species Database, *Pacifastacus leniusculus*, http://www.issg.org/database/species/ecology.asp?fr=1&si=725). The species nevertheless has beneficial effects for crayfish production, resulting in a conflict of interest between those who want to control the species and those who want to breed it. Clearly a decision should have been taken long before allowing the introduction of this species in Europe.

These complex and difficult decisions are taken on the basis of risk assessment, which is a time-consuming exercise. Furthermore, even with a very good risk assessment system, new outbreaks of IAS could still occur, making the need for a system of rapid early warning and effective eradication response necessary. The decision on where to draw the line on the acceptable environmental risks versus the introduction of new species or new communities that may carry invasive alien species then becomes a value judgement to be taken by governments. The question of the proportionality of the measures to be taken (allowing the entry of any species versus prohibiting the entry of all non-native species) is very delicate and should involve, in addition to the strategic position of governments, a societal debate. This would imply, in the first place, a good knowledge by the public of the phenomenon and of the impacts of invasive alien species. The stakeholders involved in introducing IAS, and the public who are often responsible for the entry or further spread of these species, both need to be engaged in the debate. Another element of 'proportionality' that makes legislative measures complex lies in the geographical range over which measures should be taken. A species might be a problem only in a given bioclimatic area, but free movement and trade might occur between this area and others, particularly in the free-trade space of the EU. Should this species therefore be prohibited in the whole free movement and trade area, even if it only has detrimental effects in part of it? Such concern is being raised for the development of a European legislative framework on IAS. In other words, should the attractive water hyacinth (*Eichhornia crassipes*), which in Europe may only become naturalised and be invasive in Mediterranean countries, be prohibited from trade in the United Kingdom where it is harmless? The UK nursery industry might like to make use of a plant that does not threaten UK biodiversity, but its introduction, given the free movement of persons and goods within the EU, might compromise management efforts in areas at risk. The question of balance between legislative and voluntary approaches in dealing with IAS is crucial. As many stakeholders are involved, both approaches are needed, the one reinforcing the other.

20.8 Applying the precautionary principle to invasive alien species

Because of the lack of robust criteria for predicting invasiveness, and because most research on biological invasions assumes that alien species are 'guilty until proven innocent', rigid application of the precautionary principle in managing biological invasions is problematic in the context of free-trade agreements. New Zealand, for example, requires that every species imported to the country is assessed for risks, and only if found to pose a low risk can an authorisation be issued. Some countries, however, regulate the introduction only of species

on a list of 'unwanted' invasive or potentially invasive species ([10]). This approach is also proposed by the International Plant Protection Convention (IPPC).

Another way of applying the precautionary principle, while not preventing the entry of IAS, is to eradicate new invaders in a timely manner. The case of *Caulerpa taxifolia* is a good illustration of a missed opportunity to undertake early action in Europe. The alien alga was detected in France in 1984 at a very early stage of invasion, and could have been quickly removed. However, the management of *C. taxifolia* only started when it had already expanded to a large portion of the Mediterranean, when eradication was no longer possible. When the same species was recorded in California in 2000, eradication started only 17 days after its discovery, leading to its successful removal (Genovesi, 2007).

The precautionary principle is the first of the CBD's Guiding Principles for the Prevention, Introduction and Mitigation of Impacts of Alien Species ('The Guiding Principles' Annex Decision VI/23 ([11])) (see Cooney, 2004). It is applied to some extent by the IPPC, when considering all sources of uncertainty in performing a pest risk analysis. Biosecurity is a very dynamic field of research that seeks to integrate the latest techniques and concepts in its methods to assess risks: the modelling of a species' potential area of establishment, pathway analysis, etc. Such techniques face the challenge of identifying species that may be invasive, and also those that may be invasive under novel conditions created by climate change and/or other facets of global change. Approaches for addressing such situations are being developed, such as consideration of the impacts of IAS on ecosystem services through the elaboration of different scenarios (EFSA, 2011; Chytrý et al., 2012).

20.9 Addressing invasion pathways: a late engagement with the stakeholders

A pathway for engagement: Codes of conduct

Managing IAS now consists of placing more emphasis on pathways of introduction of IAS, as well as identifying the stakeholders involved, although such aspects have been adopted quite recently considering the history of the discipline. This has shifted the focus away from preventing particular species to managing risks associated with introduction pathways, including the human activities that create, shape and sustain such pathways (Wilson et al., 2009; Richardson, 2011b), involving local knowledge. Researchers in the social sciences have become interested in exploring perceptions of alien and invasive species and their impacts (Menozzi, 2007; Andreu et al., 2009; Kueffer and Hirsch Hadorn, 2008; Javelle et al., 2010). Cooperation with stakeholders involved in introducing and disseminating IAS is becoming increasingly common.

For invasive alien plants, the horticultural trade is the primary invasion pathway (Reichard and White, 2001; Dehnen-Schmutz et al., 2007; Drew et al., 2010; Richardson and Rejmánek, 2011). As a response, some countries have prepared voluntary codes of conduct or good practice for the horticultural industry, for example the United States (Fay et al., 2001) and Europe (Heywood and Brunel, 2009). Such approaches have so far had limited effectiveness and buy-in (Drew et al., 2010), although 12 European countries report initiatives related to the implementation of a code of conduct on horticulture and invasive alien plants. The effectiveness of such voluntary codes depends largely on how well they are promoted (Dehnen-Schmutz and Touza, 2008; Brundu et al., 2011); this requires continuing communication and dialogue with the stakeholders (Gibbs, 2011). When developing this code of conduct in Europe, the International Association of Horticulture Producers (AIPH) was involved in the drafting of the document. For the specific case of invasive alien plants, the industry cannot be seen as preventing legislation from happening, and although playing its role in challenging the issue, it has been collaborative in considering that if some species present a problem, then some alternative can be found.

Pathway approaches are also emerging in the field of plant health. It is increasingly considered that a species-by-species regulatory approach relying on inspections is more and more difficult in today's markets context. As a consequence, the forest entomology and pathology science communities recommend a pathway approach for regulating nursery stock, similar to that adopted for wood packaging material. This is based on the principle that best management practices that effectively

([10]) Such lists used to be called 'Black lists', but such a term is now not considered politically correct.
([11]) See http://www.cbd.int/decision/cop/?id=7197.

prevent known IAS will significantly reduce the risk of also introducing unknown pests. In this regard, the IPPC is developing an international standard for plants for planting (see the UK Forestry Commission website: http://www.forestry.gov.uk/fr/INFD-6YUJRD).

Other initiatives to prepare codes of conduct involve botanical gardens (see Heywood, 2011 for Europe; Fay et al., 2001 for the US), the pet industry, hunting, recreational fishing, zoos and aquaria, aquaculture, marine ballast waters, commercial forestry and other sectors.

Stakeholders: what forces lie behind action and inaction?

Scientists and experts have been active in communicating the dangers of IAS for biodiversity — although not necessarily in the most coherent way, as most scientists are not trained in public relations or communication. Dissenting views have probably had little influence on government decisions on IAS, where the consensus is now that this is a serious problem requiring some degree of attention. Other interest groups have been silently watching the growing interest in IAS with much attention and a degree of reluctance. This includes not only animal welfare activists, alarmed at the possible eradication of animals, but also industries and lobbying groups, for whom restrictions on the trade of some species would hinder or complicate business. Horticulture would have to change its current practices substantially if serious measures to avoid new introductions were put in place. But as they feel that their industry is part of the environment business, they do not want to be seen as environmentally unfriendly. A number of other stakeholders who deal with animals and plants may not welcome restrictions, i.e. foresters, the pet trade, aquaculture, recreational fishing and, to a lesser extent, hunters, zoological gardens, aquaria and botanical gardens. Many of these groups are generally aware of the problem and display in general a cooperative attitude with governments and scientists, but prefer a voluntary approach with agreed codes of conduct to hard laws. The industry may also be divided in some cases. While few businesses are in favour of more bureaucracy, some think they might be at a disadvantage compared with those who decide not to apply codes and therefore that legislation would be fairer. The pet industry is more favourable to a voluntary approach and has been actively engaged in the drafting of a European Code of Conduct on Pets and Invasive Alien Species. It would certainly not welcome some mandatory regulations, for instance any relating to the shipping of all pets, as these would increase costs and imply new complex procedures and operations. Yet it is clear that responsibility for the introduction of many invasive species lies partly with the industry and its activities, although it is also a consequence of the slowness of governments to take action or introduce legislation.

20.10 Lessons learnt on invasive alien species: towards more transdisciplinarity in a rapidly changing world?

During the past few decades, we have acquired greatly increased awareness of the extent of biological invasions, the impacts they have on biodiversity and the economy, and a much better understanding of how to prevent and manage them. Faced with the uncertainties posed by a rapidly changing world, we need to learn lessons from this large body of experience so as to avoid further losses.

Biological invasions currently interest a large and growing body of people, including researchers and students in academic institutions, conservation agencies and NGOs, civil servants, park managers, activists, volunteers and a growing number of concerned citizens in many parts of the world. This network of people, interests and perspectives has assembled over the past 30 years worldwide. The 'game rules' for interactions between different parties are still being defined, tested, and debated. Governments and institutions charged with making decisions have access to considerable knowledge on the topic, but the lack of rules of interactions between multiple parties regularly thwarts effective decision-making. Governance of IAS needs to be achieved before the introduction of species, which means dealing with uncertainties and setting a level of protection. Lessons can, nonetheless, be learnt that could pave the way to more effective interaction and communication between parties, which should result in more effective and transparent decisions. Some of these lessons are late ones (EEA, 2001).

Align concepts for a better understanding by society and public engagement

Public understanding of the threats posed by IAS is fundamental for effective governance. Occasional divergence of opinion among experts in the field of biological invasions may weaken public confidence in the advice of 'experts'. Rather than talking with one voice to the public and insisting on convergent opinions, it is more important to ensure that different opinions are made clearly understandable and transparent to the public and decision makers.

In the historical framing of the phenomenon of biological invasions (see above), it was assumed that the problem could be solved by identifying the biological traits of potentially invasive species and preventing their introduction to new areas. Fifty years of research have shown that the identity (alien or native) and traits of the species are indeed highly relevant, but it has become increasingly obvious that other factors are also involved (e.g. propagule ([12]) pressure, habitat factors, land use). In particular, several studies have shown that biological invasions are strongly correlated with economic factors (Essl et al., 2011; Jeschke and Genovesi, 2011; Pyšek et al., 2010). A comparison of plant invasions on oceanic islands highlighted the fact that economic development (measured as gross domestic product) is the most important predictor of invasive species richness on islands (Kueffer et al., 2010). Human activities are an essential factor in the understanding and solution of the IAS issue, so that public engagement is vital if we are to adopt effective measures and ensure good governance.

Harmonise concepts for improved coordination of on-the-ground actions

The lack of clear and common concepts and definitions of IAS has led to serious problems in obtaining reliable information on species involved in biological invasions and has undoubtedly hampered the development of detailed databases. This is a key element to be addressed when considering ways of strengthening strategies for the management of IAS. This is indeed one of the reasons why some countries do not have a comprehensive list of alien or invasive alien species and is exacerbated by the fact that some countries do not appear to be aware of the extent or seriousness of biological invasions. Another cogent reason is the dynamic nature of biological invasions, so that existing lists need to be regularly updated, requiring budgets and trained staff. A better connection between science and management would help increase and improve policy and legislative action. Initially, most research questions were disconnected from management concerns, and arose from the issues of population and community ecology (Kueffer and Hirsch Hadorn, 2008). Also, impacts were considered without explicitly clarifying the broader human and economic context, and it was often assumed that any detectable effect of an alien species on an ecosystem would be undesirable (Kueffer and Hirsch Hadorn, 2008). Researching global concepts may have hindered the provision of concrete and simple actions. With time, the study of biological invasions has become much more interdisciplinary, and links to management agencies have strengthened. The valuation of costs and benefits associated with alien species (including IAS) and their management has become an important research focus (Kueffer and Hirsch Hadorn, 2008). Consequently, the problem of IAS, initially recognised and brought forward by scientists, is now being more firmly rooted in civil society (e.g. NGO groups).

A late lesson not yet learnt: take account of wider social interests and values

As mentioned in *Late lessons from early warnings* Vol. 1 (EEA, 2001), 'taking account of wider social interests and values' has been overlooked when dealing with IAS. Further social studies are needed to understand human perceptions of biological invasions, so as to eventually adapt the concepts and reconcile diverging opinions between experts and stakeholders. It has for example been shown that the alien origin of a species is of minor importance for stakeholders, while the role that humans play in the spread of a species, its aesthetic and cultural value, or personal experiences with the impacts and management of a particular invasive species in a specific site, are of high importance in their valuation (Bardsley and Edwards-Jones 2007; Bremner and Park, 2007; Gobster, 2011; Selge et al., 2012). Additional care and thought must also be given to the language used in communicating on the topic (Larson, 2010; Hattingh, 2011). For problems associated with IAS, it is crucial to involve all stakeholders, including those who introduce species and members of the public who have divergent ideas about the species. Identifying the pathways of introduction of the invaders and implementing any regulations that affect these demands ongoing dialogue with stakeholders (e.g. in formulating codes of conduct), which, to be effective, should be undertaken at an early stage. It is important to recognise that sociological aspects are very important in addressing this problem, and some of the research questions still need to be explored and the results acted on, such as personal attitudes to IAS and those of interest groups such as animal rights groups.

Another late lesson: avoid paralysis by analysis

Much progress has been made in enhancing the consistency and transparency of protocols for (pest) risk analysis and cost-benefit studies, such as research undertaken for the PRATIQUE project at the European scale (see EPPO, 2011). Such progress in evaluating the risks that species pose has become

([12]) A propagule is defined as any plant organ or part, as a spore, seed or cutting, used to propagate a new plant.

increasingly sophisticated and multidisciplinary, bringing together zoologists, botanists, managers, policy makers and economists (Hulme, 2011a). However, despite the significant advances in predicting the risks related to species introductions, the complexity of the relationships between the many potential explanatory variables still limits the precision of current risk assessment tools (Hulme, 2011b). In addition, the discipline known as 'biosecurity' ([13]) which encompasses all aspects and measures that deal with the prevention of pests will also need to address the emerging challenges of a changing world.

A specific lesson for Europe which concerns the need to act without waiting for coordinated European action is presented in Box 20.4.

Anticipate further challenges and 'blind spots' in a changing world

Kueffer and Hirsch Hadorn (2008) suggest that biological invasions represent a complex societal issue because knowledge is highly uncertain, and because conflicts of interest and values are central to the problem. A wider and more intense debate is expected on options for preventing and managing invasions, and on how to deal with the risks related to novel approaches to conservation and the economy such as biofuel crop planting and managed relocation. Contextual factors are amplified through the global changes that we are currently witnessing: climate change, habitat change, land-use change, etc. Consequently, criteria currently used to consider the invasive behaviour of a species in particular areas are likely to be increasingly challenged (Kueffer, 2010). For example, in montane areas, future invaders may be mountain specialists directly introduced through human activity between high-elevation habitats, rather than the current situation where most invaders of montane regions are climatically plastic species that spread from lowlands (McDougall et al., 2011). As already described, increasing interest in 'novel ecosystems' (Hobbs et al., 2006) as well as novel crops, and in radical conservation measures such as managed relocation, pose new challenges for nature conservation which will demand in-depth discussion.

Box 20.4 A lesson for Europe: do not take the need for European coordination as an excuse for inaction

A particular problem for Europe has been the long time taken by European institutions to propose coordinated stringent measures to control the introduction, trade and spread of IAS and to promote eradication or containment measures. It is likely that a dedicated legislative instrument will be prepared before 2013, to be implemented in the following years, but 2013 is twenty years after scientists alerted governments to the dimension of the problem and the growing risks to European native biological diversity from IAS. During that time the problem has grown worse. Many governments were reluctant to pass legislation on the grounds that the free movement of goods in the EU did not permit them to restrict the import of alien species that might threaten their native biodiversity through national laws. This remains a doubtful claim, as a few European governments did not hesitate to take that step. However many European governments have been slow to act.

As environment is a competence of the EU and resources are scarce, some EU states, when fixing their priorities for conservation action, pay a greater attention to the legal requirement for implementation of EU legal instruments and tend to pay less attention to other issues not specifically covered by European legislation, including much-needed action on IAS. Although the 1992 EU Habitats Directive contains obligations on the introduction of IAS and the European Commission has since the late 1990s invested substantial funds on research, data gathering and eradication operations, government awareness of the need for a more stringent legislative instrument has only come since the growing economic and environmental costs of invasive species have become difficult to ignore. The problem is complex, awareness only relatively recent, government interest limited, and public resources scarce. Hard times for native species!

([13]) The FAO notes that 'Biosecurity is a strategic and integrated approach that encompasses the policy and regulatory frameworks (including instruments and activities) that analyse and manage risks in the sectors of food safety, animal life and health, and plant life and health, including associated environmental risk. Biosecurity covers the introduction of plant pests, animal pests and diseases, and zoonoses, the introduction and release of genetically modified organisms (GMOs) and their products, and the introduction and management of invasive alien species and genotypes. Biosecurity is a holistic concept of direct relevance to the sustainability of agriculture, food safety, and the protection of the environment, including biodiversity.' http://www.fao.org/biosecurity.

Do not allow philosophical debates to create blockages in tackling the problem

Biological invasions occupy a position between 'nature' and 'culture', as they have both biological and social aspects. While many problems that affect biodiversity directly relate to human activities (destruction of habitats, pollution), issues related to IAS are 'nature threatening nature' through human activities, making the role of humans difficult to unravel. This is particularly true in Europe, where ecosystems have been modified since prehistoric times. Such uneasiness sends us back to the classical argument 'it is natural therefore it is safe'. The emerging questioning of IAS reflects the difficulties inherent in defining what nature is and how to protect it, in particular in a context of climate and global change. Global change will increasingly challenge current assumptions and concepts relating to biological invasions. The risk of invasion should be perceived not only as coming from alien species, but rather as a socio-ecological phenomenon in which our perceptions about how humans move species and manage land are considered as a whole (Kueffer, 2010). The response to invasions therefore needs to take into account the human dimension, combining the need to consider the rapidly changing patterns of our society with the urgent need to respond to the threats posed by invasive species.

Table 20.1 Early warnings and actions

77 AD	Pliny the Elder wrote in his *Naturalis Historia* that the invasion of rabbits in the Balearic Islands, Spain, was a very severe problem requiring effective control
1830s	Charles Darwin noted the invasive behaviour of some alien species during his explorations on the *HMS Beagle*, which contributed to the development of his theory of natural selection
1958	Publication by the British zoologist and ecologist Charles S. Elton of his landmark monograph *The Ecology of Invasions by Animals and Plants* which is seen by many as a starting point for the understanding of invasion biology as a distinct field of study
1980s	International research programme on the Ecology of Biological Invasions by the Scientific Committee on Problems of the Environment (SCOPE I) which was important in shaping the research agenda on IAS and led to an explosive growth in invasion biology
1993	Entry into force of the Convention on Biological Diversity (CBD) and of its Article 8(h) on invasive alien species, requiring parties to: Prevent the introduction of, control or eradicate those alien species which threaten ecosystems, habitats or species. Establishment of the IUCN SSC Invasive Species Specialist Group, first interdisciplinary specialist group of IUCN
1997	Launch of a second SCOPE research programme ('SCOPE II') on IAS, which was more inter/transdisciplinary than SCOPE I, and considered economic valuation, stakeholder participation, pathway analysis and management. SCOPE II was run under auspices of a consortium of scientific organizations including SCOPE, IUCN, and CABI which developed the Global Invasive Species Programme (GISP), with the explicit objective of providing new tools for understanding and coping with IAS
2002	Adoption, by the Convention on Biological Diversity (CBD) of Guiding Principles for the Prevention, Introduction and Mitigation of Impacts of Alien Species that Threaten Ecosystems, Habitats or Species (COP decision VI/23)
2000s	Development of national, regional and international databases and information systems, web portals and clearing house mechanisms such as the Global Invasive Species Information Network (GISIN) ([a]), the Global Invasive Species Database ([b]), the Invasive Species Compendium (ISC), the Inter-American IABIN Invasives Information Network (I3N) ([c]) for the Americas, DAISIE ([d]) for Europe and NOBANIS ([e]) for North Europe and the Baltic

Note: ([a]) GISIN: http://www.gisin.org.
([b]) GISD: http://www.issg.org/database/welcome.
([c]) IABIN: http://i3n.iabin.net.
([d]) DAISIE: www.europe-aliens.org.
([e]) NOBANIS: www.nobanis.org.

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21 Mobile phone use and brain tumour risk: early warnings, early actions?

Lennart Hardell, Michael Carlberg and David Gee [1]

In 2011 the World Health Organization's International Agency for Research on Cancer (IARC) categorised the radiation fields from mobile phones and other devices that emit similar non-ionizing electromagnetic fields (EMFs), as a Group 2B i.e. 'possible' human carcinogen. Nine years earlier IARC gave the same classification to the magnetic fields from overhead electric power lines.

The IARC decision on mobile phones was principally based on two sets of case-control human studies of possible links between mobile phone use and brain tumours: the IARC Interphone study and the Hardell group studies from Sweden. Both provided complementary and generally mutually supportive results. This chapter gives an account of the studies by these two groups — and others coming to different conclusions — as well as reviews and discussions leading up to the IARC decision in 2011. The chapter also describes how different groups have interpreted the authoritative IARC evaluation very differently.

There are by now several meta-analyses and reviews on mobile phones and brain tumours, which describe the challenges of doing epidemiology on this issue, the methodological limitations of the major studies published so far and the difficulties of interpreting their results.

It has been suggested that national incidence data on brain tumours could be used to qualify or disqualify the association between mobile phones and brain tumours observed in the case-control studies. However, in addition to methodological shortcomings, there might be other factors that influence the overall incidence rate such as changes in exposure to other risk factors for brain tumours that are unknown in descriptive studies. Cancer incidence depends on initiation, promotion and progression of the disease. As the mechanism for radiofrequency electromagnetic fields carcinogenesis is unclear, it supports the view that descriptive data on brain tumour incidence is of limited value.

The chapter points to mobile phone industry inertia in considering the various studies and taking the IARC carcinogenic classification into account and a failings from the media in providing the public with robust and consistent information on potential health risks. The IARC carcinogenic classification also appears not to have had any significant impact on governments' perceptions of their responsibilities to protect public health from this widespread source of radiation.

The benefits of mobile telecommunications are many but such benefits need to be accompanied by consideration of the possibility of widespread harms. Precautionary actions now to reduce head exposures would limit the size and seriousness of any brain tumour risk that may exist. Reducing exposures may also help to reduce the other possible harms that are not considered in this case study.

Evidence is increasing that workers with heavy long-term use of wireless phones who develop glioma or acoustic neuroma should be compensated. The first case in the world was established on 12 October 2012. The Italian Supreme Court affirmed a previous ruling that the Insurance Body for Work (INAIL) must grant worker's compensation to a businessman who had used wireless phones for 12 years and developed a neuroma in the brain.

([1]) This chapter was supported by grants from Cancer- och Allergifonden and Cancerhjälpen. Contributions by co-workers in the various Hardell group publications are acknowledged.

21.1 Introduction

On May 31, 2011 the WHO International Agency for Research on Cancer (IARC) categorised the radiation fields from mobile phones, and from other devices that emit similar non-ionizing electromagnetic fields (EMFs), as a Group 2B i.e. a 'possible' human carcinogen. Nine years earlier IARC had also classified the magnetic fields from overhead electric power lines as a Group 2B carcinogen.

The IARC decision on mobile phones was principally based on two sets of case-control human studies: the IARC Interphone study and the Hardell group studies from Sweden. Both provided complementary but generally mutually supportive results.

But why were these case-control studies into possible brain tumours from mobile phones initiated?

21.2 The Hardell group studies — 1999–2011

Sweden, along with Israel, was one of the first countries in the world to widely adopt wireless telecommunications technology. Analogue phones (NMT; Nordic Mobile Telephone System) were introduced in the early 1980's using both 450 and 900 Megahertz (MHz) fields. NMT 450 was used in Sweden since 1981 but closed down in 31 December, 2007, whereas NMT 900 operated during 1986–2000.

The digital system (GSM; Global System for Mobile Communication) using dual band, 900 and 1 800 MHz, started to operate in 1991 and now dominates the market. The third generation of mobile phones, 3G or UMTS (Universal Mobile Telecommunication System), using 1900/2100 MHz RF fields has been introduced worldwide since a few years, in Sweden in 2003. Currently the fourth generation, 4G, operating at 800/2 600 MHz, and Trunked Radio Communication (TETRA, 380–400 MHz) are being established in Sweden and elsewhere in Europe.

Desktop cordless phones (e.g. Digital Enhanced Cordless Telecommunications; DECT) have been used in Sweden since 1988, first using analogue 800–900 MHz RF fields, but since early 1990's the digital 1900 MHz system has been used.

Nowadays mobile phones are used more than landline phones in Sweden. (http://www.pts.se/upload/Rapporter/Tele/2011/sv-telemarknad-halvar-2011-pts-er-2011-21.pdf).

The real increase in use and exposures to their radiation fields has been since the end of the 1990's. Wireless phones emit radiofrequency (RF) EMFs and the brain is the main target organ during use of the handheld phone (Cardis et al., 2008).

One of the author's (LH) interest in this research area was initiated by his involvement in a Swedish committee that evaluated cancer risks from exposure to extremely low frequency (ELF) EMFs from power lines. The conclusion was that there was an increased risk for childhood leukemia based on distance to power lines (Hardell et al., 1995). In 2002 IARC concluded that ELF electric and magnetic fields from power lines etc. is a human Group 2B carcinogen (IARC, 2002).

From a review of the literature there seemed to be an increased risk for brain tumours in the electronics industry (Hardell et al., 1995). It was decided to study it further in a case-control study. However, at that time there was also some media attention to a US lawsuit against cell phone industry companies.

It was alleged that repeated use of mobile phone had caused a fatal brain tumour in a woman. The head line in Los Angeles Times was *'Suit Over Cellular Radiation Raises Hazard Questions'* (Carlo and Schram, 2001). It was therefore decided to add questions on mobile phone use in the first of 4 linked case-control studies that are briefly described below.

This is followed by the results of the other major publications with some data on long-term use, the Interphone study, and the IARC evaluation of the RF and cancer evidence, and related responses and discussions.

The aim is not to give a thorough review of this research area, nor to deal with possible other effects of RF exposures which can be found in other publications including meta-analyses of the risk of brain tumours related to use of wireless phones (Hardell et al., 2006d; 2009; Myung et al., 2009; Kundi, 2009; Cardis and Sadetzki, 2011; Levis et al., 2011; IARC Monograph, in press).

21.3 First Hardell group study on mobile phone use and brain tumours — 1999

In 1999 the Hardell group in Sweden published results from their first case-control study on brain tumours and use of mobile phones (Hardell et al.,

1999a). In total 209 (90 %) of the cases and 425 (91 %) of the controls that fullfilled the inclusion criteria answered the mailed questionnaire. Overall no association between use of mobile phones and brain tumours was found.

A slightly increased (but not statistically significant) risk was found for analogue phone (NMT) use and for a *latency* period greater than 10 years, Odds Ratio (OR) = 1.20 (95 % Confidence Interval; CI = 0.56–2.59). For tumours located in the temporal ([2]), occipital or temporoparietal lobe areas of the brain an increased risk was found for ipsilateral ([3]) exposure, OR = 2.42 (95 % CI = 0.97–6.05) (Hardell et al., 1999a, 2001). However, all results were based on low numbers of exposed subjects and different histopathological types of brain tumours so no firm conclusions could be drawn. Furthermore, in this first study use of cordless phones was not included.

Authors of an Editorial in 2001, in commenting on a 'negative' US study (Inskip et al., 2001) that was published after the first Hardell et al. (1999a) study, stated that *…the use of cellular telephones does not detectably increase the risk of brain tumors'* and that *'This study allays fears raised by alarmist reports that the use of cellular telephones causes brain tumors* (Trichopoulos and Adami, 2001). This statement goes far beyond what was scientifically defensible. For example, among the 782 patients with brain tumours only 22 had 5 years or more of mobile phone use and no data with longer latencies were presented. The Editorial illustrates a common misconception which is that a 'non–positive' study is often assumed to be a 'negative' study when in fact the data do not support this assumption.

21.4 Second and third Hardell group studies — 2002–2006

This initial study by the Hardell group gave some support for an association between use of mobile phones and brain tumours. However, the results were based on low numbers especially regarding tumour type and long-term use. The first study was thus followed by two larger studies with cases diagnosed during the time period 1997–2003. The second study encompassed cases diagnosed during 1 January 1997 to 30 June 2000 and the third study 1 July 2000 to 31 December 2003. The methods were the same including an identical questionnaire in both studies. Results for these two study periods were published separately (Hardell et al., 2002, 2005, 2006a), but here pooled results for the whole study period 1997–2003 are presented (Hardell et al., 2006b, 2006c; Hardell and Carlberg 2009). More details can be found in the different publications.

In short, all cases were reported to a cancer registry and had histopathological verfication of tumour diagnosis. Both men and women aged 20–80 years at the time of diagnosis were included. Matched controls were identified from the Swedish Population Registry. The study included use of both mobile and cordless (DECT) phones (wireless phones), the latter an exposure which most other studies ignore ([4]). Also questions e.g. about occupational exposures were asked. Use of wireless phones was assessed by a self-administered questionnaire. The information was supplemented over the phone, if necessary.

The ear that had mostly been used during calls with mobile phone and/or cordless phone was assessed by separate questions; more than 50 % of the time for one side, or equally both sides. This information was checked during the supplementary phone call. Moreover every person that had used a wireless phone received after that a letter asking them again to specify the ear that had been used during phone calls and to what extent that side of the head was mostly used. There was a very good agreement for the result using these three methods to assess these data.

Separately, tumour localisation was defined by using medical records, such as computer tomography (CT) and/or magnetic resonance imaging (MRI). Use of mobile and cordless phones was defined as ipsilateral (more than 50 % of the time), equally ipsi/contralateral or contralateral (less than 50 %) in relation to tumour side. Calculation of cumulative hours of use over the years was based on information on first and last year of use (time period) and average number of minutes per day during that period. Use in a car with external antenna was disregarded as well as use of a handsfree device. A minimum latency period of one year was adopted. Hence, latency period and cumulative use for the different phone types could be defined.

([2]) A review of 110 phone models showed that exposure to radiations is generally higher in the temporal lobe, which is a part of the brain that is near to the ear, (Cardis et al., 2008).
([3]) i.e. the tumour appears on the side of head at which the phone is normally used.
([4]) The Interphone study (see Section 20.9) had some questions on cordless phone use at least in some countries but that information has never been properly analysed or published.

Box 21.1 Some concepts and tools for identifying cancer risks in human studies

OR: Odds ratio. The odds ratio is an estimate of the relative risk, showing how much more likely it is that someone who is exposed to a factor (e.g. cell phones) will develop an outcome (e.g. brain tumour) compared to someone who is not exposed. An OR of 1 indicates no risk, OR < 1 decreased risk and OR > 1 increased risk. For example, an OR of 1.5 indicates that those who are exposed have a 1.5 times higher risk of developing a disease compared to those who are not exposed.

SIR: Standardized incidence ratio. The SIR compares the observed number of cases in a specific population (e.g. cell phone subscribers) to the number of cases expected would the same rates apply as observed in a reference population (e.g. general population). A SIR of 1 indicates no risk, SIR < 1 decreased risk and SIR > 1 increased risk.

CI: Confidence interval. A confidence interval shows the uncertainty of the statistical estimate. In the case of OR and SIR, if the corresponding CI range does not cover 1.0, the result is considered **statistically significant**. Usually 95 % confidence intervals are reported indicating the range of the true OR/SIR with 95 % statistical confidence. The absence of 'statistical significance' can often be a weak guide to the strength of evidence for a risk compared to the power of a study to detect a risk ([5]).

Latency period. Time between first exposure and identification of the disease. For cancer, particularly the solid tumours like brain cancers in contrast to cancers of the blood, such as leukemia, the latency period can be from 15–45 years on average, depending on age at exposure, type and intensity of exposure ([6]) etc. This means that any study of cancer has to be at least as long as the average latent period for the tumour being studied before there will be any clear evidence of a cancer risk.

21.5 Fourth Hardell group study — 2010

In a review commissioned by the former Swedish Radiation Protection Agency (now called the Swedish Radiation Safety Authority) it was suggested that the exclusion of deceased cases was a source of bias in the Hardell group studies (Boice and McLaughlin, 2002). The scientific reason for this suggestion was not given.

As a response to that critique a fourth study was performed. This included the cases with a malignant brain tumour who had died before inclusion in the case-control studies 1997–2003. These cases represented patients with a poor prognosis, mostly with a astrocytoma grade IV tumour. Controls were selected from the Death Registry in Sweden.

Two groups of controls were included, one group consisted of controls that had died from other types of malignant diseases than brain tumour and one group of controls that had died from other diseases than cancer. Relatives to both cases and controls were identified through the Swedish Population Registry at the Swedish Tax Agency. The study encompassed 464 cases and 464 controls that had died from a malignant disease and 463 controls with other causes of death. A similar questionnaire as in previous studies was used and exposure was assessed by a questionnaire sent to the next of kin to each deceased case and control.

Replies were obtained for 346 (75 %) cases, 343 (74 %) cancer controls and 276 (60 %) controls with other diseases. Use of mobile phones gave an increased risk, highest in the >10 years latency group yielding an OR of 2.4 (95 % CI = 1.4–4.1). The risk increased with cumulative number of life-time hours of use, being highest in the more than 2000 hours group who had an OR of 3.4 (95 % CI = 1.6–7.1).

([5]) See Sir Bradford Hill's classic epidemiology paper, 'The Environment and Disease: Association or Causation?' (Proceedings of the Royal Society of Medicine, 1965) where he warned not to overrate the value of statistical significance since it often led people to 'grasp the shadow and loose the substance' of what was in the data. See Chapter 26 on science for precautionary decision-making.

([6]) Stein, Y., Levy-Nativ, O., Richter, E.D., 'A sentinel case series of cancer patients with occupational exposures to electromagnetic non-ionising radiation and other agents', *Eur. J. Oncol.*, 2011, (16/1) 21–54. It has taken almost 50 years to be sure that the atomic bomb dropped on Japan in 1945 also caused brain cancers: the data before then were not clear or robust enough. (Shibata, Y. et al., 'Intercranial meningiomas among Nagasaki atomic bomb survivors', *Lancet*, 1994, (344) 1 770).

No clear association was found for use of cordless phones, although an OR of 1.7 (95 % CI = 0.8–3.4) was found in the group with more than 2000 hours cumulative use. This investigation confirmed the previous results of an association between mobile phones and malignant brain tumours (Hardell et al., 2010). It was concluded that the critique made by Boice and McLaughlin (2002) was scientifically unfounded.

21.6 Some Swedish responses to the Hardell group studies

The first publication on mobile phone use and brain tumour risk (Hardell et al., 1999a) was quickly followed by a letter to the journal (Ahlbom and Feychting, 1999). They suggested that selection bias of cases might have created the high response rate in the Hardell study. However, the critique was unfounded and easy to rebut (Hardell et al., 1999b). In all of the Hardell et al. studies there has usually been a high response rate to the oncologists who have been trained in cancer epidemiology. This applies as well to studies not related to mobile phone use.

Interestingly in the Swedish part of the Interphone studies, one of the authors (Anders Ahlbom) had stated, even before the study started, that an association between cellular telephones and brain tumours was *biologically bizarre* in an 'opinion' letter (Adami et al., 2001). Ahlbom's own work provided evidence for an association between exposure to magnetic fields from overhead power lines and childhood leukemia: an association that would also have to be regarded as *biologically bizarre* (Feychting and Ahlbom, 1993).

Maria Feychting, who participated in the Swedish part of the Interphone studies, queried whether *'the questions really were placed in the same way to cases and controls'* (Björkstén, 2006). Indeed they were in the Hardell studies, however, different methods do seem to have been used for the interviews with cases and controls in the Interphone study, for example, when bed-side interviews were done of cases only.

Meanwhile, the Hardell studies and other evidence of possible health risks from EMF inspired a group of scientists to summarise this evidence in their BioInitiative Report (BioInitiative Working Group, 2007). This had considerable impact in alerting many people to the emerging evidence of risks and to the presence of a small but growing minority of experts who did not agree with the WHO EMF Project statements and other reports that there was no evidence of risk (e.g. of SCENIHR 2007).

The European Environment Agency (EEA), having produced a report *Late lessons from early warnings* (EEA, 2001) was invited by the Biointiative group to submit a chapter about the relevance of the 14 well known 'Late lessons' case studies to the emerging issue of EMF. Having considered the published evidence, the EEA decided it was timely to issue a guarded early warning about the possible risk of brain tumours from mobile phones in September 2007 (see Box 21.2).

21.7 A pooled analysis of the Hardell group studies

Pooled analysis of the two case-control studies on brain tumour cases (glioma, meningioma and acoustic neuroma ([7]), Table 21.1) diagnosed for the whole time period 1997–2003 was made and results were reported for both malignant (Hardell et al., 2006b) and benign (Hardell, 2006c) tumours. This was possible since the same methods were used in both studies with an identical questionnaire. In this presentation results for glioma in the fourth study were added (Hardell et al., 2010; Hardell et al., 2011a).

Latency was divided in three categories, > 1–5 year, > 5–10 year, and > 10 year from first use of a wireless phone until diagnosis. Both use of mobile and cordless phones gave an increased risk overall for **glioma**, highest in the latency group > 10 years, increasing further for *ipsilateral* use; mobile phone OR of 2.9 (95 % CI = 1.8–4.7) and cordless phone OR of 3.8 (95 % CI = 1.8–8.1). Highest OR was found in the > 10 year latency group for total wireless phone use as well.

Table 21.1 gives the same calculations for **meningioma** (n = 916). There was no consistent pattern of an increased risk, although highest risk was found for ***ipsilateral*** exposure in the > 10 year latency period, mobile phone OR = 1.6 (95 % CI = 0.9–2.9). Also ipsilateral use of cordless phone in the same latency category yielded an increased risk, OR = 3.0 (95 % CI = 1.3–7.2).

Regarding **acoustic neuroma** (n = 243) wireless phone use gave OR = 2.2 (95 % CI = 1.3–3.7) in the > 10 y latency period. *Ipsilateral* use gave higher risks than contralateral use for both mobile phone and cordless phone use.

([7]) Studying especially long-term use and laterality.

21.8 Risks to children

Use of wireless phones is widespread among children and adolescents (Söderqvist et al., 2007, 2008). Children's brain absorbs higher radiation from RF-EMF emissions than adults (Cardis et al., 2008; Christ et al., 2010; Gandhi et al., 2012). This is due to the smaller head, thinner skull bone and higher conductivity of the brain tissue. The developing brain is more sensitive to toxins (Kheifets et al., 2005) and the brain is still developing until about 20 years of age (Dosenbach et al., 2010). The greater absorption of RF energy per unit of time, the greater sensitivity of their brain, and the longer lifetimes within which to develop a brain tumour leaves children at a higher risk than adults from mobile phone radiations.

Analyses of the Hardell group results revealed that first use before age of 20 is associated with the highest risk for glioma and acoustic neuroma, see Table 21.2 (Hardell, Carlberg, 2009).

Three age groups for first use of a wireless phone were used; < 20 years, 20–49 years and 50–80 years. For glioma, first use of a mobile phone < 20 y of age gave OR = 3.1 (95 % CI = 1.4–6.7). A similar pattern was found also for cordless phone use (data not shown). Also for acoustic neuroma the risk was highest in the youngest age group; OR = 5.0 (95 % CI = 1.5–16), but no conclusions could be drawn regarding cordless phones since only 1 case had first use before the age of 20 years. These ORs increased further for *ipsilateral* mobile phone use in the youngest age group; glioma OR = 4.4 (95 % CI = 1.3–15), acoustic neuroma OR = 6.8 (95 % CI = 1.4–3.4). No clear age dependent pattern of increased risk was found for meningioma.

There have been very few other studies of children and mobile phone use except the CEFALO study (Aydin et al., 2011) and that of the EU, Mobikids ([8]), which is ongoing.

The multi-centre case–control study CEFALO, conducted in Denmark, Sweden, Norway, and Switzerland has been commented in detail by Söderqvist et al. (2011) since serious methodological problems exist as exemplified below.

In the summary of the study the authors wrote that they *did not observe that regular use of a mobile phone increased the risk for brain tumors.* This conclusion was accompanied by an editorial stating that the study showed *no increased risk of brain tumors* (Boice and Tarone, 2011) as well as by a news release from the Karolinska Institute in Stockholm that the results of no increased risk were 'reassuring' (Karolinska Institute, 2011). However, the statements go far beyond what the study really showed.

For example the data collection and analyses of use of cordless phones was not valid. Use of cordless phones was assessed only *in the first 3 years* of use, a most peculiar definition for which the authors gave no explanation for or reference to. Furthermore, the study never considered wireless phone use, including both mobile and cordless phones, as an exposure category. IARC categorised wireless phone use as a relevant exposure group (Baan et al., 2011). Instead, Aydin et al. (2011) included use of cordless phones in the 'unexposed' category, so risk estimates for mobile phone use might therefore be underestimated. Similarly mobile phone use was included among the 'unexposed' when considering use of cordless phones and thereby potentially concealing an increased risk.

The study yielded a statistically non-significant increased risk for brain tumours among regular users of mobile phones, OR = 1.36 (95 % CI = 0.92–2.02). This OR increased somewhat with cumulative duration of subscriptions and duration of calls (Aydin et al., 2011). Only latency time of 5 years or more was presented with very few cases within this category. Further support of a true association was found in the results based on operator-recorded use for 62 cases and 101 controls, which for time since first subscription > 2.8 years yielded a statistically significant OR of 2.15 (95 % CI = 1.07–4.29) with a statistically significant trend (p = 0.001).

Although the authors do not emphasize that the results yielded an increased risk, the data indicate a moderately increased risk, in spite of low exposure, short latency period and limitations in study design and analyses. Certainly it cannot be used as reassuring evidence *against* an association, as discussed in the commentary (Söderqvist et al., 2011).

Unfortunately, the CEFALO study (Aydin et al., 2011) was published after the IARC meeting in May 2011. Had it been available at the IARC meeting it would have provided additional evidence to support the IARC conclusion that human exposure to RF-EMF is a group 2B carcinogen.

([8]) Contact: ecardis@creal.cat for details.

Box 21.2 The EEA early warnings on brain tumour from mobile phones, 2007–2011

'There are many examples of the failure to use the precautionary principle in the past, which have resulted in serious and often irreversible damage to health and environments. Appropriate, precautionary and proportionate actions taken now to avoid plausible and potentially serious threats to health from EMF are likely to be seen as prudent and wise from future perspectives' (EEA, 2007).

This early warning was updated in 2009 to include:

'The evidence for a head tumour risk from mobile phones, although still very limited, and much contested, is, unfortunately, stronger than two years ago when we first issued our early warning'.

The evidence is now strong enough, using the precautionary principle, to justify the following steps (EEA, 2009):

1. For governments, the mobile phone industry, and the public to take all **reasonable measures to reduce exposures to EMF, especially to radio frequencies from mobile phones, and particularly the exposures to children and young adults who seem to be most at risk from head tumours**. Such measures would include stopping the use of a mobile phone by placing it next to the brain. This can be achieved by the use of texting; hands free sets; and by the use of phones of an improved design which could generate less radiation and make it convenient to use hands free sets ([9]).

2. **To reconsider the scientific basis for the present EMF exposure standards which have serious limitations** such as reliance on the contested thermal effects paradigm; and simplistic assumptions about the complexities of radio frequency exposures.

3. To provide **effective labelling and warnings** about potential risks for users of mobile phones. Across the European Union, the vast majority (80 %) of citizens do not feel that they are informed on the existing protection framework relating to potential health risks of electromagnetic fields. 65 % of citizens say that they are not satisfied with the information they receive concerning the potential health risks linked to EMF. (Special Euro barometer report on EMF, Fieldwork Oct/Nov 2006, published 2007).

4. To **generate the funds needed to finance and organise the urgently needed research** into the health effects of phones and associated masts (base stations). **Such funds could include grants from industry and possibly a small levy on the purchase and or use of mobile phones**. This idea of a research levy is a practice that we think the US pioneered in the rubber industry with a research levy on rubber industry activities in the 1970s when lung and stomach cancer was an emerging problem for that industry. The research funds would be used by independent bodies ([10]) (http://latelessons.ew.eea.europa.eu/fol572324/statements/Benefits_of_mobile_phones_and_potential_hazards_of_EMF.doc).

This was updated in 2011 when evidence was presented to the Council of Europe hearing on mobile phones, February 2011 (EEA, 2011a).

([9]) The EEA has since noted, with some relief, what appears to be an increased use of hands free devices, particularly in the younger generation, due to enhanced applications.

([10]) The EEA has noted the increasing evidence of 'funding bias' in scientific research whereby results outcomes are strongly linked to source of funding. This observation is based on evidence from pharmaceuticals, tobacco, lead, asbestos, BPA and EMF, as well as on evidence from other fields such as cost-benefit analysis and transport construction project cost estimations.

Table 21.1 Odds ratio (OR) and 95 % confidence interval (CI) for glioma, meningioma and acoustic neuroma and use of wireless phones (mobile phones and/or cordless phones)

	Ipsilateral, > 10 year latency	> 10 year latency	Total, > 1 year latency
	OR, CI	OR, CI	OR, CI
Glioma (n = 1148)			
Wireless phone	-	**2.1 1.6–2.8**	**1.3 1.1–1.5**
Mobile phone	**2.9 1.8–4.7**	**2.5 1.8–3.3**	**1.3 1.1–1.6**
Cordless phone	**3.8 1.8–8.1**	**1.7 1.1–2.6**	**1.3 1.1–1.6**
Meningioma (n = 916)			
Wireless phone	-	1.4 0.97–2.0	1.0 0.9–1.2
Mobile phone	1.6 0.9–2.9	1.4 0.9–2.1	1.1 0.9–1.3
Cordless phone	**3.0 1.3–7.2**	1.6 0.9–2.8	1.1 0.9–1.4
Acoustic neuroma (n = 243)			
Wireless phone	-	**2.2 1.3–3.7**	**1.5 1.1–2.0**
Mobile phone	**3.0 1.4–6.2**	**2.6 1.5–4.6**	**1.7 1.2–2.3**
Cordless phone	2.3 0.6–8.8	1.0 0.3–2.9	**1.5 1.04–2.0**

Note: Bold = statistically significant. Number of controls = 2438 in analyses of glioma (living and deceased controls), 2162 for meningioma and acoustic neuroma (only living controls). Only living cases and controls included in analyses of ipsilateral use of mobile and cordless phones.

Adjustment was made for age, gender, socioeconomic-code and year of diagnosis. For glioma adjustment was also made for vital status.

Source: Hardell et al., 2006b, 2006c, 2010, 2011a.

Table 21.2 Odds ratio (OR) and 95 % confidence interval (CI) for glioma, meningioma and acoustic neuroma in different age groups for age at first use of a mobile phone

	Glioma (n = 1148)	Meningioma (n = 916)	Acoustic neuroma (n = 243)
	OR, (CI)	OR, (CI)	OR, (CI)
Mobile phone	**1.3 (1.1–1.6)**	1.1 (0.9–1.3)	**1.7 (1.2–2.3)**
< 20 years old	**3.1 1.4–6.7**	1.9 0.6–5.6	**5.0 1.5–16**
20–49 years old	**1.4 1.1–1.7**	1.3 0.99–1.6	**2.0 1.3–2.9**
≥ 50 years old	**1.3 1.01–1.6**	1.0 0.8–1.3	1.4 0.9–2.2

Note: Bold = statistically significant. Number of controls=2438 in analyses of glioma (living and deceased controls), 2162 for meningioma and acoustic neuroma (only living controls).

Adjustment was made for age, gender, socioeconomic-code, year of diagnosis. For glioma adjustment was also made for vital status.

Source: Hardell et al., 2006b, 2006c, 2010, 2011a.

21.9 The Interphone study 2000–2010: disagreements and delays

The Interphone study was an international collaboration on brain tumour risk and mobile phone use conducted under the guidance of IARC, which is an independent agency of WHO. The investigation was inititated by recommendations from several expert groups to study possible health effects of exposure to RF-fields (McKinlay, 1997; Cardis et al., 2007). It was conducted at 16 research centres in 13 countries during varying time periods between 2000 and 2004. It cost nearly EUR 20 million of which industry contibuted 5.5 million (IARC, 2010) ([11]).

Some of the separate country analyses of the Interphone study produced different results, with some being positive i.e. finding increased brain tumour risks, and some negative i.e. finding decreased risks, i.e. seemingly a 'protective' effect of the radiation.

The authors therefore found it hard to come to an agreed conclusion and there was a 4 year delay between publication of the country results and of the overall study results. One group reportedly thought that the Interphone study overall had found indications of a positive link between mobile phone use and brain tumours, especially when the results of the 10+ year exposure group were analysed separately. Another group thought that they had found no indication of a risk and that the apparent excess of brain tumour was an artifact of the study design and methodology. A third group could agree to neither position.

The publication of the overall Interphone results was finally initiated by the Director of IARC, Christopher Wild, who brokered sufficient agreement between the scientists to finally get the results published in May 2010.

No association between mobile phone use and meningioma was found in the overall Interphone results whereas subgroup analyses showed statistically significant increased risk for glioma in the highest exposure group, i.e. those who had used their mobile phones for 1 640 hours or more, which corresponds to about half an hour of use per day for ten years (Interphone Study Group, 2010), OR = 1.40 (95 % CI = 1.03–1.89). The risk increased further for ipsilateral exposure (OR = 1.96, 95 % CI = 1.22–3.16) and for tumours in the most exposed part of the brain, the temporal lobe, (OR = 1.87, 95 % CI = 1.09–3.22) in the highest exposure group for glioma.

However, the compromise reached between the opposing scientists involved the juxtaposition of two contrasting sentences that were pointing in different directions: *There were suggestions of an increased risk of glioma, and much less so meningioma, at the highest exposure levels, for ipsilateral exposures and, for glioma, for tumours in the temporal lobe* followed by *…biases and errors limit the strength of the conclusions we can draw from these analyses and prevent a* ***causal*** [our emphasis] *interpretation* (Interphone Study Group, 2010).

There was no explanation about how the strength of a link between a cause and an effect can vary from a 'scientific suspicion of risk' to a 'strong association' through 'reasonable certainty' and on to 'causality' which requires the strongest of evidence. This continuum in strengths of evidence, which was illustrated in Bradford Hill's paper written at the height of the tobacco and lung cancer controversy (Hill, 1965), was not explained in the Interphone paper. This meant that the media and the public could assume that 'not causal' meant 'no link' between mobile phones and brain tumours. Other epidemiologists did pick up this rather significant nuance.

In an Editorial accompanying the Interphone results (Saracci and Samet, 2010), published in the International Journal of Epidemiology, the main conclusion of the Interphone results, was described as *both elegant and oracular…(which) tolerates diametrically opposite readings*. They also pointed out several methodological reasons why the Interphone results were likely to have underestimated the risks, such as the short latency period since first exposures became widespread: less than 10 % of the Interphone cases had more than 10 years exposure.

None of the today's established carcinogens, including tobacco, could have been firmly identified as increasing risk in the first 10 years or so since first exposure.

The 'oracular' concluding sentences from the Interphone study therefore allowed the media to report opposite conclusions. For example, on 17 May, 2010 the UK Daily Telegraph reported that the Interphone study provided evidence of a brain tumour risk from mobile phones (http://

([11]) The Hardell studies cost approximately EUR 410 000 and were financed by the Swedish Work Environment Fund, Cancer- och Allergifonden, Cancerhjälpen, Telia, Fondkistan, and the Örebro University Hospital Cancer Fund.

www.telegraph.co.uk/health/7729676/Half-an-hour-of-mobile-use-a-day-increases-brain-cancer-risk.html) whilst the BBC News reported on the same day that there was no risk (http://news.bbc.co.uk/2/hi/health/8685839.stm). This conflicting media reporting pattern was widely repeated elsewhere ([12]).

Further confusion for the public and policymakers followed as a result of the differences in the statements of the Interphone scientists reported in the media. For example, Microwave News reported on 17 May that Elisabeth Cardis, the coordinator of the Interphone study, thought that *Overall...the results show a real effect;* Bruce Armstrong, the Australian Interphone participant, thought that *It shows some indication of an increased risk of gliomas, but I cannot say this with certainty;* and Siegal Sadetzki from Israel thought the results had consistency in indicating a risk but, whilst not *strong enough for a* ***causal*** [our emphasis] *interpretation, they are sufficient to support precautionary policies* (http://www.microwavenews.com/Interphone.Main.html).

In contrast, another co-author, Feychting, thought, *the use of mobile phones for over ten years shows no increased risk of brain tumours* (http://www.i-sis.org.uk/EEA_Highlight_Mobile_Phone_Cancer_Risks.php) and Ahlbom, also from the Swedish Interphone part, told Chinese Television that *there is nothing in these data or in previous data, really, to indicate that there is any risk involved in this* (http://www.youtube.com/watch?v=TllmreWZdoA).

In later publications of Interphone data the estimated RF dose from mobile phone use in the tumour area was also associated with an increased risk for glioma in parts of the Interphone group. The OR increased with increasing total cumulative dose of specific energy (J/kg) absorbed at the estimated tumour centre for more than 7 years before diagnosis with an OR of 1.91 (95 % CI = 1.05–3.47) in the highest quintile of exposure (Cardis et al., 2011).

This important result, which for the first time linked amount of radiation absorbed (rather than just its proxy which is years of exposure/cumulative hours of use) to tumour induction, received very little media attention.

A similar study based on less sound methods was later published by another part of the Interphone study group, see below (Larjavaara et al., 2011).

Results have also now been published for **acoustic neuroma** (Interphone study group, 2011). An increased risk was found for start of *ipsilateral* mobile phone use ≥ 10 year before reference date and cumulative use ≥1 640 h; OR = 3.74 (95 % CI = 1.58–8.83).

The total Interphone results for tumours of the parotid gland ([13]) have never been published. Since the IARC has now terminated the Interphone study ([14]) only the results from Sweden (Lönn et al., 2006) and Israel (Sadetzki et al., 2008) are available. Subgroup analyses that considered laterality (side of use and risk of tumour) and/or amount of use (cumulative hours) indicated increased risks. However, results from other studies do not indicate a consistent pattern of increased risk (Auvinen et al., 2002; Hardell et al., 2004; Duan et al., 2011; Söderqvist et al., 2012a). Results on long-term use are, however, scarce.

21.10 Some reviews and discussions of the Hardell group and Interphone studies

There are by now several meta-analyses and reviews on mobile phones and cancer and they describe the challenges of doing epidemiology on this issue, the methodological limitations of the major studies published so far and the difficulties of interpreting their results.

For example, several of the Interphone findings display differential misclassification of exposure due to observational and recall bias which would tend to underestimate the risk. There were low participation rates for both cases and controls in the Interphone studies, for example in some countries only about 50 % of the cases and about 40 % of the controls participated. This is to be compared with 90 % response rate for cases with malignant brain tumours, 88 % for benign and 89 % for controls in the Hardell-group studies on living subjects (Hardell et al., 2006b, 2006c). Deceased cases were included in the calculations of participation in Interphone, but in

([12]) The EEA had anticipated this confusion and had earlier proposed to IARC that the conflicting opinions of the different Interphone groups should be published alongside each other, with their different arguments and data interpretations clearly illustrated in the same scientific article. This would have helped the media and the public to better understand the reasons for the divergent views amongst the Interphone scientists. However, this suggestion was not adopted.
([13]) A tumour in a gland on the cheek in front of the ear.
([14]) According to the official website (http://interphone.iarc.fr/) the Interphone Study was completed in February 2012.

the Hardell studies deceased cases were included in a separate sub-study on malignant brain tumours.

About 40 % of the cases were interviewed at hospitals in the Interphone studies. Further, it was always known to the interviewer if it was a case or a control that was interviewed. Use of cordless phones was not properly assessed in the Interphone study, or at least not reported. Further discussion on these methodological points may be found elsewhere (Hardell et al., 2008; Kundi, 2009).

Myung et al. (2009) subsequently compared methods and results in all the published studies on the use of mobile phones and the risk for brain tumours. They concluded that the Hardell studies were of higher quality compared with the Interphone study based on the Interphone results from different countries that were then available.

However, one important issue was not covered in the Myung et al. (2009) review, namely that the Hardell group also assessed use of cordless phones in contrast to the Interphone study group. RF-EMF emissions from a cordless phone are of the same magnitude as that from a digital mobile phone, something that has been pointed out several times (Hardell et al., 2006d; Kundi, 2009; Redmayne et al., 2010). Moreover cordless phones are typically used for longer calls than mobile phones (Hardell et al., 2006b, 2006c). Including cordless phone use in the 'unexposed' group, as was done in the Interphone study, would bias estimates against a risk.

The use of bedside interviews of cases, as in the Interphone study, can be a major disadvantage and is ethically questionable. At that time the patient has not fully recovered from e.g. surgery, may not have been fully informed about the diagnosis, treatment and prognosis and may even be under sedation by drugs. In fact patients scored significantly lower than controls due to problems in recalling words (aphasia), problems with writing and drawing due to paralysis in the Danish part of Interphone (Christensen et al., 2005). Obviously observational bias could have been introduced thereby during these bedside interviews.

In contrast, the Hardell group cases received a postal questionnaire approximately 2 months after diagnosis and could give the answers in a relaxed manner, a situation similar to the controls. All cases and controls were later interviewed over the phone to verify and clarify different exposures. This was done blinded as to case or control status.

The possibility of recall and observational bias was investigated in the second case-control study by Hardell et al. (2002). Use of a wireless phone was similar among cases and controls regardless if they reported a previous cancer or if a relative helped to fill in the questionnaire. Potential observational bias during phone interviews was analysed by comparing change of exposure in cases and controls after these interviews. No significant differences were found, showing that the results could not be explained by observational bias: for further details see discussion in that publication (Hardell et al., 2002). All interviews were performed by trained persons using structured instructions and protocols.

The article by Myung et al. was commented on by e.g. Rowley and Milligan (2010) representing the mobile phone industry. They claimed that the Interphone studies were independent of industry influence. However, the mobile phone industry provided 5.5 million euro for the Interphone study and additional funding was provided by the industry in some countries. Furthermore, according to the study protocol *Other parties may also be involved in the Study Group as observers or consultants. These may include representatives of industry, other concerned organisations...* In addition, *representatives of industry and other concerned organisations… shall be informed shortly (maximum of seven days) before publication,* and before the scientific community and laymen have access to the study results (IARC, 2001).

Rowley and Milligan claim that there is *evidence of selection, information, and recall bias, and unusually high reported participation rates* in the Hardell studies (Rowley and Milligan, 2010). These ad hoc statements are not substantiated by the authors or in their references. A high participation rate is a pre-requiste for high quality in case-control studies.

Other scientists have analysed the Hardell results more favourably (Kundi, 2009; Myung et al., 2009; Mead, 2009; Cardis and Sadetzki, 2011; Levis et al., 2011) and IARC relied mainly on the Hardell group and Interphone study group results for its evaluation of the RF evidence.

The Cardis review was particulary interesting as she was the coordinator of the Interphone study. In the review with Sadetzki, another Interphone study participant, they concluded, after a full discussion of the methodological strengths and weaknesses of the Hardell and Interphone studies, that:

> *It is not possible to evaluate the magnitude and direction of the different possible biases on the study results and to estimate the net effect of mobile phones on the risk of brain tumours. The overall balance of the above mentioned arguments,*

> *however, suggest the existence of a possible association* (i.e. between mobile phones and brain tumour).

They ended by concluding that:

> *Simple and low cost measures, such as the use of text messages, handsfree kits and/or the loudspeaker mode of the phone could substantially reduce exposure to the brain from mobile phones. Therefore, until definitive scientific answers are available, the adoption of such precautions, particularly among young people, is advisable* (Cardis and Sadetzki, 2011, p. 170).

21.11 IARC evaluation of the carcinogenicity of RF-EMFs 2011

In 2011 IARC evaluated the carcinogenic effect to humans for RF-EMF emissions during a 8 days (24–31 May) meeting at Lyon in France. This included all sources of radiofrequency radiation, not only mobile and cordless phones. Regarding use of wireless phones all of the published studies by the Hardell group were included as well as overall results for Interphone (Interphone Study Group, 2010, 2011; Cardis et al., 2011). The results on glioma are similar in the Hardell group and Interphone studies if the same inclusion and exclusion criteria are used (Hardell et al., 2011b). This is in contrast to widespread claims that the results of the two sets of studies differed significantly.

The IARC Working Group consisted of 30 scientists ([15]) representing four areas: 'animal cancer studies', 'epidemiology', 'exposure' and 'mechanistic and other relevant data'. The different expert groups had initially a draft written before the meeting by some of the experts. Further work was done in the expert groups and a final agreement, sentence by sentence, was obtained during plenary sessions with all experts participating.

The Working Group concluded that there is 'limited evidence in humans' for the carcinogenicity of RF-EMF, based on positive associations between glioma and acoustic neuroma and exposure to RF-EMF from wireless phones. This conclusion was based on the Interphone study and the Hardell group studies. No conclusions could be drawn from the Danish cohort study on mobile phone subscribers due to considerable misclassification in exposure assessment (Baan et al., 2011).

The final conclusion was obtained by voting by all 30 scientists and there was a very large majority for the conclusion that RF-EMF radiation is 'possibly carcinogenic' to humans, Group 2B, based also on occupational studies.

21.12 Some responses to the IARC conclusion

It is interesting to see that even the authoritative IARC evaluation has been interpreted very differently by different groups.

To date, no adverse health effects have been established as being caused by mobile phone use. This was stated in a fact sheet in June 2011 from WHO EMF Program after the IARC decision (http://www.who.int/mediacentre/factsheets/fs193/en/), and furthermore that *Tissue heating is the principal mechanism of interaction between radiofrequency energy and the human body* without acknowledging any of the non-thermal effects that could explain the evidence on brain tumours (Guiliani and Soffriti, 2010).

Michael Milligan from the Mobile Manufacturers Forum (MMF) said:

> *…After reviewing the available scientific evidence, it is significant that IARC has concluded that RF electromagnetic fields are not a definite nor a probable human carcinogen…* (http://www.mmfai.org/public/docs/eng/MMF_PR_310511_IARC.pdf).

Jack Rowley from GSM Association (GSMA) said:

> *…The IARC classification suggests that a hazard is possible but not likely…* (http://www.gsma.com/articles/gsma-statement-on-the-iarc-classification/17567/).

([15]) David Gee of the EEA had been invited by IARC to join the group as 'a representative of your organization, rather than as an observer' (for a definition of representatives and observers, please see the Preamble: http://monographs.iarc.fr/ENG/Preamble/currenta5participants0706.php). However, a few days before the IARC meeting began the EEA wrote to IARC to say they were withdrawing because of further delays in publishing the full Interphone results and because of the intellectual bias of Ahlbom who was then the Chair of the epidemiology group for the meeting. The day before the meeting began Ahlbom was removed from the Chair by IARC as a result of a reported conflict of interest: and the meeting was also given part of the unpublished Interphone data. However, this was too late for the EEA to then participate.

Patrick Frostell from the Federation of Finnish Technology Industries (FFTI) said:

> *…IARC's classification is in line with the dominant interpretation of current research data, according to which radiofrequency electromagnetic fields are neither carcinogenic to humans nor probably carcinogenic to humans…* (http://www.teknologiateollisuus.fi/en/news/announcements/2011-6/no-change-in-international-assessment-of-the-health-effects-of-mobile-phones).

Professor **Dariuz Leszczynski** from the Finnish Radiation and Nuclear Safety Authority (STUK) and member of the IARC expert panel wrote:

> *Recent IARC evaluation of mobile phone radiation potential to cause cancer and classification of it as a 2B carcinogen has caused a stir of pro and contra opinions among the scientists, industry and news media. Unfortunately, the only outcome of this broad attention leads to only one — **confusion**. Regular mobile phone user, whether highly or not so highly educated, can only be **confused** by this flurry of contradictory opinions and spin-statements* (http://betweenrockandhardplace.wordpress.com/2011/06/29/%e2%80%a2viva-confusion/).

The Economist wrote:

> *..your correspondent thinks the whole brouhaha over mobile phones causing brain cancer is monumentally irrelevant compared with all the other things there are to worry about* (http://www.economist.com/blogs/babbage/2011/06/mobile-phones-and-health).

Microwave News has followed this area for a long time. Much of the whole IARC story and the aftermath can be found at its website, for example regarding ICNIRP's standpoint:

> *ICNIRP is a self-perpetuating group that declines to disclose its finances. Its Standing Committee on Epidemiology, which wrote the new commentary, has only welcomed the like-minded. Its previous chairman, Anders Ahlbom, has also registered his opinion that cell phone tumor risks are nonexistent. (He was the lead author of the last ICNIRP review of cell phones and cancer.) Another former member, Maria Blettner, was the lone dissenting voice in the final vote of the IARC working group. Both Blettner and Ahlbom worked on Interphone* (http://www.microwavenews.com/ICNIRP.Interphone.html).

Perhaps even IARC has contributed to this confusion by seeming to agree with the largely non-positive but much criticized Danish cohort study, see below (http://www.microwavenews.com).

No doubt the IARC decision started a world-wide spinning machine perhaps similar to the one launched by the tobacco industry when IARC was studying and evaluating passive smoking as a carcinogen in the 1990s (Ong and Glanz, 2000) ([16]). Sowing confusion and 'manufacturing doubt' is a well known strategy used by the tobacco and other industries (Michaels, 2008; McGarity and Wagner, 2008; Oreskes and Conway, 2010).

21.13 Some further studies published since the IARC conclusion

The Nordic part of Interphone published a study relating brain tumour location to mobile phone radiation (Larjavaara et al., 2011). The results seemed to contradict the findings by Cardis et al. (2011) as discussed above, but used a different, less clear method. Only 42 cases had used the mobile phone for more than 10 years and no analysis was made of the highest exposed group with longest duration of use. Thus, this study is much less informative and less sophisticated that the one by Cardis et al. (2011).

In Denmark a cohort of mobile phone subscribers was designed and started in cooperation between The International Epidemiology Institute (IEI), Rockville, MD, USA, and the Danish Cancer Society. The cohort was established by grants from two Danish telecom operation companies (TeleDenmark Mobil and Sonafon), by IEI, and by the Danish Cancer Society. The source of money for the IEI has not been disclosed.

([16]) In the early 1990s the Philip Morris tobacco company feared that an IARC study and a possible IARC monograph on second-hand smoke would lead to increased restrictions in Europe so they spearheaded an inter-industry, three-prong strategy to subvert IARC's work. The scientific strategy attempted to undercut IARC's research and to develop industry-directed research to counter the anticipated findings. The communications strategy planned to shape opinion by manipulating the media and the public. The government strategy sought to prevent increased smoking restrictions. The IARC study cost USD 2 million over ten years; Philip Morris planned to spend USD 2 million in one year alone and up to USD 4 million on research (Ong and Glanz, 2000).

Box 21.3 IARC and its classifications of carcinogens

IARC evaluates the *hazard* from potential carcinogens, i.e. 'an agent that is capable of causing cancer under some circumstances', while a cancer *risk* is an estimate of the carcinogenic effects expected from an exposure to a cancer hazard. The IARC monographs are an exercise in evaluating cancer hazards, despite the historical presence of the word 'risks' in the title.

IARC has categorised nearly 1000 potentially carcinogenic **hazardous** agents, that it has studied over the last 40 years, into 5 classifications. These are differentiated by different strengths of evidence. In *descending order of strengths of evidence* they are: **Group 1**, which are '**established'** human carcinogens, such as asbestos, diesel engine exhaust, tobacco, and X-rays (*108 agents*); **Group 2A**, which are **probable** carcinogens, such as perchloroethylene (*64 agents*); **Group 2B,** which are **possible carcinogens,** such as other traffic fumes, lead, DDT and now radiofrequency electromagnetic fields, including mobile phones (*272 agents*); **Group 3**, where the agent is **not classifiable** because the evidence is inadequate and does not permit another classification *(508 agents);* and **Group 4**, where the agent is **probably not carcinogenic to humans,** based on fairly strong evidence *against* a cancer effect in both humans and animals (*1 agent*) (IARC, 2012).

It may be helpful to clarify the meaning of the particularly contentious groups. i.e. 2A and 2B.

IARC chooses 3 main different strengths of evidence when it is evaluating the different types of cancer evidence that may be available. The evidence evaluated comes mainly from humans; from animals; and from consideration of the biological mechanisms for cancer causation: this last can provide understanding about *how* carcinogens cause cancer, in contrast to *whether* they cause cancer.

The main strengths of evidence groups used by IARC are: 'sufficient', 'limited', and 'inadequate'. For example, while Group 1 consists of those agents where there is 'sufficient evidence of carcinogenicity' in humans; Group 2A includes those agents where there is 'limited evidence of cancer in humans' but 'sufficient evidence of cancer in animals'; and Group 2B, which is the radiofrequency EMF category, is those agents where there is 'limited evidence of cancer in humans and less than sufficient evidence in animals' and where 'chance, bias or confounding cannot be ruled out with reasonable confidence'. 'Evidence suggesting lack of carcinogenicity' is used for Group 4 (IARC, 2006, p. 19–20).

Different agents in the same classification group are evaluated on the basis of very different kinds of evidence and exposure conditions that are specific for each substance. Some 2B agents will be at the lower end of the probability range, others will be close to the nearly one in two probability and the rest are somewhere in between, depending on their very specific characteristics. By loosely lumping together several randomly chosen carcinogens from the 271 in Group 2B such as dry cleaning fumes and coffee, which invites comparison to mobile phones, journalists and others help to complicate the already difficult discussion about the likelihood of cancer risks. Each agent needs to be considered on its own evidence.

The first results from the Danish study on brain tumour risk among mobile phone subscribers were published in 2001 and updated in 2006 and 2011 (Johansen et al., 2001; Schüz et al., 2006, 2011; Frei et al., 2011). It included subjects from 1 January, 1982 until 31 December, 1995 identified from the computerized files of the two Danish operating companies, TeleDenmark Mobil and Sonafon. A total of 723 421 subscribers were identified but the initial cohort consisted of only 58 % of these subscribers.

The IARC working group's main reason for not using the Danish study as evidence for its evaluation was that it *could have resulted in considerable misclassification in exposure assessment* (Baan et al., 2011).

The authors of the Danish study have themselves pointed out the main causes of such considerable exposure misclassification (Frei et al., 2011): mobile phone subscription holders not using the phone were classified as 'exposed'; non-subscribers using the mobile phone were classified as 'unexposed'; corporate subscribers of mobile phones (200 507 people), which are likely to have been heavy users, were classified as 'unexposed'; persons with a mobile phone subscription later than 1995 (which is over 80 % of the Danish population) were classified as 'unexposed'; and many users of cordless phones, which Hardell et al. have linked to excess risks of brain cancers, were also classified as 'unexposed'.

Other limitations are the absence of analysis by laterality (the side of head were the phone is used in relation to the side of the tumour) and the complete absence of actual exposure data. These and other shortcomings in this cohort study have been discussed elsewhere in more detail (Ahlbom et al., 2007; Söderqvist et al., 2012b).

It is clear from these limitations that the authors conclusion that 'In this update of a large nationwide cohort study of mobile phone use, there were no increased risks of tumours of the central nervous system, providing little evidence for a causal association' is not soundly based (Frei et al., 2011).

21.14 Need for monitoring long term trends in country wide nervous system tumours

It has been suggested that overall incidence data on brain tumours for countries may be used to qualify or disqualify the association between mobile phones and brain tumours observed in the case-control studies (Aydin et al., 2011; Ahlbom and Feychting, 2011; Deltour et al., 2012; Little et al., 2012). In support of the findings that Frei et al. (2011) presented for Denmark, Ahlbom and Feychting (2011) refer to data on overall brain tumour incidence from the Swedish Cancer Registry (which does not show an overall increase in brain tumour incidence since the 1990s) rather than from the Danish Cancer Registry which would have been more relevant.

The quality of the Swedish Cancer Registry in reporting of central nervous system tumours, particularly high grade glioma, has been seriously questioned (Bergenheim et al., 2007; Barlow et al., 2009). In the Deltour et al. paper (2012) Sweden accounted for about 40 % of the population and cases. Thus, underreporting of brain tumour cases to the Swedish Cancer Register would make the conclusions in the Deltour et al. study less valid.

In Denmark a statistically significant increase in incidence rate per year for brain and central nervous system tumours (combined) was seen during 2000–2009, in men +2.7 % (95 % CI = 1.1 to 4.3) and in women + 2.9 % (95 % CI = 0.7 to 5.2) (NORDCAN). Recently updated results for brain and central nervous system tumours were released in Denmark. The age-standardized incidence of brain and central nervous system tumours increased by 40 % among men and by 29 % among women between 2001–2010 (Sundhedsstyrelsen, 2010).

A more recent news release based on the Danish Cancer Register states that during the last 10 years there has been an almost 4-fold increase in the incidence of the most malignant glioma type, glioblastoma (http://www.cancer.dk/Nyheder/nyhedsartikler/2012kv4/Kraftig+stigning+i+hjernesvulster.htm). So far these incidence data are not generally available.

Little et al. (2012) studied the incidence rates of glioma during 1992–2008 in the United States and compared the results with odds ratios for glioma associated with mobile phone use in the 2010 Interphone publication (Interphone Study Group, 2010) and the Hardell group pooled results published in 2011 (Hardell et al., 2011a). However, an important methodological issue that was not stated in the abstract or in Figures, but can be found in the web appendix, is that observed rates were based on men aged 60–64 years from the Los Angeles SEER registry as the baseline category. These data were used to estimate rates in the entire dataset, men and women aged ≥ 18 years and all 12 SEER registries. Thereby numerous assumptions were made. The conclusion by Little et al. that 'Raised risk of glioma with mobile phone use, as reported by one (Swedish) study … are not consistent with observed incidence trends in the US population data...' goes far beyond scientific evidence and what would be possible to show with the faulty methods used in the study. On the contrary, it is of interest that they in fact showed statistically significant yearly increasing incidence of high-grade glioma in the SEER data for 1992–2008, + 0.64 %, 95 % CI 0.33 to 0.95, a result not commented further by the research group.

Much care is needed when using *descriptive* data, as in Aydin et al. (2011), Deltour et al. (2012) and Little et al. (2012), to dismiss results from *analytical* epidemiology. In addition to methodological shortcomings, there might be other factors that influence the overall incidence rate such as changes in exposure to other risk factors for brain tumours that are unknown in descriptive studies. Cancer incidence depends on initiation, promotion and progression of the disease (Hazleton et al., 2005). As the mechanism for RF-EMF carcinogenesis is unclear it supports the view that descriptive data on brain tumour incidence is of limited value.

21.15 Concluding remarks

It is sometimes claimed by the telecommunications industry and others that:

- the scientific basis for the current ICNIRP limits for exposure to EMF is adequate to protect the public from cancer risks;
- that children are no more sensitive than adults to the RF from mobile phones;
- that there are no biologically significant effects from **non-thermal** levels of EMF, and
- that, if there are such effects, there are no acceptable mechanisms of action that could explain these effects.

However the recent 400-page review by the Ramazzini Institute and The International Commission for Electromagnetic Safety (ICEMS) provides a wealth of evidence on the non–thermal biological and ecological effects of EMF (Giuliani and Soffritti, 2010). The EEA summarised the main findings of this report in its evidence to the Council of Europe' hearing on RF and mobile phones in 2011 (EEA, 2011a, 2011b).

Results from the Hardell-group as well as from the Interphone group show an increased risk for glioma and acoustic neuroma associated with long term mobile phone use. Also use of cordless phones increases the risk when properly assessed and analysed. The risk is highest for ipsilateral exposure to the brain of RF-EMF emissions. Adolescents seem to be at higher risk than adults. For meningioma there is no consistent pattern of increased risk.

Furthermore, of interest is that in the same studies different results were obtained for different tumour types. This strongly argues against systematic bias as an explanation of the findings. In that case the results would have been similar regardless of tumour type.

The IARC conclusion that RF-EMF emissions overall, e.g. occupational and from wireless phones, are possibly carcinogenic to humans, Group 2B (Baan et al., 2011) has been questioned by e.g. members of ICNIRP (Swerdlow et al., 2011). That article appeared online 1 July, 2011, one month after the IARC decision, and concluded that *the trend in the accumulating evidence is increasingly against the hypotheses that mobile phone use can cause brain tumors in adults*. There has also been unfounded attacks on individual researchers as exemplified in this article, a pattern that repeats similar experiences in the asbestos, lead and tobacco histories. Published results on health effects are questioned by using obscure methods and citing single results out of context without considering the overall pattern.

There is a lack of investigating journalists who can produce nuanced reports in the media. Most journalists seem to make only reference to news reports or press releases without making their own evaluations or without seeming to have read the original articles. Many limitations of epidemiological studies are to be found in the text, but rarely in the abstract which is most often all that is read. Without accurate and reliable reporting in the media the public do not get a robust and consistent information on potential health risks to make their own judgements about how precautionary they should be.

It is remarkable that the IARC carcinogenic classification does not seem to have had any significant impact on governments' perceptions of their responsibilities to protect public health from this widespread source of radiation, especially given the ease with which exposures can be reduced (i.e. texting, handsfree devices and better phone design).

Independent research into the many unknowns about the biological and ecological effects of RF radiations are urgently needed, given the global exposure of over 5 billion people and many other species, especially those, like bees and some birds whose navigation systems are possibly being affected by such radiations (Balmori, 2005, 2009; Sharma and Kumar, 2010), and effects on breeding of wild birds (Everaert and Bauwens, 2007). Research could be in part funded by relevant industries from levies on phones and masts but used independent from their influence.

The benefits of mobile telecommunications are many, but, as with other case studies in the *Late lessons from early warnings* Volume 1 (EEA, 2001) and the present report, such benefits need not to be accompanied by the possibility of widespread harms. Precautionary actions now to reduce head exposures, as pointed out by the EEA in 2007, and many others since, would limit the size and seriousness of any brain tumour risk that may exist. Reducing exposures may also help to reduce the other possible harms that are not considered in this case study.

21.16 Epilogue

The Italian Supreme Court affirmed a previous ruling that the Insurance Body for Work (INAIL) must grant worker's compensation to a businessman who had used wireless phones for 12 years and developed a neurinoma in the brain (http://www.applelettrosmog.it/public/news.php?id_news=44;

http://microwavenews.com/news-center/italian-supreme-court-affirms-tumor-risk). He had used both mobile and cordless phones for five to six hours per day preferably on the same side as the tumour developed. The neurinoma was located in the trigeminal Gasser's ganglion in the brain. This 5th cranial nerve controls facial sensations and muscles. It is the same type of tumour as the acoustic neuroma in the 8th cranial nerve located in the similar area of the brain. Although neurinoma is a benign tumour it causes persistent disabling symptoms after treatment with neurological impairment that severely affects the daily life. The Italian case fulfils the criteria for a causal association; more than 10 years use of wireless phones, high cumulative exposure on the same side as the tumour appeared, and a tumour type that would be predicted based on previous research on use of wireless phones and brain tumour risk. No further appeal of the Supreme Court decision is possible.

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22 Nanotechnology — early lessons from early warnings

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Nanotechnology is the latest in a long series of technologies heralded as ushering in a new era of technology-driven prosperity. Current and future applications of nanotechnology are expected to lead to substantial societal and environmental benefits, increasing economic development and employment, generating better materials at lower environmental costs, and offering new ways to diagnose and treat medical conditions. Nevertheless, as new materials based on nanoscale engineering move from the lab to the marketplace, have we learnt the lessons of past 'wonder technologies' or are we destined to repeat past mistakes?

This chapter first introduces nanotechnology, clarifies the terminology of nanomaterials and describes current uses of these unique materials. Some of the early warning signs of possible adverse impacts of some nanomaterials are summarised, along with regulatory responses of some governments. Inspired by the EEA's first volume of *Late lessons from early warnings*, the chapter looks critically at what lessons can already be learned, notwithstanding nanotechnology's immaturity ([1]).

Nanotechnology development has occurred in the absence of clear design rules for chemists and materials developers on how to integrate health, safety and environmental concerns into design. The emerging area of 'green nanotechnology' offers promise for the future with its focus on preventive design. To gain traction, however, it is important that research on the sustainability of materials is funded at levels significant enough to identify early warnings, and that regulatory systems provide incentives for safer and sustainable materials.

Political decision-makers have yet to address many of the shortcomings in legislation, research and development, and limitations in risk assessment, management and governance of nanotechnologies and other emerging technologies. As a result, there remains a developmental environment that hinders the adoption of precautionary yet socially and economically responsive strategies in the field of nanotechnology. If left unresolved, this could hamper society's ability to ensure responsible development of nanotechnologies.

([1]) This chapter is based on and in parts identical to Hansen, S.F., Maynard, A., Baun, A., Tickner, J.A. 2008. 'Late lessons from early warnings for nanotechnology', *Nature Nanotechnology*, (3/8) 444–447.

22.1 What is nanotechnology and what are nanomaterials?

Nanotechnology is often described as having roots in a wide range of scientific and technical fields, including physics, chemistry, biology, material science and electronics. The field of nanotechnology is thus broad and covers a multitude of materials, techniques, scientific and commercial applications and products (RS and RAE, 2004). Originally the term nanotechnology, first used by Taniguchi in 1974, referred to the ability to engineer materials precisely at the nanometre (nm) level (Taniguchi, 1974). The term has since been framed and reframed by various actors over the decades and, despite the desire for a unifying all embracing definition of nanotechnology, many versions of the definition exist today. Here, we use the widely-accepted definition suggested by the United States National Nanotechnology Initiative (NNI):

> Nanotechnology is the understanding and control of matter at dimensions between approximately 1 and 100 nanometers, where unique phenomena enable novel applications. Encompassing nanoscale science, engineering, and technology, nanotechnology involves imaging, measuring, modelling, and manipulating matter at this length scale (NNI, 2009).

Chemistry typically deals with large numbers of atoms and molecules acting together. The behaviour of individual atoms and molecules can best be understood within a quantum physics-based framework, while the motion of massive collections of atoms and molecules such as physical objects under the influence of force are best described through classical mechanics or Newtonian physics. Nanotechnology falls between these two domains and holds the possibility of revealing and exploiting unique novel phenomena as a result.

Although the wordings differ, a number of definitions require that two criteria must be fulfilled for materials to be considered as engineered nanomaterials ([2]):

- they must have some purposely engineered structure with at least one dimension in the approximate range 1–100 nm;
- this nanostructure must give the system properties that differ from those of the bulk forms of the same material.

Although the definition is broad, in most materials or systems it can be determined whether they involve nanomaterials or not (Hansen et al., 2007).

The range of nanomaterials that can be manufactured is extremely broad. However the techniques used to produce them can, roughly speaking, be divided into top-down and bottom-up approaches. Top-down techniques involve starting from a larger unit of material, and etching or milling it down to smaller units of desired shape, whereas bottom-up involves progressing from smaller sub-units (e.g. atoms or molecules) to make larger and functionally richer structures (RS and RAE, 2004; BSI, 2007b). Top-down techniques include processes such as high-energy ball milling, etching, sonication and laser ablation, whereas bottom-up techniques include sol-gel, chemical vapour deposition, plasma or flame spraying, supercritical fluid, spinning and self-assembly (Biswas and Wu, 2005). Both approaches pose specific challenges. Creating smaller and smaller structures with sufficient accuracy is a critical challenge for top-down manufacturing, whereas the challenge for bottom-up techniques is to make structures large enough and of sufficient quality (RS and RAE, 2004).

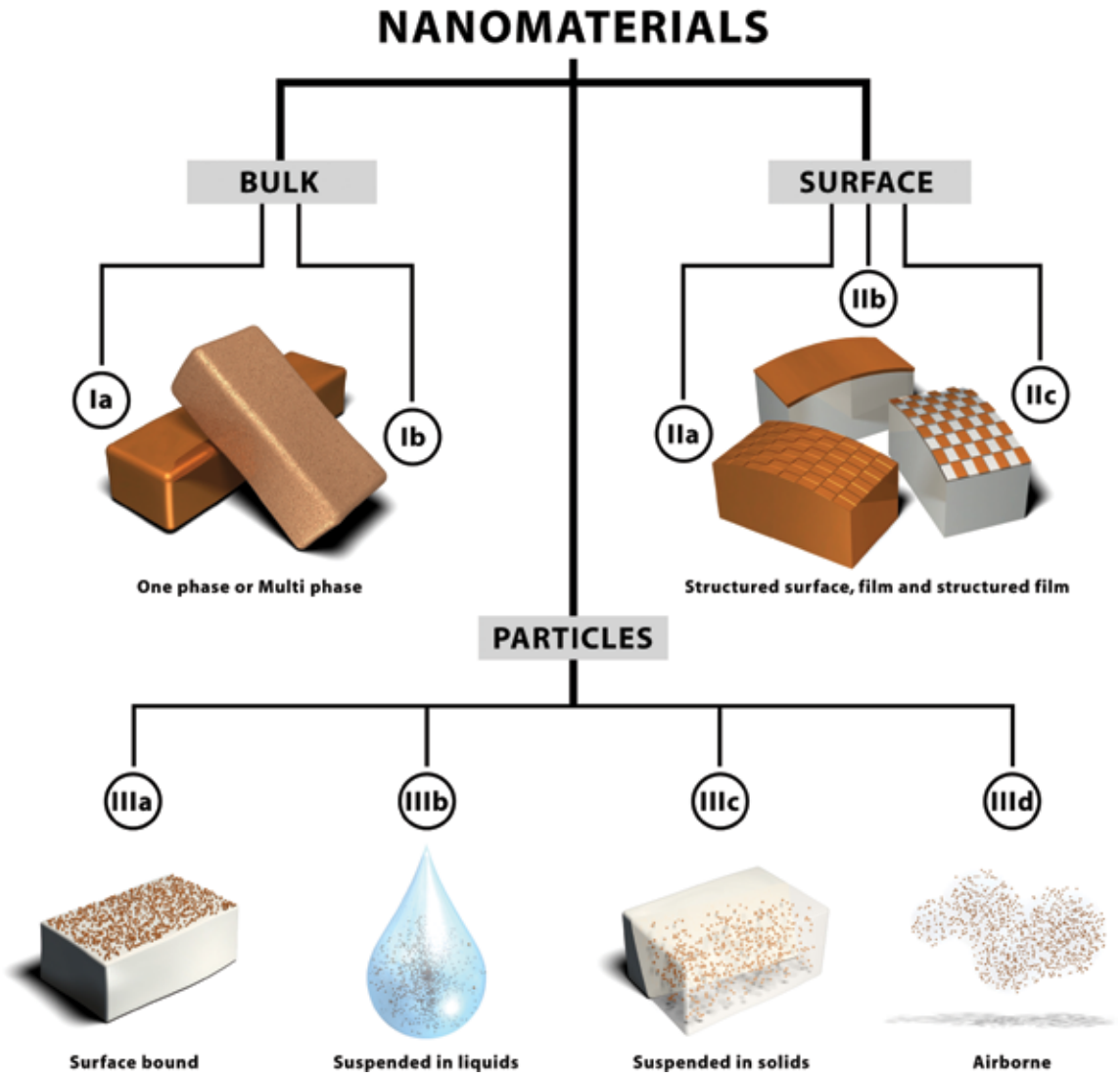
Starting with a palette of conventional materials, new nanomaterials may be formed by subtly altering the shape, size and form of these materials at the nanoscale. A further range of nanomaterials with new properties may be developed by combining two or more nanoscale materials. Familiar chemicals may also be used to construct new nanometre-scale molecules and structures, such as carbon-60 and carbon-70 molecules (C60 and C70), carbon nanotubes, nanoscale liposomes, self-assemble monolayers, dendrimers and aerogels. Various international standardisation institutes have expanded their focus of attention from trying to define nanotechnology to defining the nature of the many different kinds of nanomaterials such as carbon nanostructures, nanorods and nano-objects (BSI, 2007; ISO, 2008).

In order to facilitate hazard identification and focus risk assessment, a procedure for dividing nanomaterials into relevant subcategories has been developed by Hansen et al. (2007), as illustrated by Figure 22.1.

Hansen et al. (2007) suggest categorisation of nanomaterials depending on the location of the

([2]) Nanomaterials in this context specifically refer to materials that have been purposely engineered to have nanoscale structure.

Figure 22.1 The categorisation framework for nanomaterials. The nanomaterials are categorised according to the location of the nanostructure in the material



Source: Hansen et al., 2007, reprinted with permission.

nanoscale structure in the system. This leads to a division of nanomaterials into three main categories:

- materials that are nanostructured in the bulk;
- materials that have nanostructure on the surface;
- materials that contain nanostructured particles.

Nanoparticles have been defined by the ISO (2008) as particles having three external dimensions between 1 and 100 nanometre ([3]). Category III above contains nanostructured nanoparticles that can have various forms and shapes and this category includes, for example, quantum dots, fullerenes, nanotubes and nanowires (Maynard and Aitken, 2007). There are four subcategories of systems with nanoparticles, depending on the environment around the nanoparticles:

- subcategory IIIa has nanoparticles bound to the surface of another solid structure;

([3]) It is important to note that this is not a universally accepted definition and that, as with the term nanotechnology, a number of different definitions as to what constitutes a nanomaterial exists. The articulation by the European Commission of their recommendation for a definition is discussed in detail in Section 22.5 of this chapter.

- subcategory IIIb consists of systems where nanoparticles are suspended in a liquid;
- subcategory IIIc is nanoparticles suspended in solids;
- subcategory IIId consists of airborne nanoparticles.

Most health and environmental impact concerns have been raised over nanoparticles that fall into subcategories IIIc and IIId (see, for example, SCENIHR, 2009; RCEP, 2008; Madl and Pinkerton, 2009). A major benefit of the proposed categorisation framework is that it provides a tool for dividing nanosystems into identifiable parts, thereby facilitating evaluations of, for example, relevant exposure routes or analysis of effect studies according to relevance to the material tested.

22.2 Development of nanotechnology and nanomaterials

The development of nanotechnology has been rapid when assessed by a number of metrics, including government funding and number of research publications and industrial patents (see, for example, Chen and Roco, 2009; Youtie et al., 2008; Sylvester and Bowman, 2011). Early nanotechnology development was driven by advances in materials science and scientific breakthroughs such as the discovery of fullerenes, quantum dots and carbon nanotubes (Iijima, 1991) along with innovations that allowed nanostructures to be visualised, such as the invention of the scanning tunnelling microscope and the atomic force microscope (Kroto et al., 1986; Iijima, 1991; Binning et al., 1982 and 1986).

One of the key turning points in science and technology policy in relation to nanotechnology was the establishment of the National Nanotechnology Initiative (NNI) by the United States of America (USA) Government in 2000, along with significant increases in research and development (R&D) funding for nanotechnology-related research (Igami and Okazaki, 2007). Since then, most developed and many emerging economies have launched national initiatives or prioritise research in nanotechnology (Roco, 2011). Although somewhat speculative in nature, Lux Research (2008) estimated that in 2008 alone global nanotechnology R&D investment was around USD 18.2 billion, representing USD 8.4 billion from governments, USD 8.6 billion from corporate sources and USD 1.2 billion from venture capital investors. Government funding of academic research has lead to a significant increase in the number of scientific research publications in nanotechnology (Linkov et al., 2009). Scientific activities sparked by government funding have had a crucial role in nanotechnology-related knowledge creation and technology transfer, although there is often some time lag before scientific knowledge is diffused into useful inventions and applications (Igami and Okazaki, 2007).

22.3 Current production and application of nanotechnology and nanomaterials

According to the Nanotechnology Company Database, there are now about 2 000 nanotechnology-focused companies around the world; the majority of these are based in the US (estimates suggest 1 100), and 670 have their headquarters within the European Union (Nanowerk, 2010). These companies range from multinationals to small and medium-size companies and university spin-offs. They span a wide range of sectors and applications including energy, analysis, textiles, anti-microbial wound dressings, paints and coatings, fuel catalysts and additives, lubricants, cosmetics and food packaging (Chaundry et al., 2006; Hodge et al., 2010).

Till now, the emerging nature of the technology has ensured that much of the public and private sector attention has been on R&D activities. However, one could argue that nanotechnology is entering in a new era in which both the number of products containing nanomaterials and the sophistication of these nanomaterials have increased spectacularly. Mundane products will soon, it would appear, be superseded by a range of innovative nanotechnology-based products.

In 2006, the Project for Emerging Nanotechnologies (PEN) at the Woodrow Wilson International Center for Scholars launched an online inventory of consumer products that are reported to include nanomaterials (the Consumer Products Inventory). At the time of its launch in March 2006, the global inventory contained 212 different products available for purchase. This number increased to 580 products in 2007, and in March 2011 the inventory contained 1 317 products from about 30 countries (PEN, 2011). These products fall into a number of different categories including health and fitness, home and garden, and electronics and computers. More than half (738) were considered to be health and fitness-related and included products as diverse as hair straighteners, sporting equipment and cosmetics. The primary material in many of the products was nanoscale silver (PEN, 2011). The

Woodrow Wilson Consumer Products Inventory contains information such as product name, company, manufacturer or supplier, country of origin, and a short product description. However, it does not contain information about how many units of a given product are produced and sold or the mass/volume of nanomaterial in each product. Such information is only available if the producers themselves make it available, which occurs rarely. It is therefore not surprising that the public, and even the relevant regulators themselves, have limited knowledge about the current production volumes of nanomaterials. Moreover, the veracity of the available information must be considered, given its scattered and incomplete nature.

Publicly available information on commercially produced engineered nanomaterials is at best patchy. For example, in 2001, the global production of carbon-based nanomaterials was estimated to be around several hundred tonnes per year; by 2003 global production of nanotubes alone was estimated to be about 900 tonnes (Kleiner and Hogan, 2003). Frontier Carbon Corp, a Japanese-based company, produces more than 40 tonnes of C60 per annum, mainly for use in a range of goods including sporting goods, batteries, lubricants and polymer additives (Fujitani et al., 2008). The consulting firm Cientifica (2006) has estimated that in 2006 the global annual production of nanotubes and fibres was 65 tonnes, giving it a commercial value of about EUR 144 million. Cientifica (2006) has suggested that the value of nanotubes and fibres will exceed EUR 3 billion by 2010, representing an annual growth rate of well over 60 %. The veracity of these claims is still to be tested. Even though information about the production of carbon-based nanomaterials is scarce, more is known, or at least guessed at, about such materials than about many other nanomaterials such as quantum dots, nano-metals and materials with nanostructured surfaces.

22.4 Signs of early warnings

Concerns have been raised about the potential risks of nanotechnology and nanomaterials almost since the emergence of nanotechnology (Drexler, 1986), and historical analogies have been made with both ambient ultrafine particles and asbestos (RS and RAE, 2004; Seaton et al., 2009; Mullins, 2010). Ambient ultrafine particles, which can come from multiple sources, are defined as airborne nanoscale particles, including particles incidentally produced such as those in diesel exhaust and incinerator stacks. Ultrafine particles are typically considered to be smaller than 0.1 micron (i.e. < 100 nm). Research on ultrafine particles has found an increased morbidity and mortality from cardiovascular and pulmonary diseases inversely correlated with size i.e. the smaller the particles, the more dangerous (Oberdorster et al., 2005a; Pope and Dockery, 2006). Since nanomaterials are in the same size range as ultrafine particles, concerns have been raised on whether nanomaterials could have the same hazardous properties as ultrafine particles.

Much of the research performed on ultrafine particles in the 1990s now feeds into what we know about the potential risk of nanomaterials and lays the foundation for many of the current scientific research hypotheses in the field of nano(eco) toxicology (Oberdorster et al., 2007). One of the most important hypotheses is that the hazard properties of nanoparticles might be related to inherent physico-chemical properties different from those traditionally used for industrial chemicals, e.g. particle size, shape, crystal structure, surface area, surface chemistry and surface charge. As early as 1990 Oberdorster et al. (1990) and Ferin et al (1990) reported that ultrafine titanium dioxide (TiO_2) and aluminium oxide (Al_2O_3) of 30 and 20 nm, respectively, induced a very striking inflammatory reaction in the lung of rats compared to larger particles of 250 and 500 nm. Two years later Oberdorster et al. (1992) reported that the crystallinity of TiO_2 nanoparticles influenced their toxicity and that surface area was a better descriptor than mass for the adverse effects observed in rats. Donaldson et al. (2002) have since observed a similar correlation for carbon black, when studying the ability of nano and micron particles to cause inflammatory effects in rats. Warheit et al. (2006) and Sayes et al. (2007), however, did not observe any correlation with surface area when evaluating biological response in rats after exposure to nano-sized TiO_2, SiO_2 and other particles.

One study has found a statistically significant increase in malignant lung tumours in rats following chronic inhalation of nano-sized TiO_2 (Heinrich et al., 1995) and, on the basis of this study, NIOSH (2011) has determined that ultrafine TiO_2 should be considered a potential occupational carcinogen. NIOSH further concluded that TiO_2 is not a direct-acting carcinogen, but acts through a secondary genotoxicity mechanism that is not specific to TiO_2 but primarily related to particle size and surface area and surface area was found to be the critical metric for occupational inhalation exposure to TiO_2.

Visual similarities between carbon nanotubes (CNTs) and asbestos fibres have led to others raising

concerns about them having the same hazardous properties (Huczko et al., 2001; Warheit, 2009). In 2004 Lam et al. (2004) published a study in which they exposed mice to a number of single-walled CNTs of different purity and found that all nanotubes induced dose-dependent granulomas and interstitial inflammation in the lungs. The results presented by Lam and co-workers were supported by observations by Warheit et al. (2004) who also observed pulmonary granulomas in rats after exposure to single-walled CNT soot. However, in contrast to Lam et al., the effects observed by Warheit et al. (2004) were not dose-dependent. Absence of pulmonary biomarkers suggests a potentially new mechanism of pulmonary toxicity and induced injury (Warheit et al., 2004). More recently, Poland et al. (2008) compared the toxicity of four kinds of multi-walled carbon nanotubes (MWCNTs) of various diameters, lengths, shape and chemical composition by exposing the mesothelial lining of the body cavity of three mice to 50 mg MWCNT for 24 hours or 7 days. This method was used as a surrogate for the mesothelial lining of the chest cavity. They found that long MWCNTs produced length dependent inflammation, foreign body giant cells and granulomas that were qualitatively and quantitatively similar to the foreign body inflammatory response caused by long asbestos. Only the long MWCNTs caused significant increase in polymorphonuclear leukocytes or protein exudation. The short MWCNTs failed to cause any significant inflammation at 1 day or giant cell formation at 7 days. The finding that the length of CNTs affects their biological activity is supported by findings by Takagi et al. (2008) and Muller et al. (2009). Poland et al. (2008) also found that water-soluble components of MWCNTs did not produce significant inflammatory effects 24 hours after injection, which rules out the concern that residue metals were the cause of the observed effects, an association that other researchers had previously hypothesised on the basis of *in vitro* studies (Shvedova et al., 2005; Kagan et al., 2006).

Most studies of CNTs have used intra-tracheal or intra-peritoneal administration. Intra-tracheal and intra-peritoneal instillation bypasses upper respiratory tract defences and does not deposit particles evenly in the lung in a manner similar to inhalation. This has historically led to the biological relevance of such studies being questioned (Oiser et al., 1997). Recently, however, a number of nose-only inhalation studies on CNTs have been published in peer-reviewed journals by industry (BASF, Nanocyl and Bayer) that support previous findings such as Ellinger-Ziegelbauer and Pauluhn (2009), Ma-Hock et al. (2009) and Pauluhn (2010). For example, in a 90-day nose-only inhalation toxicity study of MWCNTs, Ma-Hock et al. (2009) found that the incidence and severity of granulomatous inflammation of the lung and the lung-draining lymph nodes were concentration-dependent, something which has previously been demonstrated for intra-tracheally instilled single-walled carbon nanotubes (SWCNTs) (Lam et al., 2004) and MWCNTs (Muller et al., 2005). Interestingly, exposure via inhalation revealed inflammation in the nasal cavity, larynx and trachea, where the particles are deposited during inhalation, as well as alveolar lipoproteinosis. This had not been observed using intra-tracheal or intra-peritoneal administration (Ma-Hock et al., 2009).

In addition to CNTs, substantial concerns have been raised over the use of nanometre-scale silver particles, or nanosilver, especially in regard to its widespread prevalence in everyday consumer products. Nanosilver is reportedly one of the most widely used nanomaterials in consumer products today (PEN, 2011), and the antibacterial properties of nanosilver have been exploited in a very diverse set of products and applications. These include dietary supplements, personal-care products, powdered colours, varnish, textile, paper, interior and exterior paints, printing colours, water and air purification, polymer-based products and foils for antibacterial protection such as washing machines, kitchenware and food storage (PEN, 2011). The scale of use is currently unknown as there are no labelling requirements for nanoproducts, and the concentrations used are also unknown for most of the products on the market (Boxall et al., 2008).

Many applications involving nanosilver involve direct exposure of the substance to humans. This has raised concern about the potential human health effect of the material. The potential health and environmental impacts of nanosilver have been subject to many reviews (Luoma, 2008; Aitken et al., 2009; Wijnhoven et al., 2009; Pronk et al., 2009; Stone et al., 2010, Christensen et al., 2010; Mikkelsen et al., 2011). The toxicity of silver metal is generally considered to be relatively low (Wijnhoven et al., 2009). At very high concentrations, repeated ingestion or inhalation of colloidal silver has been found to lead to deposition of silver metal/silver sulphide particles in the skin, eye and other organs, leading to blue or bluish-grey discolouration of the skin. Although cosmetically undesirable and irreversible, the condition — known as argyria — is not life threatening. It has been shown that silver from nanoparticles can enter the body via oral and inhalation routes and that silver is absorbed and distributed to target organs such as the liver, olfactory bulb, lungs, skin, brain, kidneys

and testes (Sung et al., 2008 and 2009; Kim et al., 2008). The form in which the silver is transmitted through and accumulated within the body is however unclear, i.e. whether it is present as particles, ions or complexes (Mikkelsen et al., 2011). Nanosilver has been associated with inflammation as well as slight liver damage in mice after oral exposure (Cha et al., 2008; Kim et al., 2008). Prolonged exposure to nanosilver particles via inhalation has been found to produce an inflammatory response in the lungs of rats, as well as inducing alterations in lung function (Sung et al., 2008).

A number of *in vitro* studies have found that the toxicity of nanosilver is mediated by an increase in the production of reactive oxygen species, stimulating inflammation and subsequent cell death. The relevance of this is unclear and subject to scientific investigation (Stone et al., 2010; Christensen et al., 2010; Mikkelsen et al., 2011). In an extensive review of risk assessments of nanosilver, Wijnhoven et al. (2009) concluded that the number of well-controlled studies on the potential toxicities of nanosilver as well as current knowledge of the kinetics of nanosilver is too limited to provide a proper foundation for human risk assessment.

With regard to environmental organisms, concerns have been raised by the expected increased emissions and toxicity of nanoscale materials compared to bulk forms of the same material. In this respect, silver nanoparticles may serve as an example since the substance is being used in an increasing number of consumer products because of its antibacterial properties. Silver is known to be ecotoxic. However the toxicity is highly dependent on the form and speciation of the metal. In the registration of silver under REACH (Registration, Evaluation and Authorisation of CHemicals) (Regulation (EC) No 1907/2006), predicted no-effect concentrations (PNECs) are reported as 0.04 μg/L (micrograms per litre) (freshwater), 0.86 mg/L (marine water) and 0.025 mg/L (sewage treatment plants) (ECHA, 2011). Toxicity tests using silver nanoparticles also reveal very-low-effect concentrations. For freshwater algae EC50-values as low as 4 μg/L have been found, and values far below 1 mg/L have been reported for crustaceans (Navarro et al., 2008; Griffitt et al., 2008). EC50 is the maximum concentration that induces a response halfway. Inhibition of nitrifying bacteria can occur at concentrations below 1 mg/L (Hu, 2010) and the function of wastewater treatment plants may therefore be affected by the presence of silver nanoparticles. For ionic silver it is known that the speciation in aqueous media determines bioavailability and toxicity. This is likely also to be the case for elemental silver nanoparticles, but the influence of speciation on uptake, depuration and toxicity has yet to be studied in depth. The environmental concentrations resulting from the use of nanosilver in consumer products are at present uncertain, although a number of different estimates have been made (e.g. Mueller and Nowack, 2008; Gottschalk et al., 2010). Where silver nanoparticles are incorporated in textiles, they can be released during washing (Benn et al., 2010). Resulting environmental concentrations in the low ng/L range have been proposed by Gottschalk et al. (2010). It remains uncertain whether silver nanoparticles are more toxic than their bulk counterpart or ionic silver, since the effects can in many cases be ascribed to the ionic form of silver (Ag+). Some studies have documented a more pronounced effect associated with nanosilver (e.g. Navarro et al., 2008), but the data so far are not conclusive.

After reviewing the current level of scientific knowledge of nanosilver, Aitken et al. (2009) stated that there is:

> …indicative evidence of the harm of silver nanoparticles at low concentrations on aquatic invertebrates, which suggests that the environmental release of silver nanoparticles will be detrimental for the environment and that any industry/institute using silver nanoparticles should consider taking the necessary steps to reduce or eliminate the potential exposure of the environment to these nanoparticles.

The authors further stated that there is insufficient evidence to make a risk assessment feasible for nanosilver. They did however go on to state … there is sufficient evidence to suggest that silver nanoparticles may be harmful to the environment and therefore the use of the precautionary principle should be considered in this case (Aitken et al., 2009).

Although preliminary, these studies on the nanoforms of TiO_2 and silver as well as carbon nanotubes are indicative of wider concerns that materials intentionally designed and engineered at the nanoscale to exhibit novel properties may also pose emergent risks. They therefore arguably trigger indicators of early warnings regarding the potential impacts of engineered nanomaterials, and as a consequence have led to increased attention and funding on various aspects of nanotechnological health and environmental risks (Hankin et al., 2011; Aitken et al., 2011; National Academy of Sciences, 2012).

22.5 Current (lack of nano-specific) regulation for nanomaterials

Whereas there has been some government funding of environmental, health and safety research into the potential adverse effect of nanotechnology and nanomaterials, there has been limited action from regulatory decision-makers towards changing existing technology-neutral regulation to take the unique properties of these materials into account. This is not surprising given the current state of scientific understanding of nanomaterial hazards and risks. Nor is this lag in regulatory response unique to nanotechnologies. As observed by Ludlow et al. (2009), the emergence of a new technology is, for example, likely to be perceived as a period of under-regulation in which the development of a specific regulatory response will occur subsequent to an initial period of research and development (R&D) and commercialisation. It must also be remembered that the regulatory frameworks under which nanomaterials currently fall are in any case not perfect, with many current regimes outdated and needing to be overhauled. Such recasts were needed prior to the commercialisation of nanotechnology and in many respects nanomaterials highlight many of the deficiencies that have existed for some time.

In an effort to elicit information regarding the types of nanomaterials being produced and imported into their jurisdictions, some governments, for example in the United Kingdom, USA and Australia, have implemented voluntary reporting schemes for nanomaterials (see, for example, DEFRA, 2006a and 2006b; US EPA, 2007; Weiss, 2005; NICNAS, 2008). Voluntary in nature, and somewhat onerous in operation, the schemes can be described as at best underwhelming. In the United Kingdom, for example, the Department for Environment, Food and Rural Affairs (DEFRA) received a total of 13 submissions over the life of the programme (2 years). The US scheme, which ended in 2009, fared a little better with the Environmental Protection Agency (EPA) receiving submissions from a total of 31 organisations (DEFRA, 2008; Hansen, 2009; Maynard and Rejeski, 2009). Given the lack of buy-in from stakeholders, it is not surprising that other jurisdictions, including France and California, have focused their efforts on mandatory nanomaterial reporting schemes.

Nanomaterials which are defined as chemical substances are regulated by the EPA under the Toxic Substances Control Act (TSCA) (US EPA, 2009a; Breggin et al., 2009). Pursuant to the TSCA, chemical substances are typically regulated on the basis of their Chemical Abstract Service (CAS) number; this system differentiates chemicals on the basis of their novel molecular structure and not their size. Silver, for example, is an existing chemical under the TSCA with its own unique CAS number. The TSCA Inventory is not able to differentiate nanosilver from bulk silver under the current framework, as the nanoscale and bulk versions of the substances both have the same CAS number. This approach ignores evidence that size and shape often lead to nanomaterials behaving in substantially different ways from their bulk counterparts. In the case of nano-silver, this failure to trigger regulatory oversight for the nanoscale substance has already raised considerable debate among various stakeholders, including those within the scientific community, due to its increasingly widespread use in consumer products (see, for example, Chen and Schluesener, 2008; Wijnhoven et al., 2009).

It is important, however, to note that the approach adopted under the TSCA is not unique, with chemical substances traditionally regulated on the basis of being existing or new based on their CAS number in most jurisdictions. At this stage, the majority of nanoscale substances are considered to be existing chemical substances under these frameworks.

One approach that the EPA has implemented in order to gather additional data on existing chemicals manufactured at the nansocale is through the use of its significant new use rule (SNUR). As explained by Widmer and Maili (2010), Section 5(a)(2) of the TSCA provides the EPA with the regulatory authority to request addition information on existing chemicals for the purpose of regulatory review where the proposed use of the chemical has significantly changed since it was initially reviewed. This regulatory tool has so far been employed for several types of nanomaterials, including single-walled and multi-walled CNTs. The EPA has proposed a more encompassing SNUR that would require companies that intend to manufacture, import or process new nanoscale materials based on chemical substances listed on the TSCA Inventory to submit a significant new use notice (SNUN) to the EPA at least 90 days in advance (Matus et al., 2011).

Even if a nanomaterial has a novel molecular structure, the US EPA must show that it may pose an unreasonable risk of significant exposure before manufacturers are required to undertake environmental, health and safety testing. These are just the data the agency needs to determine whether the substance poses an unreasonable risk — a classic regulatory paradox. Nonetheless, the EPA has proposed a data collection rule that would require the submission of certain existing data

on nanomaterials, including production volume, methods of manufacture and processing, exposure and release information, and available health and safety data. Despite these limitations and some recent moves towards reform of the TSCA, actual amendments have yet to be implemented (Davies, 2006 and 2009; US EPA, 2009b; Breggin et al., 2009). A December 2011, EPA Office of the Inspector General report (EPA OIG, 2011) found several limitations in the EPAs evaluation and management of engineered nanomaterials, including:

- Program offices do not have a formal process to coordinate the dissemination and utilisation of the potentially mandated information;
- EPA is not communicating an overall message to external stakeholders regarding policy changes and the risks of nanomaterials;
- EPA proposes to regulate nanomaterials as chemicals and its success in managing nanomaterials will be linked to the existing limitations of those applicable statutes;
- EPAs management of nanomaterials is limited by lack of risk information and reliance on industry-submitted data.

The Office of the Inspector General concluded that:

> 'these issues present significant barriers to effective nanomaterial management when combined with existing resource challenges. If EPA does not improve its internal processes and develop a clear and consistent stakeholder communication process, the Agency will not be able to assure that it is effectively managing nanomaterial risks.'

The EUs approach towards ensuring adequate protection of human health and the environment also relies heavily on chemical legislation, in particular the REACH Regulation, which was adopted by the Council and Parliament in 2006 and has been implemented progressively within the EU since 2007 (EP and CEU, 2006). As articulated in Article 1 of REACH, the purpose of the scheme is to ensure a high level of protection of human health and the environment. To fulfil this overarching objective, the regulation has expressly incorporated the precautionary principle into its text and sets out a no data, no market requirement under Article 5. Pursuant to this Article, REACH prohibits the manufacture or sale of any substance in the EU that has not been registered with the European Chemical Agency in accordance with the regulation. In this respect, REACH applies uniformly to existing and new chemicals, thus overcoming some of the difficulties associated with systems analogous to the TSCA.

As with the US system, however, REACH relies on the CAS identification system for the registration of chemical substances. One of the limitations of REACH yet to be addressed is related to whether a nano-equivalent of a substance with different physico-chemical and (eco)toxicological properties from the bulk substance would be considered as the same or different from the bulk substance under REACH. The regulation requires that a registration dossier be submitted to the European Chemical Agency containing information about manufacture and uses, classification and labelling, and guidance for safe use. If a nanomaterial is considered to be different from its bulk equivalent, hazard information has to be generated for this registration dossier if more than 1 tonne/year is produced. On the other hand, if the nanomaterial is considered to be the same as a registered bulk material, the appropriateness of the hazard information data submitted in the registration dossier is open to discussion (Chaundry et al., 2006; Breggin et al., 2009; Milieu and RPA, 2009). To date, the only amendment has been to annul the exemption status of carbon and graphite under REACH (CEC, 2008a; Breggin et al., 2009; Milieu and RPA, 2009).

It has recently been reported that companies have set up two different data-gathering groups on carbon nanotubes — one group of companies considers them as new substances while the other, including global chemical producing companies such as Arkema and Bayer, consider them as bulk graphite (Milmo, 2009). This example shows that whether nanomaterials are to be considered new or not is not just a theoretical question, but a source of confusion among regulated parties. Clearer guidance is expected on the issue from the European Commission as a result of the review of REACH in 2012.

If nanomaterials are considered to be different from their bulk counterpart, and if they are produced or imported in quantities of more than 10 tonnes, companies have to complete a chemical safety assessment. Companies are urged to use existing guidelines, however both the Commission of the European Communities (CEC, 2008a) and SCENIHR (2007) and others have pointed out that current test guidelines that support REACH are based on conventional methodologies for assessing chemical risks and may not be appropriate for assessing risks associated with nanomaterials. This means that,

although manufacturers and importers might be required to provide a chemical safety assessment, they cannot rely on the toxicological profile of the equivalent bulk material and cannot use existing test and risk assessment guidelines since these might not provide any meaningful results or be practically applicable, because of the limitations of conventional methods (Hansen, 2009; Milmo, 2009).

Pursuant to the text of the regulation, REACH is to be reviewed in 2012. It is generally expected that the revisions will include provisions related to nanomaterials. This is not surprising given the last-minute attempts to specifically include nanomaterials in the text of REACH during the second reading speech in 2006 (Bowman and van Calster, 2007). However, how REACH can be modified to expressly regulate nanomaterials — and the extent thereof — is still up for debate among politicians, regulators and stakeholders in the EU.

Expressly differentiating nanomaterials from their bulk equivalents in legislation is not new to the European Parliament and Council, as highlighted by the recent recast of the regulatory regime for cosmetics. While this recast was not initiated in response to the increasing use of nanomaterials in cosmetic products — but rather to increase transparency and streamline human safety requirements — considerable debate centred on the issue of nanomaterials (Bowman et al., 2010).

The Cosmetic Regulation, adopted in 2009, requires that all cosmetics that contain nanomaterials — which are defined as an insoluble or bio-persistent and intentionally manufactured material with one or more external dimensions, or an internal structure, on the scale from 1 to 100 nm (Article 2(k)) — be labelled. This will be done by placing the word nano in brackets after the nanoscale ingredient (Article 19(1)(g)) and will come into effect in 2012. As observed by Bowman et al. (2010), the regulation does not set a minimum threshold for this labelling requirement, which suggests that the mere presence of any nanoparticles in the cosmetic will be enough to trigger this requirement.

In addition to the labelling requirements, producers will have to provide a safety assessment of the nanomaterial used (European Parliament, 2009). The regulation also requires the European Commission to create a publicly available catalogue of all nanomaterials used in cosmetic products placed on the market … and the reasonably foreseeable exposure conditions (Article 16(10)(a)). Titanium dioxide, zinc oxide and lipid-based nanocapsules are examples of materials used in cosmetics such as sunscreens and moisturisers, while it has been reported that fullerenes have been used in a small number of facial creams (PEN, 2011).

Although the recast of the Cosmetic Regulation could be interpreted as a successful political effort to address the potential risk and transparency concerns relating to the use of nanomaterials in such consumer products, recent controversies surrounding the recast of the EU Novel Foods Regulation is evidence of the challenges that lie ahead for implementing future nano-specific revisions to existing legislation such as REACH. In regard to the EU Novel Foods Regulation, the European Parliament and the Council of the European Union recently failed to reach an agreement about changes to the instrument that would have ensured that the regulation includes foods modified by new production processes such as nanotechnology.

In its current form, the EU Novel Foods Regulation requires pre-market approval of all new food ingredients and products as well as safety assessments by European Food Safety Authorities on the composition, nutritional value, metabolism, intended use and level of microbiological and chemical contaminants. Studies on the toxicology, allergenicity and details of the manufacturing process may also be considered. Had the proposed revisions been adopted, such information relating to nanomaterials might have assisted in addressing current concerns surrounding their use in such applications in relation to nanoparticles (CEC, 2008b; Chaudhry et al., 2012).

The failure of the political parties to reach a compromise in regard to the Novel Foods Regulation should act as a warning sign of what to expect in regard to the likely negotiations around revisions to REACH, in which the stakes appear to be significantly higher for many parties. There is, we would argue, the potential for nanomaterials to be overlooked in the 2012 REACH revision discussion, with attention focusing instead on the myriad of other issues in play, including increasing dossier quality, limiting registration bureaucracy and lessening the impact of the regulation on small to medium enterprises.

Many of these issues are so controversial that the EU Commission is trying to downplay expectations for the 2012 REACH revision, arguing that no fundamental overhaul should be expected (EurActiv, 2011). In regard to nanomaterials, such efforts to maintain the status quo are worrying given the rapidly increasing evidence of risks as well as the swift growth of production and commercialisation

of nanomaterials and products. Such political statements are further worrying given the fact that the next formal REACH revision with relevance for nanomaterials is not scheduled before 2019 (EP and CEU, 2006). Substantial time is being wasted and effective regulation of nanomaterials is being pushed even further into the future although it is clear that immediate revisions are needed to address the most obvious and short-term limitations of the current legislative framework.

Against this background of legislative reform and associated debates, a number of other policy-related activities have occurred within the EU that have the potential to impact on the longer-term regulatory approach in relation to nanomaterials. For example, in 2009 the European Parliaments Environment Committee adopted a report on regulation of nanomaterials in general which calls for application of the no data, no market principle (as already incorporated in REACH) until safety assessments can be made (Schylter, 2009). While the fate of the proposal to implement this principle is unclear, it would appear to put additional pressure on the European Commission and the Council to address the potential risks of nanomaterials in the short to medium term.

Of arguably greater significance is the October 2011 recommendation of a definition of the term nanomaterial by the European Commission specifically for legislative, policy and research purposes. As set out in the Official Journal of the European Union (2011), a nanomaterial means:

> '… a natural, incidental or manufactured material containing particles, in an unbound state or as an aggregate or as an agglomerate and where, for 50 % or more of the particles in the number size distribution, one or more external dimensions is in the size range 1 nm-100 nm.
>
> In specific cases and where warranted by concerns for the environment, health, safety or competitiveness the number size distribution threshold of 50 % may be replaced by a threshold between 1 and 50 %.'

This definition differs considerably from the one in the Cosmetic Regulation (as articulated above) and was mooted in relation to the recast of the Novel Foods Regulation. It is therefore not surprising that this recommendation for a definition has not been without considerable controversy and global debate. According to Maynard (2011), the Commissions push for a one size fits all policy-based definition has the potential to sideline the science and may fail to capture what is important for addressing risk. Others within the scientific community have similarly expressed concern about the fact that the definition fails to take into account the key physico-chemical characteristics associated with potential risks (see, for example, ChemSec, 2011). In response to such criticisms, Hermann Stamm of the European Commission Joint Research Centre Institute for Health and Consumer Protection has contended …such a definition is urgently needed, especially for particulate nanomaterials. The aim should be to identify a general class of materials for attention — whether they are benign or hazardous (Stamm, 2011). It would seem that both camps have valid points; it is important that the crafting of such a definition does not act as a barrier to the effective regulation of nanomaterials.

The fact that existing legislation may have serious shortcomings when it comes to effectively regulating nanomaterials is not a new revelation. Government and independent reviews of the current regulatory frameworks and their applicability to nanotechnologies have now been published (see, for example, Chaudhry et al., 2006; Ludlow et al., 2007; European Commission, 2008). While the reports have varied in scope, method and the instruments that they have sought to evaluate, each has concluded that nanomaterials are currently captured under the existing regimes. However, the failure of such instruments to differentiate between nano-based products and their conventional counterparts has raised a number of concerns regarding the ongoing effectiveness of these regimes. A number of cross-cutting issues that appear to be common to most jurisdictions have now been examined through these reviews. The main areas of concern include that, as discussed above, the regimes do not differentiate between novel and known substances for the purposes of triggering regulatory oversight; that requirements for regulators to undertake safety evaluations on novel substances are triggered by mass or volume thresholds that are not tailored to the current production volumes of nanoscale materials; the lack of trust in the appropriateness of conventional risk assessment protocols and technical guidelines; and that risk thresholds and exposure limits established with existing methodologies are questionable (Ludlow et al., 2007; Baun et al., 2009).

In most countries, nanomaterials are still being treated within existing regulatory frameworks, under which the nanomaterials have inherited

the scope and features of the previous analogous regime (Stokes and Bowman, 2012). At this stage of development and commercialisation, countries such as the US, Australia, China and India, as well as the Organisation for Economic Co-operation and Development (OECD) and the EU, are proposing to treat nanomaterials primarily in the same manner as their conventional chemical counterparts (CEC, 2008; US EPA, 2007 and 2009b; OECD, 2009a and 2009b). In doing so, they have opted to retain the regulatory status quo despite the growing body of literature that suggests that some nanomaterials may cause harm to human and/or environmental health. This approach is not surprising given the current knowledge deficits in the evolving state of the scientific art and a general lack of express reliance on the precautionary principle in most jurisdictions.

Australia is one country that has explicitly moved to differentiate the requirements for some new industrial nanoscale chemicals. Recent administrative changes to its National Industrial Chemicals Notification and Assessment Scheme (NICNAS) (which may be considered analogous to the TSCA), which came into effect in January 2011, have sought to remove several of the low-volume/low-concentrate exemptions that usually apply to new industrial chemicals (NICNAS, 2010). While minor and incremental in nature, such a shift is indicative of how some countries may attempt to tweak their regulatory frameworks in the first instance rather than move towards more wholesale changes.

A number of features related to engineered nanomaterials indicate that the identification of hazards may deviate from what is known about regular chemicals. While our current approach to toxicity-driven risk is based on the paradigm attributed to Parcelsus, that it is the dose that makes the poison, and most extrapolations from toxicity tests assume that there is a correlation between mass and toxicity, this may not hold true for engineered nanoparticles (Baun and Hansen, 2008). As pointed out in a number of studies, other properties such as surface area and surface chemistry may be better indicators of the toxicity of some nanoparticles. This raises the question of how to determine the relevant exposure concentrations in laboratory studies and in occupational and environmental settings. In response to this concern, SCENIHR has stated that amendments have to be made to the existing technical guideline for risk assessment of chemicals since: due to the physico-chemical properties of nanoparticles, their behaviour and their potential adverse effects are not solely dependent on exposure in terms of the mass concentration … (SCENIHR, 2007).

Another issue that makes engineered nanomaterials, especially nanoparticles, different from conventional industrial chemicals is their ability to agglomerate (form clusters of weakly bound particles) or aggregate (form clusters of strongly bound particles) into stable particles. Aggregated particles are generally considered to be less prone to biological uptake, however it is not correct to assume that they are inherently safe. While the aggregation and agglomeration behaviour of engineered nanoparticles is only partly understood, it is known that their formation is concentration-dependent and that smaller aggregates/agglomerates may be formed at lower initial concentrations. If toxicity is inversely associated with aggregation/agglomeration size, our traditional understanding of concentration-response relationships may have to be altered for nanoparticles since higher concentrations may not necessarily result in higher toxicity. Furthermore, it is not known whether larger benign agglomerates may be broken down after inhalation or ingestion, resulting in smaller, and perhaps less benign, agglomerates or single particles. For these reasons the statement that lower exposure equals lower effects should be seriously scrutinised before it can be considered valid for engineered nanoparticles (Baun and Hansen, 2008; Baun et al., 2009).

In environmental hazard identification it is not only the toxicity, but also the degradability and potential for bioaccumulation that are used as parameters to identify chemical compounds that are environmentally hazardous. Very few studies have addressed these two parameters for engineered nanomaterials (Stone et al., 2010; Mikkelsen et al., 2011) and, as described above, serious concerns have been raised about whether the knowledge built up for regular chemicals can be transferred to nanoparticles. This led the SCENIHR (2007) to conclude that: The criteria used for persistence, bioaccumulation and toxicity (PBT) assessment applied for substances in soluble form should be assessed for applicability to nanoparticles.

Finally, in order to take the unique properties of any type of nanoparticles into consideration, it has often been argued that risk assessments of nanoparticles need to be completed on a case-by-case basis (see for example, SCENIHR, 2007 and 2009; Stone et al., 2010). Past experiences with case-by-case risk assessment of regular chemicals indicates that such an approach can be very time- and resource-intensive even with well-defined data demands and hence one has to wonder whether this is the most appropriate approach when it comes to risk assessment of nanoparticles. The

situation for these is further complicated by the fact that the hazard characteristics will be linked not only to the chemical identity but also to a number of other characteristics and their combinations. For example, it has been claimed that there are up to 50 000 potential combinations of single-walled carbon nanotubes (SWCNTs), depending on their structural type, length, surface coating, manufacturing processes and purification method (Schmidt, 2007). Each of these 50 000 SWCNTs may have different chemical, physical and biological properties that determine their overall hazard. Although not all of them are expected to be of commercial relevance, there are many kinds of nanoparticles, such as fullerenes, quantum dots, and metal and metal oxide nanoparticles, which imply a great complexity in performing case-by-case risk assessments for nanoparticles.

22.6 Late lessons from early warnings for nanotechnology

A comparison between the EEA recommendations made in 2001 and the current situation for nanotechnology shows that stakeholders are doing some things right, but we are still in danger of repeating old, and potentially costly, mistakes. In this section we briefly discuss the current development of regulation and environmental, health and safety research in view of the late lessons from early warnings learned by the EEA in 2001.

22.6.1 Lessons 1–3: heed the 'warnings'

According to *Late lessons from early warning* Volume 1. 'No matter how sophisticated knowledge is, it will always be subject to some degree of ignorance (i.e. inevitable surprises, or unpredicted effects). To be alert to — and humble about — the potential gaps in those bodies of knowledge that are included in our decision-making is fundamental' (EEA, 2001).

Perhaps more than any preceding technology, the early development of nanotechnology has been characterised by discussions of potential risks and the need for regulatory reform (Grieger et al., 2009; Fiedler and Reynolds, 1994). Such discussions have always been an integral part of the government-led National Nanotechnology Initiative (NNI) in the US, for example, while in the EU the landmark report published by the Royal Society & Royal Academy of Engineering (RS and RAE) in 2004 emphasised the need to address uncertainties regarding the risks of nanomaterials (RS and RAE, 2004). Levi-Faur and Comhanester (2007) have observed that unlike other cases where the discussion of the associated risks has followed the development of new technologies, the discussion on the proper regulatory framework for the governance of nanotechnology risks is accompanying the development of the technology and the associated products themselves. While hard government action may still be limited, we have however seen the emergence of a number of nano-specific self-regulatory activities within industry, including codes of conduct, guidance documents and risk assessment/management frameworks (Bowman and Hodge, 2009; Meili and Widmer, 2010). Voluntary in nature, they sit within the shadow of formal regulatory obligations and do not seek to usurp legislative requirements.

Currently, most economies investing in nanotechnology season discussions about future directions in research with questions concerning potential risks and how to manage them. Yet despite some moves (for example, the funding of early investigations into environmental, health and safety risks) to respond to ignorance and uncertainty rather than simply discuss them, coordinated action seems slow to emerge. The EEA report recommends looking out for warning signs such as materials that are novel, bio-persistent, readily dispersed or bioaccumulative, and/or materials that lead to irreversible action (such as mesothelioma caused by the inhalation of asbestiform fibres).

These warning signs are clearly relevant to many nanomaterials, some of which have novel properties, may be capable of being incorporated in highly diverse products, may be transported to places in the human body in new ways, such as across the blood, brain or placental barriers, and may be designed to be persistent. Too little is known at this early stage of the technologys development trajectory to predict the environmental fate of many nanomaterials, and appropriate documentation of environmental dispersion through monitoring is not expected in the short term (SCENIHR, 2007). The extent to which specific nanomaterials are bioaccumulative or lead to irreversible impact is largely unknown, but the current state of knowledge suggest that the potential exists for such behaviour under some circumstances (Moore, 2006; Stone et al., 2011; Mikkelsen et al., 2011) (see Box 22.1 on how EEAs warning signs apply to C60 and CNTs).

The global response to these warning signs may be described, at least in our view, as patchy at best, with governments being slow, and sometimes complacent, regarding the need to gather essential data, for example on production, use patterns and the effectiveness of current types of personal protection

equipment (see Section 22.5 on the current regulation of nanomaterials). Saying this, it is important to acknowledge that efforts to date have been better than those seen in response to the emergence of earlier technologies, but they are still far from ideal.

A number of reports have made specific recommendations on developing responsive research strategies (see for instance Oberdorster et al., 2005b; Maynard et al., 2006; Tsuji et al., 2006; SCENIHR, 2006; National Academy of Sciences, 2012). For example Maynard et al. (2006) called for:

- the development of strategic programmes that enable relevant risk-focused research, within the next 12 months;
- the development of instruments to assess exposure to engineered nanomaterials, within the next 3–10 years;
- the development of robust systems for evaluating the health and environmental impact of engineered nanomaterials over their entire life, within the next 5 years;
- the development and validation of methods to evaluate the toxicity of engineered nanomaterials, within the next 5–15 years;
- the development of models for predicting the potential impact of engineered nanomaterials on the environment and human health, within the next 10 years.

Calls for research proposals in the European seventh framework programme reflect some of these recommendations, and a number of countries are beginning to develop integrated environment, health and safety (EHS) research programmes, such as the cross-agency risk-research strategy published by the NNI (2008). However, there are still critical gaps in our knowledge that need to be addressed in EHS research programmes. These include, but are not limited to, epidemiological investigation of exposed populations; the behaviour and impact of ingested nanomaterials; investigation of the fate, behaviour and (eco)toxicity of nanomaterials throughout the life cycle; and interactions between nanomaterials and environmental matrices such as natural organic matter and sediments and other pollutants already present in the environment (Maynard 2006; Baun et al., 2008; Grieger et al., 2009; National Academy of Sciences, 2012).

Research strategies that target recognised areas of uncertainty (including the applicability of current testing procedures and equipment, how to assess human and environmental effects, and how to do exposure assessments and characterisation of nanomaterials) should be relatively easy to develop, as the critical questions to be addressed are generally agreed (Maynard et al., 2006; Grieger et al., 2009). But the EEA report highlights the dangers of entirely missing important areas because the right questions have not been identified, leading to blind spots in our understanding. The report cites the widespread use of anti-microbials as growth promoters in food animals, methyl tert-butyl ether (MTBE) and tributyltin as three examples where conventional thinking led to inappropriate assumptions and a lack of recognition of broader issues. At present it is not clear whether the recognition of ignorance in the field of nanomaterial-related EHS risks is sufficient to avoid blind spots, or whether the novel properties of nanomaterials inherently will generate blind spots because of their novelty (see Box 22.1).

22.6.2 Lessons 4 and 11: reduce obstacles to action

Even when research throws up useful information, it may be ignored and overlooked through what the EEA authors call institutional ignorance. They cite cases where regulators have made inappropriate appraisals because of the blinkers imposed by their specific disciplines — such as the preoccupation of medical clinicians with acute effects when dealing with radiation and asbestos. There is a real danger of similar errors being made with nanotechnology, which crosses many fields of expertise. One needs to draw on physics, chemistry, computer sciences, health, environmental sciences and law to understand nanomaterial properties and risks (Karn et al., 2003). A number of multidisciplinary centres for nanoscience and nanomanufacturing have been established around the world, but only a few of these address health, environmental and social aspects. It is critical to set aside resources to create an infrastructure that gets people working together across disciplines (Lynch, 2006).

Interdisciplinary obstacles also affect regulatory oversight in decision-making (EEA, 2001). In a discussion on how nanomaterials were covered under the TSCA, the US EPA appeared to be constrained by a world-view rooted in chemistry, stating that the sole factor that determines whether a nanomaterial is legally classified as new depends on whether it has a unique molecular identity (US EPA, 2007). However, it is now clear that characteristics other than molecular identity — such as particle size and shape — can affect exposure and response to engineered nanomaterials (SCENIHR, 2007).

Box 22.1 EEA's warning signs applied to fullerenes and carbon nanotubes

To acknowledge and respond to ignorance, i.e. potential risks that you do not know (EEA, 2001), seems almost impossible when it comes to a rapidly emerging technology such as nanotechnology. In cases of ignorance, the EEA recommends being proactive, alert and humble about the state of the scientific evidence indicating harm as well as looking for warning signs such as novelty, persistence, ready dispersion, bioaccumulation, leading to potentially irreversible action. These lessons bear an uncanny resemblance to many of the concerns now being raised about various forms of nanomaterials such as the two types of nanoparticles: C60-fullerenes and carbon nanotubes (CNTs).

No single exhaustive taxonomy exists for novel materials and, as noted by the Royal Commission on Environmental Pollution (RCEP, 2008), it is unlikely that one is possible or even necessarily desirable. That said, one could argue that nanomaterials are novel by definition in the sense that many of the definitions of nanotechnology require either novel applications, whatever they might be, and/or that nanomaterials exhibit novel properties compared to bulk materials (see for example the definitions cited earlier in the chapter). In the following, C60 and CNT will be used as illustrative examples of nanomaterials that are novel in their use pattern and properties.

At present, very few studies have addressed the degradability of engineered C60 and CNT, but, because of their structure, they are expected to be persistent in the environment. Both C60 and CNT are often seen as anthropogenic, however they may also be formed in forest fires or volcanic eruptions. Although the sources of naturally occurring carbon-containing nanoparticles are different from the engineered ones, the particles are, from a chemical point of view, identical, and geological studies have shown that both C60 and CNT may be very resistant to degradation. Thus, Becker et al. (1994) observed C60 in 1.85 billion year-old shock-produced breccias of the Sudbury impact structure in Ontario, Canada and C60 has also been found in a 70 million-year-old fossil dinosaur eggshell from Xixia, China (Zhenxia et al., 1998). CNT and fullerenes have been extracted from 10 000-year-old ice-core melt samples (Murr et al., 2004).

Whether C60 and CNT are readily dispersed depends on a number of factors such as the environmental compartment considered (e.g. air, water, soil). Little is known about the fate and transport of C60 and CNT in air and soil, but under laboratory conditions hydrophobic nanoparticles such as C60 and CNT have been found to aggregate rapidly (Fortner et al., 2005; Baun et al., 2008). As a result of sedimentation, they may therefore not be readily dispersed after emission to the aquatic environment. However, the dispersivity of nanomaterials can be altered, for example by changing the surface chemistry, and hydroxylated C60, for example, is much more soluble in water (Sayes et al., 2004). What happens in the environment, and how interaction with natural substances (e.g. humic substances) and water-living organisms influence dispersion, are however unclear (Roberts et al., 2007; Hansen et al., 2009).

The potential bioaccumulation of nanomaterials is believed to depend on a combination of the specific properties of the nanomaterial (such as biodegradability, lipophilicity, aqueous solubility) that influence overall bioavailability. For example carbon nanotubes are known to be non-biodegradable, insoluble in water and lipophilic, which indicates that carbon nanotubes have a potential to bioaccumulate. However, there is a profound lack of studies addressing the issue of bioaccumulation of engineered nanomaterials (RCEP, 2008).

Because of the lack of scientific research, it is currently almost impossible to say whether or not the production and use of nanomaterials could lead to potentially irreversible action. Some studies have indicated that some CNTs might be able to cause effects that would be classified as irreversible (e.g. Poland et al., 2009; Smith et al., 2007). Widespread production and use of C60 and CNT will inevitably lead to the release of these materials into the environment, and hence an irreversible action, as they would be practically impossible to locate and recover after release (Hansen et al., 2009).

22.6.3 Lessons 5 and 8: stay in the real world

The EEA panel assertion from 2001 (EEA, 2001) that it is often assumed that technologies will perform to the specified standards. Yet real life practices can be far from ideal echoes claims made of nanotechnology. In 2006, Rick Weiss of the Washington Post visited a nanomaterial company expecting to see a high-tech work environment. Instead, he found the future looked a lot like the past with men in grease-stained blue coats […] story-tall spray-drying machines […] noisy milling operations and workers with face masks covered by a pale dust stemming from emptying buckets of freshly made powders (Weiss, 2006).

It is often assumed that nanotechnology will be conducted with small quantities of material, within sealed processes. Reality can be very different and the past tells us that persistent substances used in closed settings or incorporated in solid matrices (like PCBs) will eventually end up in the environment. Moreover, there is evidence that the R&D community is entrenched in the philosophy that basic research will ultimately solve real-world problems through a one-way process of knowledge diffusion, and that they do not need to worry about EHS issues. A study by Powell (2007) found that many scientists who are developing new nanotechnologies do not think that nanotechnologies pose new or substantial risks and that concerns about risks are based on invalid science (Powell 2007). This is a mistake in our view, and there is plenty of historical evidence to support this view in the first EEA report *Late lessons from early warnings* (EEA, 2001), including the sorry tale of asbestos. Clearly, applied researchers and the EHS community need to be involved in informing policy decisions. According to the EEA, this includes making use of the information that workers and users can bring to the regulatory appraisal process, although such knowledge of course needs as much critical appraisal as specialist knowledge.

Nanotechnology is complex, and it can be argued that non-experts have little to contribute to its safe development and use currently. But non-specialists intimately involved with a technology can bring unique insight to the table since they may have some of the clearest ideas about what is important, what has the potential to work and what may not (Gavelin et al., 2007).

22.6.4 Lessons 6 and 9: consider wider issues

Concerns have often been raised that speculation on risks overshadows real benefits, or that an unbalanced promotion of possible benefits will prevent potential risks from being critically scrutinised.

Nanotechnology is in such a position (Maynard et al., 2011). Pros include economic benefits, improved materials, reduced use of resources and new medical treatments (RS and RAE, 2004; Roco and Bainbridge, 2005), while cons mainly revolve around worker health, consumer exposure and environmental impacts. Comparisons have also been made between ultrafine particles in the atmosphere — which are known to cause health problems — and specific types of nanoparticles (RS and RAE, 2004, Oberdorster et al., 2005b; Maynard et al., 2006).

It is generally difficult to evaluate whether proclaimed pros and cons are valid both in the short and the long term. However, the process of determining more likely scenarios is vital to the future development of sustainable nanotechnologies. As we emerge from the first flush of nano-enthusiasm and begin the hard work of translating good ideas into viable products, this is a lesson that is more relevant than ever if an appropriate balance between benefits and risks is to be struck (Maynard et al., 2011).

If proclaimed pros do not materialise in the foreseeable future despite heavy public investments, or if projected cons are not investigated, but later prove to be significant, decision-making processes will be undermined, and public trust may be compromised.

A key feature of the public reaction to the emerging evidence for bovine spongiform encephalopathy (BSE) in the late 1980s was the surprised revulsion that cows and other ruminants were being fed on offal and bodily wastes. The EEA panel in 2001 speculates that accounting for wider social values at an earlier stage might have limited the scale of BSE problems. The extent to which societal interests and values can prevent real risks with emerging technologies is debatable. Yet these interests and values influence what is considered acceptable, and consequently what is accepted or rejected. Nanotechnology is proclaimed to have a tremendous potential to address major global challenges like cancer, renewable energy and provision of clean water. Yet precisely because of the widespread applications of nanotechnology, citizens around the world are as much stakeholders in the technology as the governments, industries and scientists promoting it. But so far the deliberate engagement of citizens and the public in risk-related decisions on nanotechnology has been very limited.

22.6.5 Lesson 7: evaluate alternative solutions

This lesson may simply be summarised by saying, dont become so enamoured by a new technology, that you are blinded to alternative solutions. Past lessons have shown there is a tendency for proponents to justify heavy investment in a new technology by promoting its application to every conceivable problem, with the result that alternatives are insufficiently scrutinised, and the most appropriate solution not always selected.

While nanotechnology is diverse and widely applicable, this would seem a potential pitfall as

the number of nanoscale solutions looking for a problem continues to grow. And with international nano-fever running high, everyone wants to be at the forefront of the nanotechnology revolution. In many cases, nanotechnology will provide the means to overcome challenges — but the lesson to be learnt is the need to find the best solution to a given problem, rather than to squeeze a solution out of the latest technology. This means that, in some cases, while nanotechnology **could** be used, it may be questionable whether it **should**. In the context of such discussions, assessment of alternatives can be used to provide helpful guidance in case of doubt as it provides a structured approach to examining a wide range of alternatives (e.g. technologies, processes, social changes) to potentially hazardous activities (Rossi et al., 2006).

Alternatives assessment is normally a six-step process that includes:

1) identification of target(s) for action;

2) characterisation and prioritisation of end uses;

3) identification of alternatives;

4) evaluation and comparison of alternatives;

5) selection of preferred alternative(s); and

6) review of selected alternative.

The scope of any alternatives assessment should be broad enough to examine the service and function that it requires as opposed to just examining, for example, the opportunities of substituting a hazardous chemical with a less hazardous one. In the case of nanomaterials this means that alternatives need not simply be nanomaterials, but may include the process or administrative changes that reduce the need for the materials in the first place (Rossi et al., 2006; Linkov et al., 2009). While alternatives assessment is generally applied to existing technologies and problems, the thinking about alternatives can be applied at the design phase, which did not occur in the case of nanotechnology.

22.6.6 Lesson 10: maintain regulatory independence

The EEA panel found evidence in the case studies that interested parties are often able to unduly influence regulators. As a result, decisions that might reasonably have been made on the basis of available evidence were not taken. For example according to the EEA panel one factor in the slow UK response to BSE was that the governmental regulatory body was responsible first to the industry and only second to consumers. In many countries, the organisations responsible for overseeing the development of nanotechnologies through R&D are the very ones that address health and environmental issues.

In testimony to the US Congress House Committee on Science and Technology, Richard Dennison of the Environmental Defense Fund, a non-profit environmental campaign group, wrote that:

> 'we have become convinced that a conflict of interest has arisen from the decision to house within NNI the dual functions of both seeking to develop and promote nanotechnology and its applications, while at the same time aggressively pursuing the actions needed to identify and mitigate any potential risks that arise from such applications. That conflict of interest is both slowing and compromising efforts by NNI and its member agencies and departments to effectively address nanotechnologys implications' (Denison, 2007a).

Concerns that such a conflict of interest could jeopardise effective environmental, health and safety research were most recently articulated by the US National Academies of Science in a research strategy for environmental, health and safety aspects of engineered nanomaterials:

> 'There is a concern that the dual and potentially conflicting roles of the NNI — developing and promoting nanotechnology and its applications while identifying and mitigating risks that arise from such applications — impede implementation and evaluation of the EHS risk research…To implement the research strategy effectively, a clear separation of management and budgetary authority and accountability is needed between the functions of developing and promoting applications of nanotechnology and of understanding and assessing potential health and environmental implications. Such a separation is needed to ensure that progress in implementing an effective nanotechnology-related EHS research strategy is not hampered' (National Academy of Sciences, 2012).

While an integrated approach to understanding the risks and benefits of nanotechnology is critical, when the promoters of nanotechnology, whether government or industry, have a strong

influence over oversight, independent regulatory decision-making becomes compromised. Perhaps more insidiously, research and development decisions end up being influenced by what will ultimately promote the technology, rather than what will protect producers, users and the environment.

22.6.7 Lesson 12: avoid paralysis by analysis

In the face of uncertainty, a frequent response is to call for more research before action is taken. Yet, as the EEA panel note, Experts have often argued at an early stage that we know enough to take protective action (EEA, 2001). Good policy depends on identifying the right balance between information and action while keeping the end-point (preventing harm) in mind, and building in review procedures for course corrections.

Twenty years have elapsed since first indications of nanomaterial harm were published (Ferin et al., 1990; Oberdorster et al., 1990), and in the intervening time an increasing body of literature has been developed on how nanomaterials interact with cells, mammals and aquatic organisms (Hansen et al., 2007; Stone et al., 2010). Yet many governments still call for more information as a substitute for action; there are indications that understanding and managing the risks of engineered nanomaterials are being paralysed by analysis. While it is clear that more scientific information is needed, we need to act on what we know now, to enable industry to produce and market nanotechnology-enabled products that are as safe as possible. Engineered nanomaterials are already on the market, and in some cases the risks are poorly understood and may therefore be ineffectively regulated. Applying current knowledge to nanotechnology oversight will not solve every problem, but it will help prevent basic mistakes being made while the knowledge needed for more effective oversight is developed.

One way to facilitate decision-making on nanomaterials may be to develop design criteria to identify which nanomaterials are of higher or lower concern because of their intrinsic properties or use or exposure characteristics. For example, Maynard et al. (2011) have proposed principles of emergent risk, plausibility and impact to identify materials of high concern. Further, a thorough consideration of health and safety implications at the design phase of a nanomaterial, including consideration of possible safer production methods and alternatives to the material, will facilitate decisions as economic interests are not fully entrenched at that point.

22.7 So have we learnt the lessons?

Although the EEA panel was writing about existing technologies, and some of the 12 lessons learned are not directly applicable to all emerging technologies, many of the lessons are directly relevant to nanotechnology today. Yet the picture is not as bleak as it might be. Table 22.1 provides a qualitative analysis of 10 main EU Member State national and multilateral scientific reports that have provided input to the EU regulatory and political decision-makers on nanomaterials over the course of the last decade. For each of the late lessons from the first volume of this publication (EEA, 2001) we have provided an assessment of whether the lessons there have been mentioned in passing (+), have been substantially discussed and/or analysed (++), or whether a strategy to address a given lesson has been suggested (+++). Blanks means that no noticed was taken of these lessons.

While progress in developing sustainable nanotechnologies has been slow, the qualitative analysis above indicates that policy makers and relevant stakeholders seem to have learnt at least some of the lessons: they are asking more critical questions early on about health and environmental fate and effects; developing collaborations that cross disciplines, departments and international boundaries; beginning the process of targeting research to develop relevant knowledge; engaging stakeholders; and asking whether existing oversight mechanisms are fit for purpose.

But are we doing enough? The second half of Table 22.1 provides a qualitative analysis of the main EU regulatory actions taken over the course of the last decade in response to the twelve lessons.

The Cosmetic and the Biocides regulations acknowledge that there is a high level of scientific uncertainty regarding the risks of nanomaterials. They require industry to submit data and information about physical/chemical characteristics and the exposure and toxicological profile of a given nanomaterial, thereby providing some elements of a strategy toward long-term environmental and health monitoring to help identify and reduce scientific blind spots. The burden of providing health and safety data being placed on industry also helps to overcome the problem of paralysis by analysis since companies are in theory not able to market their products without proper data and information about risks. To some extent, regulatory independence is also ensured in the Cosmetic and the Biocides regulations in the sense that the scientific

Table 22.1 Late lessons learned, as indicated in 10 EU Member State nanomaterials reports

Lessons (EEA, 2001)	Royal S& RAE (2004)	DG Sanco (2004)	Chaundry et al. (2006)	IRGB (2006)	SCENIHR (2007)	RCEP (2008)	CEC (2008)	Stone et al. (2009)	RIVM (2009)	Aitken et al. (2009)	SCENIHR (2009)	Cosmetic Regulation	Biocides Regulation	Food Additives Regulation	RoHS * and WEEE **
Acknowledge and respond to ignorance, uncertainty and risk in technology appraisal	++	++	++	++	++	++	+	++	++	++	++	++	++	+	+
Provide long-term environmental and health monitoring and research into early warnings	++	++		++	+	++	+	++	+		++	++	++	+	+
Identify and work to reduce scientific blind spots and knowledge gaps	++	+		+	++	++	+	+			++	++	++	+	+
Identify and reduce interdisciplinary obstacles to learning	++			+	+	+									
Account for real-world conditions in regulatory appraisal		+										+	+		+
Systematically scrutinise claimed benefits and risks	+	+		+		+							++		
Ensure use of lay knowledge, as well as specialist expertise	++	+		++											
Evaluate alternative options for meeting needs, and promote robust, diverse and adaptable technologies															
Account fully for the assumptions and values of different social groups	++	+		++		+									
Maintain regulatory independence of interested parties while retaining an inclusive approach to information and opinion gathering	+											++			
Identify and reduce institutional obstacles to learning and action	++			+		+									
Avoid paralysis by analysis by acting to reduce potential harm when there are reasonable grounds for concern	+	+		+	++	+						+	+	+	+

Note: A empty cell indicates no notice taken
+ mentioned in passing; ++ substantially discussed and/or analysed; +++ strategy suggested/implemented
* Restriction of Hazardous Substances Directive; ** Waste Electrical and Electronic Equipment Directive.

committees such as the European Commissions Scientific Committee on Consumer Safety and the European Food Safety Agency that are responsible for evaluating the health and safety data and the information provided by industry are independent from the regulatory agencies that promote the use of nanomaterials in those same products. However, these agencies have recently come under attack for not being independent from industry interests (Muilerman and Tweedale, 2011).

In the light of the 14 case studies in the first volume (EEA, 2001), the question here seems not to be whether we have learnt the lessons, but whether we are applying them effectively enough to prevent nanotechnology becoming yet another future case study on how not to introduce a new technology. Despite a good start, it seems that we have become distracted by the way that nanotechnology is being overseen by the very government organisations that promote it; research strategies are not leading to clear answers to critical questions; collaboration continues to be hampered by disciplinary and institutional barriers; and stakeholders are not being fully engaged, or not being engaged early enough. In part this is attributable to bureaucratic inertia, although comments from some quarters, such as risk research jeopardises innovation or regulation is bad for business, only cloud the waters when clarity of thought and action are needed.

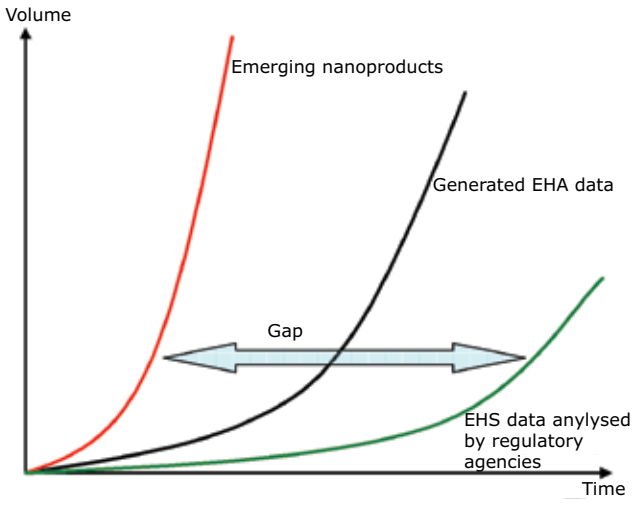
If we are to realise the commercial and social benefits of nanotechnology without leaving a legacy of harm, and to prevent nanotechnology from becoming a lesson in what not to do for future generations, perhaps it is time to go back to the classroom and re-learn these late lessons from early warnings.

22.8 Precautionary strategies for nanomaterials

Linkov et al. (2009) have pointed out that there seems to be a substantial time lag between the emergence of products containing nanomaterials, the generation of EHS data and their subsequent use by regulatory agencies (see Figure 22.2).

They argue that this results from these agencies having limited resources and that it will take time for regulatory agencies to adjust risk assessment procedures so that they are applicable to nanomaterials. The precise extent of the time lag is unclear, but there is historical evidence indicating that it will not be less than two decades. In 1977, Lawless and his team analysed 45 episodes of public alarm or strong concern over various technologies including reproduction and genetics, food and medicine, and environmental problems. A common theme identified by Lawless was that social institutions grapple with the problem for varying amounts of time while papers on effects increase in the technical literature. On average, this delay is one or two decades (Lawless, 1977). Volume 1 of this publication (EEA, 2001) found that the time gap between the first report of harm and effective regulatory action was decades, and in some cases, even over a century. Although the cases analysed by the EEA and Lawless may not reflect all emerging technologies, they do represent plausible worst-case scenarios. Given that the shelf life of specific new nanotechnology products is likely to be short because of continuous technology improvements, Linkov et al. (2009) argue that the approaches to regulating these materials should be adjusted to the evolving nature of the field. The question however is how this should be done.

Figure 22.2 Schematic representation of the emergence of nanotechnology products in comparison with generated EHS data



Source: Reprinted with permission from Linkov, I. et al., 2009.

RCEP (2008) has pointed out that existing regulatory approaches cannot be relied on to detect and manage problems before a novel technology such as nanomaterials has become ubiquitous. Although, this observation is rather bleak and discouraging, several precautionary strategies have nevertheless been suggested over the past decade. Some have focused on providing recommendations on how to adapt existing legislation, for example Chaundry et al., 2006; Fuhr et al., 2007; Franco et al., 2007; Ludlow et al., 2007 and Breggin et al., 2009. Specific recommendations include clarification of key terms and definitions of nanotechnology and material properties; ensuring the relevance of the scope and objectives of existing legislation; clear definition of thresholds relevant to nanomaterials; and risk assessment of nanomaterials prior to or after release into the environment.

Others have focused on providing recommendations on how to adapt existing risk assessment methods and risk management procedures such as the nano-risk framework jointly developed by the American non-governmental organisation Environmental Defense and the DuPont Corporation (ED and DuPont, 2007). This framework describes a process for ensuring the responsible development of nanoscale materials, and is designed to be used iteratively at different stages of development including basic R&D, prototyping, pilot testing, test marketing, and finally when new information becomes available. The suggested framework consists of six distinct steps:

- develop the nanomaterial and its intended uses;
- develop nanomaterial hazard and exposure profiles along the full life cycle;
- evaluate information generated to assess the probability of nanomaterial risks;
- evaluate risk management options and recommend a course of action;
- decide alongside key stakeholders whether to continue R&D and production;

- update and re-execute the risk evaluation regularly and share appropriate information with relevant stakeholders (ED and DuPont, 2007).

A third series of recommendations from various stakeholders and experts, for example the International Council on Risk Governance (2007) and RCEP (2009), have a much broader focus and have provided recommendations on issues more relevant to the governance of emerging technologies and innovation. In addition to a wide range of recommendations focused on restructuring risk research and regulation of chemicals and emerging technologies, RCEP (2009) has called for the development of flexible and resilient forms of adaptive management to allow us to handle such difficult situations and emergent technologies while recognising the high degree of ignorance and uncertainty and the time it will take to address these. According to RCEP (2009), key elements of such a framework should be structured around modification and extension of the existing regulatory framework as a matter of urgency, and development of an early warning system including robust arrangements for monitoring complemented (and informed) by the full range of perspectives on innovation.

Similarly, ICRG (2006, 2007) has suggested an integrated analytic framework for risk governance, consisting of pre-assessment, risk appraisal, and judgment of tolerability and acceptability, with risk management and communication as integrated elements that provide connectivity between the other elements. Application of the framework to nanotechnologies has led to a number of recommendations that fall into five categories: improve the knowledge base; strengthen risk management structures and processes; promote stakeholder communication and participation; ensure social benefits and acceptance; and collaboration between stakeholders and nations.

Recently, the German Advisory Council on the Environment for the German Government has called for a multifaceted strategy that includes intensification of risk research, promotion of social dialogue, development of a single piece of nano-specific legislation based on the precautionary principle, establishment of a labelling and product register, and a reform of the current chemical, product and environmental legislation (SRU German Advisory Council for the Environment, 2011).

In many ways, these recommendations echo those made by the Royal Society and Royal Academy of Engineering in 2004 in areas such as health, safety and environmental impacts; regulatory, social and ethical issues; stakeholder and public dialogue; and ensuring the responsible development of nanotechnologies. Key recommendations include:

- Research into possible adverse health, safety and environmental impacts of nanomaterials, which the RS and RAE (2004) argue should be an integral part of the innovation and design process of products including nanomaterials.

- Avoidance of the release of manufactured nanoparticles and nanotubes into the environment as far as possible.

- Regulatory authorities to consider whether existing regulations are appropriate to protect humans and the environment and inclusion of future applications of nanotechnologies in their horizon-scanning programmes to ensure timely identification of any regulatory gaps.

- Consideration of whether ethical and social implications of advanced technologies (such as nanotechnologies) should form part of the formal training of all research students and staff working in these areas.

- Comprehensive qualitative work involving members of the general public as well as members of interested sections of society, and government funding of public dialogue around the development of nanotechnologies.

- Establishment of a group that brings together representatives of a wide range of stakeholders to look at new and emerging technologies and identify, at the earliest possible stage, areas where potential health, safety, environmental, social, ethical and regulatory issues may arise and advise on how these might be addressed.

While a regulatory, stakeholder engagement and R&D strategy are critical elements of a precautionary approach to nanomaterials, one must not forget the critical role of design in ensuring that technology development occurs in parallel with technology assessment. Nanotechnology development has occurred in the absence of clear design rules for chemists and materials developers on how to integrate health, safety and environmental concerns into the design of nanomaterials. This is not surprising given that most chemists and materials designers are not trained to recognise these issues. The emerging area of green nanotechnology offers promise for the future. For this type of focus on preventive design to occur, we will need a cultural transition: that chemists and materials developers

are educated on health, safety and environment; that environment, health and safety become quality concerns in the development of new materials, equal to economic and performance considerations; that research on the sustainability of materials is funded at levels significant enough to identify early warnings; and that regulatory systems provide incentives for safer and sustainable materials.

When it comes to addressing R&D gaps, specific legislative gaps, limitations in current risk assessment and risk management approaches as well as risk governance of nanotechnologies and other emerging technologies, a common denominator of all of these recommendations is that many of them are not or have yet to be successfully implemented by political decision-makers. As a result, there remains a developmental environment that hinders the adoption of precautionary yet socially and economically responsive strategies in the field of nanotechnology. If left unresolved, this has the potential to hamper our ability as a society to ensure the responsible development of nanotechnologies.

Table 22.2 Early warnings and actions

1974	Taniguchi first uses the term nanotechnology referring to the ability to engineer materials precisely at the nanometre (nm) level
1981	Scanning tunnelling microscope developed
1985	Atomic force microscope developed
1985	Fullerenes discovered at Rice University
1986	Drexler raises concern about potential risks of nanotechnology
1991	Iijima discovers carbon nanotubes
1992	Surface area found to be a better descriptor than mass for the adverse effects observed in rats exposed to TiO_2
2000	National Nanotechnology Initiative (NNI) established by the US Government
2003	Making analogies with ultrafine particles and asbestos, the Royal Society and Royal Academy of Engineering in the UK calls for more research and for avoidance of the release of manufactured nanoparticles and nanotubes into the environment
2004	Single-walled carbon nanotubes of different purity found to induced dose-dependent granulomas and interstitial inflammation in the lungs of mice
2006	Project for Emerging Nanotechnologies, Woodrow Wilson International Center for Scholars launches online consumer nanoproduct inventory totalling 212 products
2006	2 year voluntary reporting program set up in the United Kingdom by DEFRA
2007	Publication of Nano-risk framework jointly developed by the American non-governmental organisation Environmental Defense and the DuPont Corporation
2007	Voluntary reporting program set up in the US by the US EPA
2008	Long multi-walled carbon nanotubes are found to produce adverse effects qualitatively and quantitatively similar those caused by long asbestos
2009	Voluntary reporting program end in the US receiving only 31 submissions
2009	Cosmetic Regulation in Europe adopted that requires labelling and safety assessment of nanomaterials
2009	European Parliaments Environment Committee call for application of the no data, no market principle in regard to regulation of nanomaterials
2011	Australia explicitly moves to differentiate the requirements for some new industrial nanoscale chemicals in its National Industrial Chemicals Notification and Assessment Scheme
2011	NIOSH (2011) has determined that ultrafine TiO_2 should be considered a potential occupational carcinogen
2011	European Commission publishes proposal of a definition of nanomaterials

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Part D Costs, justice and innovation

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23 Understanding and accounting for the costs of inaction

Mikael Skou Andersen and David Owain Clubb

In political decision-making processes, the burden of proof is often distributed such that policymakers only respond to early warning signals from environmental hazards once the costs of inaction have been estimated.

This chapter revisits some key environmental issues for which estimates of costs of inaction have been carefully developed over many years of research. The aim is to consider the methodological challenges involved in producing estimates that are credible and appropriate rather than present specific estimates for these costs.

The case studies also provide insights into how early warning signals might provide a basis for estimating the costs of inaction, when the science base is less consolidated. For example, the case of nitrates in drinking water illustrates that a precautionary approach to the costs of inaction is quite conceivable. The phase-out of ozone-depleting substances, where early-warning scientists successfully alerted the world to the damaging effects of chlorofluorocarbons (CFCs), provides another important case because additional impacts for global warming actually cause the costs of inaction to be considerably higher than initially believed. This is a reminder that figures for the costs of inaction have often been grossly underestimated.

Finally, in the case of air pollution, making use of different estimates for mortality risk avoidance will help decision-makers to see that there are higher- and lower-bound estimates for the costs of inaction. Even if the lower-bound estimates are perhaps too conservative, with a bias towards health effects, they will in many situations encourage more rather than less abatement effort. Reducing emission loads will also tend to bring relief for the intangible assets of biodiversity and nature.

Making the best use of environmental science and modelling helps to make environmental protection and precaution a priority. Producing cost estimates should not be left to economists alone, but should rather be seen as a starting point for a broader discussion, featuring also the relevant expertise in health, ecology, demography, modelling and science. Well researched estimates, based on interdisciplinary collaboration, can strengthen some of those scattered and diffuse interests, which during the ordinary processes of policy-making have difficulty making their voices heard.

23.1 Introduction

The first volume of *Late lessons from early warnings* reminded us that:

'The costs of preventive actions are usually tangible, clearly allocated and often short term, whereas the costs of failing to act are less tangible, less clearly distributed and usually longer term, posing particular problems of governance. Weighing up the overall pros and cons of action, or inaction, is therefore very difficult, involving ethical as well as economic considerations, as the case studies illustrate' (EEA, 2001:3-4).

In the decade since its publication, there has been considerable interest in addressing and understanding the possible costs of inaction. The Stern review on 'The Economics of Climate Change' for the UK government is a prominent example of how an economist specialising in risk assessment was able to provide credible estimates of the global costs of failure to prevent climate change (Stern, 2007). Stern warned that the likely consequences of continued, unabated global warming would be in the magnitude of 5 % of global GDP annually. He estimated that the costs could rise as high as 20 % when including non-market costs for health and environment and if we factor in the effects on developing countries in an equitable way. In contrast, according to Stern's review, the average expected costs of mitigation for stabilising greenhouse gas concentrations are likely to be about 1 % of GDP annually, while unlikely to exceed 3.5 % of GDP annually.

The Stern review has been subject to much attention and scrutiny, mainly over the so-called 'discount rate' (a measure of how to value costs and benefits in the future — see section below) it used. However, its basic finding that the costs of preventive action were less than the harm caused by inaction was broadly accepted. The Review influenced the political debate, and the UK government subsequently passed the Climate Change Act, which called for an 80 % reduction in greenhouse gases by 2050. The Stern review also influenced the European Council in its decision in March 2007 to embark on a more active climate policy.

The subject of the 'costs of inaction' has subsequently become a recurrent topic in deliberations over climate policy, and more recently, with respect to biodiversity. The OECD (2008) has provided an overview of studies addressing the costs of inaction for a range of other environmental issues, including air pollution, water pollution, natural resource depletion and industrial accidents. To understand the costs of inaction, one must express in monetary terms the damage that will be caused if no or limited intervention is agreed. Stern did this by taking a risk-analysis approach, which unlike the more static cost-benefit approach, emphasised a range of outcomes and the uncertainties involved in the calculations.

It is essential to understand that under an economics perspective the 'costs of inaction' are simply analogous to the benefits that can be obtained with proper controls (OECD, 2008:49). Addressing the 'costs of inaction' involves the same methods used to account for benefits in conventional cost-benefit analysis. They have in recent years been underpinned by the availability of computing and modelling capacities, that better allow environmental scientists and environmental economists to account for the complexities and uncertainties at stake, and hence to integrate a precautionary perspective.

This chapter reviews some of the methodologies used to produce estimates for the costs of inaction. Not all the case studies here will match chapters in *Late lessons from early warnings* Volumes 1 and 2. Instead, the case studies provide a generic perspective, which will be of some relevance to historical, current and future case studies.

The first case study we look at is the phasing out of lead in petrol. We use this example as a starting point for a discussion of the subtle differences between scientific proof and scientific evidence. In our second case study, we turn to the issue of nitrates in drinking water in order to show that costs of inaction can be estimated even when there are uncertainties over the long term effects of inaction. In the third case study, we explain some of the methodological controversies that have raged over how to account for the costs of inaction related to mortality risks, which is relevant for air pollution for example. By way of illustration we present in separate boxes monetary estimates of the environmental burdens related to lead and mercury, SO_2 with other air pollutants as well as to ozone-depleting substances (ODS).

23.2 Should we require proof or evidence to account for the costs of inaction: insights from lead phase-out

Heinzerling, Ackerman and Massey (2005) provide a concise overview of the role of scientific and economic analysis in eventually ending the use of

lead in gasoline in the United States. It was research by Herbert Needleman (see Chapter 3 on lead in petrol) on the relationship between lead levels in children's blood and cognitive impairment that made it possible to state in quantitative terms the loss of IQ involved. Heinzerling et al. describe how economic analysis eventually came to the rescue of the lead phase-out by translating this IQ loss into monetary figures. Lower IQ could be shown to result in lower life-time income, which could in turn be translated into an implied cost of inaction (see also Nichols, 1997).

This approach differed from the simple 'willingness-to-pay' studies that previously had been referred to by economists. In these willingness-to-pay studies, parents were asked how much they would spend to prevent exposure of their children. These studies were problematic in that they expected firm monetary preferences to emerge for a problem the dimensions of which few parents would understand. The shift in focus away from willingness-to-pay studies meant that the findings of the lead scientists were used directly in economic assessments of the costs of inaction. The human bones absorb lead, and Needleman's breakthrough was to measure the stocks of accumulated lead in the first 'baby' teeth of children, rather than the level of more recent lead exposure in their blood. One challenge was to establish to what extent blood lead levels reflected ambient concentrations of lead in air. The lead case is described in more detail in Box 23.1.

Today there are numerous hazards and challenges for which we have only limited scientific evidence, and for which it will take many years to accumulate the same understanding as was reached in the case of lead. Economists trying to estimate the costs of inaction will often ask whether there is 'scientific proof', but it must be acknowledged that there is usually not a simple answer to this question. Economic analysis should therefore consider the less certain levels of knowledge that make up scientific evidence in order to explore the magnitude and risks of potential impacts suggested through early warning signals.

We sometimes tend to think of knowledge and lack of knowledge in a simplistic way, believing that research is a process that can transform lack of knowledge into indisputable proof. More realistically, our knowledge base is less clear-cut. It often has a focused nucleus of complete understanding, with a surrounding area where many linkages and relationships are not understood with the same rigour and underpinning. Early warning signals are often located in this blurred area where linkages are not fully understood.

The Treaty on the Functioning of the European Union (TFEU), which establishes the precautionary principle as one of the guiding principles of environmental policy, does not generally mandate a requirement for scientific *proof*. For instance, TFEU art. 114 no. 5 — the so-called environmental guarantee — allows a Member State to introduce unilaterally more stringent measures in areas where there is 'scientific *evidence*'. The precautionary perspective (TFEU art. 191) is really about acting *in the absence* of scientific proof (see Chapter 2 on the precautionary principle).

Although Needleman's research was able to document a relationship between low doses of lead and IQ impacts on children, not all aspects of lead exposure were fully understood. Today we can take advantage of computerised environmental models to account for blood lead concentrations as a result of the lead accumulation over time in the various compartments of the human body. In this way, we can clarify the link between low-dose exposure and the resulting, age-dependent blood lead in children (Pizzol et al., 2010). But the use of such tools remains the exception. For example, the chemical PCB is a substance for which the abatement costs are now counted in billions of euros (von Bahr and Janson, 2004) while welfare economic damage costs are largely unknown. Therefore, when it comes to substances for which the knowledge base is less developed, it will be necessary to explore the potential costs of inaction by relying on evidence from early warning signals. These harm costs could for instance be calculated by looking first at the already-proven impacts of high doses in the work environment, and then scaling linearly to low doses.

23.3 Using warning signals to estimate the costs of inaction: risks from nitrate in drinking water

The European Union's 1980 directive on drinking water quality (80/778/EEC) introduced a maximum admissible concentration value (MAC) for nitrate contents in drinking water, based directly on WHO guidelines. Drinking water with MAC levels of nitrates is suspected to increase the occurrence of *methaemoglobinaemia* in vulnerable individuals, particularly babies (leading to the potentially fatal phenomenon of 'blue' babies, cf. NSW, 2006). At MAC-concentration levels, drinking water nitrate will double the amount of nitrates that the average person would ordinarily consume from other sources.

Box 23.1 Costs of inaction on lead and mercury

Why does lead matter?
Lead is a potent and pervasive neurotoxicant that travels widely throughout the body once ingested or inhaled, and affects virtually every organ or system in the body (Meyer et al., 2008). Children and pregnant women have a higher absorption rate of lead due to constant bone remodelling, which arises from skeletal development (Barbosa et al., 2005). The impacts upon children are profound, because not only is lead more easily absorbed, it is also more damaging to the developing nervous system. Even extremely low Bloodstream Lead Levels (BLL) can have significant impacts on future academic achievement (Miranda et al., 2011), a fact that was a material consideration in the 2005 US Centre for Disease Control's recommendation that there is no safe BLL for children (ACCLPP, 2012). These changes in development are irreversible. Exposure to even low levels of lead during pregnancy will cause permanent and irreversible developmental harm, which manifests itself in lower educational achievement in later stages (Lourdes et al., 2006).

The damages arising from lead have been described as nothing less than a 'catastrophe' for public health (Landrigan, 2002). Lead damages almost every biochemical process in the human body (Gidlow, 2004; Needleman, 2004). It damages fertility and neuropsychology, as well as distorting enzymes, structural proteins and mitochondrial cristae. It also pushes out calcium from natural neuron signalling processes (see Box 3.1 on children and lead in Chapter 3).

Recognition of the problem
Lead has been recognised as a health problem since Roman times (Reddy and Braun, 2010). But it was not until 100 years ago that an Australian doctor identified the critical vulnerability of children to lead (Taylor et al., 2010). But despite multiple early warnings, lead continued to be used as an additive in paint for many years in Europe, America and Australia.

The most harm was caused by the use of lead as an additive to motor vehicle fuel, which resulted in widespread environmental exposure and serious health impacts for hundreds of millions of people. Lead was first added to motor fuel in the 1920s, and it took many decades before developed nations began to phase out the practice.

The history of the use of lead as an additive in petrol is a sad testament to the desire of companies to make profits regardless of the consequence to human health. Other, much less harmful alternatives to lead were available to the petrochemical industry, but they were not adopted because they were not patent-protected, and would therefore have greatly reduced profits for the sector (Ackerman et al, 2005). The global harm caused by leaded gasoline is undoubtedly high, not least because extremely high BLL have been measured in different cities. For example, the average BLL of the sampled population in Bangkok in the 1980s and 1990s was 40ug/dl, levels at which effects such as headaches, slowing of motor nerve conduction and anaemia may occur. Death may occur at BLL of about 100ug/dl (Olson, 2004).

In 1981, the EU introduced a limit of 0.4 gram of lead per litre of leaded gasoline. Use of lead became less attractive following the requirements for installation of catalytic converters in cars. Germany introduced different tax levels for leaded and unleaded petrol in 1985, an approach copied in several other Member States (Hammar and Löfgren, 2004). This meant that by the time the European Union prohibited use of leaded gasoline in 2000, there was little protest from any quarter. As of January 2011, only six countries continue to allow leaded gasoline: Iraq, Yemen, Algeria, North Korea, Burma and Afghanistan.

Economic impacts
In the US, economic analysis was instrumental in convincing the Reagan administration of the desirability to phase out lead in petrol (US EPA, 1985). These analyses explored the loss of IQ in children exposed to lead, a phenomenon that had been demonstrated by scientists. Cognitive impairment of children could be shown to result in reduced expectations for life-time income (Salkever, 1995). Statistically, a loss of one IQ-point can be shown to cause a loss in life-time income of 2-3 % (highest for females). There is no lower threshold for the lead-induced cognitive impairment of young children, so all emissions impair cognitive function (Schwartz, 1994).

Because the harm from lead relates to a future stream of income over a lifetime, the discount rate used to convert future earnings into a net present value decisively influences the final monetary estimate for the

Box 23.1 Costs of inaction on lead and mercury (cont.)

harm caused. In studying the harm cause by lead, US economists used a discount rate of 10 %, while an EU study abstained from any discounting ([1]). Early childhood IQ-losses, such as those that arise from undernourishment or poisoning, can be significant. IQ levels have been demonstrated to influence dramatically the relative affluence of nations, and are therefore a social good (see Figure 23.1).

When using a *social* discount rate of 1.4 % (cf. Stern, 2007; European Commission, 2008) the result is a damage estimate of EUR 1.50 per gram of lead emitted in urban areas (Andersen, 2010). The discount rate is not the only factor that influences the cost estimate. Estimates of the cost of damage can also be greatly influenced by assumptions about how lead enters the food chain ([2]) and by assumptions about so-called 'resuspension'. Resuspension is the process by which lead emitted years ago is deposited on the soil, but then blown up into the air again by the wind.

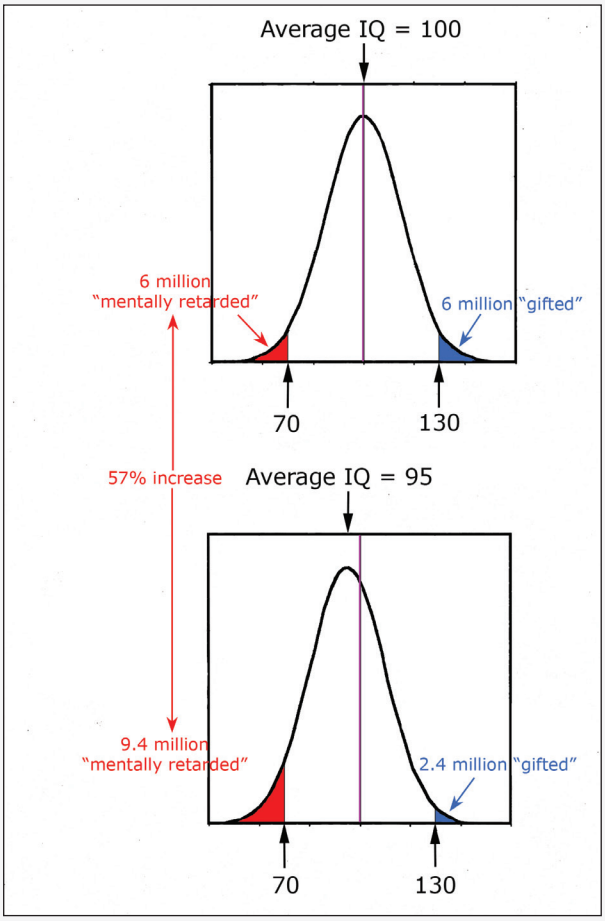
Considering that until the 1970's, gasoline contained about 1 gram of lead per litre, valuing lead-associated IQ damages at EUR 1.50 per gram (EUR 1.50 per litre) implies significant annual costs of about 4–6 % of GDP in EU Member States.

Today, lead emissions in the European Union have decreased greatly, and the magnitude of damages from new emissions, mainly from waste incineration and industry, amounts to less than 0.1 % of GDP. Still, further reduction of lead in products (e.g. paints, toys) remains desirable to prevent continued harm to children.

All the lead emitted during the 20th century is dispersed across the environment, contributing each year to renewed harm as some of the lead finds its way back into our atmosphere. Many urban areas have chronically high levels of lead in top-soils. This is sufficient reason to recommend the resurfacing of playgrounds and areas of high activity for young children, as the intake of even a few micrograms may suffice to induce IQ-damage.

Economic damage estimates are based on scientific research on the impact of human exposure to a particular substance. But not all risks are factored into cost-benefit analysis. For example, the ability of lead to trigger cardiovascular diseases in adults (hypertension, nonfatal heart attacks and premature deaths, cf. Menke et al. 2006) has not been included in the above-mentioned damage estimate. Thus, some damage estimates are lower-bound conservative values (Gould, 2009). This tendency for cost-benefit analysis to lean toward conservative values further strengthens the case for adopting a precautionary perspective.

Figure 23.1 Diminished IQ stunts economic development



Note: This graph shows the social impact of a drop in average population IQ. For example a 5-point drop could raise by 57 % the number of individuals considered neurologically impaired, with implications for social and economic development. It also significantly lowers the number of intellectually gifted children.

Source: www.ourstolenfuture.org.

([1]) The US EPA study due to its use of a private discount rate implied a damage cost of 8 US cents$_{1983}$ per gram lead, while the European study with no discounting implied a damage cost of 5.9 EUR$_{2004}$ per gram lead.
([2]) Spadaro and Rabl (2004) indicate a ratio of 1:25 between inhalation and ingestion (intake) from food.

Box 23.1 Costs of inaction on lead and mercury (cont.)

Why does Mercury matter?
Mercury has a long atmospheric lifetime (6–18 months), which means that once it is released from a source anywhere in the world, it can be transported globally, hence its characterisation as a 'global pollutant'. After deposition in ground or water, mercury can be transformed. The process by which this happens is primarily microbial action, which turns mercury into methylmercury. Methylmercury can 'accumulate' as it progresses up the food chain. For example, an animal could eat a smaller animal that has eaten mercury, exposing the larger animal to all the mercury consumed by the smaller animal in its lifetime. This results in ever higher levels of mercury being found in larger predator animals. Human health can be adversely affected by this process of accumulation if organisms with high concentrations of mercury are ingested. This is a particular problem in consumption of predatory fish, notably tuna and shark (Shimshack and Ward, 2010). Pregnant women are at particular risk, as mercury readily passes through the placenta, concentrates in umbilical tissues and leaches into breast milk. Methylmercury is a developmental neurotoxicant , and high environmental exposure to this compound is associated with a statistically significant reduction in IQ in developing children.

Recognition of the problem
Despite the official acknowledgement of Minamata Disease (a sickness affecting people exposed to methylmercury in the Japanese city of Minamata, see Chapter 5) in the spring of 1956, success in tracing the cause to the mercury discharges from an industrial facility took several years. It was not until 1968 that the Japanese Government 'announced its opinion', that factory effluent was directly responsible. An official apology was finally made at the 50th anniversary of the discovery of the disease (Japan Times, 2006) ([3]). Although large-scale acute cases of mercury poisoning are relatively rare, the more general result of lower IQ due to the developmental neurotoxicant effects of methylmercury continues.

Economic impacts
Mercury damages the developing brain and reduces IQ, just like lead (see above). And like lead, it is a substance that has only harmful effects. This is in contrast to other metals that are also toxic at high doses, but of which the human body needs a certain minimum to survive. Several studies have attempted to calculate the costs for diffuse poisoning (i.e. poisoning from many different sources) by mercury. Despite the wide uncertainty in these figures, they demonstrate that the impact is far from trivial.

Axelrad et al. (2007) created a 'dose-response' model to assess the effect on IQ of each additional 'dose' of mercury exposure by performing an integrative analysis of studies from New Zealand, the Seychelles and the Faroe islands. Their central estimate is that for every 'part per million' increase in mercury in the hair of an expectant mother, the child suffered a 0.18 point decline in their IQ ([4]). Concentrations of mercury in hair can be converted into blood concentrations, or concentrations in the umbilical cord, using established factors. As is the case with other mercury studies, the authors assume that there is a minimum threshold (0.1 ug per day per kilogram bodyweight) below which no effects of mercury occur.

For low doses, the time window during which the brain is affected by mercury needs to be considered. The sensitivity of the brain to mercury is greatest during the early development of the body. The epidemiological studies all assume that once a person is exposed to mercury, the effects on their IQ are both measurable and irreversible, remaining with the person throughout their lives. Since the dose-response function refers to maternal hair concentration and effect on children's IQ, it implicitly includes the effect of mothers' diet during pregnancy and early infancy of her child while she is nursing.

Spadaro and Rabl (2008) have calculated the marginal impact of low-dose mercury emissions. Applying an estimate for the monetary value of a 'global' IQ-point (i.e. the value that an extra IQ point brings a person in terms of lifetime income), Spadaro and Rabl report a marginal damage cost per kilogram of mercury emitted of about USD 1 500. If not assuming any threshold to the impact of low doses, the cost is reported to be USD 3 400 per kg. These estimates are conservative compared with the average damage cost of over USD 6 000 USD per kg implied by one US EPA study (where a 33 tonne change in mercury emissions would cost USD 210 million), which used a different methodology and did not have any threshold for pre-natal exposures (Griffiths et al., 2007).

A study in Greenland, where three quarters of newborns have elevated blood concentrations of mercury, even though there are hardly any local emissions, estimated a damage of 59 million dollars per year (Hylander and Goodwin, 2006). This translates to about USD 59 000 for each new born child. The traditional diet in the Arctic region of fish and sea mammals serves as a sink for global mercury emissions by means of the accumulation process described above. Global mercury emissions are projected to increase by 20 % by 2020 (relative to 2005 cf. AMAP, 2011:143).

([3]) 'Koizumi issues official Minamata apology', The Japan Times Online, 29 April, 2006, http://search.japantimes.co.jp/cgi-bin/nn20060429a4.html.
([4]) A part per million is roughly equivalent to the concentration of a single drop of a substance in 50 litres of water.

In addition to a MAC-value of 50 mg NO_3 per litre, the directive introduced a complementary 'guide value' of 25 mg NO_3 per litre. When revising the directive in 1998, the precautionary guide value for nitrate in potable water was deleted and only the MAC-value retained. The main reason for abandoning a guide value was the absence of scientific proof to underpin it.

Starting with the introduction of the drinking water directive (80/778/EEC), the European Union introduced several initiatives to reduce environmental pressures from nitrogen. One such initiative is the nitrogen application ceiling for agricultural land, and the associated regulations on animal manure that were introduced with the Nitrate Directive (91/676/EEC). The Urban Waste Water Directive (91/271/EEC) also introduced constraints for emissions of nitrogen from sewage and industrial effluents. The protection of drinking water was not the only goal in these efforts to reduce nitrate leaching and emissions. Policy makers were also motivated by concerns over eutrophication in shallow and open coastal waters. Over the years, many conflicts have appeared over the costs associated with both these directives. Farming interests in particular have requested derogations and exemptions from regulatory requirements aiming to reduce nitrate loads.

No analysis has so far been carried out in Europe to explore how the possible benefits of these nitrate regulations compare to the costs of implementing them. The evidence that nitrates have adverse health effects is contested. In particular, there has been controversy over the extent to which gastric cancer is related to nitrate intake. The World Health Organization experts maintain that 'a link between cancer risk and endogenous nitrosation as a result of high intake of nitrate and/or nitrite and nitrosatable compounds is possible' (WHO, 2007:12). WHO normally requires at least three different studies establishing comparable evidence before accepting a link to exposure as conclusive, but in the case of nitrate there are few well-designed epidemiological studies in the international scientific literature.

Chronic impacts resulting from exposure over longer periods of time due to elevated levels of nitrate in drinking water have caused particular concern. In order to detect such influences, epidemiological cohort studies, which monitor health effects in a large population sample over a series of years, are required. Such cohort studies are both laborious and costly, and they often face difficulties with establishing the specific historical exposures. At present, the international scientific literature reports results only from two cohort studies regarding nitrate, and their results are ambiguous.

One study by Weyer et al. (2001) reports an increased incidence of bladder cancers in a population cohort of 10 000 women aged 55 or more from Iowa, US — a state with intensive agricultural practices, and high levels of nitrate in public utility water supply. A more recent study could not detect an increased incidence of bladder cancers in a population cohort in the Netherlands, presumably because nitrate levels in Dutch public water supply are rather low.

The Iowa study was published after the EU Council of Ministers abandoned the 25 mg NO_3 per litre guide value for nitrate in drinking water. Along with other types of studies, the Iowa study suggests that health effects can be detected well below the MAC-value and with lower thresholds of 15–25 mg NO_3 per litre. Hence there appear to be costs of inaction at stake, but a relevant question is: how significant are they?

The studies provide evidence from which nitrate health effects can be quantified. A quantification of these health effects is useful for estimating the *potential* costs of inaction — the risks in other words. For instance, the World Bank (2007) has used those studies that show a connection between ill health and nitrate exposure as a basis for providing rough estimates of the health benefits associated with reducing nitrate exposures. More detailed studies have taken a similar point of departure. Van Grinsven et al. (2010) explore the health risk costs related to colon cancer from nitrates, and arrive at a level of EUR 0.7 per kg of fertiliser nitrogen. Andersen et al. (2011), in the EU FP7 EXIOPOL project, explored different river catchment areas and arrived at site-specific estimates based mainly on figures for bladder cancers derived from Weyer et al. (2001). Their mean estimate is EUR 0.3 per kgN-loss, but they report higher health risk costs for specific Member States, for example the United Kingdom and Belgium at a level of EUR 1.3 per kgN. In some urban areas, the health risk costs are much higher. Consequently, it can be estimated that the risk costs of inaction on nitrate in drinking water amount to EUR 2.6 billion annually for the United Kingdom alone. This figure is comparable to a previous estimate for all external costs of UK agriculture combined (Pretty et al., 2001).

Since there are also other costs related to nitrogen, arising from the pollution of surface waters, ammonia evaporation, and greenhouse gas emissions of N_2O, these figures taken together

would suggest that a precautionary approach is warranted. The abandoned guide value for nitrate in drinking water also deserves reconsideration.

23.4 Air pollution: how to account for the mortality risks from inaction?

The willingness of individuals to make economic sacrifices in order to reduce potential statistical mortality risk is determined by their risk aversion. People make decisions to this effect with many everyday choices, such as adding airbags and other safety devices to their car. In the United States, the authorities have determined risk aversion by resorting to wage-risk analysis. This involves exploring what wage premiums individuals require for more risk-prone occupations, and on that basis have estimated the value of preventing a fatality at about 5.5 million USD_{1999} (1999 prices).

In Europe, there has been more emphasis on applying specific values comparable to figures used in transport economics for avoiding fatalities. Still, air pollution has a risk profile different from road traffic: The average road victim is middle-aged, while victims of air pollution are believed to be mainly people over 65 (Pope, 2002). While a road victim on average loses 30–40 years of life expectancy, the average air-pollution victim may stand to lose only a few years. The European Commission, on the basis of expert advice, has opted to value a statistical life (VSL) at 1.4 million EUR_{2000}, but has adjusted it downwards to about EUR 1 million for air pollution to account for the advanced age of the typical air pollution victim. Similar adjustments proposed in the United States were however met with public outcry and were branded as a 'senior death discount' (NYT, 2011).

In the economics literature, VSL remains the conventional metric for the valuation of statistical fatalities. In recent years, it has been challenged by the adoption of more conservative estimates, based on the specific number of life-years lost. There has therefore been a debate over whether it would be reasonable to exchange VSL-figures with VOLY: the value of a life-year (Hofstetter and Hammitt, 2002). Questions that have been addressed include whether life-years towards the end of an individual's life should be valued more highly than an average life-year (as more precious) or rather should be valued lower, as reduced health and vigour is likely to reduce life-quality. VOLY-values can be derived schematically from VSL, by assuming that the average VSL represents a loss of life expectancy of 3–40 years as in road traffic.

OECD (2006) guidelines for environmental cost-benefit analysis recommend the use of VSL for acute mortality (as in road transport) and to introduce VOLY for cases of so-called 'chronic' mortality, (the result of elevated exposures to harmful substances over longer periods of time), such as air pollution or nitrate in drinking water (See Box 23.2 on SO_2 and other air pollutants for results obtained with the OECD approach).

In contrast, the Science Advisory Board of the US EPA maintains that the only solid value available for quantifying risk aversion in monetary terms is the VSL (US EPA, 2010:12). The obvious implication of the US approach is that it accords a higher monetary value to environmental risk reduction than Europe. Unfortunately, US economists are facing decreased political acceptance of the recommended approach. This was reflected in the recent decision by the Obama administration — acting under political pressures — to withdraw proposed restrictions on ozone pollution, despite the high costs of inaction.

VOLY-based figures provide perhaps only a lower-bound estimate for the benefits of action, but in many cases these conservative values are already sufficient to justify abatement action. The European Commission's impact assessment of the thematic strategy on air pollution (CAFÉ; Clean Air For Europe cf. AEA, 2005) programme decided to tackle the ambiguity over VSL and VOLY values simply by reporting different sets of benefit estimates. It then left it to policymakers to make a decision based on these two different pieces of information. While the most conservative estimate suggests that air pollution costs account for roughly 3 % of GDP in EU-25, the highest estimate amounts to 5 % (see Box 23.2 on SO_2 and other air pollutants). The acknowledgement that economics may not offer a mature consensus corroborates the role and significance of the precautionary principle. The Stern review of climate change reflected similar uncertainties, reporting different estimates, rather than presenting one specific economic figure.

23.5 Should we accept a discount on costs of inaction arising in the future?

The costs of inaction will often only be felt in the future. This is certainly the case for the impact of lead on IQ-loss or the health implications of living with high levels of air pollution and drinking water nitrate. In the case of the skin cancers induced by the ozone 'hole', impacts are expected to peak only after

Box 23.2 Costs of inaction on sulphur dioxide (SO_2) and other air pollutants

Why does air pollution matter?
Sulphur dioxide (SO_2) is a colourless, pungent gas that is a by-product of combustion at power plants, and also arises from natural sources such as volcanic eruptions. SO_2 emissions are a particularly important issue because they are produced in the combustion of coal, which is a major component of the electricity generation systems of many major economies (see Figure 23.2).

Sulphur dioxide has many potential environmental impacts, including its conversion to various acidic compounds (sulphuric acid, sulphurous acid) that can damage tree, plant and animal life (see EEA, 2001, Ch. 10 on sulphur dioxide, lungs and lakes). The converted and hence secondary formation of particulates (for example SO_4) after transport and chemical action cause severe health problems too.

Health impacts
Inhaled sulphur dioxide readily reacts with the moisture of mucous membranes to form sulphurous acid (H_2SO_3), which is a severe irritant. People with asthma can experience increased airway resistance with sulphur dioxide concentrations of less than 0.1 ppm when exercising. Healthy adults experience increased airway resistance at 5 ppm, sneeze and cough at 10 ppm, and experience 'bronchospasm' at 20 ppm (ATSDR, 2011).

The further risk posed by SO_2 is in its subsequent conversion to sulphate particles, and as a precursor to PM (particulate matter), contributing to ill-effects caused by PM_{10} (particulates of larger size) and $PM_{2.5}$ (particulates of smaller size). A meta-study of the mortality effects of ambient particulate sulphates demonstrates a strong correlation between mortality and the atmospheric density of the pollutant (i.e. the amount of pollutant present in the air, Smith et al., 2009).

Recognition of the problem
The first deadly impacts of an air pollution episode had been reported as early as 1929 in Wallonia, Belgium. Another significant and widely-recognised case of health impacts from sulphur dioxide was the Great Smog which affected London in 1952, causing an excess mortality of as many as 13 000 deaths (Bell et al., 2003). The smog was caused by a high level of air-borne pollutants, which remained in the city due to unusually still weather conditions. The response to this event was to propose remedies such as increasing the height of chimneys. Whilst this alleviated the problem, it also dispersed the pollution more regionally, and caused the acidification of rain, lakes and rivers in Scandinavia.

Japan also suffered badly from sulphur dioxide pollution in the three decades of industrialisation that started in about 1950. In all, more than 100 000 people were registered by the Japanese ministry of the environment as having suffered health impacts as a result. Sulphur dioxide pollution, known at the time as Yokkaichi Asthma, is listed as one of the four 'big pollution diseases of Japan' (Committee, 1997).

Economic impacts
In the 1970s, some claimed that the problem of sulphur dioxide pollution were not severe enough to warrant expensive action. Some even called it a 'million dollar problem with a billion dollar solution' (Opinion, 1977). The link between atmospheric concentrations of sulphur dioxide and sulphate to increased mortality rates was only gradually accepted. However, when one factors in not only the costs of morbidity (the sickness caused by sulphur dioxide) but also those of mortality (the deaths caused by sulphur dioxide) it is clear that the health costs of inaction on air pollution damages should indeed have been counted in billions too.

Pope et al. (1995, 2002) showed how increased rates of mortality are consistently associated with high ambient levels of pollutants. Most of the deaths were seen to occur in response to chronic exposures over extended time periods, rather than in response to shorter periods of exposure. Their findings were based on a population cohort of more than 500 000 individuals, who had been interviewed about health status, smoking habits and other potentially confounding variables. The American Cancer Society had obtained individual death certificates from deceased participants in the cohort, which allowed control for death caused by air pollution exposure. The US EPA decided to require a complete reanalysis of the data by an independent research team before finally accepting the findings — it led to the same results.

In 2005, the European Commission commissioned a comprehensive cost-benefit analysis when preparing its Thematic Strategy for Air Pollution. It also invited the World Health Organization (WHO) to review the

Box 23.2 Costs of inaction on sulphur dioxide (SO_2) and other air pollutants (cont.)

health effects evidence available. Because of the methodological debate over the appropriate valuation metric for the risks to human lives (see discussion in main text of this chapter), the assessment presented different estimates. The lowest estimate, based on a VOLY metric, came to a total cost of air pollution for the EU-25 of EUR 276 billion, equivalent to 3 % of GDP. The highest estimate, based on a VSL metric, came to a total cost of EUR 427 billion, close to 5 % of GDP (AEA, 2005).

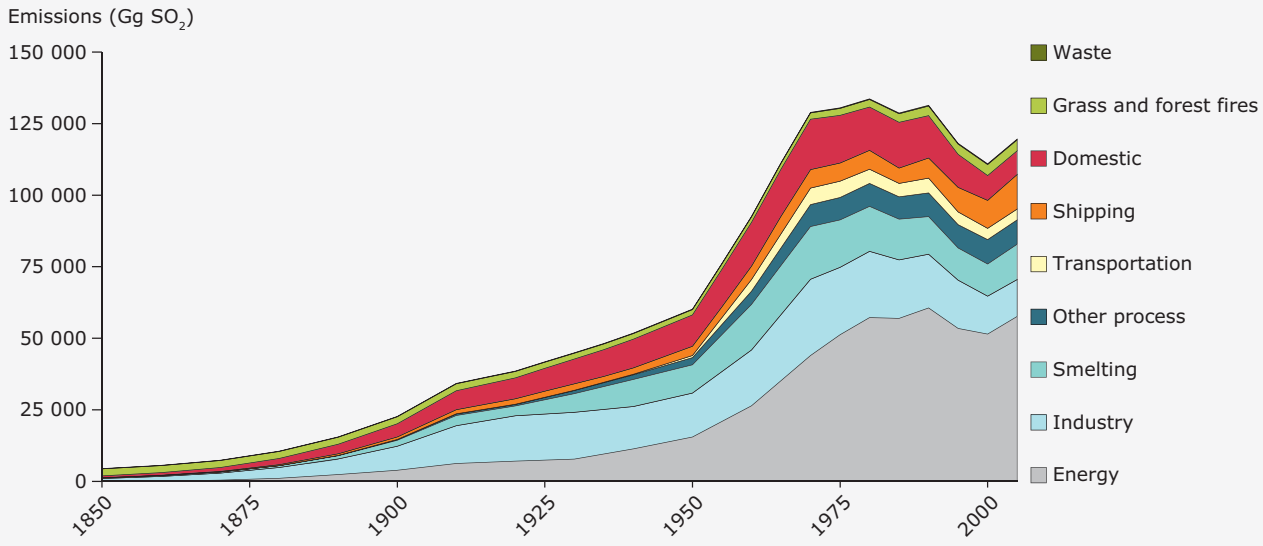
The costs were seen to differ considerably among Member States. In Poland and other new Member States, the air pollution costs (using 2000 as the reference year) varied between approximately 15 % and 22 % of GDP depending on the metric (AEA, 2005). These costs referred to the combined exposure to particles from SO_2, NO_X and primary PM.

Although these figures do not include all relevant costs of inaction — for instance in relation to biodiversity — the figures suffice to justify further action to reduce air pollutants. While the damage cost per kilo of SO_2 ranges from EUR 5 to 9 per kg SO_2, marginal abatement costs start from below EUR 1 per kg SO_2 (Rive, 2010). Theoretically, it would be desirable to pick the lowest-hanging fruit first and focus on the most cost-effective measures, but in reality there are large benefits for nearly all efforts regarding SO_2 abatement.

A cost-benefit assessment becomes highly complex when multiple types of emissions are considered jointly (SO_2, NO_X, VOC, O_3, NH_3 and PM). There are non-linearities at play in the atmospheric transport and chemistry, for instance relating to ozone, which must be taken into account. Some integrated assessment models have been created to study these situations that feature complex mixtures of emissions. They typically produce scenarios for different levels of pollutants (e.g. SO_X, NO_X) and come up with a best-cost solution for meeting various environmental outcomes. The technically feasible reduction of air pollution has been estimated at EUR 56–181 billion equivalent to 0.6–2 % of GDP in EU, which are the costs that could be avoided by introducing appropriate controls (AEA, 2005).

Japanese industry was a pioneer in air pollution abatement. In 1975, investment in air pollution abatement accounted for 18 % of Japanese capital investment and 6.5 % of GDP. The OECD (1977) has reviewed the experience and concludes that 'the impact of relatively high pollution abatement costs on macro-economic magnitudes, such as GNP, employment, prices and foreign trade is practically negligible'. In fact, these investments accelerated technological innovation, raised product quality and lowered technical costs. Even today, Japanese companies control many of the patents and licenses for air pollution control equipment, and benefit from sales globally, demonstrating the economic significance of being a pioneer in environmental technology.

Figure 23.2 Global SO_2 emissions 1850–2005 by end-use sector



Source: Smith et al., 2011.

60 years. These delayed effects present a particular problem for estimating the costs of inaction.

To allow for the comparison of monetary estimates at different points of time, economists typically use 'discounting' techniques, whereby all estimates of future costs are discounted — or reduced in absolute terms — into net present values. There are two textbook reasons why economists assume the future is not worth the same as the present to an investor. Firstly the investor may not be alive when the return on the 'investment' is made, and secondly, the prospect of continued economic growth and technological progress means an investor expects to be richer when the return is made, meaning that the return will have less value in the future. For this reason economists apply a discount rate, reflecting mainly these two aspects, and adjusting them for time preferences and consumption value.

To many non-economists, the implied shrinking of future values with the discounting technique is at odds with the core idea of intergenerational equity that is central to sustainability. A related problem is that many economists are applying discount rates that are typically used in the corporate sector — rising up to as much as 10 % — without reflecting on the specific context of environmental challenges.

As pointed out in the Stern report, time preference discounting is less relevant for a society than to an individual. Firstly, society is not mortal. There is only a small risk that societies would be discontinued, whereas an individual investor faces a much greater risk. For this reason, Stern recommends representing this risk of social 'mortality' with a tiny discount rate of 0.1 %. As for the second aspect of discounting, the consumption discount rate that seeks to compensate for continued economic growth in the future, Stern maintains it should be based on expectations for future economic growth, net of inflation. Only a very small number of countries have expectations for annual economic growth rates of 10 %. In Stern's analysis of climate change policy with the PAGE model, he simulated many different trajectories of economic growth for the future decades and came to an average expectation of 1.3 % per annum. Stern's review argued that even when discounting the stream of future benefits, the aggregate sum of avoided damages — from 5 to 20 % of annual consumption — would well exceed the involved costs. Table 23.1 illustrates how the social cost of carbon depends crucially on the discount rate chosen.

Many environmental projects have much shorter time horizons than climate change policy. For example, investments in sulphur scrubbers for air pollution abatement have only a 10 or 20 year lifetime. With shorter project lifetimes than in climate change policy, there will be less 'shrinking' of the future, even for the lifetime-loss of income of the lead-poisoned child (see estimates in Box 23.1 on lead). For mortality risks, discounting is not very important because the VSL must be adjusted upwards for expected economic growth, which will cancel out the consumption component of the discounting, leaving only the 0.1 %.

Table 23.1 Effect of the discount rate on the estimated costs of inaction

Discount rate (%)	Discounted costs of inaction (% of GDP-equivalents)
1.3	14.7
1.8	10.6
2.3	6.7
2.8	4.2

Source: Stern, cited from OECD, 2008:96.

23.6 Concluding remarks

We have discussed above some of the problems with the willingness to pay model of estimating the costs of inaction. In what has become a classic discussion of this model, Diamond and Hausman (1994) raise two other difficulties with willingness-to-pay and the so-called 'contingent valuation method' (CVM) it uses. Firstly, because stated willingness-to-pay is hypothetical, there is an inherent risk that any respondent will overstate their preferences, neglecting their level of income and therefore their real ability to actually pay. Secondly, there is the tendency of willingness-to-pay results to be inconsistent across different surveys. For example, the willingness-to-pay for cleaning up one lake might be similar to the willingness to pay for cleaning up five. People may simply express a desire to contribute EUR 50 for a good purpose, but have no specific individual preference as to the amount of the public good in question. These are strong methodological critiques to the use of monetary estimates derived from CVM.

Europe has acted cautiously in mandating formal requirements for cost-benefit analysis. At Member State level, there is a fairly limited tradition as part of formal legislative processes. Although the concept has found its way into common-day language across the European continent (Germans for instance speak of 'Kosten-Nutzen analyse'), it is perceived by many as a somewhat American-style approach to policymaking processes. The Dutch felt compelled to rename it as

Box 23.3 Benefits of early action on ozone depleting substances

Why do ODS matter?

The ozone layer absorbs most of the high-frequency ultraviolet radiation that could cause damage to life on Earth. Ozone Depleting Substances (ODS) are chemicals that can survive long enough in the atmosphere to migrate to ozone-rich areas, in the upper atmosphere, some 25 km high. At this altitude, ODS then undergo reactions that break down ozone molecules (see also Figure 23.3). If the emission of ODS is allowed to continue or increase, the ozone layer will reduce in thickness, increasing the quantity of harmful UV radiation that reaches the surface of the Earth (Molina and Rowland, 1974 — see also Chapter 7 on halocarbons and the ozone layer in *Late lessons from early warning* Volume 1 (EEA, 2001)).

Exposure to UV radiation has significant health implications for many forms of life, including humans. Excessive exposure is linked to increasing rates of skin cancer, cataract development and reduced capacity to resist bacterial and viral infection (WHO, 1994). Insufficient exposure can also create problems, notably by leading to vitamin D deficiency, and damaging crop productivity.

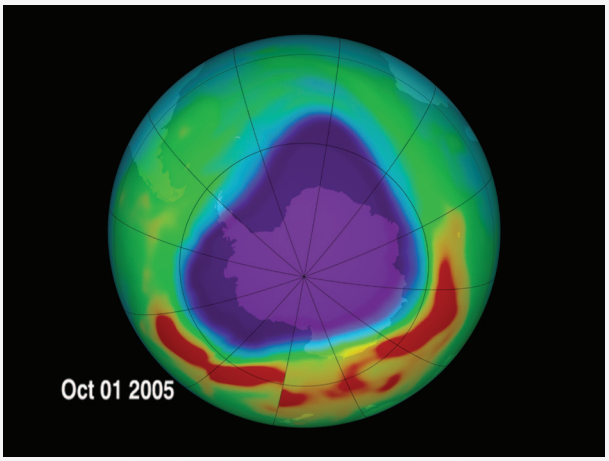
UVB radiation is a major causal factor in the development of melanoma and non-melanoma skin cancer (NMSC). A reduction in the thickness of the stratospheric concentration of ozone allows a greater proportion of UVB radiation to reach the Earth's surface, and will generate an increase in UVB-related cancers. Although NMSC is not as serious as melanoma, it accounts for the majority of skin cancers.

Recognition of the problem

Scientist Richard Scorer of Britain's Imperial College was a respected environmentalist, but sided with industry on the safety of CFC's, claiming in 1975 that 'The only thing that has been accumulated so far is a number of theories' (Roan, 1989:61).

In spite of scepticism about the ozone depletion theory from some quarters, the case for limiting the production and emission of ODS is often viewed as a *cause célèbre* for international agreements. This is because it was one of the first cases of successful coordinated, international action on phasing out a chemical (CFCs were the first of the ODS to be banned) that was in widespread use, and that was shown to be causing an environmental impact on a global scale. The Montreal Protocol entered into force on 1 January 1989, and was recognised by Kofi Annan in 2003 as 'perhaps the single most successful international environmental agreement to date'. It went on to become the first international treaty to be universally ratified, on 16 September 2009, by 196 countries, and has shown demonstrable success in achieving its stated objectives. This means that the ozone layer should return to its pre-1980 levels sometime between 2050 and 2075 (UNEP, 2009a).

Figure 23.3 Region of exceptionally depleted ozone in the stratosphere over the Antarctic



Source: NASA/Goddard Space Flight Center Scientific Visualization Studio.

A study undertaken in 2009 attempted to predict the future that was avoided by the Montreal Protocol and by subsequent international agreements on ozone-depleting chemicals (Newman et al., 2009). The benefits of early action are starkly illustrated in the predicted 'World Avoided' ultraviolet (UV) radiation index compiled by that study (see Figure 23.4). This figure shows the impact of the increasing amount of harmful UV radiation that would have been permitted to reach the Earth's surface. Without international agreements to eliminate ODS production and emissions, the ozone layer could have reduced in thickness by as much as 67 % by 2065, with highly damaging consequences for humans and many other organisms.

Box 23.3 Benefits of early action on ozone depleting substances (ODS) (cont.)

Economic impacts

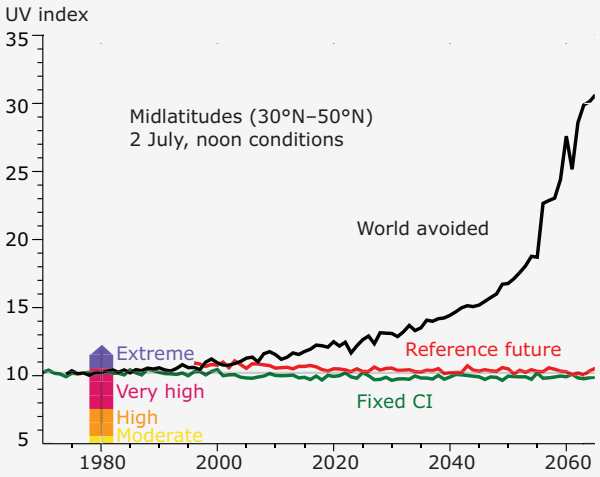
Health

Incidence of skin cancers in response to increased UV radiation are expected to peak about 60 years from exposure. Assuming prevention of a 48 % decrease in the ozone layer by 2050, UNEP (2009b) has estimated that more than 20 million skin cancers and 130 million cataract cases have been prevented globally as a result of the Montreal protocol.

The stabilisation of the ozone layer means that by 2050 annually about 47 000 skin cancer cases will be avoided in north-western Europe, although 14 000 additional cases of skin cancer are still to be expected as a result of the damage to the ozone layer that has already been done and the 60 year latency period (Slaper et al., 1998:83; Velders et al., 2001:8). 99.5 % of skin cancers are likely to be non-melanoma with a mortality rate of 1 %, while 0.5 % will be melanomas with a mortality rate of 24 %. The implication is about 500 fatalities avoided annually in north-western Europe towards the middle of the 21st century.

Assuming the same ratio between fatality reduction and other avoided UV-radiation effects (mainly health-related) as in US studies (Sunstein, 2007), these figures imply that annual benefits of early action from the Montreal Protocol are not less than EUR 3 billion for Europe. Scaling results for north-western Europe to all of the European Union must take into account higher exposure risks in southern Europe, with likely annual benefits of EUR 10–11 billion for EU-27.

Figure 23.4 The 'world avoided' UV index as a result of international agreement



Source: Newman et al., 2009.

Climate change benefits of early action

ODSs have had a considerable impact upon so-called 'radiative forcing', and therefore on global warming (Radiative forcing is a measure of the influence a factor has in altering the balance of incoming and outgoing energy in the earth-atmosphere system). It is estimated that 13 % of the present total global warming effect is due to the release from year 1750 to 2000 of Halocarbons and ODSs (IPCC, 2007).

The *avoided* impacts of ODSs on climate change are substantial. The combined effect in 1990 was 7.5 ± 0.4 $GtCO_2$-equivalent/year, or about 33 % of the annual CO_2 emissions due to global fossil fuel combustion (IEA, 2009). If we assume — in the absence of a Montreal protocol — a 3 % annual increase in ODS and halocarbon production, the 2010 emissions would have amounted to ~ 14 $GtCO_2$-equivalent/year. In other words the Montreal protocol has over two decades saved the atmosphere for about 215 $GtCO_2$-equivalent in emissions. Assuming that ODS had not been regulated separately, but also were to be counted under the Kyoto Protocol, these emissions, that stem mainly from developed countries, should have been offset and could have represented a cost of about EUR 2 150 billion (assuming a price of EUR 10 per tCO_2-equivalent) — about 0.5 % of annual GDP of OECD countries over these two decades.

The CO_2-equivalent of ODS-reduction is bigger than cuts required by developed countries under the Kyoto Protocol. Important is also the time delay achieved in relation to climate change. It will take between 7 and 12 years for CO_2-emissions to increase by the amount of ODS abated with the Montreal Protocol. If considering the full reduction achieved since the 'early warning' scientists Molina and Rowland (1974) first called attention to the ozone layer break-down, as many as 30 to 45 years may have been gained (Velders et al., 2007). These estimates further underscore how early warning scientists must be attributed a role in curbing ODS-consumption being equally important to the Montreal protocol itself.

SCBA — social cost benefit analysis — to sweeten the pill (RMNO, 2008). The uptake of cost-benefit analysis has been most significant in the United Kingdom. And because the United Kingdom has promoted the extension of the method to EU regulations — with occasional support from other Member States — there are examples of formal requirements for cost benefit analysis in EU programmes. Findings from cost-benefit analysis are also referred to in impact assessments of new legislative proposals prepared by the Commission. There has been a rule in place for the past 15 years requiring a cost-benefit analysis as part of the screening of projects set to receive EU support under the Structural Fund programmes and a manual is available to guide these assessments, published by the European Commission (2008).

Obviously there are great methodological challenges in further expanding the use of cost-benefit analysis. However, there has also been some progress in these methodologies. For example, improvements in scientific knowledge and modelling techniques have helped to significantly influence the ratios of benefits to costs in favour of regulation.

Precautionary action can be justified by using credible estimates of the costs of inaction. The lead case illustrates that even if we have an understanding of only some of the benefits, making good use of the science base can be enough to prompt action. The nitrate case demonstrates that risk calculations can be useful and help prompt immediate action, even though the time-lag effects of exposure means that full proof will likely take decades to materialise. Finally, in the case of air pollution, making use of different estimates for mortality risk avoidance will help decision-makers to see that there are higher- and lower-bound estimates for the costs of inaction. Even if the lower-bound estimates are perhaps too conservative, with a bias towards health-effects, they will in many situations encourage more rather than less abatement effort. Reducing emission loads will also tend to bring relief for the intangible assets of biodiversity and nature.

Making the best use of environmental science and modelling helps to make environmental protection and precaution a priority. Producing cost estimates should not be left to economists alone, but should rather be seen as a starting point for a broader discussion, featuring also the relevant expertise in health, ecology, demography, modelling and science. Well-researched estimates, based on inter-disciplinary collaboration, can strengthen some of those scattered and diffuse interests, which during the ordinary processes of policymaking have difficulty making their voices heard.

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24 Protecting early warners and late victims

Carl Cranor

Many *Late lessons from early warnings* chapters provide examples of early warning scientists who were harassed for bringing inconvenient truths about impending harm to the attention of the public and regulators. There is also some evidence that young scientists are being discouraged from entering controversial fields for fear of such harassment. In addition, where warnings have been ignored and damage has ensued, it has often proven difficult in the past to achieve prompt and fair compensation for the victims. Some ideas for reform, building on some current institutional models are explored here.

This chapter first explores the idea of extending whistleblowing laws to help encourage and protect early-warning scientists and others who identify evidence of impending harm. Complementary measures, such as greater involvement of professional societies and the use of recognition awards, as for example in Germany, could also be helpful.

Next, the chapter explores improved mechanisms for compensating victims of pollution and contamination. The chapter on the Minamata Bay disaster provides an extreme example of long delays in getting adequate compensation for the victims of methylmercury poisoning. It was almost fifty years, between 1956 and 2004, before the victims attained equitable levels of compensation and legal recognition of responsibility. Other case studies illustrate similar examples of long delays in receiving adequate compensation.

Options are examined for providing justice to any future victims of those emerging technologies such as nanotechnology, genetically modified crops and mobile phone use, which currently can provide broad public benefits but potentially at a cost to small groups of victims. The potential for widespread exposure and uncertain science could justify 'no-fault' administrative schemes that provide more efficient and equitable redress in situations where the benefit of scientific doubt would be given to victims. The use of anticipatory assurance bonds to help minimise and meet the costs of future environmental damage from large scale technologies is also explored.

A supplementary panel text describes cases of asbestos and mesothelioma, where the senior courts in the United Kingdom have developed innovative ways of dealing with both joint and several liability, and the foreseeability of subsequent asbestos cancers, after the initial recognition of the respiratory disease, asbestosis. Such legal developments in the field of personal injury could illustrate the future direction of long-tail liability in both environmental damage and personal injury.

Implementing a precautionary approach to managing new technologies requires, first and foremost, administrative laws aimed at detecting and addressing risks before they materialise into harms. But in addition to precautionary policies towards chemical, genetic and other technologies, additional legal tools can support the precautionary approach, better protecting public health and environment.

Since most statements of the precautionary principle emphasise acting on the basis of early warnings of threats to health and the environment and to minimise harm, at least two significant kinds of supporting laws should be considered.

First, in order to encourage the identification of impending threats to health or environment as early as possible, current whistleblowing laws could be extended to protect early warning scientists and others from harassment. Such people should feel free, and be free, to research and report early warnings without the threat of adverse actions that would discourage them.

Second, for those foreseeable and surprise events that cause future harm despite precautionary actions, measures could be taken to provide prompt and fair compensation without having to prove negligence by specific parties.

These two issues are explored below.

24.1 Encouraging and protecting early warning scientists and others

It is not hard to imagine situations where rules or personal risks could prevent potential 'whistleblowers' from sharing important information. Employees in academia, business or government might become aware of serious risks to health and the environment, but internal policies might pose threats of retaliation to those who report these early warnings. Private company employees in particular might be at risk of being fired, demoted, denied raises and so on for bringing environmental risks to the attention of appropriate authorities. Government employees could be at a similar risk for bringing threats to health or the environment to public attention, although perhaps this is less likely ([1]).

Several democracies in the developed world have implemented whistleblower laws and policies to foster and protect those who call attention to legal wrongs, often but not only regarding corruption. Such laws provide models for how to think about whistleblower protections in a precautionary world.

> 'Whistleblower protection laws are intended to make it safe for employees to disclose misconduct that they discover during the course of their employment. Indeed, when accompanied by other initiatives, such laws can actually help foster an environment that rewards and encourages whistleblowing' (Kaplan, 2001).

Countries that have constitutional guarantees of free speech can also assist in protecting public employees, in particular those who call attention to issues of public concern.

While some may praise whistleblowers for taking on their own companies or misconduct in government, others may regard them as disloyal, malcontents, grumpy employees, even bitter individuals who have been passed over for merits or promotions and are seeking to create problems. When they are regarded in this negative light, it becomes clear why there might be a need to foster and protect whistleblowing in order to encourage the revelation of misconduct, wrongdoing and harm, along with warnings that actions have occurred or are about to occur.

Some whistleblower protections in the United States

In the United States, the Civil Service Reform Act of 1978, as amended by the Whistleblower Protection Act of 1989 (WPA), provides some of these protections. As Kaplan (2001) explains:

1. The WPA 'makes it illegal to take or threaten to take a 'personnel action' against a federal employee because the employee has made a protected disclosure' where 'personnel action' is broadly defined.

2. This prohibition should be backed by sanctions for taking or threatening a 'personnel action' against a federal employee because the employee has a made a protected disclosure. This would be information that the employee 'reasonably believes evidences a violation of the

([1]) The US Union of Concerned Scientists has recently reported cases of government employees in food and other areas who have been restricted from speaking out in the past. There are now attempts to restore the integrity of science across the US government following an initiative from the administration (UCS, 2012).

law, rule or regulation, a gross waste of funds, gross mismanagement, an abuse of authority, or a significant and specific danger to public health or safety.' Moreover, such a disclosure 'need not prove ultimately accurate in order to be protected — it is enough if the person making it is acting in good faith and with an objectively reasonable belief in its accuracy.'

3. In the US, the Office of Special Counsel (OSC) enforces the whistleblower protection provisions of the WPA and has a great deal of independence from other government and private sector bodies to carry out its work.

4. The OSC has authority to correct an adverse personnel action or to prosecute any retaliation.

5. It also operates a 'secure channel', which government employees can use to report misconduct.

6. It is comparatively easy for a whistleblower to make a 'prima facie case of retaliation'. It is sufficient that an employee's public disclosure be a 'contributing factor' to an adverse personnel action.

Following the recent financial crisis, the US Congress passed financial reform legislation that included protections for whistleblowers in order to improve early warnings of violations of securities laws (Harvard Law Review, 2011). The new law provides substantial bounties to people reporting information that the Securities and Exchange Commission (SEC) finds useful in identifying securities law violations, enhances protections for those providing the information, and establishes a two-tiered system for whistleblowers reporting to the SEC. The bounties can be 10–30 % of sanctions exceeding USD 1 million.

The law 'prohibits employers from discharging, demoting, suspending, threatening, harassing, or in any other manner discriminating against a whistleblower "because of any lawful act done by the whistleblower"' (Harvard Law Review, 2011). Protections for whistleblowers are greater for those who report directly to the SEC, but somewhat lesser for those who report to the company. These two tiers strongly encourage a person to report to the SEC rather than going to the company that has committed the violation. This could be a strength — boosting the hand of SEC enforcers, but discouraging local corrections for abuses — or a weakness, undermining internal compliance systems within companies.

Some whistleblower protections in the United Kingdom and South Africa

The United Kingdom's Public Interest Disclosure Act (PIDA) differs in some respects from the US approach (House of Commons, 1998). In the United Kingdom the PIDA governs both public and private employees, providing that 'a worker has the right not to be subjected to any detriment by any act, or any deliberate failure to act, done on the ground that the worker has made a protected disclosure.'

Based on 'reasonable belief', whistleblowers are protected if reporting criminal offenses, miscarriages of justice or that 'the health or safety or an individual, is being or is likely to be endangered.' There are defined channels by which a whistleblower may disclose violations but in the United Kingdom there is a preference for disclosing to the private employer or some public agency identified by the Secretary of State to hear such reports. Whistleblowers are at some risk if they go outside the recognised reporting channels (Kaplan, 2001).

In contrast to the US approach, the UK law encourages employers to specify internal procedures for disclosures and responses to them, but employees are not restricted to these. Moreover, there is no 'independent agency of the State to investigate or prosecute whistleblower complaints' as there is in the US (Kaplan, 2001).

In 2000, South Africa passed 'the Protected Disclosures Act', largely modelled on the UK's PIDA and covering both private and public employees. In addition to covering dismissals, demotions, involuntary transfers and suspensions, it goes beyond the US laws by 'explicitly including harassment and intimidation, as well as the refusal to provide an employment reference, or provision of an adverse reference as "occupational detriments"'. Reports of misconduct may be made to employers or a specified public agency, but there is no independent agency of the State to conduct investigations. The whistleblower has to invoke a court or tribunal for protection (Kaplan, 2001).

Whistleblower provisions have been enacted in some established democracies but many emerging democracies have been slow to institute them. In addition, countries with constitutional or other free speech protections appear to have a wider range of protections for those who identify and report wrongdoing (Kaplan, 2001).

In order for whistleblower provisions to function well employees must be aware of both statutory protections and the variety of channels through which disclosures or wrongdoing may be reported. The protections must be sufficiently effective to overcome employee reluctance to use them. In addition, government agencies and private entities must 'change their cultures, to make them receptive, rather than hostile, to employees who "rock the boat"' and this must be communicated from the top (Kaplan, 2001).

Desirable features of whistleblower laws

Whistleblower protections for those who report threats to the environment or public health from genetic, chemical or other technologies can supplement laws implementing the precautionary principle. Existing models suggest that such laws should protect public and private employees from adverse personnel actions, broadly construed.

Employees should be protected as long as they have a reasonable belief that private or government actions are a violation of the law or pose threats to the environment or public health. There should be a secure channel by which misconduct can be reported and it should be fairly easy for an employee to make a prima facie case that he or she has suffered retaliation. There should be an office with considerable independence from private or government bodies to provide protection and prosecute any retaliation. Finally, if a country desires to encourage whistleblowing more strongly, it could offer bounties amounting to some percentage of the fines issued against wrongdoers.

Panel 24.1 Better scientific support for early warning scientists?

David Gee

An early warning scientist is not the same as a whistleblower who reports on wrongdoing. However, the *Late lessons from early warnings* case studies have provided several examples of early warning scientists who, like whistleblowers, were harassed after issuing or publishing their views. Examples include Snow (in relation to his work on cholera); Selikoff (regarding asbestos); Henderson, Byers, Patterson and Needleman (regarding leaded petrol); Osakawa (regarding mercury); Putzai and Chapella (regarding GMOs); Schneider (regarding climate change); and several scientists in the French bees story. In addition there are others who wish to remain anonymous.

Other examples from beyond the *Late lessons* case studies include public servants who have been prevented from speaking out on environment or health issues (UCS, 2012; Martin 1999 and 2008).

Generally, recognition that scientists were harassed seems to increase over time, alongside acceptance that the early warning has been vindicated by unfolding science. The luxury of such hindsight is of little use to harassed early warning scientists, however, who, unlike Nobel prize winners, need fairly immediate recognition for their 'inconvenient truth' and resulting personal difficulties.

The price of providing early peer group support to harassed early warning scientists could be that some warnings turn out to be false alarms. However, this may be seen as an acceptable price to pay for defending the rights of scientists to issue an early warning based on reasonably plausible evidence.

As we have seen, there are some legal precedents from the field of whistleblowing that could be used to help characterise the situations in which responsible early warning scientists would be encouraged and protected by their scientific peers. Relevant considerations include the following:

- the scientists have acted in good faith in drawing attention to threats to health and/or the environment based on evidence that they reasonably believe;
- the belief need not necessarily prove 'ultimately accurate' in order for them to be protected, (Kaplan, 2001);
- the early warning scientist suffers from some form of serious harassment, including personal attacks (distinct from scientific criticism) in the scientific literature and elsewhere; being preventing from speaking out, or publishing; removal from their scientific work; loss of contracts or funding; unreasonable difficulties in getting their science in the relevant literature; accusations of scientific misconduct; being by-passed for promotion; loss of their facilities or staff; and threats of legal action.

Panel 24.1 Better scientific support for early warning scientists? (cont.)

In contrast to whistleblowers, where the law is the main measure used in their protection, it would be more constructive if early warning scientists were encouraged from the outset by a culture within science that explicitly supported challenges to conventional scientific ideas and paradigms and the scientists who may suffer as a result of producing the challenges. There is a long history of scientific and other dissenters, which illustrates their frequent value to societies (Sunstein, 2005; Mercer, 2010).

It may be asking too much of individual scientists, whose lifelong work is challenged by an early warning scientist, to respond positively to the challenge. It would be reasonable, however, to expect more independent professional associations of scientists, who have the integrity of science as a whole to uphold, to produce explicit policies that encourage early warning scientists and defend them if they are harassed.

Early warning scientists would be further encouraged if there were a European award to an early warning scientist who had produced a reasonably credible challenge to conventional science and who subsequently suffered harassment.

Such an award would follow the precedent of rewards to successful whistleblowers, which began with a law against lead in alcohol production in the USA in the 18th century (see Chapter 3) and which continue today under US financial regulations.

The award would need to be made by an authoritative and independent scientific body of scientists, free from direct bias (i.e. their own scientific work would not be challenged by affording credibility to the early warning science).

An interesting legal view of such 'intellectual bias' comes from a World Trade Organization case in which scientists acting as expert witnesses were asked to review science that was critical of their own work. The WTO Appellate Body considered that as 'coauthors' of the JECFA reports that were being criticised, they 'cannot be considered to be independent and impartial in these circumstances, because this would amount to asking them to review and criticise reports that are their own doing' (WTO, 2008).

An appropriate title for such an award could be 'The Henrik Ibsen award for early warning scientists' in recognition of Ibsen's play, 'An enemy of the people' which concerns the harassment of an early warning public health doctor. The harassed Chisso company doctor in the Minamata chapter of the present volume of *Late lessons from early warnings*, like many others in similar situations drew support from reading that Ibsen play.

An existing award that could provide some relevant lessons is the German Whistleblower Award, which honours individuals who have exposed grave abuses, dangers or aberrations in their professional field for the public good. It is awarded by The Federation of German Scientists (VDW/FGS) and the German section of the International Association of Lawyers Against Nuclear Arms (IALANA). info@vdw-ev.de / info@ialana.de.

In addition to possible legal remedies, early warning scientists could receive greater support from scientific communities (see Panel 24.1).

24.2 Providing compensation in a precautionary world

If we have precaution, do we need compensation?
How necessary are compensation policies in a legal system committed to precaution in protecting health and the environment? Compensation might seem unnecessary in a world guided by precautionary approaches. Effective precautionary approaches would result in fewer wrongs to right; wholly successful policies might not leave any.

In reality, of course, flawless implementation of precautionary approaches is unattainable. Compensatory schemes are needed to address harms that occur despite precautionary efforts.

Harms can also arise because society accepts certain risks, which benefit society as a whole but may result in harm to individuals. For example, we use lead or cadmium in batteries and other electronic devices despite the hazards to people and the environment. Alternatively, accepting one risk of

harm potentially mitigates other, more serious dangers to human or environmental health. The use of some pesticides is an example of such a risk-risk trade-offs. Even if such harms do not involve wrongful acts by individuals or companies, justice arguably demands that society compensate those adversely affected

In addition, there may continue to be less visible threats to health and the environment. For instance, substances that contribute to disease during early human development can trigger subtle diseases or dysfunctions that can be difficult to detect via human studies. Some will have extremely long causal tails, delaying the manifestation of disease by decades. Some will be comparatively rare. For example, early or mid-life exposures to substances such as the pesticide paraquat or the industrial degreaser trichloroethylene (TCE) may hasten the early onset of Parkinson's disease, as shown by animal and human studies (Cranor, 2011). Other substances may pose long-delayed risks to wildlife or the broader environment, as has been seen in the Arctic (Cone, 2005).

Genetically modified plants may cause subtle genetic or other changes in vegetation or the environment that may not be immediately perceptible, or that will only be revealed over a longer period of time. For example, there have been proposals to use transgenic plants to extract organic mercury from the soil and volatilise it into elemental mercury (National Research Council, 2002). While this might be of some benefit at a local level, on a larger scale this proposal could easily have long-term adverse environmental and health consequences. Concentrations of atmospheric mercury would probably increase in local areas and then be deposited further away into aquatic or terrestrial ecosystems via precipitation and condensation. Once there, it would again be converted into more toxic organic mercury, although in a different location. This would add to organic mercury from other sources, exacerbating existing effects (National Research Council, 2002). Decision-makers must clearly be alert to such long-term, subtle environmental consequences of new technologies.

Finally, it is worth noting that imposing an obligation to compensate those harmed by technological hazards can also help deter firms from undertaking harmful activities.

Compensation systems

There are different rationales for compensation. One comes from the tort law. As Priest (2003) explains: 'Tort law is designed to deal with harms inflicted by some identifiable person who was in a position to have prevented the harm'. The tort system shifts the costs of injuries to parties judged to be responsible, sometimes 'at fault' for the harm, 'in order to create incentives to reduce the level of harm suffered in the society'. It awards full damages to injured parties in order to ensure that the full costs of the legal violation are paid by the tortfeasor and to provide some degree of deterrence.

In contrast, **insurance** addresses 'losses that cannot realistically be prevented'. Typically private insurance is funded by parties seeking to protect themselves from future costs and placed into 'self-supporting risk pools in ways that serve to reduce effective risks while amassing resources to compensate those who ultimately suffer losses'. **Government insurance**, another form of risk sharing, is ordinarily 'provided for more generalised societal risks for which no, or less of a, market exists, such as the risks of unemployment or disaster' (Priest, 2003).

Contrasted with all of these, but somewhat similar to tort law, are systems of **compensatory reparations**. Reparations presuppose that one person has acted wrongly, causing harm to another person who deserves compensation as a consequence (Boxill, 2011). The best reparations would also include an acknowledgement by the wrongdoer of the wrongdoing in order to help restore relationships severed by the wrongful act ([2]). Institutionalising acceptance of wrongdoing presents difficulties, however, and there is likely to be greater success in securing compensation for injured parties if it is not required.

The existing institutions discussed below do not always carefully distinguish these different dimensions of restitution. The central idea, however, is to provide some substantial degree of recompense to those who have suffered losses as a result of new technologies.

One ideal would be to ensure that the full social costs of a technology are incorporated into the costs of the activity (removing negative externalities), or at least to ensure that the costs are not left to fall on innocent bystanders or the environment. However,

([2]) As noted in Chapter 5, victims of methylmercury poisoning in Minamata, Japan, have sought such acknowledgement but have not secured it.

not all compensatory approaches accomplish the first goal. For example, the creator of a technology that causes harm may not be have acted wrongfully according to the requirements of tort law or compensatory reparation systems.

Guidance for compensation in a precautionary world

The above discussion suggests the outline for compensatory approaches in a precautionary world:

1. Successful precautionary policies should reduce the need for compensation.

2. Compensatory approaches should seek to minimise any harm as quickly as is institutionally reasonable and to shorten its duration, if possible.

3. Some past environmental, health and new technological issues suggest that compensation is needed to address difficult situations such as long-tailed, less visible, low probability, and subtle consequences of a technology. These could be long-tailed in two senses: both highly unlikely and possibly years into the future.

4. Any reasonable compensation should also be combined with an adequate deterrence mechanism to discourage firms from negligence or recklessness toward public health or the environment.

5. Finally, in some countries with single-payer health systems that provide medical care to all citizens, compensation for injured people would be less than under medical systems with private insurance. Nonetheless, there would still be a need to compensate for income loss, personal suffering, losses of loved ones, and other non-medical losses.

What compensatory 'institutions' or policies might be adopted for a precautionary world to set matters right, once people or the environment have been harmed? Of those compensatory approaches, which might be most compatible with a precautionary approach towards people and environmental resources?

With these questions in mind, the strengths and weaknesses of several compensatory approaches are assessed below: traditional personal injury law, workers' compensation, and individual compensatory schemes tailored to particular classes of potential harms such as the US Vaccine Injury Compensation Program and the UK's radiation compensation programme. In addition, general no fault compensatory arrangements like those used in New Zealand are considered, and flexible assurance bonds instituted upfront to provide compensation if technological risks materialise.

24.2.1 Tort or personal injury law

Tort or personal injury law is a major institution in the US and the United Kingdom (with analogues in other countries). It aims to provide compensation for injuries that people suffer because of the conduct of others. In bringing a tort action, a party (the plaintiff), who believes another party (the defendant) has caused him or her harm, must show that defendant breached a legal duty, that the plaintiff suffered a legally compensable injury, and that defendant's breach was the cause in fact and the legally proximate cause of the injury. Each element of the cause of action must be established by the preponderance of the evidence — the balance of the quality and quantity of evidence must favour the plaintiff.

The duty that the defendant breached in most cases is a duty in negligence — to take reasonable care that one's actions do not cause legally compensable injuries to others. In the US, tort duties in strict liability (liability without fault) exist for products, ultra-hazardous activities and trespass. Under strict liability a plaintiff need only show that the defendant's action caused and was the proximate cause of a plaintiff's injuries. A plaintiff need not show lack of reasonable care by the defendant.

When torts came into prominence in the 19th century, it was quite cramped and restricted in principle at the outset and quite limited in application in achieving compensation goals. Nineteenth century courts never considered holding defendants accountable in strict liability, instead basing liability on 'moral fault,' interpreted as negligence. Defendants were also provided a number of defences that greatly limited many tort actions for harm caused by railroads or factories during the industrial age, reducing the number of injuries entitled to compensation. Courts were concerned that more extensive tort liability would too greatly burden enterprises; and they had a suspicion of juries, who might be overly sympathetic to injured parties. Both continue in current debates (Friedman, 1985).

As the tort law developed, some of these liability-limiting features were moderated. Strict

liability became the basis for some legal actions: for harm caused by ultra-hazardous activities and for products liability. Proximate causation rules were liberalised. In the early 20th century workplace torts largely disappeared in favour of a government-managed workers' compensation programme designed to expedite compensation, remove long, costly disputes, and provide a more consistent legal framework for addressing workplace injuries (Friedman, 1985).

Doctrines more favourable to plaintiffs continued to develop until about 1980. Various cause-in-fact rules were adopted to ease the burden on plaintiffs in establishing causal claims, recognising the multifactorial nature of causation (Anderson v. Minneapolis, St. Paul & S. St. M.R.R. Co., 1920; Summers v. Tice, 1948; Sindell v. Abbott Laboratories, 1980). Doctrines of joint and several liability better ensured that plaintiffs received compensation from some defendant to an action.

About this time, firms required to defend tort suits, with support from some legal scholars, began efforts to roll back doctrines that had eased the burden on plaintiffs. At the same time, other scholars argued that the tort law had never served well to express moral outrage about wrongs (likely never its aim), poorly compensated plaintiffs and did not function especially well to deter harmful conduct (Abel, 1988).

Defence arguments yielded some success in the United States during the late-1980s and early-1990s. Some jurisdictions limited compensation, especially for pain and suffering. Some sought to limit joint liability. And, there was considerable pressure to ensure high standards for scientific evidence in cases requiring it.

As a consequence, the US Supreme Court intervened, ultimately invalidating a long-standing rule concerning the admissibility of scientific testimony. The Court had initially seemed to liberalise admissibility rules for experts in Daubert v. Merrell-Dow Pharmaceuticals (1993). However, as that decision was implemented by lower courts and expanded by two later Supreme Court decisions (General Electric v. Joiner (1997) and Kumho Tire v. Carmichael (1999)), in many jurisdictions it substantially burdened experts, especially those for plaintiffs (Cranor, 2006). Some state and federal circuits are especially onerous (Merrell Dow Pharmaceuticals, Inc. v. Havner, 1997). Although in principle these rules impartially apply to both plaintiffs and defendants, in reality they asymmetrically hamper plaintiffs, who bear the burden of proof to establish the key elements of a tort.

This series of decisions reduced plaintiffs' access to the law because lawyers must invest greater resources upfront to ensure experts have good scientific foundations for testimony, which in turn means they only take cases they are more certain to win. This development likely reduces somewhat any deterrent effect of tort law (Cranor, 2006).

Too often judicial interpretations of the admissibility of scientists erected unscientific barriers against expert testimony (Cranor, 2007 and 2008b). Recently, however, a decision from the US First Circuit Court of Appeals has marked a change. In that circuit, with jurisdiction over about one-twelfth of the US, scientists may now use in the courtroom the same kinds of arguments that they would use in the lab to draw scientific conclusions. In addition, there is no priority of evidence for cancer causation, such as human epidemiological evidence (Milward v. Acuity Specialty Products, Inc., 2011). This decision removes some judicially created unscientific barriers to expert testimony.

In large measure current US tort law does not compensate injured parties well or quickly. They bear the initial burden of proof to establish legal violations, injuries and causation. When scientific or technical evidence is needed, this increases the hurdles. In some US federal jurisdictions plaintiffs must have human epidemiological evidence showing that toxic exposures double the relative risk of disease from which a plaintiff suffers, a further barrier because of the insensitivity of epidemiological research. In some jurisdictions compensation is capped at a sufficiently low level that it is inadequate for some injuries. Even when plaintiffs are successful, resolution can take considerable time.

Milward v. Acuity Specialty Products was filed in 2007 and stopped by the trial judge for inadequate scientific testimony in 2010. It was reinstated by the First Circuit Court of appeals in 2011 with many of the original twenty-two defendants settling. As of 2012 one defendant continued to seek a jury trial to conclude the issues. This case involves a single plaintiff (but many defendants) and in this respect may be typical of many tort cases.

Class actions involving many plaintiffs and sometimes many defendants are more difficult and can take longer to resolve. However, once there is a sufficient record of injury types, as with asbestos, and a long history of litigation,

subsequent compensation disputes will generally be settled much more quickly, often without trial. In addition, class action cases can reach a point at which the issues are clear and there is no need to litigate compensation for each plaintiff. At that time, defence and plaintiff attorneys, perhaps with encouragement from the judge, agree to a 'settlement matrix' — a classification system for groups of plaintiffs with similar exposures, adverse health outcomes and possible confounding factors, e.g. health status or smoking. The matrix enables comparatively easy classification of each plaintiff to receive greater or lesser compensation depending on the circumstances for the injuries suffered. In this respect, some tort law settlements can resemble the classification of injured parties under the compensation schemes described below, such as worker compensation or vaccine injury compensation.

In addition to the shortcomings of the tort system outlined above, it is essential to note that when there is clear harm to people, injured parties rarely bring legal cases to set matters right. For instance, Saks (2000) observes that in cases of clear medical malpractice just 4 % or fewer of injured parties even approach a lawyer to consider redress.

Based on the above, existing US tort law appears to be a poor legal model for providing rapid and adequate compensation for those who have been wrongly injured by the actions or products of others. Tort law persists but its achievements fall far short of its goals.

Battery and trespass are two other causes of action in the US tort system that could provide some compensation for citizens, short of people being actually harmed. Battery is the 'foundational tort cause of action. It protects bodily integrity and individual autonomy, creating the essential status and space for social interactions' (Lyndon, 2012). The idea is that by giving citizens a cause of action for offense against them or for violation of bodily integrity without their consent, this lessens the chances of retaliatory harm needing criminal intervention; historically it was a means of helping to keep the King's peace in the United Kingdom.

To establish a battery a plaintiff must show that 'the defendant committed a voluntary act with the intent to cause a wrongful [offensive or harmful] contact and the contact occurred.' Intent is widely construed for this purpose and it applies to the contact only; one need not intend offensiveness or harm (Lyndon, 2012; Cranor, 2011). For intentional invasions of one's body by potentially harmful chemical substances without consent that one would reasonably regard as offensive, one could bring a battery cause of action. A special advantage of battery compared with the main body of tort law is that one need not show harm as the result of the invasion, offensive contact is sufficient. Consequently, if one's bodily integrity has been invaded by potentially harmful substances in a manner one would reasonably regard as offensive, whether or not one has been harmed and before one could even show harm, one potentially has a cause of action in battery.

Trespass is also a vindication of a legal right against invasion. What remains of early trespass law largely concerns property but also applies to invasions of individuals. If someone enters property or causes molecules, particles, or toxic substances to enter property without 'authorization' or without permission, the person has trespassed on the property. Trespass also applies to violations of the integrity of persons, e.g. as when blasting trees injure a party on a public highway (Cranor, 2011). Both battery and trespass are founded on deep considerations concerning the integrity of one's person (or property) and 'rights over aspects of one's life'. Without doing harm one can be accountable for either battery or trespass and merit compensation. Compensation for battery would consist of 'Proof of the technical invasion of the integrity of the plaintiff's person by even an entirely harmless, but offensive, contact [which] entitles him to vindication of his legal right by an award of nominal damages, and the establishment of the tort cause of action entitles him also to compensation for the mental disturbance inflicted upon him' (Cranor, 2011).

A larger number of citizens could potentially bring battery or trespass causes of action than could bring actions in torts for harm caused by toxicants. This might better facilitate safety testing and better deter invasions by potentially harmful substances than would successful tort suits alleging (and even proving) harm. Battery and trespass would likely be much quicker and easier to resolve than would tort suits for harm. Compensation for each individual invaded in a battery/trespass action would likely be much less than for each individual harmed in a typical tort action, but total compensation paid out by a company that caused the invasion (or harm, respectively) could be substantial.

One aspect of the tort law, whether for actions for harm or battery/trespass, is quite important both in supporting health protections and providing compensation for plaintiffs. This is a pre-trial stage called 'discovery'. During discovery each litigant in

the dispute can interrogate the other party about information it may have about the background of the dispute, try to determine what legal issues are or could be easily agreed upon, request documents related to the issue, and conduct depositions (questioning of witnesses on the issues). This process can reveal a good deal of information about a case that might expedite settlement or narrow issues. It can also serve the wider public good, by revealing hidden data about adverse health effects, decisions made by responsible people that contributed to harm, policies that might have exacerbated problems and so on. If information unearthed during discovery is publicised, as it has been for asbestos, lead, and vinyl chloride in the US, it can alert public health officials to other problems, issues meriting further investigation, scientists who have acted without integrity, or even other serious legal wrongdoings (Brodeur, 1983; Markowitz and Rosner, 2002).

In a legal system that greatly emphasised precautionary policies toward risks and harms, tort law with its emphasis on showing harm would be a poor compensatory model simply because bringing a successful tort action is normally burdensome and slow. This would greatly slow efforts to reduce harm and clean up environmental contamination. Tort actions for battery/trespass would be less burdensome and slow, but lesser compensation for each individual would result; total compensation paid out could be substantial.

Of course, tort law can be modified; it is not set in stone. For instance, there are some developments in the tort system of the United Kingdom that merit attention because they may expand the range of compensation available to plaintiffs for injuries suffered from some kinds of environmental exposures. For asbestos-caused mesothelioma possibly resulting from exposures due to the activities of two or more defendants, a plaintiff need not rule out other possible causes (because all or virtually all mesothelioma is caused by asbestos exposure). Also, once liability has been established for particular defendants, all defendants must pay full compensation for the mesothelioma-related injuries. Other court decisions have applied the same principle to dermatitis caused by coal dust (discussed below).

Just because medical science cannot determine which of several liable defendants' asbestos fibres caused plaintiff's injuries does not bar recovery for mesothelioma. In short, 'where there are multiple potential tortfeasors ... in the case of an 'indivisible injury' such as mesothelioma, **any tortfeasor** could be liable for the whole of the injury once liability has been established' (McIntyre, 2004 (emphasis added)). UK courts treat asbestosis (which also results from asbestos exposures) differently: each liable defendant in a group need not pay for the full costs of the disease but only for the portion of time plaintiff had asbestos exposures at their facilities (McIntyre, 2004).

A second UK innovation concerns foreseeability for harm from an asbestos facility to those outside the plant boundaries. Where a defendant should have reasonably foreseen a risk of pulmonary injury, not necessarily mesothelioma, it has been found liable for mesothelioma in people who reside near to asbestos plants (see Panel 24.2.). Generalising from this, it suggests that companies might be liable not merely for known toxic injuries to employees but also for other types of harm to local residents of a type that emerged after the initial exposure (McIntyre, 2004).

24.2.2 Alternatives to the tort system

Workers' compensation

The tort system's shortcomings in addressing compensation for **occupational** injuries and illnesses led to the development of an alternative compensatory arrangement. Under tort law, employees seeking compensation historically bore the burden of proof to show that employment caused an injury and that the employer was negligent. Employers had an incentive to delay legal proceedings because injured employees probably had more limited means to support themselves, to secure medical care and to bring legal actions. Such suits were slow to resolve and unpredictable, and damages were often inadequate. Employees were often afraid to sue their employers, and witnesses among fellow workers were often difficult to find (Franklin, 1979).

Workers' compensation programmes were implemented as an alternative to torts for employees. They hold employers liable without fault for injuries suffered by employees in the course of and arising out of their employment. Employees 'exchange their common law damage actions for smaller but more reliable recoveries whenever they [are] hurt on the job even if they [are] at fault and the employer [is] not' (Franklin, 1979). The discussion that follows provides the general outlines of workers' compensation within various states in the United States, since this is a state, not a federal issue.

Panel 24.2 Liability for asbestos-related illness: redefining the rules on 'toxic torts'

Owen McIntyre

In recent years litigation over diseases resulting from exposure to asbestos has led to the progressive development of UK common law principles as they apply to two issues that have traditionally proven very onerous for plaintiffs claiming for 'toxic torts' (Cranor, 2006). These are the burdens of establishing the necessary causal link between an activity and disease and of establishing that harm that only becomes apparent long after the period of exposure, when scientific understanding of the risks may have been less developed, ought to have been reasonably foreseeable. Considerations of justice and injustice played a major role in each of these innovative developments in tort cases on asbestos-induced mesothelioma.

The UK House of Lords has recently ruled that the traditional 'but for' test for causation need not apply in mesothelioma ([3]) claims entered by employees who suffered periods of exposure to asbestos with more than one employer and where medical science cannot prove who among a number of employers caused the condition ([4]). This decision effectively creates joint and several liability whereby the claimant will be entitled to recover damages in full against each defendant.

In addition, and with strong implications for the precautionary principle, the English Court of Appeal ruled in 1996 that liability **arose in respect of exposure to asbestos resulting in mesothelioma despite the fact that the disease was not known to medical science at any time** during the relevant period of exposure ([5]). The Court reached this decision by employing a broad concept of injury for the purposes of establishing reasonable **foreseeability**. This development is significant in light of the emphasis placed on the requirement of foreseeability in environmental claims by the House of Lords decision in Cambridge Water Co. v. Eastern Counties Leather ([6]).

Causation

Establishing causation in toxic tort actions has long proven a difficult and even insurmountable task. The Scottish case of Graham and Graham v. ReChem ([7]) provides an extreme example of the practical problems which can be involved in establishing causation in such cases, involving an action in negligence and nuisance against the operator of a hazardous waste incinerator by local farmers for alleged damage to their cattle. The case lasted for 896 hours in court, spread over 198 days, and involved 80 lay witnesses and 21 expert witnesses on such issues as veterinary toxicology, agricultural accountancy, incinerator design, dioxin formation, pollution dispersion, analysis of trace organics and meteorology. The defendant's costs were estimated at GBP 4.5 million and the cost to the Legal Aid Board at GBP 1.5 million (see Wooley et al., 2000). Ultimately, the case failed on the issue of causation as there were other possible explanations of the cattle's injuries.

The cancer mesothelioma is classified by the UK courts as an 'indivisible' disease, as distinct from the respiratory disease, asbestosis, which is 'divisible' or cumulative. In the case of asbestosis, once the threshold for exposure is exceeded, all inhaled fibres are considered to contribute proportionately and progressively to lung dysfunction. The 'indivisibility' of mesothelioma creates obvious difficulty for a plaintiff mesothelioma victim who has been negligently exposed to asbestos by a number of defendants, usually successive employers, in terms of establishing causation.

In Fairchild, Curtis J. refused recovery at first instance to the estate of a mesothelioma victim suing two former owners of buildings containing asbestos in which he had worked ([8]). The Court found that there was no evidence of significant differences between the respective levels of exposure and was 'unable to establish on the balance of probabilities that the breaches of duty by either defendant were a cause or a material contribution to the deceased's mesothelioma'.

([3]) Mesothelioma is cancer of the lining of the lung or stomach. See the chapter on asbestos in Volume 1 of *Late lessons from early warnings* (EEA, 2001).
([4]) Joined cases Fairchild v. Glenhaven Funeral Services Ltd, Fox v. Spousal (Midlands) Ltd, and Matthews v. Associated Portland Cement Manufacturers (1978) Ltd and others, (2002), UKHL 22, NLJ Law Reports, 28 June 2002. See also, Morgan (2002).
([5]) Unrep. 17 April 1996. See further, McIntyre (2004).
([6]) (1994) 1 All ER 53 (H.L.)
([7]) (1996) EnvLR.
([8]) QBD, 1 February 2001.

Panel 24.2 Liability for asbestos-related illness: redefining the rules on 'toxic torts' (cont.)

However, a mere five months after Curtis J.'s decision in Fairchild, the English High Court reached a very different conclusion on very similar facts ([9]). Where a mesothelioma victim sued two of 15 employers who had exposed him to asbestos during the course of his working life, Mitting J., relying on the 1972 decision of the House of Lords in McGhee ([10]), justified his award of full damages against both defendants stating: 'The claimant was exposed by each defendant and by both defendants, to asbestos fibres, in quantities sufficient greatly to increase his risk of contracting mesothelioma.'

This followed the earlier ruling of Philips J. in a 1987 case ([11]) where he stated:

'Whether the defendants' breaches of duty merely added to the number of possible initiators of mesothelioma within the lungs of Mr Bryce, or whether they also produced a cumulative effect on the reduction of his body's defence mechanism, they increase the risk of his developing mesothelioma. He developed mesothelioma. Each of the defendants must accordingly be taken to have caused the mesothelioma by its breach of duty.'

The House of Lords later judgment in Fairchild relaxed the traditional test for establishing causation where there are multiple potential tortfeasors, holding that, in the case of an 'indivisible injury' such as mesothelioma, any tortfeasor could be liable for the whole of the injury once liability has been established. The House of Lords relied on its earlier decision in McGhee where it held that an employer who causes an indivisible disease such as dermatitis through exposure, only some of which is negligent, shall be liable in full for that injury.

The Lords stressed in McGhee that theirs was a 'common sense' understanding of causation having regard to the circumstances of such cases. According to Lord Reid:

' … it has often been said that the legal concept of causation is not based on logic or philosophy. It is based on the practical way in which the ordinary man's mind works in the everyday affairs of life. From a broad and practical viewpoint I can see no substantial difference between saying that what the respondents did materially increased the *risk* of injury to the appellant and saying that what the respondents did made a material *contribution* to his injury' (emphasis added).

Lord Hoffman stated that 'I think it would be both inconsistent with the policy of the law imposing the duty and morally wrong for your Lordships to impose causal requirements which exclude liability'.

Lord Hoffman approved the test for causation proposed by the Supreme Court of California in Rutherford v. Owens-Illinois Inc., stating that 'the causal requirements of the tort were satisfied by proving that exposure to a particular product was a substantial factor contributing to the … risk of developing cancer'.

Lord Bingham stated that '… such injustice as may be involved in imposing liability on a duty-breaking employer in these circumstances is heavily outweighed by the injustice of denying redress to a victim'.

Foreseeability of the 'surprise' disease of mesothelioma

The unique characteristics associated with the disease of mesothelioma have also resulted in the English courts taking an innovative approach to the issue of foreseeability of damage for the purposes of liability. The disease can develop from a very short period of exposure, even from a single instance of exposure but only manifests itself many years after exposure. According to statistics published by the insurer Munich Re, the average latency period (i.e. from first exposure to diagnosis of the cancer) for asbestos-related mesothelioma is 34 years ([12]) and epidemiology suggests that it is so rare for the latency period to be less than ten years that exposures within ten years of diagnosis may be excluded as causal (see Miller, 2002).

([9]) Matthews v. Associated Portland Cement and British Uralite PLC, QBD, 11 July 2001. Indeed, Dr Rudd, the principle expert witness in Fairchild, also acted in Matthews giving substantially similar evidence. See Miller (2002).
([10]) McGhee v. National Coal Board (1972) 3 All ER 1008, where it held that an employer who causes an indivisible disease such as dermatitis through exposure, only some of which is negligent, shall be liable in full for that injury.
([11]) Bryce v. Swan Hunter Group plc and others (1988), 1 All ER 658.
([12]) Munich Re, Employers Liability Handbook. See further, Buckley, supra, n. 1, at 192.

Panel 24.2 Liability for asbestos-related illness: redefining the rules on 'toxic torts' (cont)

In the joined cases Margereson v. JW Roberts Ltd and Hancock v. JW Roberts Ltd, ([13]) the plaintiffs sued an asbestos manufacturer after having contracted mesothelioma due to the defendant's extensive asbestos contamination of the district of Armley in Leeds where both plaintiffs had lived as children. Both sued in negligence and strict liability ([14]) and/or nuisance, though only liability in negligence was considered by the court. It was never disputed by the defendant that the steps taken by them to mitigate the problems of asbestos dust contamination were woefully inadequate. At trial, Holland J. found for the plaintiffs despite the fact that at no material time was mesothelioma a concept known to medical science.

The defendant appealed on the ground that there was no culpable lack of foresight on their part as they did not know and had no reason to believe that the risk of mesothelioma existed.

The Court of Appeal rejected the appeal stating that liability would arise where the applicant should reasonably have foreseen a risk of some pulmonary injury, not necessarily mesothelioma, and, that the damage occurred at a time when the applicant was on actual or constructive notice as to the potential pulmonary damage that exposure to asbestos could cause.

The Court also considered whether any distinction could sensibly be made between employees working within the factory and local residents. It asked 'did the factory wall pose such a barrier that risk of injury to persons on the other side … amount at worst to no more than a "mere possibility which would never occur to the mind of a reasonable man"?' and agreed with the trial judge that if the conditions outside the factory are not materially different to those giving rise to a duty of care within, there is 'no reason not to extend to that extramural neighbour a comparable duty of care'.

Lady Justice Hale has elsewhere ([15]) stated:

'The point which impressed the [trial] judge was the certain knowledge that asbestos dust was dangerous and the absence of any knowledge, and indeed any means of knowledge, about what constituted a safe level of exposure. … But just as courts must beware using such later developments to inflate the knowledge which should have been available earlier, they must beware using it to the contrary effect. The fact that other and graver risks emerged later does not detract from the power of what was already known …'

It remains to be seen whether this decision has implications beyond personal injury actions ([16]) and whether the courts are prepared to apply a less onerous test of foreseeability in cases of environmental damage generally. Where any particular class of environmental damage was foreseeable, liability might arise for any other type of damage in that class which arises much later. Several of the case studies in volume 1 of *Late lessons from early warnings* and the present report demonstrate that much harm arises after the first wave of harm, e.g. with PCS, mercury, CFCs, benzene and radiations. If the courts were to examine foreseeability in the context of broad classes of damage, the test of foreseeability (seen by many commentators as one of the factors responsible for tort's failure to compensate for historic pollution), would effectively be relaxed. The test may now relate to the foreseeability of some relevant damage.

([13]) *The Times,* 17 April 1996.
([14]) Rylands v. Fletcher (1868), L.R. 3 H.L. 330.
([15]) Shell Tankers UK Ltd. v. Betty Irene Jeromson (2001), EWCA Civ 101, 2 February 2001.
([16]) Following the House of Lords decision in Page v. Smith (1996) AC 155, it is sufficient if any personal injury to a 'primary' victim is foreseeable.

Part of the rationale is that the since the 'employment of labor involves the risk of disability, by social policy the employer must defray its costs.' Expressed succinctly: 'The cost of the product should bear the blood of the workingman' (Franklin, 1979). When employees are harmed, there are costs; workers' compensation seeks to internalise those costs to the commercial activity that produces profits and harms employees.

Workers' compensation is financed by employers' contributions based on the hazards of particular kinds of employment ranging from quite hazardous jobs to office work. General tax revenues could fund such a system but this would likely disconnect compensation from current modest incentives for employers to provide a safer work environment. Moreover, since funding is largely employer based, it could and often does reflect a particular employer's safety record (Franklin, 1979). In addition, like tort law, workers' compensation laws in some jurisdictions permit discovery — but with a twist. Some jurisdictions only permit an impartial adjudicator to conduct discovery concerning injuries, while others allow the injured party to conduct discovery much like under tort law. While either option provides some of the same information benefits of tort, it slows the process, thus interfering to some extent with one of the strengths of workers' compensation: quick compensation and resolution of issues.

Initially workers' compensation only covered injuries resulting from the workplace, not diseases. Coverage has subsequently been extended, however, to include at least some diseases resulting from workplace exposures. Sometimes particular diseases resulting from particular working conditions are dealt with by separate legislation, e.g. black lung from coal mining. Many but not quite all workers are covered in the US. Domestic service employees, agricultural workers, casual employees, and possibly employees of small businesses tend to be excluded by statute (Franklin, 1979).

Injuries or diseases for which employees are authorised to receive compensation must fall within prescribed legislative categories. The injuries must be both explicitly authorised by the legislation or enabling regulations and attributable to a person's employment (Franklin, 1979). A back injury for which compensation is sought must be due to a workplace event, not weekend soccer.

Compensation typically consists of cash payments to an employee or his/her survivors, reflecting lost income, costs of medical care, and rehabilitative services. Lost income payments tend to be some percentage of the worker's weekly earnings at the time injuries were suffered, usually with a maximum payout, for example up to two thirds of the total earnings. This can vary depending upon marital status and whether the person has dependent children. Moreover, compensation is based on the generic kind of injury suffered, whether it was a temporary but partial disability, a temporary total disability, a permanent total disability, or death resulting from the workplace.

Payment amounts can be quite specific for a lost arm, leg, or particular finger, for example. When an employee dies as a result of a workplace injury, typically his or her survivors receive compensation based on the levels of earnings at the time and the number of his or her dependents. Medical and rehabilitative services provided by workers' compensation 'are generally considered to be the most effective single part of the system'. This is typically provided at once following an injury or disease (Franklin, 1979). Rehabilitative services can avoid other long-term costs that would otherwise result.

Finally, if the workers' compensation law in question does not cover a person or an injury or disease, remedies in tort law may be available. Ordinarily, workers' compensation is the exclusive remedy for workplace-caused diseases but if employees for some reason are not covered or poorly compensated for injuries, in some instances they may have recourse to the tort law.

In the US there are additional variations on workers' compensation. A federal version covers federal non-military employees. The Black-Lung Benefits Act 'provides compensation for [coal] miners suffering from 'black lung' (pneumoconiosis)'. Other laws provide compensation for employees injured by railroads, those working on ships, and those working for private maritime employers, but most of these provide compensation only if employers were negligent (Cornell University Law School, 2010). Some shortcomings of workers' compensation are considered at the end of the next section.

Analogues to workers compensation for a precautionary world

How well might generic strict liability analogues to workers' compensation laws function within a legal system oriented toward a precautionary approach to environmental health and environmental protection?

Imagine a generic compensation scheme that could compensate workers or citizens for injuries, diseases, dysfunctions or death as a result of an

environmental hazard, such as a chemical or other exposure. Imagine also that it provided compensation for environmental damage caused by products whose causal consequences were missed by prior review. How well would such a system function?

A well functioning system analogous to workers' compensation could have aspects consistent with a more precautionary approach to environmental and occupational health harms. It could provide compensation quickly to repair and rehabilitate people from injuries suffered. Once harms were identified, this would shorten their duration. But could analogues for environmental damages be devised? This more difficult issue would need to be addressed.

There is one major limitation. Workers' compensation laws function as well as they do is because many injuries tend to be immediately cognisable and causally traceable to a source, e.g. a worker cuts off a finger or is in a car accident. Obvious and immediate traumatic injuries are easy to identify under workers' compensation programmes. Provisions for other injuries, such as diseases associated with workplace exposures, would need to be created as understanding of disease processes develops and as diseases can be causally attributed to exposures, e.g. how coke oven emissions can contribute to lung cancer (very easy) or bisphenol A can contribute to metabolic syndrome, breast cancer or adverse reproductive effects (extremely difficult). In a precautionary world creating categories of identifiable injuries, diseases or dysfunctions from many chemical exposures becomes more difficult when harms are not obvious, are not obviously traceable to a particular exposure or are not causally proximate to the time of exposure.

As a first step for comparatively new or poorly understood exposures to technologies, decision-makers could assess potential causes of harm from what is known about the technologies and any plausible adverse effects that might result. These could be used together with background information and analogies to the same adverse effect caused by other exposures or sources to create presumptive categories of adverse outcomes and appropriate compensation. For example, at present the evidence may or may not be sufficient to identify various forms of electromagnetic waves as contributors to brain cancer. However, there is surely considerable knowledge about the costs of treating different brain cancers and how much these forms of cancer disrupt people's lives so that if it turns out that cell phones do contribute to some forms of brain cancer, compensation tables could begin to be developed even before the causal evidence is fully sufficient to support a case for compensation.

In addition, decision-makers could 'learn as they go', and assess and evaluate kinds of diseases and dysfunction based on the causal properties of the substance as they are revealed over time. It would take some time to build up categories of injuries that would be more or less automatically compensable. For known hazardous but socially important chemical products whose toxicity was better understood, compensation tables could be developed somewhat quicker.

Another amendment might be a procedure for monitoring for any potential adverse health or environmental effects from risky but socially important products or activities, such as lead. This is highly toxic product with no known safe level of exposure but it is likely to have continued use in batteries (Wigle and Lanphear, 2005). Lead companies would need to continue monitoring the health status of their employees for known adverse effects of lead exposure. Neighbourhoods or communities downwind or downstream from lead battery factories or recycling plants would need to be monitored in order quickly to detect health or environmental effects from fugitive lead exposures for compensation and to expedite its delivery.

For environmental harms there would need to be categories of plausible or even remote harms for which there would be compensation based on liability without fault. There would also need to be monitoring programmes in place to identify long-tailed risks as early as possible so that harm could be minimised and its duration shortened. Such efforts could probably be expedited by experts giving careful thought to potential adverse effects, where these estimates would be made on the basis of existing information and analogies to similar outcomes caused by other sources. For instance, for a genetically modified weed killer new to the market, there might well be recent historical examples of other weed killers, genetically modified or not, that when released into the environment posed problems of killing beneficial plants from which decision-makers could learn. For genetically modified plants with in-built pesticides that are close relatives to wild types that could pose problems, decision-makers could learn from analogies.

Despite the appearance that workers' compensation is more efficient, faster and without many of the transaction costs of tort law, over time it appears that this system's apparent attractiveness has been reduced in practice. Compensation rarely appears to

be adequate, some employees engage in fraud, and companies resist workers' compensation provisions. The public perceives that system as substantially flawed at present. An additional worry for long-tailed risks would be whether companies that caused harms continued to exist long enough for the results of their activities to appear.

Analogues to the US Vaccine Injury Compensation System

The Vaccine Injury Compensation System, a hybrid of the regulatory and tort systems in the US, constitutes another model. Pharmaceutical manufacturers at one time argued that they could no longer manufacture vaccines because there was too little profit margin and even that could quickly disappear if the few people who suffered adverse reactions to vaccines were permitted to sue. Congress created the Vaccine Injury Compensation Program to encourage the production of needed vaccines by providing a streamlined procedure to compensate those who, in rare instances, experienced a vaccine-related injury. This was an alternative to traditional tort actions concerning injuries caused by vaccines and companies were immunised from suits by the legislation.

The Program has two main parts: compensation for so-called 'on table' injuries from vaccines, and compensation for 'off-table' injuries. On-table injuries are identifiable and have typical adverse effects from particular vaccinations. These receive fairly automatic compensation with minimal evidentiary showings.

Off-table injuries are those that might be causally attributable to a vaccine but the injury is atypical. People using this remedy may file a petition 'against the Department of Health and Human Services in the US Court of Federal Claims seeking compensation from the Vaccine Trust Fund'. They must specify who was injured, the vaccine that caused it, when and where it was given, the type of injury, when the first symptoms appeared and how long any adverse effects lasted (USHRSA, 2010).

For off-table injuries, tort law standards of proof apply, but the requirements on expert testimony set out in Daubert v. Merrell-Dow Pharmaceuticals (1993) do not because the magistrate hearing the case is both judge and juror. There is no need to screen a jury from experts; judges simply assess such testimony and give it appropriate weight. In addition, there are fewer formal procedures than in a typical tort case and the magistrates in this system appear to have a much more sophisticated grasp of scientific evidence than the general federal district judges that hear tort cases (Stevens v. the Secretary of Health and Human Services, 2001).

Successful petitioners may receive compensation for past and future non-reimbursable medical, custodial care, and rehabilitation costs, as well as up to USD 250 000 for pain and suffering, lost earnings and/or reasonable lawyer expenses. Death benefits of up to USD 250 000 plus reasonable legal fees are also permitted (USHRSA, 2010).

The Program is funded by an excise tax of USD 0.75 on each dose of vaccine (USHRSA, 2010). Thus, the costs of VICP seem likely to be paid by patients, their insurance companies or the government (in the case of those with government aid). During the 12 years of its existence it has provided 'a less adversarial, less expensive and less time-consuming system of recovery than the traditional tort system that governs medical malpractice, personal injury and product liability cases. More than 1 500 people have been paid in excess of USD 1.18 billion' since its inception. This averages to about USD 78 000 per plaintiff (US Department of Justice, 2010).

In principle, an analogue to the VICP appears to be a superior compensation system to torts and might function well in a legal system that emphasised the importance of precautionary policies. How might it work?

If a potentially hazardous product has been tested and subject to pre-market review (for example under Europe's Registration, Authorisation and Restriction of Chemicals (REACH) system) or is subject to post-market health regulations, neither might be sufficient to protect all those contaminated by the substance. Some will be more susceptible, some less so, because of life-stage, genetic heterogeneity, variation in detoxifying enzymes, age, pre-existing illnesses and so on. Some provisions need to be provided for citizens who are harmed because health standards failed to protect them (Cranor, 2008a).

For injuries that are typical of such exposures — analogous to 'on-table' injuries — there should be virtually automatic compensation. (The list of such injuries would obviously need to be developed and revised over time.) For injuries that were not typical but were suspected of being causally traceable to the toxic exposure subject to regulation, injured parties could make an argument that the compensation system should recognise such injuries with a standard of evidence similar to those employed in the VICP.

How well might such a system function? First, there would need to be a table of expected or not atypical injuries to people or damage to the environment from exposures in order to create the equivalent of 'on-table' injuries subject to compensation. This is a necessary element to expedite compensation. How difficult it might be to create such tables for more subtle diseases and dysfunctions is difficult to know but it should be addressed.

Second, there would need to be some showing that appropriate exposure had occurred that would support the connection between the technology and the adverse effects. Unlike vaccines where exposures are typically known with some degree of confidence, for environmental and even some workplace exposures, this critical element would likely be subject to numerous disputes.

Third, explicit provisions would be needed for long-tailed, subtle, adverse consequences of the technology, making it possible, with reduced procedural requirements, to argue that people or the environment had been damaged as a consequence. One might think of these as something like the off-table injuries if they were more atypical adverse effects.

A possible shortcoming of analogues to VICP is that tort law's preponderance of evidence standard is needed for off-table injuries. This attenuates the chances of compensation for those whose injuries that may have been caused by exposures — at least compared to the United Kingdom's Compensation Scheme for Radiation-Linked Diseases (discussed below).

September 11 Victim Compensation Fund

This fund was created by a separate law passed following the 11 September 2001 terrorist attack on New York city. Its aim was 'to provide compensation to any individual (or relatives of a deceased individual) who was physically injured or killed as a result of [the 11 September attacks].' Congress sought 'in part, to establish a mechanism that would provide financial security and assistance to the victims of the attacks without the uncertainties, delays and costs of traditional litigation' (Feinberg, 2004).

The legislation creates an administrative alternative to traditional tort litigation for the victims of the terrorist attacks. Injured parties were permitted to seek tort compensation instead but with substantial limitations. The law created a 'Special Master' with substantial powers to issue any 'procedural and substantive rules' and to determine eligibility under them. The Special Master had authority to determine the amount of compensation for harms suffered by those making the claims where this includes both economic and non-economic damages. Neither liability nor punitive damages could be considered. Congress authorised the funds necessary to pay compensation costs, but placed no aggregate limit on the total fund or on individual claimants (Feinberg, 2004).

The result was a hybrid system utilising some aspects of tort law but precluding liability and punitive damages. It authorised reduction of compensatory awards 'by payments that the claimant received from certain collateral sources'. Congress tried to create a comparatively quick and fair system for the victims. This was enforced by imposition of 'strict time limits' during which claims could be evaluated. Not everyone harmed by the attacks was eligible — only those 'individuals physically harmed or killed at the sites and in the immediate aftermath of the attacks.' Congress sought to ensure awards that were individualised between parties but not overly disparate between them. The details of these regulations and how they were implemented are described in the final report (Feinberg, 2004).

The Compensation Fund was created following a major tragedy and the enabling legislation passed in less than one week. There was no debate about the need or justification for compensation, which is likely to be quite different from analogous legislation that might cover environmental or environmental health harms. Moreover, there is a critical feature of this law that differs from traditional tort law. It was enacted and implemented in a manner similar to administrative or regulatory law: the Justice Department and Special Master had to implement regulations that would guide the award of compensation and considerations the Special Master had to take into account. The Master also had considerable discretion in deciding on individual amounts of compensation. There was provision for one to appeal these decisions, but appeals were considered within the same organisation that made the initial compensation decision instead of a separate appellate court. Once an appellate decision was issued, no further appeals were available. Thus, unlike the tort law or US administrative law, appeals were quite limited and were heard by lawyers within the structure created by the legislation (Feinberg, 2004).

This example does suggest that a compensation fund might be created under administrative procedures

rather than procedures more closely analogous to tort law. There could be rules issued for guiding an administrator or administrative agency in awarding damages and damage awards would be upheld on appeal as long as the administrative agency did not act to violate administrative procedures for adjudicating compensation under the rules.

In the US, an agency awarding compensation would probably be reviewed to determine whether it had 'substantial evidence' for its conclusion, assuming it had otherwise followed proper procedures. Thus, a reviewing court would consider whether, on the record established by the agency, it 'could reasonably make the finding'. Substantial evidence is 'such relevant evidence as a reasonable mind might accept as adequate to support a conclusion . . . [or provides] a substantial basis of fact from which the fact in issue can be reasonably inferred' (Davis, 1972). While this is somewhat vague, it conveys the idea that such decisions are reviewable, and acknowledges deference to the decisionmaker, but is not so strict as to force frequent second-guessing.

UK Compensation Scheme for Radiation-Linked Diseases

In 1965 the United Kingdom passed the Nuclear Installations Act to provide for civil liability for injuries from nuclear installations. This imposed strict or absolute liability for such injuries, rather than requiring proof of negligence. Despite this, subsequent litigation concerning such damages was complex, contentious and slow.

Consequently, this led to a voluntary Compensation Scheme for Radiation-Linked Diseases (CSRLD) in 1982. This was a joint agreement between British Nuclear Fuels Ltd (BNFL) and trade unions that worked within it. The aim was to create a quicker, more generous alternative to the normal litigation process, and reduce stressful and expensive litigation for complainants and expensive litigation for BNFL. Ultimately this was expanded to include other employers using radiation, and their unions. The Compensation Scheme initially permitted only compensation for mortality but later expanded to include morbidity. This agreement was possible because the causes of radiation-induced cancers were well understood as a result of past experience (CSRLD, 2010).

In order to make a claim under this programme, an employee must have worked for one of the companies that is a party to the agreement and have received a radiation dose during employment with one of the signatory companies. He or she must also be a member of a union that was party to the agreement, with some exceptions. The person must have been diagnosed with a disease that is typical of radiation exposure. Most cancers are considered eligible.

Compensation is determined by a person's radiation dose record from signatory employers, which is then used to assess the likelihood that a disease was caused by the exposure in question. Signatories have guidelines for determining the dose to which a person was exposed. The methodology to determine probabilities of causation and interpretation of uncertainties are generous toward claimants.

If a claimant is found to have radiation-induced cancer as a result of workplace exposure, the full value of a settlement is agreed by the parties and then discounted by the probability that it was the result of workplace exposure. Minimal compensation is awarded if the causation probability is 20 %, whereas in tort litigation the requirement for compensation would be at least 50 % (more likely than not).

If the odds of radiation-caused cancer are between 20 and 29.9 %, a quarter of the full value of a settlement is provided. If it is between 30 and 39.9 %, half is compensated, and from 40 to 49.9 %, 75 % of the full value is paid. If the probability of cancer is greater than 50 % then the full value of the disease is compensated. Most compensation that has been dispensed is for probabilities of causation below 50 %. One hundred and six people have received compensation for radiation-induced injuries, with payments totalling GBP 5.3 million or about GBP 50 000 per person on average.

Claimants have been much more likely to be successful than if their cases had been considered under tort law. They have received some compensation for their diseases based on the best information available, which was probably much quicker and more generous than civil litigation would have provided. The Scheme had therefore achieved its goals (CSRLD, 2010).

The United Kingdom also has a single-payer health system, the National Health Service (NHS), under which all citizens, including those suffering from illnesses caused by radiation, would receive essentially free health care for any diseases. Consequently, it would be difficult to compare compensation received under the CSRLD with compensation received in a country such as the US with myriad private health care providers and insurers.

In the United Kingdom, radiation-exposed employees would receive diagnosis and treatment for their diseases as quickly as the NHS provides it; this seems independent of the timeliness of compensation under the CSRLD. CSRLD compensation assists in setting right other matters beyond health care and rehabilitation for radiation-caused diseases. Clearly, countries with a single-payer system have quite important institutional resources that permit harm to be minimised and shortened as much as can be achieved through medical care and the rate at which patients are considered by the medical system.

Compensation under the CSRLD is possible because there is a substantial medical and exposure history with radiation. Well-designed, scientifically based compensation tables can be provided based on past injuries to earlier employees. Such a scheme could not be instituted quickly because creating the compensation tables depends so critically on a history of previous diseases. For new and subtle diseases, more likely to be typical of contemporary technological risks, this would be a limitation.

There appear to be modest incentives for companies to control exposures to radiation and reduce diseases and death as a result of this programme. If employees contract radiation-caused diseases, the company responsible must pay the required compensation, which is considered 'generous', and some packages are awarded based on probabilities well short of the preponderance of evidence. How successful this is likely to be in deterring dangerous exposure is difficult to judge. Will compensation packages in at least some cases be much less than the costs of preventing the diseases in the first place, especially when they involve substantial capital commitments? If so, the compensatory payouts by themselves would lack deterrence value. Of course, there could be other protective mechanisms, such as regulatory rules, inspections and so on.

New Zealand's no-fault compensation law

In 1972 New Zealand abolished almost all of its existing tort system and moved toward expanding a no-fault injury compensation scheme for compensating workers for personal injuries under the Accident Compensation Corporation (ACC). Initially covering workplace and automobile injuries, this was later expanded 'to cover virtually all accidental injuries and to confer very broad benefits on victims' (Schuck, 2008). Covered categories include motor vehicle accidents, work-related injuries both to employees and self-employed people, employees injured outside the workplace, medical treatment injuries, and coverage for those outside the workforce, such as children and the elderly.

Compensation is provided for injuries suffered, medical and rehabilitation costs associated with treating injuries, replacement of wages up to 80 % of average weekly earnings, impairment of earning capacity, loss of bodily function, possibly lump sum payments for permanent injuries, and benefits for surviving spouses and children, as well as funeral expenses. Injured people 'receive free hospital care and subsidized pharmaceuticals' (Bismark and Paterson, 2006). Compensation comes from different accounts corresponding to accident types and the category of victim involved. Peter Schuck observes that 'New Zealanders today generally regard their system … as a mainstay of their social policy' (Schuck, 2008). Others note that the 'ACC system is one of the simplest in the world for patients to navigate' (Bismark and Paterson, 2006).

Compensating all medical treatment injuries led to substantial costs and, consequently, for medical injuries subsequent legislation reduced 'the scope of covered injuries, shortened the time within which claims could be brought, and eliminated lump sum payments for pain and suffering' (Schuck, 2008). The programme reintroduced the notion of fault, similar to the US requirement of negligence for medical malpractice. In this New Zealand reverted to the previous standard of care that had been used in tort medical malpractice suits before instituting the ACC. There do not appear to be such restrictions for other 'accidents' in the workplace — from automobiles, and so on.

Illnesses not caused by accidents and wilful self-inflicted injuries are excluded from compensation, creating tensions within the system (Henderson, 1981). Injured parties who are not employed, such as children and the elderly, may not be similarly compensated, since they receive no earnings equivalent (Bismark and Paterson, 2006).

Aspects of the New Zealand system in large part seem consistent with a precautionary view of the world. It is relatively simple to navigate and claims are dealt with expeditiously, minimising the time before injuries are addressed. This in turn should shorten the duration of harm that must be endured. It appears that all accidents (with minor exceptions) are eligible for compensation.

A serious shortcoming appears to be the ineligibility of illnesses, at least with respect to the

medical compensation system. Moreover, the focus on 'accidents' might suggest that it is traceable to earlier views in which illnesses were seen as resulting from 'natural' processes, not induced by human activities. The result is that the system might underemphasise illnesses, dysfunctions or death traceable to toxic and other environmental exposures. In addition, the system appears to lack deterrents discouraging activities that lead to accidents (or illnesses).

Precautionary assurance bonds for environmental damage

Liability regimes for environmental damage are helpful but apply after the damage is done (EC, 2008, 2009 and 2010). A more precautionary approach to future environmental damage could involve the use of assurance bonds.

An assurance bonding system is an arrangement in which commercial entities whose activities might have adverse impacts on the environment must 'pay in advance for the costs they might inflict on society if they adopted the most harmful method of disposal, [it] reverses the usual presumption of 'innocence' over 'guilt' as applied to environmental damages' (Costanza and Perrings, 1990). A simple example is a refundable deposit on glass bottles. This encourages users to dispose of the bottles by returning them to a location where they would be recycled instead of their becoming litter, thus providing incentives for better disposal.

Because it is difficult or impossible to calculate the costs of future damage, it is unlikely that a private insurance market could encourage similar behaviour. There are therefore two alternatives: costs from future damage could be imposed on public agencies or privately injured parties when damage occurs, or they could be imposed on the party engaging in an activity that could have possible adverse future consequences.

Assurance bonds impose responsibility and costs on the entity undertaking the activity that might adversely affect health or the environment. A government body would estimate potential future costs of adverse environmental consequences and impose a fee for those on any party whose activities threatened environmental resources.

Under the scheme, each resource user would be required to post bonds, refundable at specified dates if the intertemporal external costs of the activity turned out to be less than those assessed by the environmental authority. The value of the bond at the date of posting would be a function of the environmental authority's [best] estimate of the costs of environmental repair or rehabilitation if the worst happened between the date of posting and the refund date. The value of the bond would be higher, the greater the estimate of the worst case costs (Costanza and Perrings, 1990**).**

The bond would be refundable in whole or part if the resource users could demonstrate lower damages than those assumed by the agency setting the bond. The burden of proof that the estimate of the agency was incorrect would lie with the user of the resource**.** The system should therefore provide a strong economic incentive to firms to research the future environmental costs of their activities, and so to improve their environmental performance. If the environmental authority's estimate of the worst case costs were revised downwards during the life of the bond it would be reduced; if revised upwards it would be increased. This feature of the scheme provides the incentive to resource users to research the future environmental effects of their activities (Costanza and Perrings, 1990).

Such bonds provide a means for addressing ignorance and uncertainty associated with possible future environmental hazards, as well as deterring undesirable behaviour. When businesses are required to post bonds, if harm from their activities occurs, there are resources that can assist in whole (the preferred alternative) or in part (less preferred) in compensating those whose property or person have been harmed and assist in repairing damage to the environment. The greater the upfront bond, the more likely adequate resources would be available to address adverse consequences. Of course, a bonding scheme would need to be supported by an appropriately quick and adequate compensation system similar to the best ones we have considered above.

Assurance bonds have a number of virtues. They provide incentives for private parties and government agencies to conduct research and improve estimates of adverse environmental impacts before the activities are instituted. They also internalise these calculations into the procedures of a commercial enterprise with nudging from environmental agencies. They help correct underinvestment in research on such adverse effects. The funding of environmental protection through the bonds would be proportionate to the size of the problem insofar as this could be determined. And the inducement for research would also be approximately proportional to the assessed social costs of permitting the activity to proceed in ignorance (Costanza and Perrings, 1990).

If companies cannot afford the upfront bonds, they would not be permitted to engage in the activity; in short, no bond, no market.

Importantly, bonds help protect against economically marginal firms whose activities might turn out to be especially environmentally damaging. If they are marginal, they would likely lack resources to address the problems after they occurred and simply go out of business or declare bankruptcy rather than provide compensation for damage caused. Bonds required for activities prior to instituting a potentially hazardous activity would provide funds when firms are optimistic about their activities to ensure that there will be resources to address problems when they arise, even if the firms are no longer in business (provided funding is held in trust). This resembles a common rationale for administrative regulation of risks rather than post-market injury suits to repair damage when risks materialise into harm (Cranor, 1993).

Assurance bonds promote a precautionary approach, placing approximate upfront costs on commercial activities insofar as these can be determined. They do not require testing or estimates of adverse effects of products or activities as does REACH, but they provide incentives for it. If in fact harm occurs, there is then a fund, hopefully adequate, to begin to repair, minimise and shorten damage.

Moreover, because bonds provide incentives to conduct research to discover future harms, they might assist in discovering long-tailed, less visible adverse consequences of technology earlier. They might provide some incentives for businesses to reveal risks earlier in order to increase funds that might be returned should harms be minimised. While there is no explicit deterrence in the form of punishments or penalties, the equivalent of some deterrence exists because firms have resources at stake, which they would lose if there were adverse consequences, but which would be refunded if there were not.

A possible downside is that assurance bonds might overly burden new technologies, possibly discouraging investment in new but potentially risky activities. This concern might be addressed by requiring upfront bonds commensurate with the extent of risks. For low probability, relatively contained risks when enterprises are small, lesser bonds could be required, but as commercial activities grow and the range of risks increases, bonds should probably be increased appropriate to potential costs of risks. The size of commercial activities would need to be monitored in order for the bond fund to keep pace with potential risks. Governmental agencies may or may not be up to the task of on-going monitoring. An illustration of how an assurance bond scheme could have been applied to the Deepwater Horizon disaster is provided in Panel 24.3.

24.2.3 Desirable features of compensation systems

Comparatively quick measures to identify diseases and environmental damage due to poorly understood technologies and quickly minimise and shorten them would promote precautionary approaches better than slower systems. There are tensions between the rationales of the different compensatory systems reviewed above. Different ones might be more appropriate for the varying circumstances and institutions of individual countries, e.g. the presence of universal health care or existing compensation systems like New Zealand's.

The best compensation systems appear to have nearly automatic provisions for many classes of injuries (ideally all). It may be difficult to provide tables for automatically compensable health injuries and illnesses, and for environmental damage from less well understood technologies, but decision-makers must do the best they can. This might be more difficult for subtle, long-tailed risks. Some of these problems would be eased in countries with single-payer, universal health care such as many countries in Europe have, and in New Zealand's no-fault compensation system for accidents, with extensions to diseases and the environment.

A compensation arrangement with some similarities to administrative law and some features of the September 11 Fund in the US might be desirable. In this an administrator would have considerable discretion to award compensation and it would likely be more efficient in quickly providing resources to repair damages suffered. There would, however, need to be some constraints on decision-maker discretion to ensure justice between applicants and to utilise funds efficiently.

The generous compensation system of the UK's Compensation Scheme for Radiation-Linked Diseases, with allowances for compensating for cancers with probabilities less than 50 % is notable. It could be difficult to duplicate, however, because it rests on a long, well understood history of radiation-caused diseases with prior victims. It is nevertheless worth considering.

Panel 24.3 Precautionary assurance bonds for potentially serious environmental risks

Robert Costanza has long advocated anticipatory assurance bonds on corporations as a means of internalising and helping to minimise future environmental costs from their large scale, potentially hazardous technologies (Costanza and Perrins, 1990). His argument is summarised below, based on lessons from the Deepwater Horizon oil spill (Costanza et al., 2010).

The spill from the *Deepwater Horizon* is causing enormous economic and ecological damage. The spill has directly and indirectly affected at least 20 categories of valuable ecosystem services in and around the Gulf of Mexico. The USD 2.5 billion per year Louisiana commercial fishery has been almost completely shut down. As the oil extends to popular Gulf Coast beaches, the loss of tourism revenue will also be enormous. In addition, the spill has damaged several important natural capital assets whose value in supporting human well-being is both huge and largely outside the market system. These non-marketed ecosystem services include climate regulation via the sequestration of carbon by coastal marshes and open water systems, hurricane protection by coastal wetlands, and cultural, recreational, and aesthetic values.

A recent study estimated the total value of these ecosystem services for the Mississippi River Delta to be in the range of USD 12–47 billion per year (Batker et al., 2010). Based on the flow of these services into the future, the value of the Delta as a natural asset was estimated to be in the range of USD 330 billion to USD 1.3 trillion, far more than the total market value of BP (USD 189 billion) before the spill. Unlike BP, ecosystem service values are outside the market. They continue to produce benefits unless an action like the spill damages them.

One major lesson is that our natural capital assets and other public goods are far too valuable to continue to put them at such high risk from private interests. We need better (not necessarily more) regulation and strong incentives to protect these assets against actions that put them at risk. Our current approach to dealing with the risk of private interests damaging public environmental assets is to assign liability to the private interests, but with the burden of proof on the public. The public must demonstrate damages after the fact, claim compensation, endure a lengthy judicial process, and finally hope to recover just reparations. In addition, the total liability is often limited, as with oil spill and nuclear accident cots. This gives private interests strong incentives to take large risks with public assets — far larger than they should from society's point of view.

The long-term solutions to these problems require fundamental changes to business-as-usual practices, including assessment and incorporation of the full value of public natural capital assets into both corporate and public accounting and decision-making, a reversal of the burden of proof from public to private interest, and a requirement of corporations and other private interests to internalise and monetise their risks to public goods.

One way to internalise and monetise these risks would be to require private interests to post an 'assurance bond' large enough to cover the worst-case damages. Portions of the bond (plus interest) would be returned if and when the private interests could demonstrate that the suspected worst-case damages had not occurred or would be less than was originally assessed. If damages did occur, portions of the bond would be used to rehabilitate or repair the environment and to compensate injured parties. The critical feature is that the risk to the public asset is apparent to the private interests in financial terms before the fact, not as a liability that may or may not be enforced after the damage occurs.

Imagine how this system might have worked had it been in place prior to the Deepwater Horizon incident. What actually occurred is pretty close to the 'worst-case' scenario that might have been envisioned before the fact. Our best guess of the potential damages would thus be in the range of USD 34–670 billion. Let's say that a scientific review panel, after assessing the risk in more detail, settled on an estimate of USD 50 billion. This immediately makes it very apparent to BP and others drilling in deep water in the Gulf of Mexico that they are engaged in a *very* risky business — several orders of magnitude riskier than the USD 50 million liability limit previously in force. What could they do? Either not drill at all or find ways to reduce the size of the risk and the bond. They might be able to do this very cost-effectively if they spent some money on risk-reduction procedures or technology, such as the acoustic blowout preventer costing a mere USD 500 000 which they failed to install on Deepwater Horizon. These

Panel 24.3 Precautionary assurance bonds for potentially serious environmental risks (cont.)

measures might convince the scientific review panel to change its assessment of the worst-case scenario and reduce the bond. There would be very strong economic incentives for BP to find creative ways to reduce the risks rather than ignoring the risks and cutting corners.

The *Deepwater Horizon* incident offers a strong lesson in risk management. Our entire society is taking far too many risks with public assets whose real value we are only now beginning to recognise. By shifting the financial burden of those risks onto the private interests who benefit from them, we can establish the right incentives, shift investment to less risky, more productive pursuits, and create a more sustainable and desirable future.

Source: Costanza et al., 2010.

Funding for some of the systems suggests useful features of a model. Workers' compensation and the Vaccine Injury Compensation Program in the US all institute a fee on the covered activities to create a monetary source from which compensation can be paid. This is likely to be attractive to government agencies facing tightened budgets or long-term budgetary concerns. Moreover, if contributions to a compensation fund are based to some extent on a company's safety record with regard to the activity, this may provide some modest deterrence feedback to the company to modify its safety practices toward the new technology. Workers' compensation funds do this explicitly; there is no 'deterrence surcharge' in the VICP and it is not clear that there is such a surcharge in the UK's radiation compensation programme.

Health care and rehabilitation services, likely to be part of some but not all health care systems do not exhaust compensatory needs. People's loss of earning capacity and long-term care, as well as compensation for families left poorly supported, must be addressed.

Assurance bonds or insurance if it is available in the markets, paid for upfront by companies whose technologies appear to pose health or environmental risks, provides important resources to help fund anticipatory research into risks and to provide compensation so that society does not have to pay for any future damage. When companies put up their own money, this provides incentives for better research on risks associated with their technologies and deters carelessness or recklessness in creating such risks.

24.3 Conclusion

Early warning scientists and others who identify potential impending harm have sometimes been discouraged in the past or actually lost positions or suffered various kinds of losses. However. they often bring forth useful and timely knowledge and therefore need to be encouraged and not harmed for their efforts. Good public policy suggests laws should discourage such actions in the first place and justice requires rectification if they are the subjects of retaliation. And if warnings are not heeded and damage results, or if damage results even when there were not warnings, it has often proved difficult in the past to achieve prompt and fair compensation for the victims.

This chapter has explored some ideas for reform, building on some current institutional models in the hope that this will raise awareness of these issues among the wider public and suggest plausible improvements in current law and practices.

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25 Why did business not react with precaution to early warnings?

Marc Le Menestrel and Julian Rode

In the past, companies have frequently neglected early warning signals about potential hazards for human health or the environment associated with their products or operations. This chapter reviews and analyses relevant interdisciplinary literature and prominent case studies — in particular those documented in both volumes of *Late lessons from early warnings* — and identifies main factors responsible for the disregard of early warning signals.

The chapter shows how economic motives often drive non-precautionary business decisions. In virtually all reviewed cases it was perceived to be profitable for industries to continue using potentially harmful products or operations. However, decisions are also influenced by a complex mix of epistemological, regulatory, cultural and psychological aspects. For instance, characteristics of the research environment and the regulatory context can provide business actors with opportunities to enter into 'political actions' to deny or even suppress early warning signals. Also, business decision-makers face psychological barriers to awareness and acceptance of the conflicts of values and interests entailed by early warning signals. Cultural business context may further contribute to the denial of conflicts of values.

The chapter concludes with a set of reflections on how to support more precautionary business decision making. A prominent policy response to the conflicting interests of business and society is introducing regulations that attempt to steer business rationality towards internalising external effects. Innovative solutions such as assurance bonding should be considered.

There is a need to better understand and expose why business actors do not respond voluntarily to early warning signals with precautionary actions. Blaming business, in particular with hindsight, tends to be common reaction that may not always be constructive. It often misses the complex or even contradictory set of motives and drivers that business actors face.

Public institutions could support progressive business by analysing and publically disclosing the dilemmas and temptations entailed by early warning signals, for example for different industries and for the specific societal and regulatory context of decisions. Rigorous and explicit exposition of the dilemmas will create further incentives for responsible actors to share and communicate their precautionary responses.

An additional reflection centres on the role of political actions of business actors, in particular those actions aimed at suppressing early warning signals. Regulatory efforts that make the political actions of business more transparent can help to sustain a sound balance of power, thereby maintaining our ability to benefit from early warning signals and reducing the likelihood of health and environmental hazards.

25.1 Introduction

Late lessons from early warnings (EEA, 2001) describes a number of prominent cases in which early warning signals about potential hazards from the use of commercial products or operations have been neglected over long periods of time, eventually with grave consequences for human health and the environment. While the volume derives lessons which focus primarily on improving decision-making by regulatory agencies, it becomes also very clear that decisions to act with precaution — or the failure to do so — often involved business actors. Private companies have been the main drivers of innovative activity and, notwithstanding the benefits they have generated for society, their business practices and products have in many instances also caused considerable harm. In essence, EEA (2001) shows that business decisions played a major role when things went wrong.

So why did companies not act with precaution when early warning signals were available? In this paper, we review case studies from EEA (2001) as well as some additional 'early warnings' cases which appear in this volume. We look for patterns in these past experiences and study relevant interdisciplinary academic literature with the aim to analyse and better understand the situation of companies that are confronted with early warnings. We identify several potential impediments for business decision-makers to act in a precautionary manner, which we summarise in three 'lessons about business'. We conclude with some reflections on how to support more precautionary business decision-making in the face of early warning.

There is no doubt that many business actors recognise their responsibility to strive for economic benefits, in line with a wider regard for human welfare and with respect for the natural environment (see WBCSD, 2010). This analysis should be useful for decision-makers to be aware and better understand the challenges and potential pitfalls of business behaviours when dealing with early warnings. For policy makers as well as the general public, the analysis should foster a more integrative and differentiated judgement of the role of (different) types of business actions towards society.

25.2 Impediments for companies to respond to early warnings in a precautionary manner

25.2.1 Economic rationality

The standard economic paradigm that underlies typical present day business decisions takes root in the times of classical industrial society (Shrivastava, 1995). Private corporations in a market economy are regarded as systems of production with the purpose of profit maximisation. In such a worldview, economic value created by business actors is understood primarily as financial returns to owners, typically the shareholders. Though a variety of novel approaches have been brought forward (e.g. Kelly, 2001, 2012), this paradigm is the main driver behind management decisions. It is embedded in decision tools across corporate units, and remains the core element of management education. Since half a century, it has been to a large extent shared and supported by mainstream ideology and the public perception of the role of business within a free market society (Friedman, 1970; Karnani, 2010).

The idea of profit maximising firms embraces a rationality according to which ethical values are reasons to act if and only if they contribute to the expected economic benefits for the business actor (Le Menestrel, 2002). In particular, nature and society at large are external to the business environment, and potential societal and environmental costs are not to be taken into account in business decisions unless they imply potential costs for the business actor. Accordingly, the internal risk evaluation that is part of the standard cost-benefit analysis toolbox is typically limited to minimising financial business risk, i.e. the comparison of expected revenue or profit figures (Sommerfeld, 2010). External risks to human health or the environment may enter the calculations, but only insofar as they indirectly pose a business risk via legal liabilities, regulatory restrictions or reputation risks for the company.

Economic rationality is thus remote from a proactive precautionary response to early warning signals. Virtually all reviewed cases have in common that early warnings about harmful effects were available, but that the prospect of short-term profit generated strong economic incentives for companies to continue with their practices. The most efficient fishing methods (EEA, 2001, Ch. 2), the sales and use of cheap and effective substances such as benzene (EEA, 2001, Ch. 4), lead in petrol (Chapter 3), asbestos (EEA, 2001, Ch. 5), insecticides (Maxim and van der Sluijs, 2007 and Chapter 16), or growth hormones for meat production (EEA, 2001, Ch. 14) are only some of many examples. Moreover, competitive market forces can further increase the economic pressure for using potentially hazardous product or for gaining a monopoly position from early introduction of innovative products or methods (Gollier and Treich, 2003; Maxim and van der

Sluijs, 2007). Voluntary preventive measures and costly scientific research that may confirm the harm or the involved risks are usually expected to be detrimental to financial performance.

Reputation
Public concerns or 'conscious consumer' preferences for safe products and operations have the potential to induce economic incentives for socially or environmentally responsible business behaviour (Banerjee et al, 2003; Rode et al., 2008). A company that is economically rational will not sell a product that, for reasons of public concern or lack of consumer trust, may not be profitable or give rise to consumer boycotts. The eventual termination of the use of antimicrobials (EEA, 2001, Ch. 9) and of growth hormones (EEA, 2001, Ch. 14) for meat production in Europe was driven to some extent by growing public concern about potential health risks. Such public concern can be a powerful force, no matter whether it is driven by the available scientific evidence or, in some cases, unrelated to evidence, or even overrating the dangers (Sunstein, 2003). In many cases, however, the public lacks knowledge about early warnings, underrates the risks (see also Section 25.2.4 on psychological factors), or does not feel affected. Under these circumstances, public concern about specific uncertain hazards of a particular product or industry is generally absent or weak. Consequently, reputation does not provide a sufficient economic incentive for precautionary behaviour.

Moreover, economically rational companies can decide to influence public opinion in their favour when this appears cheaper than reducing or terminating the potentially harmful practice. If companies themselves hold information about potential harm of their products or operations, they can choose not to disclose it. Voluntarily disclosing early warning signals about a potential hazard creates the risk that consumers refrain from buying the product, and consumers seem to reward transparency and honest disclosure of negative information only under very limited conditions (Aktar and Le Menestrel, 2010). When negative information is generated outside the company and becomes public, we describe below that companies have in the past employed a variety of measures to influence public opinion in order to prevent or at least weaken reputation risks.

Economic interest in preventing harm
In some instances, specific industries stand to lose from potential hazards and have an economic interest in precautionary termination of the potentially harmful activities. For example, when inshore cod fishers in Newfoundland suffered from falling catches due to unsustainable off-shore fishing practices (EEA, 2001, Ch. 2), they reacted with protests and the commissioning of a report, which gained media attention and eventually lead to an official reappraisal of the situation on depleted fish stocks. The Arcachon oyster industry feared the harmful effects of TBT as antifouling biocides for boats and strongly supported the implementation of restrictions on the use of TBT (EEA, 2001, Ch. 13). Beekeepers suspected early on a toxic effect of the insecticide Gaucho on bee populations and fought hard for the recognition of the evidence (Maxim and van der Sluijs, 2007 and Chapter 16). These cases, however, seem to be a minority compared to those where industries have direct and strong economic motives against taking precautionary measures.

25.2.2 *Uncertainty in science and the research environment*

Scientific uncertainty
The research community is expected to provide the necessary scientific evidence for determining whether early warnings of hazards are credible and substantial enough to justify precautionary measures. However, the prevalence of scientific uncertainty about hazards can weaken acceptance of such evidence and act as an impediment to precautionary responses to early warning signals. Here it is important to consider, however, that the uncertainties that companies face today are increasingly characterised by indeterminacy and even ignorance (Stirling, 2003). Typical examples are the effects of industrial operations and substances on (marine) ecosystems (EEA, 2001, Ch. 2) and the uncertainties regarding environmental or health effects of mobile phones (Chapter 20), GMOs (Chapter 18) or nano-technologies (Chapter 21). It seems difficult for people to cognitively deal with and to act upon such strong uncertainty (Weber, 2006 — see also Section 25.2.4 on psychological aspects below) and to comprehend the complexity of natural systems (Sivakumar, 2008; Kysar, 2009). Moreover, it becomes problematic to apply the standard risk analysis tools that are based on cost-benefit analysis and require knowledge of the set of possible outcomes and estimated probabilities of their occurrence, which are not always available (Ashford, 2005). It remains a challenge for social science, and in particular for business research, to develop appropriate concepts and operational tools that help companies deal with this type of uncertainty (e.g. Kunsch et al., 2009).

Secondly, it is often not recognised — and not communicated sufficiently to the general public — that even when scientific evidence with probabilistic data exists, uncertainty is an intrinsic and essential characteristic of science. There is no scientific justification of a 'sufficient level of confidence' or for the appropriateness of a confidence interval of 99 % or 95 % (Crawford-Brown et al., 2004; Ashford, 2005), and it is an ethical or political issue rather than a scientific one to determine an 'acceptable level of risk' for a 'reasonable fraction of the population' (Crawford-Brown et al., 2004). Moreover, in light of different scientific methods (e.g. based on direct evidence, correlations, model predictions), levels of data quality (e.g. with respect to statistical properties, reliability, relevance or level of scrutiny), and different lines of evidential reasoning (e.g. with respect to conceptual clarity, logical deduction, methodological rigor) the 'weight of evidence' from scientific results is almost always open to subjective judgment and interpretation (Crawford-Brown et al., 2004; Rauschmayer et al., 2009).

Interpreting and 'manufacturing' uncertainty

The uncertain and sometimes ambiguous nature of scientific evidence seems to stand in a stark contrast to the perceptions and idealistic expectations of science by the general public (Ravetz, 2005; van den Hove, 2007) and to its preference for complete certainty for justifying actions, in particular when the actions involve concrete costs (Dana, 2003). This allows industry lobbyists to oppose or prolong precautionary measures by 'manufacturing uncertainty' and generating doubt on the state of scientific evidence. Examples abound where corporate public relations efforts have exploited the subjectivity in judgment and interpretation of particular results, and used rhetorical tricks to emphasise the remaining uncertainty and the need for further research. Rampton and Stauber (2001) give an early account of such processes, while Oreskes and Conway (2010) provide a historical perspective of this controversial interface between science and business. One may also look at Sismondo (2008) for an example in the pharmaceutical industry.

According to Maxim and van der Sluijs, (2007 and Chapter 16), Bayer seems to have repeatedly used selective knowledge and 'semantic slips' to blur the evidence of a toxic effect of Gaucho on bee populations. In the case of benzene, manufacturers hired consultants to downplay the importance of scientific evidence and to introduce irresolvable arguments about dose-response analysis, which delayed governmental regulation (EEA, 2001, Ch. 4). Monsanto in the 1960s launched a public defense of PCBs, arguing that scientific evidence was not clear, and that it would take extensive research, on a worldwide basis, to confirm or deny the initial scientific conclusions (EEA, 2001, Ch. 6; Francis, 1998). Shell in 1967 circumstantiated its denial of a causal relationship between leaking chemicals and effects on wildlife and human health in the Great Lakes area by publishing a report saying that fish killed due to chemical contamination had not been verified by recent studies (EEA, 2001, Ch. 12).

Brush Wellmann in the 1980s hired PR specialists to create a more favourable public opinion and to reassure customers of the safety of beryllium, for instance by claiming that any reports of disease at less exposure than the current limit were scientifically unsound. In the late 1990s, when it was beyond doubt that the established beryllium exposure limit was not effective in protecting workers, Brush Wellmann initiated more research and convened a conference that propagated the need for further research before any new limit could be set (see the analysis at the end of Chapter 6). The millions of pages of previously secret internal tobacco industry documents, made public in the Minnesota trial, revealed the extent to which the effects of nicotine were known and intentionally blurred for consumers by creating doubt about the health risk (Hurt and Robertson, 1998). Similarly, in order to 'keep the debate alive', the tobacco industry financed the creation of new research institutions to carry out research on the effects of second hand smoking (Hong and Bero, 2002 and Chapter 7).

In the early days of the debate about climate change, Exxon was publicly contesting the science, based on its complexity and associated uncertainties. While presenting itself as 'a science and technology-based company', its strategy of preventing political action on climate change was chiefly implemented through efforts in publicly denying the existence of the problem that they had privately identified (van den Hove et al., 2002). In essence, by emphasising the lack of scientific certainty companies can contribute effectively to a 'paralysis by analysis' that prevents precautionary measures in response to early warning signals (EEA, 2001).

Corporate influence on scientific research

When industry and research are interacting closely, for instance in medicine (Sismondo, 2008), companies can also directly influence scientific results. They do not even have to manipulate results or engage in other forms of misconduct, which may happen in some cases (Francis, 1998), but they can effectively bias research results in their own interest by inducing so-called (pro-industry) design

and publication biases. It is common that the main indicator of scientific confidence of a harmful effect is the number of published studies that provide evidence for the effect vs. the number of studies that do not find one. This overall impression of sheer number of scientific results, however, can easily be altered through the selection of which scientific studies to actually carry out (Lexchin and O'Donovan, 2010). In particular since companies typically have significant financial means, they can strive to misrepresent the weight of results in their favour by sponsoring those scientific studies and methods which can be expected to produce favourable results.

As prominently done by the tobacco industry (Grüning et al., 2006), companies can further enhance this bias by organising symposia and publishing their proceedings. Symposia proceedings are typically not peer-reviewed, but still cited as published results. Another example where these strategies were applied is research on the health effects of lead in petrol. As reported in Chapter 3, the relevant studies were conducted and funded exclusively by the Ethyl Corporation and General Motors for over 40 years, and General Motors controlled the publication of results and imposed tight reporting constraints on the regulating US Bureau of Mines. In this case, it is even said that critical independent scientists had their funding withdrawn and their jobs and lives threatened. In the Gaucho debate in the 1990s, Bayer relied almost exclusively on their own research to argue against evidence of toxicity (Maxim and van der Sluijs, 2007 and Chapter 16). In the case of beryllium (Chapter 6), Brush Wellmann financed new publications within the beryllium health and safety literature under the names of well-known academics.

Unfortunately, these cases weaken the credibility of privately sponsored research and create a difficulty for companies that have a genuine and honest interest in objective and unbiased research about the risks of their products or operations.

25.2.3 *Gaps and loopholes in the regulatory framework*

A perfectly operating regulatory system would employ appropriate mechanisms to assure that companies only take the risks that are deemed acceptable by society at large. Commonly used regulatory mechanisms are legal constraints that limit or prohibit certain activities, laws that prescribe safety standards, or liability and tax systems that align the economic interests of the company with the interests of society (Pigou, 1912). The Precautionary Principle is widely recognised as guidance to 'err on the side of caution' and to opt for preventive regulatory measures when an activity is believed to threaten human health or the environment, even if there is no scientifically established evidence (Tickner and Raffensberger, 1998). Within a perfect regulatory system, it may be argued that the sole responsibility of a company is 'to increase its profits so long as it stays within the rules of the game' (Friedman, 1970). Many of the reviewed cases revealed, however, that the regulation which actually constrained corporate decision-making in the face of early warning signals, were far from such an ideal regulatory system. The following paragraphs highlight some key gaps and loopholes of the regulatory framework.

Incomplete information for regulation

First, regulators often do not have the complete information that would be necessary for imposing all appropriate constraints. On the one hand, this is of course due to the high degree of uncertainty or ignorance inherent in the activities, such as currently for nanotechnology or for GMOs. In addition, however, regulatory measures such as legal bans, safety standards or contingency plans often rely on information that is generated within the companies whose products or activities have to be assessed (EEA, 2001). For instance, companies may be the ones to first recognise early warning signals, as exemplified in the famous article of Bill Joy, the co-founder and Chief Scientist Officer of Sun Microsystem, alerting the public about the risks of genetically modified organisms, robotics and nanotechnology (Joy, 2000). Even in the presence of information disclosure rules, it is frequently up to the companies to reveal such 'private information' to the regulatory agencies. Not revealing important information can hence delay or distort regulatory action.

Regulation rarely induces full internalisation of externalities

Apart from their *ex post* role of ensuring justice, liability regimes are meant to provide *ex ante* the incentive for companies to internalise potential harm to society or the environment in their business decisions, to make sure that companies have the financial means for compensation, and to motivate complete risk assessment as well as precautionary measures (Boyd, 1997). In accordance with the 'polluter pays' principle, financial responsibility rules would take the form of strict liability to pay for potential harm. Alternatively, 'assurance bonding' can require companies to deposit a premium that

would cover the costs of potential damage before undertaking the dangerous activity (Kysar, 2009).

In many past cases, however, limited or even complete absence of liability have undermined the polluter pays principle and left companies without economic incentives to internalise external risks. Then, external costs from corporate action are typically borne by society at large. In the case of fisheries (EEA, 2001, Ch. 2) there was no corporate liability in place to account for externalities of overfishing and the costs to restore stock is to be paid by governments of the respective adjacent states. Similarly, the majority of external costs from MTBE in petrol (treatment of contaminated water, alternative water supply, health costs etc.) were borne by society (EEA, 2001, Ch. 11). For asbestos in the United Kingdom, it is argued that the market price of asbestos was so low since it did not internalise the external costs, which remained with families, health service, insurance carriers and building owners (EEA, 2001, Ch. 5). Even though laws on prevention, compensation, and sanctions existed as early as in the 1930s, they were simply not appropriately implemented.

There are other important aspects that determine the effectiveness of liability regimes in steering corporate conduct. For instance, the evidentiary strength to determine when liability comes into effect may be more or less strict, ranging from the need of 'clear and convincing evidence' vs. 'more probable than not' vs. 'preponderance of evidence', or the requirement of a 'substantial cause or factor' vs. 'contributing factor'. In addition, it is crucial whether the legal burden of persuasion is with those who suffer the harm or whether it is the responsibility of the industry to prove that no harm was done (Ashford, 2005). Clearly, a company facing a legal situation in which the victim has to provide convincing evidence that the corporate activity was a substantial cause for the suffered harm can expect fewer costs than in other situations, e.g. in which the burden of proof of no harm lies on the company.

It has also been noted that insolvency risk can further undermine full cost internalisation by companies, especially when harm would only occur in the far future (Boyd, 1997). For instance, Manville Corporation filed for bankruptcy in 1982 as a means of dealing with asbestos pollution claims (EEA, 2001, Ch. 5), when it was far too late to act with precaution towards asbestos.

Conflicting mandates of regulatory agencies

The implementation of a regulatory framework that adequately constrains companies for protecting society from potential hazards requires that the responsible governmental agencies have a clear mandate to do so. Governmental agencies sometimes have conflicting mandates. Before establishment of the US EPA, for instance, the US Department of Agriculture was responsible for environmental regulation in the debate on chemical contamination of the Great Lakes. As a supporter of the economic interests of the agro-industry, it tended to align itself with the pesticide manufacturers and the farmers, demanding proof of causal relationship before 'massive' approbations and expenditures of public and private funds on remedial works' (EEA, 2001, Ch. 12). In a similar fashion, the US Department of Fisheries and Oceans (DFO), which was responsible for reporting the scientific evidence on overfishing, is said to have followed the interests of the fishery sector (EEA, 2001, Ch. 2). The DFO is accused of having presented biased results, referring to remaining uncertainties, and of arguing against 'pseudo-science' and bad faith of early warnings.

Conflicting mandates of regulatory agencies are reported in further instances. In the case of the 'mad-cow disease', the responsible British Ministry of Agriculture, Fisheries and Food (MAFF) was expected simultaneously to promote the economic interests of farmers and the food industry whilst also protecting public health from food-borne hazards (EEA, 2001, Ch. 15). In the debate on the toxic effects of Gaucho, the French Ministry of Agriculture was responsible for the contradictory demands of intensive agriculture and beekeepers and at the same time for the management of risks issuing from the agricultural sector's activities (Maxim and van der Sluijs, 2007, and Chapter 16). The US Department of Energy (DOE) was responsible both for the cheap production of nuclear weapons and the protection of workers through appropriate beryllium exposure limit (Chapter 6).

Corporate influence on regulation

Regulators have in the past not always judged and decided objectively and independently with respect to corporate interests. In several cases, regulatory agencies and committees included experts with a conflict of interest, who could shape policy recommendations by interpreting scientific evidence in the interests of the industry. Again, the tobacco documents have revealed the extent to which industry is able to subvert public institutions. In a report about the strategies to undermine tobacco control activities of the World Health Organization, authors write that 'evidence from tobacco industry documents reveals that tobacco companies have operated for many years with the deliberate

purpose of subverting the efforts of the World Health Organization (WHO) to control tobacco use. The attempted subversion has been elaborate, well financed, sophisticated, and usually invisible' (Zelltner, 2000).

In the case of benzene (EEA, 2001, Ch. 4), the American Conference of Governmental Industrial Hygienists (ACGIH) repeatedly recommended benzene limits higher than those in line with scientific evidence on benzene poisoning. Scientists employed by various corporations participated in the Threshold Limit Value Committee that made exposure recommendations (Castleman and Ziem, 1988). In the early phase of using lead in petrol in the 1920s (see Chapter 3), public health specialists acted as paid consultants to the Ethyl Corporation while at the same time advising the US Government's Bureau of Mines, providing assurances of 'complete safety' for public health. In the pharmaceutical domain, conflicts of interest seem pervasive. Reviewing three European drug regulatory agencies, Lexchin and O'Donavan (2010) find evidence of widespread potential conflict of interests among scientific experts.

Last, companies can also influence regulation indirectly through the above mentioned influence on public perception of the involved risks. In an increasingly demand driven economy, public trust, consumer perceptions or NGOs can have a considerable influence on the politics and decisions of regulatory agencies (Aerni, 2004; Carter, 2002).

25.2.4 Psychological factors

There is ample evidence from the behavioural sciences indicating that people's capacity for proper recognition and evaluation of early warnings is limited. This section outlines prominent findings and assesses their role for business decisions and the perceptions of the general public.

Bounded rationality

A large body of psychological and 'behavioural economics' research is dedicated to the 'bounded rationality' of risk perception and decision-making under uncertainty, (Kahneman and Tversky, 1982). Psychological theories of judgment and decision-making provide a number of explanations for human failure to adequately process risks and probabilistic information. Note that the manifestation of potential hazards may be either described as low-probability events (e.g. a nuclear catastrophe), or, when the scientific evidence of an adverse effect is scarce, the likelihood of the effect will be formulated in terms of a low probability (e.g. the increase of cancer rates caused by exposure to a chemical substance). While low-probability events can be overestimated when they are vivid in people's mind (Kahneman, 2011), it has been shown that awareness of risks is more effectively communicated by engaging in direct experience and the associated emotions, rather than abstract statistical descriptions (Weber, 2006). Also, concrete losses or events have a much higher impact on people's beliefs than information about uncertain, abstract ones (Dana, 2003).

This focus on direct experiences as basis for decisions, however, leads human cognition to struggle with an appropriate consideration of low-probability risks as indicated by early warning signals. When early warnings signals occur, people have typically not directly experienced the hazards themselves. In that case, people tend to neglect the likelihood of rare events (Hertwig and Erev, 2009). As Kahneman (2011) emphasises, 'when it comes to rare probabilities, our mind is not designed to get it quite right. For the residents of a planet that may be exposed to events no one has yet experienced, this is not good news.' The psychological hurdles for a proper recognition and evaluation of early warnings apply to business decision-makers and the general public alike (Boyd, 1997). Note that in exceptional cases, this psychological disposition can trigger an opposite effect, namely when a low-probability event does indeed occur. Then, people may even — at least temporarily — overrate the probability of occurrence (Sunstein, 2003), and increased public concern may lead to faster regulatory measures. This may have been the case for the German decision to phase out nuclear energy after the Fukushima accident in 2011. In most situations, however, human risk perception seems to impede precautionary corporate action as well as public pressure for responding to early warnings with precaution.

A related phenomenon is the so-called 'pensioner's party fallacy', according to which people tend to overrate the fact that some people live long in spite of exposure to harmful substances and are hence still present at pensioners' parties — as opposed to their deceased colleagues — and this presence is perceived as evidence against the existence of harm (EEA, 2001). Here, people neglect the fact that their personal experience with formerly exposed colleagues is biased towards meeting the survivors. For instance, this effect is likely to play a role also for the perception of risks from smoking.

Another well documented characteristic of risk perception is that immediate losses or harm have

a larger bearing on people's beliefs than losses or harm in the future (Dana, 2003; Weber 2006). Economic models capture this systematic bias in preferences over time by using discount factors for present value calculation. Recent 'behavioural economics' approaches even use hyperbolic discounting to represent the seemingly exponential diminishing of value over time. This systematic bias works against precautionary measures since those measures typically involve direct costs in the present in order to avoid uncertain costs from harm in the — often far away — future. One may argue that people should decide freely on their 'time preferences' and that any type of paternalism on how to trade off present versus future consequences is inappropriate. Nevertheless, uncertain future hazards also involve consequences for future generations and discounting such consequences based on the time preferences only of the present generation may be questionable from an ethical point of view (O'Neill et al., 2008). There is currently a heated debate about an appropriate discounting of the effects of climate change and of biodiversity loss (Stern, 2006; Weitzman, 2007; Spash, 2007; TEEB, 2009).

Other findings on the limits to taking into account information about risks are noteworthy. For instance, the 'finite-pool-of-worries' hypothesis reflects that the degree of concern for a certain issue depends on the presence of other, perhaps more direct worries, such as the financial crisis, job security etc. (Weber, 2006). For most people, uncertain future hazards may not be high enough on the agenda to invoke any action. The 'single action bias' reflects the tendency not to take further action after one initial step, which leads to suboptimal behaviour when a portfolio of actions or a constant change in behaviour would be appropriate (Weber, 2006). Moreover, there is evidence for cultural differences in how health and safety risks affects decision-making (Biana and Keller, 1999). Last, even though we have not found psychological studies on the phenomenon, several reviewed cases reported that companies exploited people's tendency to interpret 'no evidence of harm' as 'evidence of no harm' (Chapter 3; Chapter 6; Zelltner, 2000).

Bounded ethicality

Apart from 'bounded rationality' in risk perception, there are psychological findings revealing 'ethical blindness' (Palazzo et al., 2012), 'ethical biases' (Banaji et al., 2003) or 'bounded ethicality' (Gino et al., 2008). A prominent and widely studied phenomenon is the 'self-serving bias', which refers to people's general tendency to interpret ambiguous situation in their self-interest (Babcock and Loewenstein, 1997). For decisions where self-interest conflicts with ethics, this implies that people engage in self-deception that helps them reinterpret or disguise that acting in their self-interest violates ethical principles. Such phenomena can be largely unconscious and psychologists tend to relate them to the reduction of a 'cognitive dissonance' (Festinger, 1957) that stems from conflicting goals such as making profit and acting ethical.

Self-deception may be enabled through different mechanisms, including language euphemisms and 'slippery-slope' decisions, where a series of small infractions of ethical standards can lead to a journey towards immoral conduct (Tenbrusel and Messik, 2004). In addition, people tend to hide from relevant knowledge on ethical attributes of decisions (Ehrich and Irwin, 2005) and to neglect those arguments or types of reasoning that may reveal them as responsible for immoral action (Rode and Le Menestrel, 2011). The self-serving bias seems of high relevance when business decision-makers face uncertain early warnings signals but precautionary measures are not in the economic interest of the company (Gollier and Treich, 2003). Strong uncertainty may not only be inherently difficult to integrate into risk assessment, but it may also serve as a welcome 'excuse' and justification about why the profitable action may not be so unethical after all.

Other research has shown that people tend to engage in self-deception also when evaluating potentially harmful behaviour of others, in particular that they overlook unethical behaviour of others that may harm them when that behaviour is not clear, immediate and direct, and when it has not yet resulted in a bad outcome (Gino et al., 2008). With respect to our analysis, such a tendency may further explain the public lack of awareness of inappropriate corporate responses to early warnings, and hence the public's reluctance to react with potentially supportive actions in their role as consumers, voters or engaged citizens.

For the case of asbestos, Sells (1994) provides testimony of the relevance of self-deception and denial as critical factors for why business actors fail to act with precaution in the face of early warning signals. He cites one of the presidents of Manville Corporation saying that 'the blunder that cost thousands of lives and destroyed an industry was a management blunder, and the blunder was denial. …Manville managers at every level were unwilling or unable to believe in the long-term consequences of these known hazards. They denied, or at least failed to acknowledge, the depth and persistence of management accountability' (Sells, 1994). It is as

if the combination of economic interests, scientific uncertainty, and psychological factors concur to trap business executives in an organisational culture where the danger is minimised and alternative business solutions unattainable: 'If an organisation's culture encourages denial, problems get buried. Corporate cultures are built by successful people, good men and women who are often pillars of their communities as well as business leaders. The executives at Manville were good people too, and nevertheless they fostered a culture of self-deception and denial' (Sells, 1994).

Evidence from the same company, however, also shows that such cultural factors can be reversed. The tragedy of asbestos and the eventual bankruptcy acted for Manville Corporation as a lesson for the company to stop its culture of denial and changed its approach towards products stewardship. In 1986, shortly after learning that its fiberglass products could be related to an increase in cancer rate, the company's leadership took precautionary action with regards to its operations and voluntary re-labeled these products as possibly carcinogenic despite the reluctance of their lawyers. The company benefited from this proactive strategy thanks to a successful indemnification and marketing strategy, proving that what may be perceived as a conflict of interest could well lead to a successful alignment of business and social values. It took then nearly five years to realise that the excess detected in respiratory cancer in fiberglass manufacturing workers were not sufficiently significant to justify such a warning label (Sells, 1994; Paine and Gant, 2009).

25.3 Lessons and reflections about business and early warnings

We now provide a set of lessons and reflections that summarise our findings and whose consideration may promote more precautionary business decision-making.

Lesson 1: early warning signals often entail conflict of values for business actors, who expect to be in their economic interest not to respond with precautionary 'business actions'

The cases we have studied here illustrate that early warning signals often raise conflicts between short term economic gains for business actors on the one hand and long term human health and environmental values on the other. Given that health and environment are regarded as issues pertaining to society at large or at least to multiple societal actors or groups, these conflicts of values are often conflicts of interest between business actors and public interest.

The reviewed cases illustrate how business actors tended to give priority to their short-term economic interest and did not respond to early warnings. This behaviour is in line with the standard economic and management paradigm, which regards maximising profits as the main objective of companies, as long as this is done respecting the relevant regulatory frameworks. In other words, when early warning signals entailed potential conflicts between profit and other societal values, economic interests pushed business to dismiss those business actions that would respond with precaution, such as modifying or terminating potentially hazardous products or operations.

Lesson 2: characteristics of the research environment and the regulatory context can provide business actors with opportunities to enter into 'political actions' to undermine early warning signals

When companies respond to early warning signals by giving priority to their business interest at the expense of public interest, they have a further incentive to suppress, contradict or downplay these early warning signals, both to maintain favourable public opinion and to avoid regulatory constraints. Many of the reviewed cases were characterised by a regulatory and societal context that allowed companies to effectively pressure science, lobby for favourable regulation and influence public opinion against the recognition and acceptance of early warning signals. In some cases, like tobacco, such actions contributed to discrediting national and international institutions and NGOs, weakening their ability to produce or relay early warnings signals. Because these actions go beyond strictly speaking 'business actions' but rather influence the societal context of business, they can be seen as 'political actions' and illustrate a political role of business actors (Scherrer and Palazzo, 2010). It seems therefore important to distinguish these types of actions from 'business actions', such as decisions to continue or not with a potentially hazardous product or operation. 'Political actions' are not aimed at maximising profits within the political and regulatory contexts but rather aim at influencing these political and regulatory contexts in the pursuit of profits.

Lesson 3: psychological and cultural factors contribute to neglecting early warning signals

Business decision-makers face psychological barriers to awareness and acceptance of the conflicts of values and of interest entailed by early warning

signals. Human risk perception and time preferences are biased towards underrating uncertain hazards, and there is a tendency to avoid the cognitive and emotional dissonances generated by the presence of value conflicts. In particular when own interests are at stake, it is well documented that people tend to reveal self-serving biases in their perception of the situation. Hence, when business actors have an economic interest in producing or using potentially hazardous substances, they are tempted to justify their behaviour by dismissing early warning signals and the conflicts of values they entail.

The cultural business context further contributes to the denial of conflicts of values entailed by early warning signals. Typically, the idea that the main objective of business is to maximise profit and the belief that this is the most appropriate way for business to serve society provide a powerful justification for dismissing the relevance of these value conflicts for business actors and to increase self-perception of responsibility. As in the asbestos example, organisational cultures can also explain the difficulty in facing the conflicts of values and of interest entailed by early warning signals.

Reflections about business and early warning signals

A prominent policy response to conflicting interests between business and society are regulatory measures that attempt to steer business rationality towards internalisation of external effects. We would agree that for uncertain hazards, proposals for legal, fiscal, and financial regulatory mechanisms still have a large potential to further align business interests with interests of society. Innovative solutions such as assurance bonding should be considered (Kysar, 2009). Yet, our article has outlined that precautionary business operations face further barriers that are of epistemological, psychological, political and cultural nature. Given the variety and complexity of these barriers, it seems unrealistic to believe that complete alignment of business interests with interests of society at large will always be feasible. At least in the short term, or until business actors indeed face the ideal societal and regulatory context, business decision-makers will face difficult situations with value conflicts. In our opinion, the possibility to discuss these conflicts of values rationally and openly is an absolute necessity to mature our responses towards them.

In particular, and notwithstanding the necessity to strengthen the accountability of business actors, we believe there is a need to better understand and expose the rationale for business actors not to respond voluntarily to early warning signals with precautionary actions. Blaming business, in particular with hindsight, tends to be a rather typical reaction that may not always be constructive. It often misses the complex or even contradictory set of motives and drivers that business actors are facing. When companies give priority to their business interest at the expense of precautionary actions, it is not necessarily because they willingly act against the interests of society or to harm the environment. Some business actors may well acknowledge the need to sacrifice some business interest, but may consider in good faith that the early warning signals are not strong enough to justify precautionary measures. Others may be unaware of the full extent of their conflicting interests and of their self-serving biases, for instance because of a cultural or an organisational context that is trapping them in a short-sighted economic approach.

We thus believe that a crucial first step towards any solution is awareness and acceptance of the dilemmas business actors are facing, and of the various temptations for business to act in a way that is harmful to society. Here, we can imagine that public institutions could support progressive business by analysing and publically disclosing the dilemmas and temptations entailed by early warning signals, e.g. for different industries and for the specific societal and regulatory context of decisions. This includes disclosure of the conflicts between making profit and causing potential societal harm, but also the psychological temptations to hide from such value conflicts, the temptations to use gaps and loopholes of regulation or to influence the regulators, as well as the temptations to influence the scientific evidence. Rather than prescribing specific precautionary business actions, such institutions could then promote more open, transparent, and stakeholder-inclusive participatory decision frameworks that recognise the reality and the difficulty of the complex trade-offs (Stirling, 2008).

Rigorous and explicit exposition of the dilemmas will create further incentives for responsible actors to share and communicate their precautionary responses. Clear and factual descriptions of these difficult situations, if possible devoid of judgemental considerations, may contribute to reducing unconscious denials, force business organisations to openly discuss the factors driving their decision-making (see Tenbrusel and Messik, 2004), and promote more transparency, proactive attitudes and innovative responses to difficult business decisions. Because they would make explicit the conflict of values, such institutional approaches

would more realistically complement initiatives based on the idealised principle that being socially responsible is economically profitable, typical of Corporate Social Responsibility (Porter and Kramer, 2011).

An additional reflection lies more specifically on the role of political actions of business actors, in particular those actions aimed at suppressing early warning signals. Even though they could be regarded as a natural tendency to justify and protect one's own interest, such political actions have the potential to disrupt an honest debate and to prevent the development of an appropriate context within which business actions lead to positive consequences for society. The fact that some business actors spend sophisticated efforts to hide or keep secret their political actions can be seen as a signal that their behaviour is of bad faith and would not be socially acceptable. Regulatory efforts that make more transparent the political actions of business can help to sustain a sound balance of power, thereby maintaining our ability to benefit from early warning signals and reducing the likelihood of health and environmental hazards.

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Part E Implications for science and governance

Contents — Part E

26 Science for precautionary decision-making

Philippe Grandjean ([1])

The goals of academic researchers may differ from those of regulatory agencies responsible for protecting the environment. Thus, research must take into account issues such as feasibility, merit and institutional agendas, which may lead to inflexibility and inertia.

A large proportion of academic research on environmental hazards therefore seems to focus on a small number of well studied environmental chemicals, such as metals. Research on environmental hazards should therefore to a greater extent consider poorly known problems, especially the potential hazards about which new information is in particular need.

Misinterpretation may occur when results published in scientific journals are expressed in hedged language. For example, a study that fails to document with statistical significance the presence of a hazard is often said to be negative, and the results may be misinterpreted as evidence that a hazard is absent. Such erroneous conclusions are inspired by science traditions, which demand meticulous and repeated examination before a hypothesis can be said to be substantiated.

For prioritising needs for action, research should instead focus on identifying the possible magnitude of potential hazards. Research is always affected by uncertainties and many of them can blur a real association between an environmental hazard and its adverse effects, thereby resulting in an underestimated risk. Environmental health research therefore needs to address the following question: are we sufficiently confident that this exposure to a potential hazard leads to adverse effects serious enough to initiate transparent and democratic procedures to decide on appropriate intervention?

The choice of research topics must consider societal needs for information on poorly known and potentially dangerous risks. The research should be complementary and extend current knowledge, rather than being repetitive for verification purposes, as required by the traditional science paradigm. Research findings should be openly available and reported so that they inform judgements concerning the possible magnitude of suspected environmental hazards, thereby facilitating precautionary and timely decision-making.

([1]) The author would like to thank Mette Eriksen for conducting the searches on SciFinder. Helpful contributions on earlier versions were made by John Bailar, Carl Cranor, David Gee and David Kriebel.

26.1 Science and the Precautionary Principle

The case studies in this volume illustrate that science can provide powerful evidence for targeted prevention to protect against hazards to the environment and public health. However, the chapters also shows how science can be insufficient, and it can be misinterpreted or ignored, so that appropriate intervention is deferred or abandoned. This chapter explores the strengths and weaknesses of environmental health research seen from the perspective of the wider needs of society and the use of 'Precautionary Principle' (PP).

At the outset, societal investment in environmental research would seem unwise if it is irrelevant, poor, or difficult to access. Research support should favour studies that stimulate timely decision-making and prudent action to prevent hazards. While not disregarding the need for basic research, I shall focus primarily on the weaknesses of current applied research in the environmental field and the possible avenues for science to become more useful for future environmental health decision-making.

Some researchers have raised the concern that the PP may potentially make further research redundant, given that an intervention has already been decided upon (Goldstein and Carruth, 2004). But any decision on environmental health hazards should be considered tentative and amenable to change, as justified by further research (including intervention studies to determine if the action had the intended effect). The basic problem is that prevention has too often been deferred due in part to the alleged absence of convincing scientific evidence, as illustrated by the case studies in this volume ([2]). The error is recognised only when decisive evidence has finally been gathered, and it is realised that action should have been initiated much earlier on. With time, nearly all exposure limits for hazardous agents have decreased as new evidence documented that harm occurred at lower exposure levels than previously believed. Thus, when scientific evidence is incomplete, environmental standards are more lenient. But can science provide better support for prudent decision-making, so that adequate protection may be decided upon from the beginning?

For research to provide sufficient documentation for potential intervention, it has to be both reliable and pertinent. Thus, the quality of research has two sides — the methodology and the utility. One could also refer to these two aspects as the validity and the relevance. The two are of course related, but even research considered 'poor' from a narrow methodological perspective could nonetheless be highly relevant. Still, a study of limited validity is most likely also to have little impact, especially if the conclusions cannot be trusted. While the researchers should focus on securing a high methodological level, that should not turn them into sceptical ivory-tower nit-pickers preoccupied with methodological precision and technical detail. On the other hand, focusing mainly on environmental implications of the research can lead to inappropriate (or apparent) advocacy for particular policies or precautionary action that may be inspired, though perhaps not justified, by the research.

Environmental health is often considered a field of applied research, usually multidisciplinary. Researchers and their employers are engaged in science not just for purely altruistic reasons. Universities and other research institutions are enterprises that need to fulfil the institution's mandates, satisfy requirements stipulated by funding sources, and avoid going into debt. Within the EU, more than half of the research and development activities carried out are funded by industry, while slightly more than one-third is paid for from public sources (Eurostat, 2011). The EU's new Horizon 2020 research programme is intended to increase the public financing of 'smart investment' in research and innovation while dealing with pressing societal challenges, including climate change and environmental health problems (EC, 2011). Given the substantial public investment in research (van den Hove et al., 2011), one would anticipate that environmental research, especially the part of it that is reported in academic journals, would somehow reflect priorities expressed by regulatory agencies and other public bodies. The next section of this chapter will therefore examine the research coverage of environmental chemicals and whether poorly documented and potential hazards receive appropriate attention. But there is more to it than the coverage of priority topics.

([2]) As the preface to the first volume of *Late lessons from early warnings* (EEA, 2001) pointed out, 'the absence of political will to take action to reduce hazards in the face of conflicting costs and benefits seems to be an even more important factor in these histories than is the availability of trusted information'.

Under PP-based decision-making, scientific proof or a very high degree of certainty are not required. Incomplete, but reliable evidence can be sufficient to justify a precautionary intervention. On the other hand, if extensive evidence is available, then a conventional risk assessment and subsequent prevention are indicated, and there would be little need to invoke the PP. However, traditional risk assessment is sometimes anti-precautionary when it demands convincing evidence and thus ignores emerging insight and incomplete documentation. Due to its focus on scientific justification, risk assessment may inspire continued elaboration of fairly well documented hazards, so that remaining uncertainties can be resolved to allow firm decisions. When decisions are PP-based, less extensive evidence is required, and some uncertainties are accepted as being inevitable or impossible to remove in the time available for preventing plausible harm. The less extensive requirement regarding scientific evidence can have significant implications for the ways that research is planned, performed, analysed, interpreted and reported (Grandjean, 2008b).

We rely on science as evidence to help justify decisions on environmental hazards. But, as the case studies in the present and the first volume of *Late lessons from early warnings* (EEA, 2001) clearly demonstrate, science does not automatically lead to appropriate prevention or precautionary action. Thus, neither the quality nor the relevance of the science as such will necessarily translate into responsible and prudent decisions. Still, the interpretation of incomplete research data, the evaluation of uncertainties and misunderstandings of the findings can obfuscate the discussion on the urgency of possible environmental protection. So the question must therefore be asked: Can science somehow better serve to support better public policy decisions?

I think that the answer is yes, although better quality and relevance in terms of PP-based decision-making may not be easy to achieve. This chapter will focus on four main issues listed below.

Concerns regarding science as evidence for decisions on environmental hazards:

1) Does the research cover the societal needs for supporting information on suspected, poorly documented or potential hazards?

2) Does the research explore new and emerging hazards so that it could serve as an early warning system?

3) Is the reporting of research findings appropriate to serve as evidence for reducing environmental hazards?

4) If the research is available, is it reliable and independent of vested interests?

26.2 Current research focus is on well-known hazards

The most appropriate and feasible way to assess the topics covered by environmental research is to carry out bibliometric analyses using internet-based databases on scientific publications. Environmental journals are usually categorised in the fields of toxicology, environmental sciences and public health (a total of 78 major journals in both Web of Science and the PubMed database). The Web of Science covers scientific literature back to 1899, but searches are limited to chemical names in the titles of journal articles. However, for recent publications, it is possible to use the SciFinder database, where individual environmental chemicals can be identified from their Chemical Abstract Service (CAS) registry numbers. Using these internet resources, information can be retrieved on how often scientific publications have dealt with chemicals of interest from an environmental viewpoint (Grandjean et al., 2011).

As a starting point, we first used Web of Science to examine the coverage of the seven chemical substances from the 14 case studies reviewed in *Late lessons from early warnings* Volume 1 (EEA, 2001). Table 26.1 shows the number of articles published in the relevant journals during the years 2000–2009, i.e. the 10 years right after the completion of the report. One could have expected that these early warning substances would have faded somewhat from the science radar, given that their environmental impact had already been recognised during the 20th century and that some had been banned several decades ago. However, the number of scientific publications on these substances during 2000–2009 corresponded to about 40 % of all articles available since 1899. The relative coverage before and after year 2000 differed somewhat between the substances. Both sulfur dioxide and DES clearly faded during recent years, with only about one quarter of all titles available in environmental and toxicological publications since 1899 being published during 2000–2009. On the other hand, MTBE became more popular, with three-quarters of all papers available since 1899 having been published during the first decade of this century.

Table 26.1 Total numbers of articles published 1899–2009 and during the most recent 10 years (and percent of total) in environmental and toxicology journals listing 'early warnings' substances in the title

Name	Total number of articles 1899–2009	Articles published 2000–2009	
		Number	% of total
Polychlorinated biphenyls (PCBs)	5 809	2 738	47
Asbestos	2 735	809	30
Sulfur dioxide	2 380	548	23
Benzene	2 075	879	42
Tributyltin (TBT)	672	344	51
Diethylstilboestrol (DES)	603	147	24
Methyl-tert-butyl ether (MBTE)*	542	411	76
Total	14 816	5 876	40

Note: *MBTE uses were expanded during the late 20th century, not restricted like the other substances in the table.

Source: Data from the Web of Science (Grandjean et al., 2011).

These numbers suggest that substantial research continued to be published on these substances, long after the recognition of their importance as environmental contaminants. However, the numbers extracted from the Web of Science are incomplete, as a research article might well address a chemical without the substance name appearing in the title. Thus, when extracting data from SciFinder, we obtained a greater number of articles (total of 8 267 during 2000–2009, asbestos not included). With an average of over 10 scientific articles per substance per month, these early warnings chemicals remained a significant focus of research reports published since 2000. PCBs, in particular, remained very much in focus, as I shall discuss shortly.

Given the continued attention paid to these chemicals characterised by 'early warnings', what about environmental chemicals in general? Thousands of potentially toxic chemicals are being released into the environment, and there is a need to determine their persistence, dissemination, biomagnification and toxic effects, especially when only minimal information is available. So how does published research reflect the societal needs to cover a wide range of potential hazards?

Based on CAS number links from the science journals during 2000–2009, the substances can be ranked in accordance with their numbers of publication links (as SciFinder is not limited to environmental chemicals, we had to manually exclude radioactive isotopes, enzymes, metabolites, etc.). All told, 119 636 articles were published by the 78 scientific journals during the first ten years of this millennium. SciFinder listed a total of 760 056 CAS links from these articles (Grandjean et al., 2011). Thus, on average, each of the many scientific articles had six CAS links, thus not only describing a single substance at a time. The total numbers of publications and links are large and reflect an intense publication activity. However, the coverage turned out to be extremely uneven.

We focused on the 100 most frequent environmental chemicals. Each of them was covered in a minimum of 600 articles — and up to 10 000 — during the 10-year period. Thus, each of the top-100 substances would be addressed in about five to 80 articles every month. The total number of links to the top-100 environmental chemicals was 180 822. Thus, the vast majority of the many thousand chemicals listed were far less popular than the top-100. This finding suggests that research on environmental chemicals is and has been for some time fairly narrowly focused on a limited number of substances.

This conclusion becomes very clear when we examine the 20 most commonly studied environmental chemicals. Each had between 2 000 and 10 000 CAS links during the first ten years of the millennium. The sum of article links corresponds to 12 % of all CAS number links. Assuming they also represent 12 % of all published articles, one or more of these substances would be featured in 14 264 publications during the 10 years, or 119 articles per month, on average. To keep up with the literature in the top-20 substances only, one would have to read five or six papers every work day, without holiday breaks.

All of the top-10 substances are metals (including arsenic, which is regarded as a semimetal). Also well covered are several tar chemicals (polyaromatic

hydrocarbons), solvents and the PCBs — already known from *Late lessons from early warnings* Volume 1 (EEA, 2001) and Table 26.1. For the top-20 substances, an average of 51 % of all articles available in 2009 had been published within the most recent 10 years. Some variation was present: arsenic increased in popularity (74 % during the most recent 10 years), while aluminium decreased after the year 2000 (31 %). Also, the tar chemicals often found in air pollution (e.g. benzo[a]pyrene and phenanthrene) tended to appear more often in recent article titles. Overall, these results show that the chemicals most commonly studied in recent years had already been extensively studied during the previous century. Thus, the chemicals that were popular during the previous century remained a focus (Grandjean et al., 2011).

Two of the top-20 chemicals — lead and mercury — are included in the case studies, and Table 26.2 shows the results for the main substances reviewed in this volume. Thus, whether or not the chemicals are persistent in the environment or the human body, some of them have clearly become persistent and highly prominent in the scientific literature. The tens of thousands of articles on lead, mercury, and other well recognised environmental hazards testify to the enormous investments in studying, reporting and publishing on these prominent substances. It would therefore seem that the choice of research topic in the field of environmental health greatly benefits the well-known chemicals.

The next question to consider is whether research addresses societal needs for more poorly known and potentially dangerous risks. Does academic research in environmental chemicals ignore less-well known compounds that need documentation? We conducted additional studies to examine this question.

26.3 Ignoring new potential environmental hazards

We now focus on the other end of the spectrum, as many environmental chemicals have not been adequately tested. When the US National Research Council conducted a study in the 1980s on toxicity testing, 78 % of the industrial chemicals most commonly produced was found without even minimal test data for toxicity (NRC, 1984). Later follow-up showed little improvement (US EPA, 1998). Even today, the European Chemical Agency complains that gaps in safety data remain and that little has been done to mend the problem so far (Gilbert, 2011). Thus, as metals and tar chemicals attract much research attention, are substances of importance to society being neglected by environmental researchers?

To examine this question, we looked at the high-production chemicals considered in particular need of scientific documentation (US EPA, 2009). This high-priority list was first published in 2006 and included thirteen important substances lacking both a robust hazard data set and exposure information. For the time period of 2000–2009, we found that these chemicals had a total of only 352 links to scientific articles, i.e. an average of only three per month for the entire group (Grandjean et al., 2011). Five of the thirteen high-priority substances were not encountered at all in the 78 journals during the ten years. One could excuse the lack of coverage up to 2006, when the EPA published its list, and perhaps 2007. However, when extending the search to 2010 and 2011, the result was pretty much the same — the priority listing had not inspired any increased number of publications in scientific journals. When compared with the staggering numbers for top-20 substances, the

Table 26.2 Numbers of articles published in environmental science journals during 2000–2009 on chemicals covered in the present volume, as determined from SciFinder links to the CAS numbers

Name	CAS no.	Number of links	Rank
Lead	7439-92-1	8 926	2
Mercury	7439-97-6	4 399	9
p,p'-DDT	50-29-3	1 968	21
Bisphenol A	80-05-7	952	62
Perchlorethylene	127-18-4	898	68
Beryllium	7440-41-7	400	235
Vinylchloride	75-01-4	319	276
Dibromochloropropane (DBCP)	96-12-8	41	> 1 000

publication rates for these high-priority substances appear tiny.

Other substances may be considered likely emerging hazards, about which further information would be highly useful. Triclosan is a biocide often used in cosmetics, but releases into the environment have raised concern (Dann and Hontela, 2011). There were 259 articles on this chemical during 2000–2009, much better than the high-priority substances listed by the US EPA, but way below the popularity of toxic metals. Likewise, the perfluorinated compounds have been in use for decades, and concerns about their environmental fate and toxicity have grown (Lindstrom et al., 2011). The most prevalent member of this group, perfluorinated octanoic sulfate was covered in 271 articles, about the same as triclosan. Thus, each of them was addressed only in about two dozen scientific articles in the scientific journals every year. Accordingly, about 35 articles would focus on lead (and close to 20 on mercury) each time a single article would present evidence on one of these emerging hazards. But can we trust these numbers?

Although the bibliometric data do not distinguish between short, descriptive reports and thorough reviews, the overwhelming emphasis on a small minority of environmental chemicals cannot be explained away. Also, the scientific journals may not reflect research activities outside academic institutions, but one would have to imagine huge numbers of reports outside the mainstream journals to make up for the differences. The conclusion therefore seems inevitable that the long-term prominence of substances commonly covered in articles in environmental journals does not match the societal needs or those of regulatory agencies. Substances that were highly popular in research during the previous century remained so during the first ten years of the present millennium, despite the changing needs for evidence on environmental impacts.

26.4 Inertia and its reasons

An important reason for such inertia and continued focus on well-known substances may relate to the traditional science paradigm, where solid conclusions depend on replication and verification. While a single study should not be relied upon as firm evidence, the extent to which replication is needed seems to have been stretched to the extreme, when well-known environmental chemicals inspire almost 1 000 publications per year.

It may well be that academic researchers do not know or contemplate the needs for environmental health documentation. We may question environmental researchers, who keep studying lead toxicity to obtain even more detailed or perfect results ([3]). However, individual researchers and their institutions may have insufficient access to public and private funding that would allow an unrestricted choice of research topics. This limitation would especially refer to young researchers of low academic rank. Further, if students are taught to replicate and extend their mentor's own research, they will later become the seniors with the same type of expertise and narrow focus on well-known environmental hazards. Existing expertise as well as facilities may favour a continued focus on the same hazards, thereby propagating long-term traditions and ignoring society's changing needs for early warning investigations. In more general terms, a tendency to maintain a narrow focus is likely to be counter-productive in regard to scientific discovery and innovation, as there would potentially be much more to learn from studying new hazards than from replicating studies on old ones.

Several factors may contribute to the estrangement of academic research from societal needs for documentation on environmental hazards. Research institutions have an interest in maintaining highly qualified personnel and efficient use of costly infrastructure. All of the most popular chemicals can be inexpensively measured by instruments that became widely available already in the 1970s and 1980s. Analytical methodologies are already established and well documented. These instruments (atomic absorption spectrometers and gas chromatographs) make it possible within a week or so to generate results sufficient to justify a scientific paper on one or more of the top-20 substances. Under these conditions, why would ambitious researchers and their students take on new substances that might require the purchase of expensive equipment and arduous development of new methods?

The loyalty to established methods and research topics is not just a matter of convenience. In

([3]) The author has published numerous articles on lead, mercury, and other top-20 chemicals in scientific journals, thus being part of the inertia. However, as the chapters on lead and mercury show, real or alleged uncertainties were often used to argue against hazard abatement, thereby requiring more research.

academic research, competition is fierce and each researcher must demonstrate his or her qualifications by frequently publishing articles in scholarly journals. By endeavouring to research the unknown, these researchers would face longer time periods between publications, if any. The mere number of publications is a crucial metric for academic prestige and for obtaining a tenured position. By using existing instruments and methods, a researcher can more effectively expand the CV, especially if the reports can be framed into small incremental manuscripts, each of them contributing an entry on the publications list. So-called vanity publications may contaminate the scientific literature, as they contain little new information, but primarily serve to augment the author's credentials. Whether they contribute new insight then becomes a secondary concern. Similarly, the budget in many research departments is tied to the number of scientific publications, thus also favouring quantity over quality. Such a focus on publication numbers may deny the higher societal goals of environmental research while promoting earthly aspects of personal desires and academic reputation.

The pressure to complete a project on time (or even before the deadline) and to publish the findings with minimal delay also invites the use of short-cuts. Convenience and lack of funds may determine that some parameters in a study are not measured in appropriate detail, e.g. by relying on questionnaire responses rather than actual measurements, which may be too expensive. When a study claims to address an environmental hazard using study parameters that are unreliable or perhaps not representative, the results will often be non-informative. Worse, the results may be interpreted as evidence against the hazard causing any risk at all. Such misleading conclusions are sometimes referred to as Type III errors (Schwartz and Carpenter, 1999). I shall return to this problem shortly (see Section 26.5 below).

The inertia and reliance on convenience are not restricted to researchers themselves, or public research institutions, for that matter. It also affects the funding agencies. If a proposed project deals with a known environmental problem, the principal investigator probably has an impressive track record, the protocol is feasible and easy to comprehend and capable reviewers are readily recruited. That may not be the case with poorly studied substances and emerging hazards. The funding agency can feel comfortable about the proposed time schedule and the anticipated outcome of the project, as the exposures and effects rely on established methods. Uncomfortable surprises are unlikely. Hence, it may be safer and more convenient for grant managers to concentrate on the known hazards.

Scientific journals probably also play a role in maintaining a focus on well-known substances. Peer review of submitted manuscripts is rarely a problem with a manuscript on lead exposure. Bias toward publication of the report may occur when the reviewer finds that his or her own research has been cited, thus demonstrating the sound judgment of the authors of the manuscript. Some of the journals that we explored in the bibliometric databases are regarded as prestigious, with high citation rates. The possibility exists that some environmental chemicals may be held in higher esteem than others, thereby adding to their continued prominence, or publication persistence, no matter what the societal needs may be. This means that there may be an element of circular reasoning involved, where a substance is a popular research item simply because it has been widely studied in the past — a self-prophetic bias that maintains a continued prominence of a small number of scientists and their publications.

The science sociologist Robert K. Merton (Merton, 1968) dubbed this phenomenon a 'Matthew' effect, referring to the New Testament ('*For unto every one that hath shall be given, and he shall have abundance: but from him that hath not shall be taken away even that which he hath*'). Popularity among scientists in the past seems to provide justification for the importance or relevance of continued research in a particular field. The opposite strategy would appear more attractive from the point of view of innovation.

However, it must be said that some conventional research into well-known substances have identified novel scientific breakthroughs that are not only relevant to our understanding of these well-characterised substances, such as mercury and lead, but they have also been scientifically valuable, via analogy, to many other substances.

Clearly, academic research has multiple purposes, a number of constraints and some limitations, when viewed from an environmental health angle. Societal needs for evidence on priority substances or emerging risks are apparently not seen as a high priority for academic research in general. But the choice of research topic is not the only problem.

26.5 Research methodologies and assumptions

Jointly with the inertia in the choice of research topics, traditional scientific thinking may also represent

an obstacle. According to the standard paradigm, we need to justify our conclusions by replicating our findings, securing the highest possible data quality and documenting each component of the anticipated causal link. Such high standards will protect science from making mistakes by claiming, e.g. that lead is toxic to the brain, unless extensive documentation is truly available to back this assertion. The links to scientific traditions extend back to the Leonardo da Vinci's and Galileo's writings. In studying environmental health hazards, the prevalent paradigm determines how the problem is usually framed as below:

> 'The traditional scientist will address an environmental research question as follows: Have we reliably documented through meticulous study and replication that this substance is mechanistically and causally linked to an adverse biological change?'

Along with the demand for replication, tradition calls for a narrow focus. Uncertainty is commonly restricted through rigorous control of the study setting. The advantage of a well-defined study is that it addresses only a single factor under specific circumstances and therefore more likely will lead to firm or indisputable conclusions. However, due to its limited scope, the study will at best result only in an incremental increase in knowledge about the overall issue at hand, including multiple or complex exposure scenarios and the significance of individual vulnerability. Thus, the disadvantage is that this approach leads to reductionism and explores only limited or individual aspects of each hazard. Such proximate and simplistic risks poorly represent the true complexity of environmental hazards.

Examination of the chapters on human health hazards in this volume and *Late lessons from early warnings* Volume 1 (EEA, 2001) allows identification of several assumptions that were, at first, considered valid and important, but were later found to be misleading. Table 26.3 shows some of the most crucial — and erroneous — assumptions that were initially made in regard to one or more of the environmental hazards included in this volume. The case studies in this volume show that relying on these assumptions, while seemingly meaningful in terms of the prevailing research paradigm, led to proliferation of environmental hazards due to the substantial delay in their recognition.

Table 26.3 Erroneous assumptions made in initial evaluations of environmental hazards and the subsequent scientific recognition of the true complexity

Initial assumption	Late scientific lesson
1. Presence of environmental chemicals in the body can be tolerated at 'safe' or natural doses	Delayed effects, cumulated or re-mobilised doses, or toxic metabolites may occur at exposures previously thought to be safe
2. Absence of harm in adult male workers (from routine medical data or mortality) means absence of risk to the general public	Sub-populations, such as children and the elderly, may be more vulnerable to the exposure
3. Acute or short-term effects also reflect chronic or long-term effects	Dose-response relationships for acute effects may substantially differ from those for chronic effects
4. Biological effects may not necessarily be adverse and can be considered harmless	Early changes can predict more serious adverse effects which can develop later on
5. Dose-response relationships are consistent (and 'monotonic'), and no risk occurs at doses below apparent thresholds	Some substances show 'low dose' effects that are not readily predictable from responses to high doses
6. Short-term assessment of exposures from a single pathway can generally be considered sensitive and valid	Most methods for exposure assessment are imprecise, and imprecision usually results in underestimation of the toxicity
7. The placenta and the blood-brain barrier amply protect sensitive life-stages and organs from toxic chemicals	The barriers may be bypassed, as they offer limited protection against industrial chemicals
8. Average findings in exposed subjects indicate the potential for harm to the exposed population	Sensitive sub-groups may show effects that are not apparent from the average data
9. Toxicity evidence from animals and wildlife is not relevant to human toxicity	Animal data have reliably predicted most known carcinogens and many other hazards, and humans may be more vulnerable than other species

A crucial assumption was that a biological change may not necessarily reflect an adverse health effect and could therefore be ignored. Within normal variability, it may indicate adaptation or 'hormesis', therefore being innocuous. With proper justification, the assumption may be true, but biological changes should not be disregarded just because they are prevalent (or unwelcome, for some reason). For many years, researchers believed that the inhibition of an enzyme called ALAD due to lead exposure at blood-lead concentrations thought to be low, was a biological change that had no health implications (as described in the Chapter 3). That may be true in a strict sense, as the enzyme in red blood cells has no important function. However, recent research has shown that serious adverse effects do occur at lead exposures that were previously regarded as too low to be harmful.

Also, habitual levels of lead exposure were called 'natural' simply because they were normal or habitual. But prevalent lead exposures were the result of centuries of increasing lead use. Analyses of lead isotopes and of mummified tissues documented that normal lead exposure were far above what could be considered natural.

For efficiency reasons, toxicology studies have aimed at avoiding considerations of the sex, age and strain of the animals used. If focusing on inbred, adult male rats only, important sources of variability were ignored while making the study more efficient and precise. This problem became centre stage when reproductive toxicology and endocrine disruption began to attract attention (see Chapter 13 on ethinyl oestradiol in the acquatic environment and Chapter 10 on BPA, as well as PCBs, DES and TBT in *Late lessons from early warnings* Volume 1 (EEA, 2001, Ch. 6, 8, 13)). Also, it is only a recent discovery that exposures to environmental chemicals may cause much more toxicity if they happen during vulnerable developmental windows (Grandjean et al., 2008). However, prospective studies of birth cohorts take a long time and are extremely costly, and even multi-generation animal assays are often resisted due to economic burdens on industry.

The assumptions in Table 26.3 prevailed for a long time due to the failure of available, though incomplete data to show clear evidence of a risk. If adverse effects were not proven to exist, the erroneous conclusion was drawn that adverse effects must be absent. Perhaps this is the underlying assumption, which represents the greatest error. It survived, as uncertainties were ignored, whether in regard to exposure assessment, sensitivity of outcome measures, individual vulnerability, statistical analysis methodology or statistical power of the study. Overlooking imprecisions and incompleteness will most often result in underestimation and may lead to rejection of the presence of a (true) risk. Also, these uncertainties are not likely to create spurious associations, unless confounding factors are present.

26.6 Vulnerability of research to criticism

The downside of the traditional strategy to provide ample verification is that science becomes vulnerable to a critique that raises concerns about various possible sources of error or bias, particularly in regard to emerging insights and early warnings. The desire to document the truth, preferably the 'full' truth, makes science vulnerable to purported weaknesses. Thus, while careful scientists must pay meticulous attention to the methodological standards and quality assurance, some colleagues primarily exert these skills when judging the work of colleagues. Such critique may be unjust, but the halo earned from emphasis on the quality of scientific methods thrives from the collusion of admiring colleagues and students (e.g. at scientific conferences).

However, harsh critique and exaggerated scepticism may be particularly inappropriate in regard to emerging insights and early warnings which are often innovative and necessarily tentative ([4]). Thus, the case studies illustrate that astute observations by clinicians, factory inspectors, workers, anglers, bee keepers and community members can sometimes provide valid hypotheses on new hazards that are only confirmed by in-depth research much later.

A common strategy is to disregard studies that do not satisfy certain methodological criteria, sometimes abusing 'criteria' for causality. Although such criteria are useful, UK statistician Austin Bradford Hill noted:

> 'All scientific work is incomplete… All scientific work is liable to be upset or modified by

([4]) When Joe Forman first observed the hole in the ozone layer using low technology instruments he could not believe his results as they conflicted with the satellite data. He returned to the Antarctica to observe the hole three times before he — under pressure from his funding sources — felt confident enough to report his findings. See the chapter on Halocarbons in the first volume of *Late lessons from early warnings* (EEA, 2001).

> advancing knowledge. That does not confer upon us the freedom to ignore the knowledge we already have, or to postpone the action that it appears to demand at the given time' (Hill, 1965).

Despite Hill's prudent advice, some researchers may mistake the validity of their own conclusions for meticulousness in identifying presumed violations of the causal criteria or other validity requirements committed by their colleagues.

The overly sceptical focus on scientific methodology may lead to bias and narrow-mindedness. Thus, special interest groups have praised what they call 'sound science', which supports conclusions that are considered attractive (but, of course, is no more reliable than other research, and is sometimes actually less). In particular, so-called black-box epidemiology studies of health hazards have received harsh critique (Taubes, 1995). Some of that exaggerated critique is echoed in the chapters of the present volume.

Expert committees that advise national and international bodies are often tempted to express unreasonable critiques of research results and stress the preponderance of uncertainties. Such critiques may be considered appropriate for highly respected experts and is in accordance with their high methodological standards and unrelenting scepticism. However, a narrow focus on scientific methodology may be coupled with blindness to environmental degradation and social injustice. Not surprisingly, the strategy of criticising research methodologies has been vigorously explored by vested interests, often with the purpose of manufacturing doubt (Michaels, 2005; Michaels, 2008; Oreskes and Conway, 2010).

When a call for guidelines on 'Good Epidemiological Practice' was first promoted, it was at first embraced by researchers as a useful tool to stimulate high quality (and sound) science. However, strict interpretation of epidemiological rules could also be applied in order to disregard epidemiological findings that for other reasons were regarded as unwelcome. It turned out that the initiative originated with industry groups in order to disqualify unwelcome 'junk science' (as described in Chapter 7 on tobacco) (Ong and Glantz, 2001).The scientific rigour that had been considered a prerequisite in the traditional science paradigm was now turned around and became an unrealistic requirement for repetitive, controlled studies that could furnish virtual statistical certainty ([5]). Using strict criteria, unwanted results could then be criticised as junk and the uncertainties were then erroneously interpreted as an indication that no hazard was present.

26.7 Statistics and confidence limits

A key issue is the statistical data analysis. When analysing their results, researchers use statistical methods to determine whether the observed data were 'statistically significant', or whether they can be attributed to chance. The probability that their results are significant is usually expressed as *p* values, or probability values. The *p* was originally proposed by the UK statistician Ronald Fisher along with a limit of 5 % thought to be appropriate. This method allowed the researcher to identify findings that deviated significantly — unlikely due to random variation — so that the hypothesis that no difference was present would be rejected.

From its early application to agricultural plant breeding test designs, the 5 % limit has since been applied much more widely and has become almost sacrosanct amongst scientists from many disciplines. Using Fisher's *p* value limit allowed researchers to classify research findings that — when the *p* value was above 5 % — did not reliably support the 'null' hypothesis of no difference or no association, as the results could be due to random variation. Accordingly, the 'null' hypothesis could be rejected only when the *p* value was lower. A few studies and many anecdotes suggest that scientists place greater emphasis on results that have a *p* value of, say, 4.9 % than on results with a *p* value of 5.1 % (Holman et al., 2001). Statistically, there is no meaningful difference between outcomes with such similar *p* values. But if Fisher's proposed limit is applied in a strict sense beyond Fisher's own recommendations, then one set of results with a *p* value of 4.9 % would be interpreted as rejecting the hypothesis (hereby providing evidence of possible causality), whilst the other with a *p* value of 5.1 % would not refute the null hypothesis and would be considered non-informative.

([5]) An additional criterion often used was that only a 2-fold increased risk above background would be believable, e.g. from childhood leukaemia in residences close to power lines or from heart disease from environmental tobacco smoke. Apart from the much greater impact of a 2-fold increase in heart disease, there is no meaningful statistical difference between increases by a factor of 1.9 and 2.1, one of which would satisfy the criterion for a hazard, the other one not.

As commonly applied and interpreted, the *p* value is used mainly to determine the viability of a hypothesis. Although science in principle aims at falsifying hypotheses — since a definite proof cannot be obtained — it seems to make too little use of the data if we are just determining whether or not the *p* value is below 5 %. If the *p* value is high (well above 5 %), the results are rendered useless, as they failed the only criterion for success, namely to refute the hypothesis (although a hypothesis may theoretically be correct, even though the data deviate substantially from prediction). Sometimes, repeated attempts at falsifying a hypothesis fail, but a joint calculation (so-called meta-analysis) could result in an overall *p* value that perhaps finally reaches statistical significance with *p* less than 5 %, or some other specified level.

In most cases, the null hypothesis is that an exposure has no effect. Thus, in environmental research, the *p* value is used to test a null hypothesis that may be unrealistic or obviously wrong. This would seem to be a serious limitation. Would we ever be tempted to conclude that lead is not toxic, just because a small study has resulted in a *p* value that is greater than 5 %? Of course not. But the traditional use of the significance limit means that scientists are very reluctant to draw conclusions if the *p* value is 5.1 %.

The so-called frequentist tradition in statistics considers the data in isolation and evaluates them in regard to a theoretical null hypothesis, which may or may not be appropriate. Combined with a sacrosanct 5 % limit, the research results may not be as useful as they could be, and the conclusions could even be confusing and counterproductive (Goodman, 2008). The point is that we may be testing the wrong hypothesis and not making ample use of all of the available data. Thus, several case studies have shown that early warnings are often initially not statistically significant, such as the first IARC study of passive smoking, but nevertheless turned out to be robust.

Even if a study has reached statistical significance, this could still be due to chance. If we are conducting a large number of comparisons, then in all likelihood a small proportion of them could happen to be unusual and perhaps deviate from expectation at a statistically significant level. But such deviation is accidental and would be associated with a large number of comparisons. A common method is to adjust the *p* values using a procedure named after the Italian mathematician Bonferroni, thereby requiring *p* values to be significant only at lower values, the larger the number of comparisons. However, this technique, too, can also be used erroneously to disregard an unwelcome study (Perneger, 1998).

The use of an alternative approach to frequentist statistics started back in the 18th century, when UK Reverend Thomas Bayes designed a formula that let the study results modify the prior probability of a hypothesis, thereby generating a posterior probability of the hypothesis based on the new evidence obtained (Greenland, 2008). Bayes allowed inclusion of any results, whether few or large-scale, and no matter the *p* value, to help modify our reliance on a hypothesis and to determine its updated plausibility. One could still focus on the null hypothesis, or perhaps rather the overall outcome of all previous studies. This way, each study would still be useful and would be utilised to modify and fine-tune the hypothesis under consideration. Although attractive, Bayesian statistics sometimes results in serious mathematical complications that limit their usefulness. Also, we may not have a good idea about the exact hypothesis under study, and a prior probability of that hypothesis may be impossible to obtain. Bayesian statistics has therefore been criticised for being subjective and overly laborious. Still, empirical use of Bayesian statistics is gaining support (McGrayne, 2011).

Some scientists and some scientific journals now reject the use of *p* values (Lang et al., 1998). But if we are to limit our reliance on *p* values, how can we best extract a robust statistical summary of a complex study? A key parameter will always be the point estimate of the average effect. But instead of calculating whether this estimate is 'significantly' different (*p* less than 5 %) from no effect, many researchers recommend using the confidence interval (Thompson, 1987). It represents the range of values within which 95 % of averages would fall if a large number of similar studies were conducted. In other words, given the point estimate and the calculated variability, the study would be in accordance with any hypothesis that postulated an effect within the confidence interval. If zero is included in the interval, then the results do not deviate significantly from the null hypothesis. However, they also do not deviate from many other hypotheses, some perhaps suggesting a serious effect. The upper confidence limit indicates how large an effect that would be in agreement with the data. In a precautionary setting, the upper limit would often represent a plausible worst case scenario that would serve as a useful basis when considering intervention.

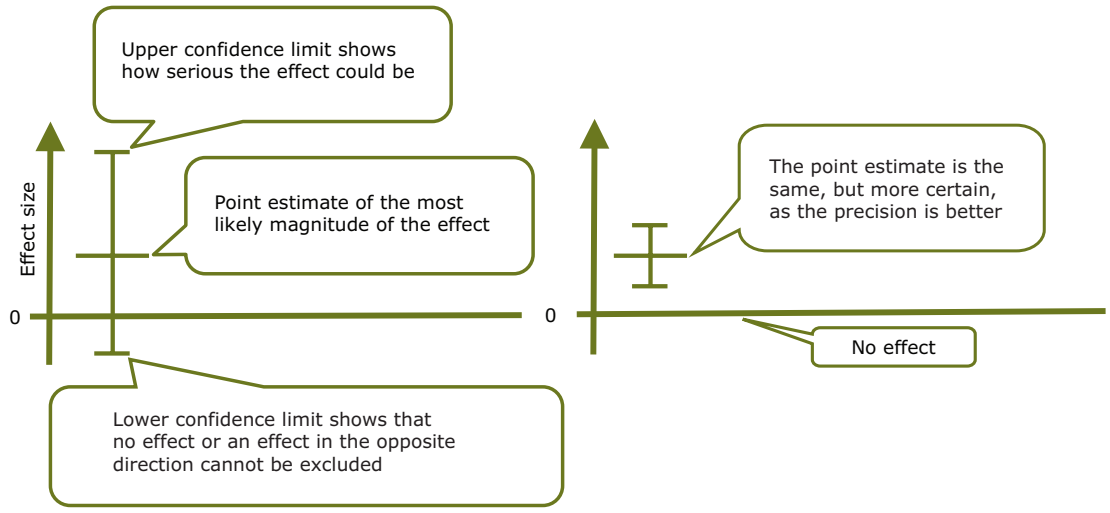
The two studies illustrated in Figure 26.1 show the same average effect, though with different degrees

of certainty. The study on the right shows an effect that is statistically significant, as the no-effect hypothesis (zero effect) can be excluded. The study on the left has less precision, perhaps because it is smaller, and the point estimate does not deviate significantly from no effect (the null hypothesis). However, the upper confidence limit suggests that the study cannot exclude a large effect. In contrast, the significant study on the right would speak against the hazard being very large. Both of these perspectives are relevant, for both studies. A focus on the upper confidence limit would have the additional advantage that it would inspire larger studies with greater precision.

From a precautionary viewpoint, the use of confidence intervals is highly attractive. Instead of concluding that we are not sure that there is an effect at all, we can now also say that the results do not contradict an effect, and that it could possibly be up to a certain magnitude. If a study is large, and when results from two or more studies are combined, the confidence interval will narrow due to the decrease in statistical uncertainty. If a small study (like the one on the left) is in accordance with a potentially large effect, it would call for extended studies to explore whether such a serious hazard is indeed realistic. However, from the 'frequentist' viewpoint, the small study cannot reject the null hypothesis and would therefore not call for any further attention. Hence, the two perspectives differ substantially as to the interpretation of research, the conclusions, and the priorities for further information. Both are useful, and a narrow focus on *p* values should be avoided (Stang et al., 2010).

The choice of statistical analysis is even more important in situations, where we do not have the option of calling for more studies. If a disease is serious but very rare, that number of subjects included will be small, and it may take a long time before enough information has been gathered in order to obtain a p value below 5 %. Perhaps most dramatically, in regard to endangered species, it is simply not possible to sample sufficiently large materials to reach 'significance'. Thus, wildlife biologists some years ago concluded: 'At least part of the blame for the spectacular overexploitation of the great whales can be placed on scientists being unable to agree… In certain circumstances, a population might go extinct before a significant decline could be detected' (Taylor and Gerrodette, 1993). When the researchers examined the frequency and precision of recent monitoring efforts, they concluded that the percentage of precipitous declines that would not be detected as statistically significant would be between 72 % and 90 % for various whale species and 55 % for polar bears. Thus, more than half of the world's polar bears and the great majority of the whales would have to disappear before current studies would be able to conclude that the decrease is 'significant' (based on a one-sided *p* value limit of 5 %) (Taylor et al., 2007). Similarly, to the extent that monitoring and effect studies of environmental hazards are patchy, we are probably overlooking adverse effects, even those

Figure 26.1 The importance of confidence limits



Note: Two studies show the same average effect (horizontal line), but the vertical line suggests that the study on the left has a larger confidence interval and more uncertainty, so that it is both in accordance with no effect (it includes zero and is therefore not statistically significant), but it also cannot exclude a large effect. The study on the right shows the same effect, now statistically significant, but due to the greater precision, this study can exclude the presence of a large effect.

that are serious, simply because the information is uncertain (like the study on the left in Figure 26.1).

To avoid inconclusive results, researchers often carry out power analyses to determine the sensitivity of a proposed study, that is, the likelihood that the proposed study will lead to conclusions on the existence of a hazard of a certain relevant magnitude. If the protocol is not able to ascertain with any confidence the presence of an important risk, then the statistical power is insufficient (as in the monitoring of polar bears). Either the study would be a waste of time and should be disbanded, or the protocol should be expanded to allow sufficient power.

26.8 Bias in research

For the reasons listed above, the research results are often non-informative. Such inconclusive studies are sometimes called 'negative', although this term could suggest that an effect was in the direction opposite to expectation. Worse, such studies have sometimes been thought to represent 'no risk', rather than 'no information'. Such aspects of the traditional science paradigm involve inherent biases toward the null hypothesis. Based on the case studies in the present and the previous volume, Table 26.4 has been revised from previous compilations (Gee, 2009; Grandjean et al., 2004).

Most of the aspects listed in Table 26.4 have to do with the design of the research study and therefore refer to the methodology, rather than the relevance of the research. So, in that respect, greater attention to methodology would be beneficial. However, the main problem is that even though the research results may be less informative than desired, the research may well contain information that is more relevant than the simple claim that the null hypothesis of no effect cannot be excluded. As illustrated in Figure 26.1, we need to ask: How large an effect can the study have overlooked? This question should also take into account the possible existence of vulnerable subgroups, long-term effects, and other issues that may have been ignored.

Two entries in the table refer to the possible existence of publication bias. It is quite likely that some science journals, and more often the mass media, prefer to publish alleged scares rather than to report that there is nothing to worry about (Ioannidis, 2008). But the bias may also be in the opposite direction (Oreskes, 2004). More importantly, our data on publication frequencies (Grandjean et al., 2011) suggest the opposite. The journals publish extensively on well-known chemicals, where new scares are rare, and only occasionally publish on the unknown and emerging environmental hazards which could possibly represent much scarier risks, given that so little attention is paid to them. So the few scares that catch occasional headlines should be interpreted in light of the overwhelming background of environmental hazards that are and have been ignored, some of which could well represent

Table 26.4 Key aspects of research likely to affect the outcome of a study, whether underestimating (false negative) or exaggerating (false positive) the possible existence of an environmental hazard

Methodological features and their main direction of error	
Inadequate statistical power	
Lost cases and inadequate follow-up for long-term effects	
Exposure misclassification	
Insensitive or imprecise outcome measures	
Adjustment for confounders with better precision than the exposure	
Failure to adjust for confounder with effects in the opposite direction	False negative
Disregarding vulnerable subgroups	
5 % probability level to minimize risk of false positives (Type I error)	
20 % probability level to minimize risk of false negatives (Type II error)	
Pressure to avoid false alarm	
Incomplete adjustment for confounders with similar effects	
Post hoc hypothesis	False positive
Publication bias towards positive findings	

serious hazards. Chapter 2 on false positives shows that erroneous alarms are fairly rare.

In summary, the context of justification needs to be balanced with the context of application or, in other words, the quality of the research must be linked with its relevance. So the focus on methodology issues and the preoccupation with verification studies should not happen at the expense of providing evidence on issues of major environmental and social relevance. While polishing the same stone over and over again, we should not ignore all the other shingles and rocks where some scientific gems may yet be hiding.

26.9 The changing research paradigm

Science sociologist Robert K. Merton characterised traditional science by the acronym CUDOS, which stands for Communalism, Universalism, Disinterestedness, Originality and Scepticism. These traits are still valued and are prevalent in many scientific disciplines, but differences occur and the research paradigm within the environmental sciences is changing. All of these attributes for science, whether basic or applied, are needed to secure a meaningful and trustworthy research activity in society. However, the preoccupation with publication, credentials and funding that is common in academia today can lead to social apathy, thereby providing fertile ground for dependence on narrow interests that may include corporate money (Grandjean, 2008b).

Of particular note, Merton characterised ideal science as 'disinterested', but vested interests of whatever origin may make research less neutral and less reliable. Several case chapters in this volume describe how industries have withheld evidence, lambasted whistle-blowers and promoted research that supported the conclusions desired (Kurland, 2003). Especially when cover-up is included in such diversions, the result is that research loses credibility. Transparency in regard to conflicts of interest has been recommended, but complete elimination of financial ties may be the best way to secure trust-worthy research (Krimsky, 2003). Although conflicts of interest undoubtedly occur within academia at large, perhaps an additional problem is that the academic agenda is likely to differ from the priorities of regulatory agencies in environmental health.

Another science culture has developed, as research contracts or privately funded research have grown. They differ in several respects from the CUDOS ideal. The results may not necessarily be published in scholarly journals (and would therefore be missed by our SciFinder searches). When the research is kept secret, it will not inspire further studies at public institutions. A particularly important chemical, bisphenol A (952 publications during 2000–2009), has enjoyed vast industrial popularity and became widely used in food packaging materials and beverage containers (see Chapter 10 on BPA). It was said to be safe at the very low exposures that consumers were likely to receive. However, after several decades of expanding use, independent research eventually uncovered evidence of health risks (Myers et al., 2009). The same pattern was seen with the perfluorinated compounds, where a major US producer for decades claimed that little would escape into the environment, and that essentially no toxicity occurred (Lindstrom et al., 2011). Only recently was it discovered that current exposures may be far from safe (Grandjean et al., 2012), but these chemicals have been disseminated into the global environment and cannot be recalled.

Physics professor John Ziman characterised the 'industrial' (or contracted) research as Proprietary, Local, Authoritarian, Commissioned, and Expert, thereby stressing that this activity builds on local expertise to reach specific goals. The same characteristics may apply to contract research carried out with public funding, but the initiator may not always be apparent. Thus, the Center for Indoor Air Research, the Electric Power Research Institute or the Chlorine Council may sound like charitable donors, rather than industry front groups. But they are in fact organisations funded by corporations with vested interests in the research outcome. However, the reader may be led to erroneously believe that the sponsored research reflects CUDOS values.

The source of funding will also affect the choice of study topics. Accordingly, comparatively little research is devoted to the risks associated with pesticide exposures and the advantages of alternative crop protection methods (Krimsky, 2003). Booster biocides (see Chapter 12), such as Diuron (389 links to articles in 2000–2009 in SciFinder) and Dichlofluanid (39 links), received only a little attention in independent research, some of them much less than the organotin compounds (see tributyltin in Table 26.1) that have been phased out. SciFinder also located only 133 links to Gaucho®, the pesticide that endangered bee populations (see Chapter 16). As there are clear commercial interests in these compounds, the paucity of complementary academic research publications is unfortunate, although perhaps not surprising. Similarly, much less attention is paid to adverse

effects of new technology than to its advantages, although this has recently changed in regard to mobile telephony. Perhaps there is a parallel to physicians collaborating with the pharmaceutical industry in clinical trials of new drugs, which, with patent protection, will be capable of yielding great monetary returns. In contrast, older drugs no longer protected by patent are the subject of far less research, but may be as effective as modern drugs costing far more (Washburn, 2005).

Because evidence is the basis upon which the evaluation of risks must rely, researchers publishing results at odds with certain vested interests have become targets of criticism and intimidation with the aim of suppressing or throwing suspicion on unwelcome information about health risks. Perhaps the best known case involves Herbert Needleman, who supplied the first, weighty documentation of prevalent lead pollution damaging brain development (see Chapter 3 on lead). He was angrily persecuted and harassed with unfounded accusations of dishonesty (Needleman, 2000).

Disagreement usually focuses on the uncertainties and the scientific inference, not the choice of study topic. Harsh critique has sometimes been voiced, as have angry accusations of bias in differing interpretations of evidence (Gori, 1996). Research that has direct implications in regard to considerations of pollution abatement usually receives more wrath than reports on already recognised hazards. Perhaps this is another key as to why researchers favour well-known hazards.

In order to introduce dissent into the literature, possible strategies involve publication in trade magazines disguised as scientific journals. The best examples are Indoor and Built Environment (Tong et al., 2005) and Regulatory Toxicology and Pharmacology (Axelson et al., 2003). These journals tend to publish articles that contain conclusions favourable to the industrial sponsors, no matter their scientific weaknesses. This strategy is counter to the Precautionary Principle, as they argue for 'no risk' when the evidence is uncertain or non-informative. In addition to the tobacco industry, other examples include studies supported by the pharmaceutical industry, which are much more likely to conclude that a drug is safe and efficacious than studies conducted without such support (Jorgensen et al., 2006), but the same seems to happen in toxicology and environmental research (Myers et al., 2009).

As a consequence, public trust is abused by deceit. The purpose of research seeking truth is betrayed, when undisclosed ties taint the research and its conclusions.

Under such contentious conditions, researchers may choose to hedge their conclusions by incessant use of words, such as 'maybe', 'perhaps', 'in theory' and similar terms (Hyland, 1998). By softening the conclusions and avoiding attribution of specific causality, the researchers protect themselves against critique by appearing well-balanced, unassuming and even sceptical toward the implications of one's own findings ([6]). However, this strategy has a downside. To the lay reader, who is not familiar with the traditions of scientific writing, the caveats and reservations may sound like the new results really do not prove anything, and that we are still left with the same uncertainty. To readers with a vested interest, the soft wording can be exploited through selective quotation and by emphasising real or alleged weaknesses (Grandjean, 2008a).

Because of the involvement of research funders, the industrialised (or contracted) science can be better characterized by the PLACE acronym (Ziman, 2000), although often posing like independent, basic research in accordance with CUDOS. If all research today earned CUDOS, no matter its funding, there would be little to worry about. But the weaknesses and biases outlined above suggest that PLACE needs to be supplemented by an additional research, one that better fits with the use of the PP in decision-making.

In this complementary paradigm, environmental research in support of PP-based decision-making would involve stake-holders and therefore become Participatory, rather than Communal or Proprietary as in the other paradigms. It would be Accessible, Transparent, Inventive and Open-minded. Although the various attributes may perhaps not be compared horizontally in Table 26.5, the PATIO characteristics would seem to fit better the research that is needed in a precautionary setting.

A key aspect is that, given the absence of final proof, an integrated evaluation must include uncertainty as a normal condition that needs to be explored and addressed, rather than minimised for the purpose of making research more efficient. An additional feature is the inclusion of the public in exploring how the uncertainty should affect

([6]) Please note how often I use the words 'may' and 'perhaps'. I do so, too, because I do not want to jump to conclusions and therefore present my case with understatement rather than the opposite.

Table 26.5 Main properties of research in three different settings

Academic (normal)	Industrial*	Precautionary
CUDOS [a]	**PLACE** [b]	**PATIO**
Communalism	**P**roprietary	**P**articipatory
Universalism	**L**ocal	**A**ccessible
Disinterestedness	**A**uthoritarian	**T**ransparent
Originality	**C**ommissioned	**I**nventive
Skepticism	**E**xpert	**O**pen-minded

Note: * 'Industrial' science is driven by private or other special interest and may violate some of the CUDOS norms in its pursuit of knowledge within fields of commercial or other defined interest, where public interest may be ignored.

Source: ([a]): Merton, 1973; ([b]): Ziman, 2000.

the decision-making. As discussed above, and in agreement with the PATIO paradigm, both study designs and the reporting of research results need to change.

In contrast to the traditional science paradigm, where replication is held as a key to supporting conclusions on causation, the PP does not inspire repetitive verification. If available, replication will be useful, but a hypothesis may well be plausible even in the (temporary) absence of supportive evidence. Given the enormous diversity and complexity of environmental hazards, one implication of the PP is that research is primarily needed to document the extent of uncertainty and, when possible, to narrow this uncertainty to better inform decision-making and eventually to support more precise risk assessments as a basis for interventions that will no longer need to be precautionary. But rather than fine-tuning risk assessments for individual hazards, the vastly incomplete information on most environmental chemicals makes research into uncertainty a very urgent need.

26.10 Precautionary science

As already discussed, the PP does not specifically demand testing of a null hypothesis that an exposure may be without a discernible effect. Rather, information is required whether a hazard could potentially be serious. This point of view should inspire new ways of planning, conducting, and reporting environmental research. So the research question outlined in the beginning of this chapter in accordance with traditional scientific paradigms now needs to be rephrased (Neutra, 2002):

> 'PP-based question on an environmental hazard: Are we sufficiently confident that this exposure to a potential hazard leads to doses of a magnitude that can result in adverse effects that are serious enough to initiate transparent and democratic procedures to decide on appropriate intervention?'

We must pay closer attention to variability and uncertainty when determining their possible magnitude. Unfortunately, standard statistical methods assume that an exposure is measured without imprecision, which is usually not true, although this problem is generally ignored, thus resulting in underestimation of a hazard (Table 26.4). Assessment of the imprecision and its implications is therefore crucial. While uncertainties may be erroneously thought to cause exaggeration of alleged risks, most often the opposite is true (Grandjean, 2008b). The extent of uncertainties can be expressed in terms of confidence limits (Figure 26.1), but the impact may often need to be explored by using sensitivity analyses. One or more worst-case scenarios deserve as careful scrutiny as the null hypothesis: How serious could the effects be; how large an effect can be reasonably ruled out?

The research evidence must be considered in light of both strengths and weaknesses. While a methodological failure may weaken the support for a particular association, the mere occurrence of some scientific weakness does not prove the absence of a risk. Unfortunate and erroneous rejection of warning signals has occurred in the past because of presumed confounding or other biases and uncertainties. As illustrated by the case chapters in this volume, inconsistencies in some methodological aspect have been used to derail conclusions otherwise adopted by the scientific community. Likewise, statistical acceptance of the null hypothesis has sometimes been interpreted as proof of safety. Further, effects within normal variability have been considered irrelevant, although a population-wide shift in the distribution may represent substantial harm. Focus on average effects may also be misleading, as populations at risk

may suffer much greater harm that can be diluted by the results of non-vulnerable groups.

By acknowledging the limitations to the research evidence, a different point of view needs to considered, i.e. what could possibly be known, given the type of evidence available? Studies e.g. with imprecise estimates of the causative exposure and insensitive and nonspecific outcome measures, are likely to detect only the most serious risks and therefore should be interpreted in light of the weight of such evidence. The fact that the null hypothesis could not be rejected with confidence may be irrelevant in such cases.

In general, all conclusions must be accepted as being provisional and temporary. While a study of often-cited publications in major medical journals found that many of the conclusions were subsequently found to be wrong (Ioannidis, 2008), this does not mean that environmental hazards are exaggerated. While accepting that a tentative conclusion based on preliminary evidence may later turn out to be wrong, public health responsibility may still demand that a serious threat be taken seriously, even though a final proof is not at hand. Any actions would then need to be adjusted later on, as more definite evidence emerges. At the same time, we should not ignore that the majority of environmental chemicals are poorly documented (Gilbert, 2011; NRC, 1984; US EPA, 1998), and ignoring such potential risks is likely to involve a very large number of false negative conclusions.

The bibliometric analyses that we conducted assume, as to regulatory agencies, that research results are published. But the science publication industry has undergone substantial change due to the electronic potentials of the internet for low-cost distribution. However, the costs of science publication need to be covered, just like the subscribers paid for the print journals. Thus, the majority of science articles are not accessible to the public on the internet, unless an access toll is paid (although access may be free after an embargo period of 6–12 months). Thus, while a citizen may view the science journal at a public library, the internet favours the academic world despite the stiff subscription charges. Some journals are open access, where the author pays a fee for quality control, processing and maintenance of the website, and the published article is then free for everybody to see. A growing number of journals now use this model. The European Commission recommends that articles arising from EC-funded research must be available after no more than 12 months. Other funding agencies, such as the Welcome Trust, have as a requirement that the results of sponsored research must be published with open access. Groups of universities, e.g. in the Netherlands, have launched a repository, where their research publications can be accessed by anyone. So in regard to the Participatory aspect of the PATIO paradigm, access to information is improving.

Even preliminary data can facilitate PP-based decision-making. While early findings may provide only tentative conclusions, they can later be included in potential meta-analyses or provide a starting point for follow-up studies. This potential assumes that the data from previous studies are available, and that may not be true. Trade secrets may allegedly be involved, and numerous cases have occurred with suppression of information and withholding of evidence (Kurland, 2003). Some public funding agencies now demand that a data-sharing strategy be worked out for major projects, so that other researchers can carry out additional analyses, including meta-analyses. But there is also a risk that such further analyses are not entirely benevolent (Pearce and Smith, 2011). Hostile analyses have occurred, thus making researchers wary with whom they share their raw data.

Given the discussion on coverage of environmental hazards, attention to the needs of regulatory agencies, traditions of science publication and the impact of other players, we can now attempt to answer the four questions posed in the beginning. Stakeholder involvement, innovation, openness and transparency should become new, important assets in environmental research to serve better as documentation and inspiration for PP-based decision-making.

Ways to improve scientific evidence for robust and precautionary decisions on environmental hazards:

1) The choice of research topic should involve stakeholders and consider the societal needs for information on poorly known hazards;

2) The research should be innovative and complementary with the aim of extending current knowledge, rather than repetitive for verification purposes;

3) The findings should be communicated in such a way as to facilitate judgements concerning the possible magnitude of suspected environmental hazards;

4) The research should be openly available and independent of vested interests.

As argued elsewhere in this volume, science does not provide a prescription for the right decisions on environmental hazards. The emphasis on research will be different for those whose first priority is scientific exactitude and those who focus on making policy in the context of environmental protection and public health. When a precautionary perspective mandates action to prevent foreseeable harms, the evidence does not have to meet the most rigorous demands of science. However, world views, political and other preferences, technical and economic feasibility, and alternative options are crucial for decision-making. As illustrated by the case studies in both volumes of *Late lessons from early warnings*, science does not have a good track record for supporting decisions on improving environmental health. This chapter has highlighted some opportunities for environmental research to provide more relevant results, interpretation, and conclusions for prudent and timely decisions on environmental hazards.

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27 More or less precaution?

David Gee

Despite its presence in a growing body of EU and national legislation and case law, the application of the precautionary principle has been strongly opposed by vested interests who perceive short term economic costs from its use. There is also intellectual resistance from scientists who fail to acknowledge that scientific ignorance and uncertainty, are excessively attached to conventional scientific paradigms, and who wait for very high strengths of evidence before accepting causal links between exposure to stressors and harm.

The chapter focuses on some of the key issues that are relevant to a more common understanding of the precautionary principle and to its wider application. These include different and confusing definitions of the precautionary principle and of related concepts such as prevention, risk, uncertainty, variability and ignorance; common myths about the meaning of the precautionary principle; different approaches to the handling of scientific complexity and uncertainty; and the use of different strengths of evidence for different purposes.

The context for applying the precautionary principle also involves considering the 'knowledge to ignorance' ratio for the agent in focus: the precautionary principle is particularly relevant where the ratio of knowledge to ignorance is low, as with emerging technologies.

A working definition of the precautionary principle is presented that aims to overcome some of the difficulties with other definitions, such as their use of triple negatives; a failure to address the context of use of the precautionary principle; no reference to the need for case specific strengths of evidence to justify precaution; and overly narrow interpretations of the pros and cons of action or inaction.

The chapter also points to the need for greater public engagement in the process of framing and decision-making about both upstream innovations and their downstream hazards, including the specification of the 'high level of protection' required by the EU treaty. A precautionary and participatory framework for risk analysis is proposed, along with some 'criteria for action' to complement criteria for causation.

The capacity to foresee and forestall disasters, especially when such action is opposed by powerful economic and political interests, appears to be limited, as the case studies in *Late lessons from early warnings* illustrate. The chapter argues that with more humility in the face of uncertainty, ignorance and complexity, and wider public engagement, societies could heed the lessons of past experience and use the precautionary principle, to anticipate and minimise many future hazards, whilst stimulating innovation. Such an approach would also encourage more participatory risk analysis; more realistic and transparent systems science; and more socially relevant and diverse innovations designed to meet the needs of people and ecosystems.

'The precautionary principle has, within the space of a decade, experienced a meteoric rise' Nicolas de Sadeleer (2010).

27.1 Introduction

Since the publication of Volume 1 of *Late lessons from early warning* in 2001, the precautionary principle (PP) has received increasing attention and is now included in many laws and constitutions. It has also been the focus of much intense public and scientific debate in the European Union and its Member States, particularly in France where it was enshrined into the national constitution in 2005.

The debate on GMOs in France in the years 1997–2005 (Marris, 2005) is just one example of how debates on the PP can trigger the examination of wider issues, moving from narrow questions of risk and scientific uncertainty to broader questions about the future of agriculture, the direction of scientific research and innovation, and public engagement. Where a political process opens up rather than closes down debates, the result can be 'empowering wider social agency in technology choice' (Stirling, 2008). Debates on future innovation pathways do not necessarily eliminate conflict between stakeholders but often clarify 'what [the] conflict is really about' (de Marchi, 2003).

These realities are reflected in Chapter 19 on genetically modified (GM) crops and agro-ecology, which analyses two contrasting innovation pathways to global food security and sustainable agriculture. It finds that, in addition to some 'top down' genetic engineering, 'bottom up' approaches to agricultural innovation 'are proving capable of getting sustainable, participatory and locally adapted solutions into the hands of those that need them most'.

A catalyst for debate and for timely action

The PP seems to have two roles. First, as a trigger for broad debates on what kind of future we want in a water-, energy- and resource-constrained world and what innovation pathways could lead towards such futures (WBCSD, 2011; WEF, 2012; WBGU, 2012; OECD, 2012; UNEP, 2011; EEA, 2010). And second as a legal and moral justification for more timely actions on early warnings about potential hazards.

The case studies in this volume furnish evidence that contributes to a wider understanding of both roles. While there is much more emphasis on its role in justifying actions on early warnings, the chapters in Parts B and C, on emerging lessons and issues, begin to illustrate the PP's role in facilitating debates around innovation pathways and technological choices. In addition, Chapter 26 on science and Chapter 24 on justice for early warning scientists and late victims, illustrate the PP's role in stimulating discussion about reforms within environmental science, the law and scientific organisations.

The case studies addressing substances or chemicals that are now widely known to be hazardous focus on the combination of early warnings and (usually) late actions. The studies address asbestos, benzene, BSE (mad cow disease), diethylstilboestrol (DES) tributyl tin (TBT) and polychlorinated biphenyls (PCBs) in Volume 1 and DDT, dibromochloropropane (DBCP), vinyl chloride monomer VCM, lead in petrol, mercury, beryllium, and booster biocides in Volume 2. They primarily illustrate how more precautionary action could be applied to chemical risks emerging now, such as those from Bisphenol A (BPA) and other chemicals, nicotinoid pesticides, and endocrine disrupting substances which are present in some consumer products, including pharmaceuticals, such as ethinyl oestrodiol in the pregnancy pill, discussed in Chapter 13.

The histories of well known technologies, such as X-rays, fishing techniques, fossil fuel power sources and early nuclear plants, can also provide lessons for prudent action on the potential hazards of such emerging technologies as nanotechnology, genetically modified (GM) food, radio-frequency from mobile phones, and the new generation of nuclear plants. The chapters on alien species, floods, and ecosystems, as well as the late actions on climate change, also provide insights into how the management of ecosystems could develop.

Taken together, the examples of late action on known hazards illustrate the high cost of inaction. Globally that cost has been paid in millions of lives and cases of disease and dysfunction, much damage to the environment and species, and very large economic penalties, some of which are described in Chapter 23 on the costs of inaction.

The case studies are not all negative, however. Five of the 34 case studies describe precautionary actions: the European ban on hormones in cattle feed; the regulations and some member state actions on GMOs in Europe; the ban on TBT in France in 1984; the ban on the pesticide Gaucho in France in 1999; and, arguably, the belated but still precautionary European ban on some antibiotics when used as growth promoters in farm animals. These actions,

along with the histories of the 88 claimed false positives analysed in this volume, also illustrate the value of the PP in minimising harm and societal costs.

There are other examples where action was taken quite quickly but only after serious and compelling human evidence became available, sometimes from an observant clinician (in the cases of DES and VCM) or from the victims themselves (DBCP). In these three examples, just four to seven cases of very rare cancers or sperm reduction (DBCP) were sufficient to justify prompt regulatory action.

Barriers to wider use of the PP

One obvious question that emerges from the case studies is 'how can the PP be more widely used, both as a justification for early policy action and as a broad trigger for wider, more upstream debates about innovation pathways?'

Looking across the case studies, there appears to be a number of common barriers to using the PP to justify more timely responses to early warnings. Taken together, these barriers explain much about the decades-long delay between warnings and action. These barriers include:

- opposition from powerful corporations — supported by some scientists, policymakers and politicians — who fear high economic, intellectual and political costs to themselves from early and sometimes even late actions to reduce risks;
- key misunderstandings about the PP's definition and meaning;
- difficulties understanding and dealing with complex biological and ecological systems that are characterised by multi-causality, scientific uncertainty, ignorance and scientific 'surprises';
- scientific and political tensions between the high strength of evidence needed for scientific causality and the lower strength of evidence needed for timely public policy;
- inadequate analysis of the costs and benefits of proposed actions and inactions; and unrealistic market prices for hazardous agents that fail to reflect the costs to society of their production, consumption and wastes;
- political and financial short-termism;
- a failure in most cases to engage with civil society and the public to help counter the power of the corporate and other stakeholders that may wish to dismiss early warnings.

Barriers 1, 6 and 7 mainly concern political and economic power, whereas barriers 2–6 primarily relate to the more technical process of applying knowledge to policymaking.

There is, of course, no clear-cut separation between these two aspects of regulatory activities or between the roles that scientists play as 'experts' in the process of evaluating the regulatory science used in the policy process. As Jasanoff (1990 and 2011) has pointed out:

> 'Policy relevant science comes into being in a territory of its own that is subject to neither purely scientific nor wholly political rules of the game.'
>
> 'It is not so much scientists (but) experts, who govern the production and evaluation of policy relevant science.'

To help encourage broad and wise use of the PP, this chapter will briefly examine the barriers to its use, focusing initially on the first barrier, relating to corporate power. This is followed by consideration of the more technical barriers 2–5, using the EEA definition of the PP as the framework for the analysis.

Thereafter, Section 27.7 of this chapter briefly addresses political and financial short-termism, before considering wider public engagement as part of the process of creating and managing innovations and their attendant hazards.

27.2 The power of corporations to oppose action

Chapter 11 on DDT notes Rachel Carson's observation that corporations have often focused on 'making a dollar at whatever the costs'. Although this overstates the situation, the case studies provide ample evidence of how corporations responded to early warnings about possible hazards from their products by organising 'product defence' campaigns. Chapter 7 on environmental tobacco smoke describes seven key strategies that the tobacco companies used to defend their products.

The tobacco industry was certainly not alone in using similar tactics, as case studies on lead, VCM, beryllium and fossil fuels illustrate. Indeed it seems

likely that other industries with hazardous products to defend today would employ similar strategies, including trying to control, directly or indirectly, the relevant scientific research.

This was a key objective of the leaded petrol industry, which maintained a virtual monopoly on leaded petrol research from immediately after the 'one day trial' of leaded petrol in 1925, when early warnings emerged from some senior public health scientists, until the 1970s. Without access to independent research the regulatory authorities were vulnerable to corporate influence on the scientific evidence made available to them. This was an issue that Clair Patterson, lead expert and eminent palaeontologist, noted with some vehemence in evidence to the US Congress:

> 'It is not just a mistake for public health agencies to cooperate and collaborate with industries in investigating and deciding whether public health is endangered; it is a direct abrogation and violation of the duties and responsibilities of those public health organisations.' ([1])

Today scientific research agendas are often determined by more independent academics and public sector organisations. However, the way in which technological and hazard problems are framed can result in research that focuses much more on developing products than on the need to find out whether those products are harmful.

For example, over the past decade public research funding by the EU on nanotechnology, biotechnology and information technology was heavily biased towards product development, with only about 1 % of the EUR 20 billion budget spent on investigating their potential hazards. There was a similar imbalance on research into genetic modification in the US, where over the period 1992–2002 the US Department of Agriculture spent USD 1.8 billion on biotechnology research, of which just 1 % went to risk-related research (Mellon, 2003, cited in Chapter 19).

In some areas where research is dominated by issues of intellectual copyright, such as GMOs, there have been problems with access to the organisms in question. There has recently been some opening up of research on GM seeds, however, following a letter of complaint from 26 academics in the US, whose research was inhibited by the lack of access to GM seeds owned by the corporations (Pollack, 2009).

The funding of different innovation pathways is also an issue. For example, the European Commission's Standing Committee on Agricultural Research (SCAR, 2012) has called for increased support for research on the economic and social dimensions of new technologies and farming practices, calling for the highest priority be given to funding low-input high-output systems, which 'integrate historical knowledge and agro-ecological principles that use nature's capacity' (cited in Chapter 19).

There is also a strong bias in the environmental sciences towards research on well known problems rather than on emerging issues (Chapter 26).

Corporations have also realised that the language used in debates about the hazards associated with their products is also important. An example of the use of loaded language was the claim by the leaded petrol industry that 'normal' levels of lead in blood were 'natural' and therefore safe. 'Sound science' was another common term taken over by public relations companies for the tobacco industry to mean science that supports the industry position (Baba et al., 2005). The term has since been used by other industries engaged in product defence who characterise science that does not support the industry position as 'unsound'.

The strategy of 'manufacturing doubt' out of uncertainties in the science was also a key part of product defence in several of the case studies, such as those on tobacco, lead, asbestos, beryllium, benzene and climate change (Michaels, 2008; Oreskes and Conway, 2010).

The long history of corporate misconduct begs the question why corporations adopt strategies of 'product defence' and how such actions could be minimised for the public good. Chapter 6 on beryllium concludes with some reflections on this question by Tee Guidotti, who suggests that corporations quickly lock themselves into product defence because of 'fear, denial and risk of loss'. His conclusion is that if corporations are expected to reverse course as the evidence of harm from their products increases, then 'there must be room for them to turn around'. It seems likely that his suggestions that this may involve 'forgiving past liabilities and reducing punitive damages' will be controversial, whereas his call for more active shareholder engagement on the question of responsible corporate behaviour is likely to be welcomed.

([1]) Senator Muskie Hearings on Air Pollution, 1966, cited in Chapter 3 on leaded petrol.

Chapter 24 addresses the question of why businesses do not react to early warnings with precaution in more depth, looking more closely at the issue of corporate behaviour. It notes that 'blaming business, in particular with hindsight ... may not always be constructive' as it often misses the 'complex or even contradictory set of motives and drivers that businesses face'. The authors, Le Menestrel and Rode, find that corporate decisions are influenced by a mixture of economic, epistemological, regulatory, cultural and psychological factors. Economic motives dominate: 'in virtually all reviewed cases from both volumes of *Late lessons from early warnings*, it was perceived to be profitable for industries to continue using potentially harmful products or operations'.

Corporate short-term interests have dominated over longer-term public interests mainly because the costs of damage to people and environments were, and still are, largely externalised to society as a whole. The external costs of climate change are described by former chief economist to the UK Treasury, Nicholas Stern, as 'the biggest market failure ever' (cited in Chapter 14). This means that corporations bear few of the costs of harm from their activities, except in cases where victims win compensation or ecosystems are restored, where possible. Even here, however, the sums may be largely covered by insurance.

As noted in Chapter 23 on the costs of inaction, external costs need to be internalised into the accounts of corporations via regulations, taxes, charges and permits. Anticipatory assurance bonds would also be helpful, as illustrated by Robert Constanza using the example of Deepwater Horizon (Chapter 24).

To deal with some of the non-economic factors influencing corporate responses to early warnings, Le Menestrel and Rode suggest distinguishing between the economic and the 'political' roles of businesses that are given ample opportunity to influence the regulatory process (Scherer and Palazzo, 2011; UCS, 2012) . They also call for new institutional arrangements involving rigorous and explicit exposition of the dilemmas and trade-offs involved in reconciling value conflicts, and the organisational pressure to deny the reality of the early warnings. These 'institutional approaches would more realistically complement initiatives based on the idealised principle that being socially responsible is economically profitable'.

Finally, the historical case studies also reveal one or two examples of responsible corporate behaviour, albeit by companies selling hazardous products rather than by their manufacturers. For example, some companies stopped using asbestos in the 1970,; and Johnson & Johnson stopped using CFCs in their aerosols in 1977, eight years before the ozone hole was discovered.

More recent case studies such as on BPA illustrate that some user companies abandoned BPA for some products some years before the European Commission took action on its use in baby toys. The marine and forest stewardship councils encourage responsible environmental actions; and some nanotechnology companies, such as BASF, are working with civil society organisations to agree codes of conduct on the responsible use of nanotechnology in both research and products (EU, 2010). Hewlett Packard has likewise been very active in getting lead and other hazardous compounds out of its electronic goods and Astra Zeneca is working on reducing the envionmental impact of pharmaceutials, by, inter alia, researching the potential for 'green' medicines.. There is even some action on the issue of more environmentally realistic accounting, with Puma leading the way.

Meanwhile, as part of the broader debate about innovation pathways from current unsustainable economic activities in an increasingly resource-, energy- and water-constrained world, the World Business Council for Sustainable Development has produced its business vision for the way forward (WBCSD, 2010).

27.3 The precautionary principle — key elements and misunderstandings

Public health decisions about moving from 'evidence to action' are a balancing act between what needs to be known and what ought to be done (Weed, 2004). It took more than 40 years of much scientific endeavour and public debate between the 1940s and the 1980s, before what was known about smoking and lung cancer was applied to protect public health, following sustained opposition from economic and political interests. In this case, the opportunity for **precautionary** action on a **likely hazard** in the 1950s and 1960s was lost. By the 1990s only **prevention of known harm** was possible.

Numerous international treaties and other instruments refer to the PP, as summarised in Box 27.1. Many share common elements but there is also variance in the definitions with respect to: the standard of scientific evidence required to invoke the PP; the extent of the obligation imposed on public bodies to apply the principle; the objectives

Box 27.1 International treaties relevant to the case studies illustrating key elements of the precautionary principle

Rio Declaration on Environment and Development, 1992: 'Where there are threats of serous or irreversible harm, lack of full scientific certainty shall not be used as a reason for postponing costs effective measures to prevent environmental degradation.'

European Union's Treaty on the Functioning of the EU, Article 191(2): 'Union policy on the environment shall aim at a high level of protection taking into account the diversity of situations in the various regions of the Union, it shall be based on the precautionary principle and on the principles that preventive action should be taken, that environmental damage should as a priority be rectified at source, and that the polluter should pay.'

Regulation (EC) No 1907/2006 concerning the Registration, Evaluation, Authorisation and Restriction of Chemicals (REACH), Preamble: 'the need to do more to protect public health and the environment in accordance with the precautionary principle'. In addition, Article 69 provides that: 'To ensure a sufficiently high level of protection for human health, including having regard to relevant human population groups and possibly to certain vulnerable sub-populations, and the environment, substances of very high concern should, in accordance with the precautionary principle, be subject to careful attention.'

UN Framework Convention on Climate Change, 1992: 'The parties should take precautionary measures to anticipate, prevent or minimize the causes of climate change and mitigate its adverse effects. Where there are threats of serious or irreversible damage, lack of full scientific certainty should not be used as a reason for postponing such measures, taking into account that policies and measures to deal with climate change should be cost-effective so as to ensure global benefits at the lowest possible cost. To achieve this, such policies and measures should take into account different socio-economic contexts, be comprehensive, cover all relevant sources, sinks and reservoirs of greenhouse gases and adaptation, and comprise all economic sectors.

EU Directive 2001/18/EC on deliberate release of GMOs, Article 4 (1): 'Member States shall, in accordance with the precautionary principle, ensure that all appropriate measures are taken to avoid adverse effects on human health and the environment which might arise from the deliberate release or the placing on the market of GMOs'.

Cartegena Protocol on Biosafety, 2000, Article 11(10): 'lack of scientific certainty due to insufficient relevant scientific information and knowledge regarding the extent of the potential adverse effects of a living modified organism on the conservation and sustainable use of biological diversity in the Party of import, taking also into account risks to human health, shall not prevent that Party from taking a decision, as appropriate, with regard to the import of that living modified organism intended for direct use as food or feed, or for processing, in order to avoid or minimize such potential adverse effects.'

Regulation (EC) No 178/2002 establishing the European Food Safety Authority and procedures in matters of food safety, Article 7: Precautionary principle: 'In specific circumstances where, following an assessment of available information, the possibility of harmful effects on health is identified but scientific uncertainty persists, provisional risk management measures necessary to ensure the high level of health protection chosen in the Community may be adopted, pending further scientific information for a more comprehensive risk assessment.'

EU Regulation 1107/2009 on plant protection products, Article 1(4): 'The provisions of this Regulation are underpinned by the precautionary principle in order to ensure that active substances or products placed on the market do not adversely affect human or animal health or the environment. In particular, Member States shall not be prevented from applying the precautionary principle where there is scientific uncertainty as to the risks with regard to human or animal health or the environment posed by the plant protection products to be authorised in their territory.'

London International Maritime Organisation Convention on the control of Harmful Anti-fouling Systems on Sips, 2000, Articles 6(3) and (4): 'Where the Commission is of the view that there is a threat of serious irreversible damage, lack of full scientific certainty shall not be used as a reason to prevent a decision to proceed with the evaluation of the proposal … (which involves considering) whether the proposal has demonstrated a potential for unreasonable risk of adverse effects on non-target organisms or human health.'

Box 27.1 International treaties relevant to the case studies illustrating key elements of the precautionary principle (cont.)

European Court of Justice in the BSE case (Case C-157/96, National Farmers Union and others, 1998, ECR 1-2211): 'Where there is uncertainty as to the existence or extent of risks to human health, the institutions may take protective measures without having to wait until the reality and seriousness of those risks become fully apparent.'

Stockholm Convention on Persistent Organic Pollutants, 2001: 'Acknowledging that precaution underlies the concerns of all the Parties and is embedded within this Convention …'

WTO Agreement on Sanitary and Phytosanitary Measures (SPS Agreement), Article 5(7): 'In cases where relevant scientific evidence is insufficient, a Member may provisionally adopt sanitary or phytosanitary measures on the basis of available pertinent information, including that from the relevant international organizations as well as from sanitary or phytosanitary measures applied by other Members.'

European Commission communication on the precautionary principle, 2 February 2000: 'The precautionary principle applies where scientific evidence is insufficient, inconclusive or uncertain and preliminary scientific evaluation indicates that there are reasonable grounds for concern that the potentially dangerous effects on the environment, human, animal or plant health may be inconsistent with the high level of protection chosen by the EU.'

of applying the PP; and the inclusion of elements such as provisions on costs and benefits or public participation.

The EEA's working definition of the PP

It is not surprising that many debates about the PP are confused and lengthy, given the variations apparent in the instruments and statements listed in Box 27.1. During the last decade of discussions arising out of Volume 1 of *Late lessons from early warnings,* the EEA has produced and refined a working definition of the PP that has proved useful in helping to achieve a more common understanding of the PP:

> 'The precautionary principle provides justification for public policy and other actions in situations of **scientific complexity, uncertainty and ignorance**, where there may be a need to act in order to avoid, or reduce, potentially serious or irreversible threats to health and/or the environment, using an **appropriate strength of scientific evidence**, and taking into account **the pros and cons of action and inaction** and their distribution.'

This definition is explicit in specifying situations of uncertainty, ignorance and risk, as contexts for considering the use of the PP. It is expressed in the affirmative rather than the triple negatives found in, for example, the Rio Declaration. It explicitly acknowledges that the strength of scientific evidence needed to justify public policy actions is determined on a case-specific basis, and only after the plausible pros and cons, including their distribution across groups, regions, and generations, have been assessed.

The three key sets of issues highlighted in the EEA definition above are explored in Sections 27.4–27.6 below.

27.4 Complex biological and ecological systems.

The *Late lessons from early warnings* case studies cover a vast range of complex systems so it is useful to focus on reproductive and developmental hazards as an illustration of such systems.

Many of the case studies have demonstrated developmental and reproductive harm from exposures to agents such as mercury at Minamata, TBT, DES, PCBs, tobacco, lead, VCM, ethinyl oestradiol from the contraceptive pill, BPA and radiation from X-rays.

These cases have shown that serious damage to health can be initiated in the early life stages of humans and other species but may not become apparent until much later in adult life, and even

Box 27.2 Reproductive and developmental harm

Developmental periods are highly sensitive to environmental factors, such as nutrients, environmental chemicals, drugs, infections and other stressors. 'Many of the major diseases — and dysfunctions — that have increased substantially in prevalence over the last 40 years seem to be related in part to developmental factors associated with either nutritional imbalance or exposures to environmental chemicals …The conditions that are affected by nutritional or environmental chemical exposures during development include the pathophysiologies, diseases, and syndromes that constitute major public health problems across the globe: obesity, diabetes, hypertension, cardiovascular disease, asthma and allergy, immune and autoimmune diseases, neurodevelopmental and neurodegenerative diseases, precocious puberty, infertility, some cancer types, osteoporosis, depression, schizophrenia and sarcopenia' (Baruoki et al., 2012).

The mechanisms of biological action in each of these earlier experiences are not yet well established, despite decades of research. However, it seems clear that it is more the timing of the dose, rather than the dose itself, which, inter alia, distinguishes harmful from harmless exposures to reproductive and developmental toxicants (Gee, 2006, 2008; Grandjean et al., 2008; Kortenkamp et al., 2011; Chemtrust, 2008; EEA, 2012).

Such harm is often irreversible and sometimes multigenerational, causing life-time personal and societal costs that cannot be offset by any benefits to the individual from intrauterine exposures. Thus, biology, economics, equity and morals all justify early actions to prevent developmental and reproductive harm. However, establishing sufficient evidence for action on such complex hazards is much more difficult than it was for tobacco and lung cancer, where there was clear evidence that just one agent, albeit a complex mixture like tobacco smoke, caused a specific cancer that was relatively rare before smoking became widespread.

in subsequent generations, as in the DES case (see EEA, 2001). Such examples illustrate the realities of complex biological and ecological systems that are characterised by multi-causality, scientific uncertainty, ignorance and scientific 'surprises'.

From monocausality to multicausality

The biological processes that lead to chronic diseases such as breast or prostate cancer, or to reproductive or developmental harm, appear to involve some or all of at least eight main events in the disease process: preparation within the host; initiation; promotion; retardation; progression; disease onset; the strengthening or weakening of severity; and prevalence of the disease. These steps in the causal chain of the disease process can be affected by many interdependent, co-causal risk factors, where the timing of exposures is usually critical. Some factors, including chance, may operate at one or several stages of the same disease process.

It is therefore a challenging task to identify the 'causal' and often co-causal factors needed to prevent or reduce the population burden of such ill health, given that exposures occur at different developmental stages; are often interactive, mixed, and usually low level; and affect people with specific environmental histories and susceptibilities.

Within the history of the public health sciences there has long been a tension between the monocausal, reductionist approach to investigating disease causation and multicausal, more holistic approaches. A similar tension exists within ecology between 'diversity' and 'variable ' approaches to complex ecosystems — see Chapter 17 on ecosystems. Some scientists frame their studies around the view that it is the germ, or the gene, the oncogene, or a single risk factor, which is mainly 'responsible' for disease. Others look to the overall environmental history of the host for the many factors and influences that, if taken together, may explain disease causation (Sing et al., 2004).

Concentrating research on particular parts of the puzzle, rather than on the causal puzzle itself, may inhibit the clarification of causality. For example, some 4 000 chemical substances have been identified in tobacco smoke, of which more than 100 are classified as toxic. However, the precise disease process that leads to cancer or heart disease in some smokers but not in others is still largely unknown after more than 40 years of research.

Despite ignorance about the disease process associated with mixtures of chemicals, it has still been possible to prevent some harm by reducing exposures to the whole mixture, such as smoke from burning tobacco and fossil fuels, from complex welding and rubber fumes, and from fine particles of air pollution.

The practical difficulties of studying and understanding complex multicausal biological processes have meant that the attraction of a monocausal approach remains strong. Reductionism and the metaphor of the body as a machine are powerful paradigms that continue to support the idea of linear relationships between specific causes, long after knowledge about irreducible uncertainties, emergent properties and non-linear dynamics became available (Di Guiliio and Benson, 2002).

From confounders to co-causal factors?

The tools available to unravel multicausal, complex and dynamic disease processes are not well developed or used (Cory-Slechta, 2005). As a consequence, most epidemiologists try to identify specific risk factors while eliminating possible confounding factors via various statistical techniques. Such 'statistical surgery' or 'context stripping' may remove many confounders from the analysis that are really co-causal factors. If the focus is on just one toxicant, then other 'environmental properties tend to be regarded as marginal and designated as covariates or confounders: treating such environmental conditions as confounders is equivalent to defining genetic differences as confounders. 'A true evaluation of toxic potential and its neurobehavioral consequences is inseparable from the ecologic setting in which they act and which creates unique, enduring individual vulnerabilities that warrant the same status as genetic predispositions and are imprinted as forcefully' (Weiss and Bellinger, 2006).

Even with a well-studied phenomenon, such as lead poisoning, there is a growing realisation that lead exposure, environmental deprivation and enrichment, and neurotoxicity are complex and 'perhaps bidirectional' (Bellinger, 2007). For example, an enriched and intellectually stimulating home environment seems to reduce the harmful effects of a toxicant such as lead, while lead exposure can reduce the benefits of such enriched environments. Similarly, a deprived socio-economic environment can increase the harmful effects of lead while reducing the beneficial effects of a reduction in lead exposure. More fundamentally, scientists have also noted that bidirectional relationships, such as cell signalling and crosstalk, imply that causality may be circular (Soto and Sonnenschein, 2006).

Similar scientific challenges emerge from the field of endocrine disruption in wildlife, as well as within ecotoxicology more generally (Newman, 2001). These arise from having to investigate and draw inference across biological scales, from population level to lower levels of biological organisation and back again, in order to show, for example, whether harm to individual fish can cause fish population decline (Chapter 13 and Kidd et al., 2007).

It would seem then that the 'key to understanding these causal processes is clearly the ability to elaborate and understand complexity: the interacting systems involved will always overwhelm predictions of independent effects of any single factor, reducing them to very limited and uncertain information' (Bellinger et al., 1985).

It also follows that in complex systems very small changes in key variables can have profound effects 'Small' can be very significant in finely balanced non-linear systems, where, as Heraclitus observed centuries ago, there is a 'harmony of opposites'. Removing even the 'smallest' link in an interdependent causal chain can sometimes break at least pathway to disease.

Such complex and multi-causal factors are also evident in ecological systems and species as illustrated in Chapter 14 on climate change, Chapter 16 on bees, Chapter 17 on ecosystems and Chapter 20 on invasive alien species.

How then can we identify possible or probable causality from observed associations in such complex biological and ecological systems, so that some co-causal priorities for public health and environmental protection can be agreed?

Multicausality and the Bradford Hill 'criteria' for causality

'With preventive medicine in mind the decisive question is whether the frequency of the undesirable event B will be influenced by a change in the environmental feature A' (Bradford Hill, 1965). Building on the tobacco controversy, Bradford Hill identified nine characteristics of scientific evidence that, if taken together, could help scientists to move with some confidence from observing associations to asserting causation. His

Box 27.3 The Bradford Hill 'criteria' for identifying causation

1. Strength of association
2. Consistency
3. Specificity
4. Temporal relationship (temporality)
5. Biological gradient (dose-response relationship)
6. Plausibility (biological plausibility)
7. Coherence
8. Experiment (reversibility)
9. Analogy

subsequently misnamed 'criteria' are still widely used today in both the health and environmental fields (WHO, 2002; Collier, 2003; Maxim and van der Sluijs, 2010).

Bradford Hill's explicit approach to deriving causation from association was essentially based on monocausality, that is, on finding the specific cause of a specific disease.

He was aware that several factors would be implicated in disease but that removing one of them may reduce its frequency, or incidence, without necessarily eliminating the disease entirely. He also acknowledged the other, simpler type of multicausality, which is where one disease can have several different independent causes, noting that: 'diseases may have more than one cause. It has always been possible to acquire a cancer of the scrotum without sweeping chimneys or taking to mule spinning in Lancashire' (Bradford Hill, 1965).

The Bradford Hill 'criteria' need to be reappraised in the light of multicausality and complexity. This is particularly important because the absence of some or all 'criteria' is often used in current controversies to deny the possibility of causality. More generally, the criteria seem less robust now as reasons for dismissing associations than they did in the world of the 1960s, when issues were perceived in largely monocausal terms.

For example, the criterion of **consistency** between the results of different studies into the same phenomena, when present, clearly adds much confidence to assertions of causality. However, multi-causality can make consistency very difficult to achieve: 'if all studies of lead showed the same relationship between variables, one would be startled, perhaps justifiably suspicious' (Needleman, 1995). The sources of variability arise both from the study and the investigator, such as the framing and initial assumptions; the models, methods and statistical analyses used; the choice of population group; the presence of susceptible sub-groups; and the data selected. Other sources of variability and bias have been noted (Bailar, 2007) and the limitations of conventional epidemiology have been explored from a precautionary perspective (Grandjean, 2008). In addition, there are the sources of variability in populations arising from the 'sociomics' of environments and the epigenetics of individuals.

It is hardly surprising therefore that, after decades of research, most lead studies can still only 'explain' 30–40 % of the variance in most lead-linked biological end-points, and sometimes far less (Bellinger, 2007). As inconsistent results are to be expected from complex biological and ecological systems the absence of consistency between studies does not imply an absence of causality.

Bradford Hill included a **linear dose-response relationship** between a toxicant and its effects as another important criterion. However, where the timing of exposure is more important than the dose itself, and where non-linear, 'low-dose' effects are present, the absence of a linear dose-response relationship does not provide robust evidence against causality.

The condition of **temporality** anticipates that a cause must precede the effect. This is obviously so, except where there are multiple causes arising at different times, and with varying rates of increase or decrease, which may therefore reverse, stabilise, or accelerate the overall disease trend, depending on their relative strengths. If this feature of reality is not taken into account then some widely used interpretations of temporality in relation to overall disease trends can lead to shaky conclusions.

For example, in a review of the evidence on falling sperm counts and endocrine-disrupting chemicals, it was concluded that, as overall sperm counts began to fall in some countries in advance of the rise of chlorine-based chemistry, such chemical exposures could not be a cause of change in the overall trend (WHO, 2002). In the context of multicausality, where the combined effects of several causes together determine the overall time trend of a disease, such a conclusion is not soundly based.

Such time-dependent factors within multicausal systems also mean that obtaining evidence based on the **experiment** criterion — i.e. demonstrating the impact of removing one cause of a disease affected by many causes — can be very difficult, as with changes in IQ or sperm counts.

Less weight should also be placed on **specificity** as a criterion, given the widespread prevalence of 'many to many' cause and effect relationships, and the capacity of many substances, such as tobacco PCBs, asbestos, lead and mercury, to cause many types of harm.

The **strength of association**, which Bradford Hill put first in his list of features, is clearly still very relevant but with caveats that arise from multicausality. Even a 'low' relative risk of say, 1.5, if replicated in several studies, can be very robust for a multicausal disease as is the case with smoking and heart disease. Such a 'low' relative risk will also represent much harm if the background rate of the disease is large.

The criteria of **biological plausibility** and **coherence** are dependent on the established knowledge of the day and therefore are not robust criteria for dismissing early warnings, where relatively novel science, at the frontiers of scientific knowledge, is often used.

Whereas multicausality seems to weaken most of the criteria, **analogy** becomes more necessary given the difficulties of establishing clear causality from complex systems. If precautionary actions are needed then analogies from past experiences may be particularly valuable. Box 27.4 provides some 'criteria for action' to complement the criteria for causation, based on experiences of past ecological and biological hazards, including by analogy, which may provide quite robust evidence of emerging potential hazards.

In judging strength of association, Bradford Hill also warned against the overuse and misuse of statistical significance testing: 'we waste a deal of time, we grasp the shadow and lose the substance, we weaken our capacity to interpret data and to take reasonable decisions whatever the value of P. And far too often we deduce "no difference" from "no significance".'

Although similar cautions have been repeated regularly since then (Cohen, 1994; Poole, 2000; Hooper, Stang and Rothman, 2011), the misinterpretation of statistical significance and the relative neglect of confidence intervals continue (see also Chapter 26 on science for precautionary decision-making).

In the circumstances of multicausality and complexity the Bradford Hill criteria are characterised by a strong element of asymmetry. The presence of the criteria can be robust evidence for a causal association, whereas the absence of the criteria is not robust evidence that there is no causal association. Bradford Hill drew attention to this asymmetry with several of his criteria but some of his followers have forgotten

Box 27.4 Criteria for precautionary action: some features of evidence about the hazardous potential of agents that may justify precautionary action

1. Intrinsic toxicity/ecotoxicity data
2. Novelty (i.e. where there is a low 'knowledge/ignorance ratio')
3. Ecological or biological persistence
4. Potential for bio-accumulation
5. Large spatial range in the environment e.g. potential for global dispersion.
6. Seriousness of potential hazards
7. Irreversibility of potential hazards
8. Analogous evidence from known hazards
9. Inequitable distribution of hazardous impacts on particular regions, people and generations
10. Availability of feasible alternatives
11. Potential for stimulating innovation
12. Potential and time scales for future learning

this in their use of the criteria to dismiss possible hazards (Ashby, 1997; WHO 2002). When addressing biological and ecological complexity, such asymmetry in the application of the Bradford Hill criteria is even more pronounced than it was when he introduced them.

Another barrier to early action arises from the systemic biases towards not finding a causal link, specifically biases within the epidemiology and toxicology methods that tend to generate false negatives (i.e. assertions that something is safe when it turns out not to be). These methodological biases are illustrated by Grandjean in Chapter 26.

Both policymakers and scientists need to acknowledge and take account of these main directions of methodological error when they evaluate the methods and results of research. Many scientists do (Grandjean, 2004 and 2005) but awareness of these methodological biases among many stakeholders appears to be low.

Finally, the issue of funding bias, whereby research results can be closely associated with the source of funding, has been observed in the tobacco literature (Barnes, 1998) and then identified in other fields such as pharmaceuticals (Goldacre, 2012; Lexchin, 2003) the food and beverage industry (Levine, 2003) BPA, (Vom Saal, 2005), mobile phones (Huss et al., 2007), food, (Levine, 2003), biomedics (Bekelman, 2003), GMOs (Diels, 2011). The explanation for this bias is not clear (Krimsky, 2006, 2010). Funding bias is also to be found in the transport and constructions fields, where underestimation of costs and construction times by the developers is routine, and in cost-benefit analysis where the direction of bias is routinely in the direction of those who fund the study.

Other concepts related to the PP and complexity are likewise often understood differently by different actors. An important example is the distinction between uncertainty and ignorance, which constitute quite different states of knowledge. For example, both the asbestos-induced mesothelioma cancer and the hole in the ozone layer caused by CFCs were complete scientific 'surprises', arising from a state of ignorance. They were not gaps or uncertainties in existing states of knowledge.

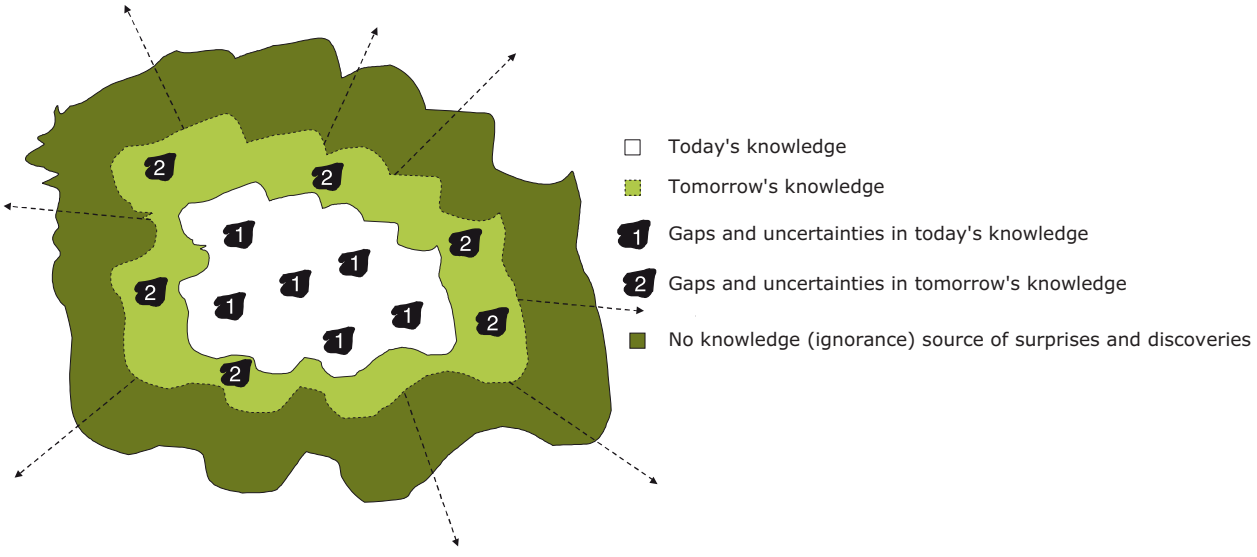
To be uncertain one has to be uncertain about something and any 'gaps' in knowledge relate to current knowledge. Both 'uncertainty' and 'gaps' relate to a stock of existing knowledge. 'Ignorance', on the other hand (or more elegantly, 'nescience', i.e. 'no knowledge') relates to 'unknown unknowns'.

More research can close some gaps in knowledge and reduce some uncertainties but such research will also uncover new sources of uncertainty and gaps in knowledge, as well as raising awareness about new areas of ignorance. Learning to live with and manage irreducible uncertainties is as necessary as trying to reduce them.

The knowledge-to-ignorance ratio

Acknowledging ignorance raises questions about how much knowledge we have in a given field

Figure 27.1 Expanding knowledge, continuing uncertainties



compared to ignorance. This issue was noted in the World Conservation Strategy (IUCN, 1980), which advised people to :

> 'keep in mind that, in spite of present knowledge, **what we know about the biosphere, ecosystems and their interrelationships is less than what we do not know.** Consequently, it is often difficult to accurately predict the effects of human actions. Gaps in knowledge should be filled where possible.. but in the meantime risks should be reduced' (emphasis added).

This may be dismissed as a trivial observation but it does draw attention to the need for scientific humility even when considering the large stocks of current knowledge on many hazards. Scientists in many of the case studies failed to show scientific humility, instead being guilty of what has been termed 'the sin of hubris' in the context of marine ecosytems and fisheries science (MacGarvin, 1994).

While the knowledge-to-ignorance ratio cannot be quantified, it is possible to get an informed qualitative appreciation of the balance in the various fields covered by the case studies. For example, there is clearly a difference between the current stock of accumulated knowledge, on, say, asbestos, ionising radiations and tobacco, compared to our stock of knowledge on nanotechnology, GM food, or on non-ionising radiations when used in recent consumer products such as mobile phones. And while there will still be a lot of new knowledge that could be gained about even a well known substance like asbestos ([2]) the practical need to search for more knowledge about asbestos is very minimal, as we know more than enough to avoid its dangers successfully.

In contrast, there is a vast ocean of scientific ignorance surrounding nanotechnologies, biotechnologies and non-ionising radiation technologies and chemicals used in consumer and other products. This remains to be explored. What is known in these relatively immature fields can perhaps be likened to the few 'pebbles' of knowledge that Sir Isaac Newton gathered from his scientific work and that he contrasted to that 'great ocean of undiscovered truth', which remained to be explored and which encouraged scientific humility ([3]).

Where the 'knowledge-to-ignorance ratio' is high (implying much knowledge and little practically necessary ignorance), as with, for example, lead, asbestos and mercury, there is little need for either more research or for precautionary (as distinct from merely preventative) measures. Where the KIR is low, however, there is a need for both precautionary measures following credible early warnings and for novel research, rather than the 'scientific inertia' of excessive research on well known substances described in the Chapter 26. As de Sadeleer (2010) has observed, 'it may be impossible to carry out a full risk assessment because such investigations operate at the frontiers of scientific knowledge, ... (where scientists) must even point to the limits of their knowledge or, where appropriate, to their ignorance.'

The limitations of scientific knowledge imply moral courage in taking precautionary action in time to avert harm. As Lewontin has observed: 'Saying that our lives are the consequence of a complex and variable interaction between internal and external causes does not concentrate the mind nearly so well as a simplistic claim; nor does it promise anything in the way of relief for individual and social miseries. It takes a certain moral courage to accept the message of scientific ignorance and all that it implies' (Orrell, 2007).

Table 27.1 attempts to clarify concepts such as ignorance and uncertainty that often arise in debates on the PP.

27.5 Conflicts between the high strength of evidence needed for scientific causality and the lower strength of evidence needed for timely public policy

All responsible applications of the precautionary principle require some plausible evidence of an association between exposures and potentially harmful impacts. For example, the European Commission's communication on the precautionary principle (EC, 2000) specifies that 'reasonable grounds for concern' are needed to justify action. However, it does not explain that these grounds will vary with the specifics of each case, nor does

([2]) It is only recently that new Dutch analyses of the epidemiological data on asbestos has shown that the difference in harmful potency between blue and white asbestos ,claimed by some scientists, practically disappears when the exposure estimates are scrutinised more carefully (Lenters et al., 2012).

([3]) 'I do not know what I may appear to the world, but to myself I seem to have been only like a boy playing on the sea-shore, and diverting myself in now and then finding a smoother pebble or a prettier shell than ordinary, whilst the great ocean of truth lay all undiscovered before me' (Newton, 1855).

Table 27.1 Some common concepts used in PP debates

Situation	Nature of knowledge	Type of action taken
Risk	**'Known' impacts** and **'known' probabilities**, e.g. regarding asbestos from 1930.	**Prevention**: action to reduce known hazards, e.g. eliminating exposure to asbestos dust
Uncertainty (*)	**'Likely' impacts** but **'unknown' probabilities**, e.g. regarding antibiotics in animal feed and associated human resistance to those antibiotics, from 1965.	**Precaution**: action taken to reduce exposure to plausible hazards, e.g. the EU ban on antibiotic growth promoters in 1999.
Ignorance	**'Unknown' impacts** and therefore **'unknown' probabilities**, e.g. the then unknown but later 'surprises' of the ozone layer 'hole' from CFCs, pre-1974; the mesothelioma cancer from asbestos pre 1959; the rate of Greenland ice sheet melting pre-2007.	**Precaution**: action taken to anticipate, identify earlier, and reduce the extent and impact of 'surprises' e.g. by using intrinsic properties of chemicals e.g. persistence, bioaccumulation, spatial range; using analogies; long-term monitoring; and using robust, diverse and adaptable technologies that can help minimise impacts of 'surprises'.
Ambiguity	Concerning the different **values and interpretations** about information used by stakeholders. E.g. in invasive alien species cases where a species can be welcomed by some but not others.	**Participatory precaution:** stakeholder engagement in decision- making about innovations and their potential hazards.
Variability	The natural differences in population or ecosystem exposures and sensitivities to harmful agents.	**Obtain more information** in order to minimise simplistic assumptions about average exposures and sensitivities
Indeterminacy	Unpredictable uses of technologies e.g. use of X-rays in children's shoe shops in the 1950s.	**Pre-market benefit assessment** of novel uses of a technology with potential hazards.

Note: * Different types, sources and levels of uncertainty can be identified (Walker, 2003).

it explicitly distinguish between risk, uncertainty and ignorance as important factors in judging the 'reasonableness' of the grounds for action.

The strength of evidence deemed to be reasonable justification for action varies between different jurisdictions and cases and can be quite low. In Sweden, for example, a 'scientific suspicion of risk' constitutes sufficient evidence for restricting an existing chemical substance. Similarly, for the World Trade Organization, 'pertinent scientific information' can be sufficient to justify protective measures under the Agreement on Sanitary and Phytosanitary Measures whenever there is an insufficiency of science to permit a comprehensive and robust risk assessment.

The strength of scientific evidence appropriate to justify public policy or other actions depends on the pros and cons of action or inaction in the specific circumstances of each case. These circumstances include the nature and distribution of potential or plausible harm; the justification for and the benefits of the agent or activity under examination; the availability of feasible alternatives; and the overall goals of public policy. Such policy goals include 'high levels of protection' of the public, consumers, and the environment, as required by the Treaty of the European Union.

The use of different strengths of evidence for different purposes is not a new idea. Legal practice has long employed several tests, such as 'beyond all reasonable doubt' in criminal courts and the lower 'balance of probabilities' used in many civil courts.

Moreover, public health practitioners have long advocated the use of varying strengths of evidence in different circumstances. For example, Bradford Hill (1965) concluded his classic paper on association and causation in environmental health with a 'call for action' in which he proposed the use of case-specific and differential strengths of evidence, observing that:

> 'It almost inevitably leads us to introduce **differential standards** before we convict. Thus on **relatively slight evidence** we might decide to restrict the use of a drug for early-morning sickness in pregnant women. If we are wrong in deducing causation from association no great harm will be done. The good lady and the pharmaceutical industry will doubtless survive. On **fair evidence** we might take action on what appears to be an occupational hazard, e.g. we might change from probable carcinogenic oil to a non-carcinogenic oil in a limited environment and without too much injustice if we are wrong. But we should need **very strong evidence**

> before we made people burn a fuel in their homes that they do not like or stop smoking the cigarettes and eating the fats and sugar that they do like' (emphasis added).

In the field of cancer, the International Agency for Research on Cancer also uses several types of scientific evidence to categorise their strengths of evidence on carcinogens (Cogliano, 2007).

Failing to acknowledge the reality of different strengths of evidence for action has led to several ill-founded debates. For example, opponents of the PP often cite the North Sea Ministerial Declaration, which calls for: 'action to avoid potentially damaging impacts of substances, **even where there is no scientific evidence to prove a causal** link between emissions and effects' (emphasis added).

Critics claim that this definition justifies action even when there is 'no scientific evidence' that associates exposures with effects. However, the North Sea Declaration clearly links the words 'no scientific evidence' with the words '**to prove a causal link**'. There is a significant difference between the evidence needed to show a **plausible link** between a pollutant and harm, and evidence which is robust enough to 'prove' a causal link. Once evidence reaches the level of 'proving' a causal link there is no need for the PP as the issue is then firmly in the 'prevention principle' area where the risks are well characterised.

Similar confusion arose in interpreting the different strengths of evidence for association and causality set out in a 13-country study of brain cancers and mobile phones (the Interphone study) (see Chapter 21 on mobile phones).

The confusion of commentators, including the media, in these cases arose because scientists were not transparent and clear about the difference between the very strong evidence needed to establish 'causality' and the suggestive evidence of plausible risks.

For example, the Interphone concluded that:

> 'There were **suggestions of an increased risk** of glioma, and much less of menigioma, at the highest level of exposure….. (but) biases and errors limit the strength of the conclusion we can draw from these analyses and **prevent a causal interpretation**'.

One consequence of not clarifying the difference between the low and high strengths of evidence embedded in these two sentences was that readers of the Interphone conclusion, particularly the media, interpreted the study as providing either no evidence of cancer or evidence of cancer. Both conclusions were strongly cited by different and similarly weighty parts of the media.

In the United Kingdom, for example, the BBC (17 May 2010) reported that 'No proof of mobile cancer risk, major study concludes'. One the same day, *The Telegraph* asserted that 'Half an hour of mobile use a day increases brain cancer risk'.

Beneath the strong evidence of 'scientific causality' there is a large evidentiary space containing a continuum of strengths of evidence that can be used to justify action under the precautionary principle, depending on the case-specific circumstances. The question remains, however, where, in that continuum, is 'sufficient evidence' located?

Identifying an appropriate strength of evidence for action has a been an important issue in climate change debates. The Intergovernmental Panel on Climate Change (IPCC) discussed this issue at length before formulating its 1995 conclusion that 'on the balance of evidence' mankind is disturbing the global climate. It further elaborated on this issue in its 2001 report, which identified seven strengths of evidence that can be used to characterise the scientific evidence for a particular climate change hypothesis (see Panel 14.1 in Chapter 14 on climate change). By 2007 the IPCC was able to conclude with 'high confidence' that the evidence for human-induced climate change had strengthened to 'very likely' (IPCC, 1995, 2001 and 2007).

Table 27.2 presents five of these strengths of evidence based on the IPPC approach and illustrates their practical application to a variety of different societal purposes.

The decision about when there is sufficient evidence to justify preventive action clearly involves more inputs to decision-making than merely science. The strength of evidence that is deemed appropriate depends on such non-scientific criteria as the costs of being wrong with actions or inactions (including their nature and distribution between different groups and generations); the justification for, and benefits of, the agents or activities that pose potential threats to health; and the availability of feasible alternatives.

The term 'no established or conclusive evidence' is often used to characterise the absence of some strength of evidence that would convince the particular scientists doing the risk assessment that an agent causes harm. The different consequences

Table 27.2 Different strengths of evidence for different purposes: some examples and illustrations

Strength of evidence	Illustrative terms	Examples of use
Very strong (90–99 %)	Statistical significance	Can be part of strong scientific evidence of 'causation'
	Beyond all reasonable doubt	Most criminal law, and the Swedish Chemical Law 1973, for evidence of 'safety' of substances under suspicion — placing the burden of proof on manufacturers
Strong (65–90 %)	Reasonably certain	US Food Quality Protection Act, 1996
	Sufficient scientific evidence	To justify a trade restriction designed to protect human, animal or plant health under World Trade Organization Sanitary and Phytosanitary Agreement, Art. 2, 1995
Moderate (33–65 %)	Balance of evidence	Intergovernmental Panel on Climate Change 1995 and 2001
	Balance of probabilities	Much civil and some administrative law
	Reasonable grounds for concern	European Commission Communication on the Precautionary Principle 2000
	Strong possibility	British Nuclear Fuels occupational radiation compensation scheme 1984 (20–50 % probabilities triggering different awards up to 50 % + which triggers full compensation)
Weak (10–33 %)	Scientific suspicion of risk	Swedish Chemical Law 1973, for sufficient evidence to take precautionary action on potential harm from substances — placing the burden of proof on the regulators
	Available pertinent information	To justify a provisional trade restriction under World Trade Organization Sanitary and Phytosanitary Agreement, Art. 5.7, where 'scientific information is insufficient'
Very weak (1–10 %)	Low risk	Household fire insurance
	Negligible and insignificant	Food Quality Protection Act, 1996 (USA)

for those for whom the evidence is 'not established' (i.e. risk takers or risk makers) is seldom discussed. Nor are the purposes for which the evidence could be conclusive discussed, for example to justify warning labels, or low cost exposure reductions, or a ban.

Decision-makers must also be aware of the common mistake of assuming that 'no evidence of harm' is 'evidence of no harm', when the relevant research has not been done, a feature of many case studies which is picked up in Chapter 26, where 'authoritative but unsubstantiated assertions of safety' are described.

Finally, interpreting 'convincing evidence' only as the high strength of evidence needed to establish 'scientific causality' is of little practical use in helping to apply the precautionary principle or in averting, as opposed to observing, future harm. This means that risk assessment committees may need to consider the consequences of their judgements as well as just causation, as Bradford Hill and the IPCC have demonstrated. It may be argued that it is for risk managers to deal with the consequences of decisions about causation. Nevertheless, scientists involved in risk assessments are well placed to contribute to analysis of consequences, as was acknowledged by the European Court when it noted that a scientific risk assessment should provide the competent public authority with sufficient, reliable and cogent information so that it also understands:

> '…the **ramifications** of the scientific question raised and can decide upon a policy in full knowledge of the facts' (ECR, 1999 and 2002) (emphasis added).

27.6 The pros and cons of actions and inactions

The EEA definition of the PP widens the conventionally narrow and quantifiable interpretation of costs and benefits to embrace wider and sometimes unquantifiable 'pros and cons'. These include, for example, a loss of trust in science after the public experiences harm that scientists had assured them would not occur. Such unquantifiable costs can sometimes be as significant as the economic costs, as in the case of BSE (EEA, 2001) and the nuclear accidents at Chernobyl and Fukushima (Chapter 18).

Chapter 23 on costs of inaction illustrates how the costs and benefits of action and inaction are

skewed towards the tangible short-term compliance costs of regulatory action, which usually fall on specific, often powerful actors, and against the long-term diffuse benefits to society as a whole of timely actions. The polluter pays principle and the internalisation of external costs are essential components of approaches to achieving a more economically efficient and equitable distribution of the pros and cons of action and inaction. Such measures would bring the market prices of hazardous agents into line with their real costs, encouraging earlier development of substitutes and other economic and technological innovations (EEA, 2012).

Several of the case studies (asbestos, lead, mercury, PCBs CFCs, benzene) indicate that early actions can stimulate innovations and conversely illustrate how late actions have consolidated technological monopolies for products, at unrealistically low prices, which served to keep smarter substitutes out of the markets for many years.

Other work has demonstrated the role that strong and smart environmental regulations, tax incentives and other measures can play in stimulating innovation (Porter, 1995; Ambec, 2011; Ashford, 1979, 2011a, 2011b and 2012).

27.7 Political and financial short-termism

The time horizons of democratic politics are very short in comparison to the long timescales associated with successfully managing the harm to environments and people illustrated in the case studies. This is a deep-seated problem but some countries have begun to devise some institutional responses to protect the long-term interests of society. For example, countries like Finland, Israel, New Zealand and Hungary have been experimenting with nominating ombudsmen or committees charged with caring for the long term (Roderick, 2010; Ward, 2012).

The financial sector is even more limited by short termism but since the financial crash there has been some effort to establish more long-term perspectives (Mainelli and Giffords, 2009).

27.8 Public participation in hazard and options analysis

There are many value judgements involved in hazard and risk analysis, from the framing of the issue and the questions to be addressed to the ethical choice of the appropriate strength of evidence that should justify action to reduce hazards in a particular case.

As several authoritative bodies have highlighted in recent years, the public should be involved in decisions about serious hazards and their avoidance, and at all stages of the risk analysis process (US PCR, 1997; RCEP, 1998; German Advisory Council on Global Change, 2001; Codex Alimentarius Commission, 2007; JRP/IPCS, 2007; Health Council for the Netherlands, 2008; NAS, 2009)

Figure 27.2**,** based on the above reports, illustrates the circular, iterative nature of risk assessment, risk management and risk communication; the links and feedback loops between them; and the involvement of stakeholders at every stage, albeit with different intensities of engagement — greater at the problem framing and options choice stages, less so at the scientific risk assessment stage.

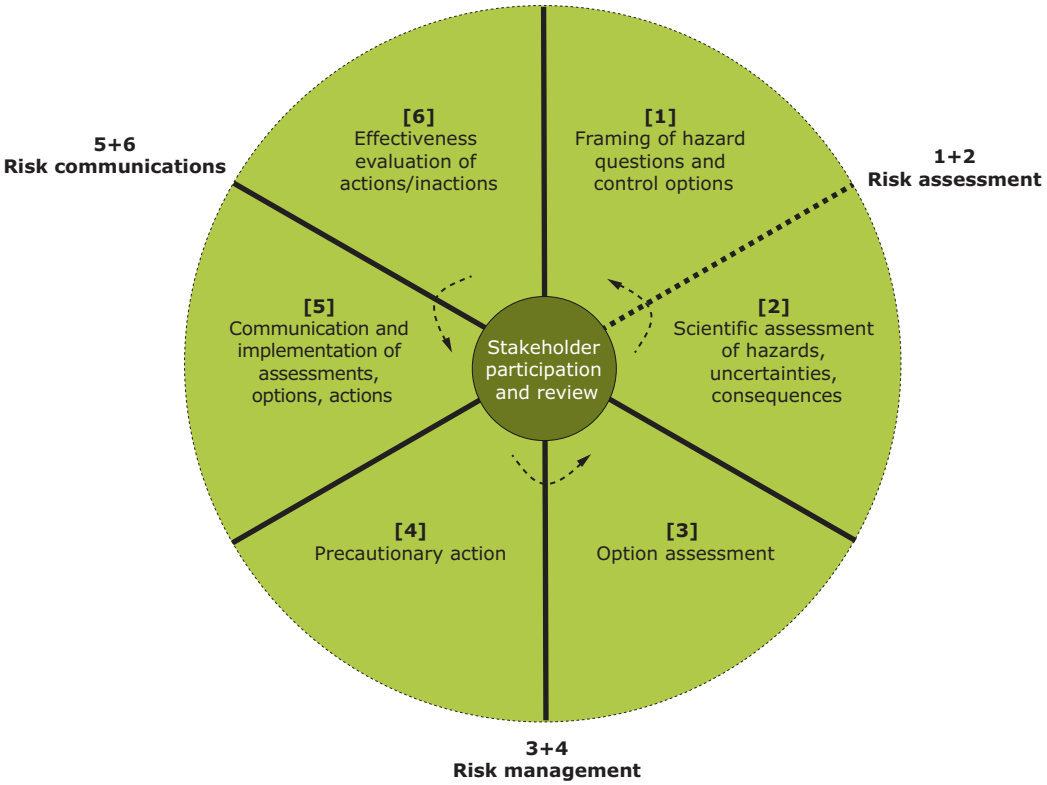
The report from the US National Academy of Sciences on Risk Assessment, *Science and decisions: advancing risk assessment* (NAS, 2009), strongly recommends such stakeholder involvement, especially at the crucial problem framing stage.

These recommendations for enhancing stakeholder participation in the hazard and options analysis process do not appear to be reflected in most existing international and European arrangements for analysing risks and setting public exposure limits e.g. relating to contaminants in food (JRC/IPTS, 2007). European authorities are continuously improving, albeit at speeds that fail to satisfy all stakeholders.

Changes are nevertheless in the air. The European Commission increasingly involves stakeholders in risk assessment by, for example, asking for public comments on the questions to be put to risk assessors and holding stakeholder consultative meetings ([4]). There have also been recent improvements in the way that uncertainties are handled in the food (EFSA, 2009; Hert, 2010) and emerging issues fields (SCENIHR, 2012), building on the earlier work of the IPCC on

([4]) See the stakeholder dialogue procedures in EC (2009). The European Food Safety Authority (EFSA), for example, organises a Stakeholder Consultative Platform for food industry stakeholders and widely publishes agendas, minutes, and scientific opinions as part of its response to Articles 38 and 39 of its founding regulation on openness and transparency in the governance of food safety risks.

Figure 27.2 A participatory and precautionary framework for analysis of hazards and options



Note: The dotted line indicates feedback.

Source: EEA, based on NRC (1996), US Presidential Commission on Risk (1997), UK Royal Commission on Environmental Pollution (1998) and NAS, 'Science and Decisions' (2009).

how to manage and communicate uncertainty. As Chapter 15 on floods illustrates, balancing timely early warnings against false alarms is a very challenging task for decision-makers under conditions of complexity, uncertainty and ignorance.

There have also been improvements in the transparency of risk assessments, including , most recently, improved public access to the scientific data submitted by companies to regulatory authorities for product authorisations (EFSA, 2013). The need for this openness has emerged as a strong lesson from several case studies — from Minamata to the bio- and nanotechnology fields — and the improvements follows recent controversies over the food additive aspartame and GM maize (Seralini et al., 2012; Genewatch, 2012).

From uncertain risks to relevant and responsible innovation?

In the introduction to this chapter the debates in France on GMOs were used to illustrate the potential of the PP to trigger or facilitate debates that go well beyond the issue of risks and into the area of responsible and socially relevant innovation.

One or two other case study chapters also raise this question. For example, the Chapter 3 on leaded petrol reviewed the technological 'roads not taken' and Chapter 19 on GM crops analysed 'top down' and 'bottom up' innovation pathways to agricultural futures. Chapter 5 on Minamata disease and Chapter 16 on bees also raised questions concerning the value of current democratic institutions in dealing with complex socio-technical issues. More involvement of the public in hazard and options analysis, discussed above, may also lead to wider discussions about technological choices and directions of innovation.

Richard Owens, co-author of the Chapter 13 on the 'birth pill' has further developed these ideas in a forthcoming book on 'responsible innovation' (Owens et al., 2013).

Box 27.5 Responsible research and innovation

Responsible research and innovation is a transparent, interactive process by which societal actors and innovators become mutually responsive to each other regarding the ethical acceptability, sustainability and social desirability of the innovation process and its marketable products. Social desirability is currently essentially determined by market mechanisms, however, as universal principles on what counts as socially desirable are not easily agreed upon.

The 'Innovation Union' flagship initiative is a central part of the EU's Europe 2020 strategy and is seen as means to deliver 'smart growth', defined as 'developing an economy based on knowledge and innovation' (EC, 2011).

From this macroeconomic perspective, innovation is assumed to be steerless but inherently good, as it produces prosperity and jobs and meets societal challenges, addressed through market mechanisms.

Modern societies lack a specific forum or policy for evaluating particular technologies in terms of benefits and risks within the legislative context. We only have formal safety, quality and efficacy assessment procedures evaluating the properties of products in the course of passing these three market hurdles.

The benefits of technologies are 'demonstrated' only by market success, whereas the potential negative consequences are evaluated under formal risk assessment schemes. The state is responsible for defining the risks of technologies under product authorisation procedures and product liability law and ensuring market operators compliance, whereas society lacks a particular responsibility for what could count as positive impacts of technologies.

Modern 'Frankensteins' are not intentionally created by a single actor. If they arise they are more likely the unforeseen side effects of collective action. Indeed, techno-scientific applications can remain ethically problematic even in cases where scientists and engineers have the best possible intentions and users have no conscious intention to misuse or abuse ([5]).

This situation constitutes the major ethical challenge we face today. An ethics focused on the intentions and/or consequence of actions of individuals is not appropriate for allocating responsibilities for the impacts of innovations.

Responsible innovation therefore requires an ethics of co-responsibility for ensuring the right impacts and avoiding negative consequences, whether these impacts are intentional or not and whether they can be fully foreseen or not.

The challenge is to arrive at a more responsive, adaptive and integrated management of the innovation process. A multidisciplinary approach involving stakeholders and other interested parties should lead to an inclusive innovation process whereby technical innovators become responsive to societal needs and societal actors become jointly responsible for the innovation process. That includes contributing to defining socially desirable products that reflect basic needs and public values, for example by focusing on the great challenges of our times such as climate change and food security.

Effecting such changes requires a paradigm shift in innovation policy. The state must assume responsibility for positive outcomes of innovation, reflect basic public values beyond consumer market preferences and move away from technology-oriented research and innovation policy and towards an issue-oriented approach.

Source: Edited extracts from von Schomberg, 2013 ([6]).

([5]) The concept of collective co-responsibility in response to the shortcomings of professional roles — responsibility in science and engineering is outlined in von Schomberg (2007).

([6]) René von Schomberg is at the European Commission, Directorate General for Research. The views expressed here are those of the author and may not in any circumstances be regarded as stating an official position of the European Commission.

Box 27.5 includes a short description of responsible innovation written by Rene Schomberg, a contributing author to the Owens book. Innovation 'with a human purpose' is also being proposed as a means to rebalance market-focused innovation and to meet the environmental challenges posed by meeting human needs in a resource-, energy- and water-constrained world (van den Hove, 2012).

The field of public engagement on risks, hazards and innovations is large (Wynne, 2007; Stirling, 2008 and 2010; Wesselink and Hoppe, 2011; Wesselink, 2011; Hoppe, 2012) and extends well beyond the bounds of the present study. However, the evidence from *Late lessons from early warnings* provides further grounds for boosting public and corporate engagement in responsible innovation.

27.9 Conclusion

The case studies and this chapter have illustrated the need for wider use of the PP both as a justification for timely actions on early warnings and as a trigger for broader debates about technological pathways to the future. Mistakes will be made, surprises will occur. But if the quality of the scientific and stakeholder processes used to arrive at such decisions are sound, and the best of science is used, then living with the consequences, of such decisions, both pleasant and unpleasant , will be more acceptable.

The capacity of people to foresee and forestall disasters appears to be limited, however, especially when such action is opposed by powerful economic and political interests, as the case studies in *Late lessons from early warnings* illustrate. It is not just corporations that have the capacity for denial when confronted with evidence of impending disaster — as the financial collapse of 2009 demonstrated. 'Wilful blindness' and human 'folly' are general human traits that thwart our capacities to do the right thing (Heffenan, 2010; Tuchman, 1984).

If we adopt optimism of the will to counter pessimism of the intellect, however, it is possible to believe that human behaviour could improve. Decision-makers could heed the lessons of past experience. Armed with more humility in the face of scientific uncertainty and ignorance, and supported by broad and effective public engagement, they could apply the precautionary principle more widely. In so doing, they would help anticipate and minimise many future hazards, while stimulating innovation.

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28 In conclusion

Since 2001: many changes, crises and lessons relearnt

The first volume of *Late lessons from early warnings* was published in 2001. Since then, the world has changed significantly. It is larger in population but smaller in interconnectivity; faster in terms of technology adoption but slower in terms of policy action in the face of complex interlinked problems; more volatile in terms of economic and environmental changes, yet more static in terms of political reflexivity and adaptations in governance. Beyond the current financial and economic crises, there are several long-term, systemic and interconnected challenges, such as depletion of natural resources, climate change, a 2-billion person increase in the world population by 2050, and diminishing ecosystem resilience (EEA, 2011a; OECD, 2012; WEF, 2012).

These developments point to two important realities. First, the systems of governance misrepresent the socio-ecological system, making societies and the environment subordinate to the economy — essentially serving as sources of human and natural capital. This misrepresentation ignores the reality that any civilisation is ultimately dependent on its ecological and social foundations and that economies function to sustain and enhance human well-being (Passet, 2001). Second, the scale, interconnectedness and sheer complexity of feedbacks between nature and human interventions have outstripped society's capacity to understand, recognise and respond to these effects.

The first volume ended with a call to action for policymakers. How much progress has been made since then? One important area is that of innovation and the effect that precaution can have on it. In volume 1, the difficulties of balancing precaution with technological innovation were recognised. However, there is now increasing evidence that precautionary measures do not stifle innovation, but can encourage it, in particular when supported by smart regulation or well-designed tax changes (EEA, 2011b, 2011c; Ambec et al., 2011; Ashford and Hall, 2011).

Volume 1 also invited policymakers to take more account of a 'richer body of information from more diverse sources'. It identified public health and the environment as two fields of science that were separate and polarised. And it suggested involving a wider range of stakeholders to expand the information base and to 'improve public trust in society's capacity to control hazards, without stifling innovation or compromising science'. These are all areas where improvements have been made since 2001.

There has been less progress with other lessons, particularly the call to 'identify and reduce institutional obstacles to learning and action'. Both political and scientific 'bureaucratic silos' do not seem to have disappeared, despite the frequent calls for policy integration and inter-departmental coordination (Hamdouch and Depret, 2010; Phoenix et al., 2012).

Worryingly, warnings of impending hazards are, in many areas, still not being heeded and the resulting damage is far more widespread, geographically, across species and extending to future generations, who will particularly suffer many of the harmful effects of our current energy systems, chemicals and technologies. Damage is now shown to be occurring at increasingly lower levels of exposure to pollution, and the polluters, for the most part, are still not paying the full costs of their pollution, partly because of a lack of incentives to do so. At the same time we see the destruction of the stocks of natural capital that underpin human well-being. It is easy to lose sight of the crucial dependence of economies on a diverse, healthy and resilient natural environment, especially in times of economic crises.

A key message in the 2001 report was the notion that 'the growing innovative powers of science seem to be outstripping its ability to predict the consequences of its applications, while the scale of human interventions in nature increases the chances that any hazardous impacts may be serious and global.' This is happening at an ever-greater pace, with globalised industries racing to introduce new technologies but with limited understanding

of what their impacts might be. National governments now have less control over globalised technologies.

More positively, however, new transformative approaches are emerging for managing the systemic and interconnected challenges that we face (e.g. Gladwell, 2012; Stirling, 2008). They are building in particular on the increasing use by consumers, citizens and shareholders of the power of the internet and social media to demand and foster increased participation, responsibility, accountability and transparency.

Such approaches also need longer-term perspectives. Greater complexity, uncertainties, scientific ignorance, broader risks and the irreversibility of many harmful impacts together necessitate the increased use of long-term scenarios and strategy analysis by citizens, governments and corporations alike (EEA, 2011a). The long-term interests of society as a whole, distinct from the partial interest of particular stakeholders and individuals, also require new political and financial institutions that can help overcome the short termism of most politics and much finance (Ward, 2012; Roderick, 2010; Mainelli and Giffords, 2009; RMNO, 2009).

The case studies in this second volume of *Late lessons from early warnings* provide some new insights from the lessons of the past that can help stimulate actions to reinforce, complement and put into practice the emerging transformative approaches, mindful of the observation that 'those who cannot remember the past are condemned to repeat it' (Santayana, 1905).

2001–2013: what new insights emerge?

Many of the cases in this report reveal similar lessons to those in the 2001 report. Some insights have been strengthened, however, as the body of evidence has increased and our understanding of ecological and biological systems has improved. The case studies in the two volumes of *Late lessons from early warnings* cover a very diverse range of both recent and historical chemical and technological innovations and their impacts on humans and nature. All cases have unique characteristics stemming from the type of the innovation, the origins and nature of the hazards, the prevailing approaches to policymaking, and the cultural influences of time and place. The studies also share common features, such as key decisions on innovation pathways made by a few people on behalf of many; a lack of institutional and other mechanisms to respond to early warning signals; misleading market prices that do not properly reflect all costs and risks to society and nature; and inadequate accounting for assets and liabilities across different types of capital.

Such features from the past raise questions for the future. How, for example, can the innovations that are driving knowledge economies, such as nanotechnologies, be developed without repeating the mistakes of the past? How can the wider and wiser application of the precautionary principle support decision-making in the face of uncertainties from within complex systems that defy prediction and where 'surprises' are inevitable? How can we ensure that the lack of 'perfect' knowledge is not a justification for inaction in the face of 'plausible' evidence of serious harm? How can conflicting interests (including public and private ones) be balanced in the development, use and impact phases? How can the distribution of costs and benefits over time be made more equitable?

The *Late lessons from early warnings* case studies demonstrate the complexities of handling the interactions between the many actors and institutions involved — governments, policymakers, businesses, entrepreneurs, scientists, civil society representatives, citizens and the media. Each comes to the debate with different and often conflicting knowledge, perceptions, interests and priorities; balancing these numerous and often antagonistic positions should be seen as a prelude to making decisions on those innovations that have broad societal implications.

The opportunities are manifold but can be boiled down to three main ones:

- to correct the prioritisation of economic and financial capital over social, human and natural capitals through the broader application of the policy principles of precaution, prevention and polluter-pays, and improved accounting systems across government and business;
- to broaden the nature of evidence and public engagement in choices about crucial innovation pathways by balancing scientific efforts more towards dealing with complex, systemic challenges and unknowns and complementing this knowledge with lay, local and traditional knowledge;
- to build greater adaptability and resilience in governance systems to deal with multiple systemic threats and surprises, through

strengthening institutional structures and deploying information technologies in support of the concept of responsible information and dialogues.

Taken together the case studies provide some lessons to support action, supplementing the conclusions of Volume 1. These findings are presented in the remainder of this section.

Reduce delays between early warnings and actions

Most of the case studies in both volumes of *Late lessons from early warnings* illustrate that if the precautionary principle had been applied on the basis of early warnings, many lives would have been saved and much morbidity and damage to ecosystems would have been avoided.

Today, several factors related to the speed, scale and breadth of technological innovation exacerbate the tendency to delay action. First, by the time evidence of harm is confirmed, the technology has often changed, leading to assumptions that, unlike yesterday's technology, today's technology is now safe. Second, for some technologies (e.g. broad-scale energy production systems or chemical plants), the huge initial investments mean that yesterday's investments will be redeemed before any serious risk reduction is implemented, creating *de facto* technological lock-ins. Third, the scale of technological development puts very difficult demands on those attempting to monitor and respond to the risks before they have become serious, widespread and irreversible.

These features of contemporary life further strengthen the case for taking early warning signals more seriously and acting on lower strengths of evidence than those normally used to adduce 'scientific causality'.

The case studies have shown that the main barriers to timely action include the short-term nature of many political and financial horizons; the novel and challenging nature of the technologies and the scientific problems that arise from their interactions with complex biological, ecological and social systems; the conservative nature of much environment and health science; the ways in which scientific and other evidence is evaluated; the different perspectives and interests of many stakeholders and the vested interests of some powerful ones; and the broader cultural and institutional circumstances of public policymaking that often favour the status quo.

Addressing these causes of delay can help to reduce the negative impacts that arise from many innovations. But tackling them is not easy. For example, the problem of the unequal distribution of political power between citizens, business and financial actors, and governments is a persistent problem of politics, which has increased through globalisation and the rise of multinational corporations, yet it is an issue that is well beyond the scope of this report. Some of the other causes of delay are more amenable to change and these are addressed in the rest of this section.

In evaluating the pros and cons of using the precautionary principle, it is important to remember that the harm from most hazards analysed in the case studies turned out to be more diverse and widespread than anticipated and such damage is often found to occur at exposures lower than initially considered dangerous.

For example, it has been known since 1960 that asbestos causes the mesothelioma cancer, in addition to lung cancer (identified in 1955) and asbestosis (identified in 1906–1929). Similarly, it is now known that smoking causes a wide range of cancers, heart disease and foetal damage, beyond the harm of lung cancer identified in 1951. PCBs are now known to cause neurological problems in children, and cancer, in addition to harming the reproduction of eagles (identified in the 1960s). Lead has also been demonstrated to be more broadly chronically harmful — it was initially recognised as damaging children's IQ but it is now known to cause heart disease in adults. Radiation has gone through a similar expansion of known hazards.

This phenomenon of 'harm expansion' is rendered more problematic by the discoveries that harm from all of the above agents has been found to occur at lower and lower levels, such that, more often than not, no 'safe' threshold of exposure can be identified. This knowledge needs to be taken into account when evaluating the potential pros and cons of future precautionary action on emerging issues. Continuous, anticipatory reductions in exposures to emerging hazards could help to avoid repeating these histories of harm expansion.

More and better prospective and retrospective analyses of the costs of action and inaction, across the full lifecycle of a technology, would highlight the value of precautionary and preventive actions, particularly the value of 'secondary benefits and costs' which can be substantial, such as the health benefits from reduced fossil fuel use, where the main objective is to mitigate climate change. They

should also consider the psychological and societal costs of both false alarms concerning a health hazard, e.g. the over-reaction to swine flu in the US in the 1970s, and misplaced reassurances concerning the safety of a technology, such as the downplaying of risks associated to nuclear power plants by Japanese authorities and utilities. Such pro and con analyses should be independent of interested parties, both commercial and political, as they often have a 'natural' tendency to exaggerate costs of hazard reduction and to underestimate the benefits of action.

As case studies from both volumes have also shown, the timely use of the precautionary principle can often stimulate rather than hamper innovation, in part by promoting a diversity of technologies and activities, which can also help to increase the resilience of societies and ecosystems to future surprises. Keeping options open and following multiple paths means that a particular option can be terminated if it turns out to pose high risks, and avoids situations of technological monopolies such as those experienced, for example, in the cases of asbestos, CFCs, and PCBs.

In contrast, technological monopolies hamper innovation. For example, it was the monopolies of lead in petrol, asbestos, CFCs and PCBs that both prolonged the harms they caused and made those harms widespread. These monopolies contributed to technological 'lock-in' but also to institutional and ideological lock-ins, which further hampered innovation and the development of alternatives. These technologies and their products were also 'cheap' in the market place, bearing little relation to their real costs in terms of harm to the environment, human health and financial compensation to victims. These artificially low market prices in turn helped to stifle the development of smart substitutes.

This past experience should be taken into account with the emerging technologies such as GMOs and nanotechnologies, where there are already signs of technological monopolies, driven by the high costs of research, development and production involved and the patent protections for developers on many of their products and processes (Stirling, 2007; van den Hove et al., 2012).

When applying the precautionary principle, there are, therefore, not only scientific issues to be considered but also ethical choices, concerning the appropriate strength of evidence for action; the equity implications arising from the costs and benefits of action and inaction; the appropriate balance between generating false negatives and false positives; and the social necessity of large-scale innovations.

Clearly, acting to avoid or reduce harm on lower strengths of evidence than that used to establish scientific causality will sometimes increase the number of false alarms — although the review of 88 cases of alleged false positives in Volume 2 of *Late lessons from early warnings* confirmed just four actual cases, suggesting that the risks are considerably less than sometimes claimed. Moreover, it is important to recognise that, in cases where there are damages over a long time span that may irreversibly alter the system, there is a fundamental asymmetry between the competing policy and scientific options of avoiding false negatives and avoiding false positives. Examples of such situations of irreversibility include climate change, modification to the genetic make-up of humans or other species, persistent chemical or radioactive contamination, and species loss.

If an early warning signal triggers a double reaction of precautionary policy measures and more intensive research on risks and alternatives, then at some point the research may show that this was a false alarm and the precautionary measure can be cancelled. The loss in this case will be a delay in economic and social benefits from the technology (or the cost of mitigating actions in cases such as climate change) during the time it took to show that there was no cause for concern. But the system will not be irreversibly altered. In contrast, if the early warning triggers no precautionary action but more research shows, only much later, that there was indeed real cause for concern then irreversible systemic damages will already have taken place. Acknowledging this asymmetry is central to understanding when precautionary and preventive approaches are best deployed.

Tipping the overall balance of public policy towards avoiding harm, even at the cost of more false alarms, would seem to be a price that is well worth paying, given the costs of being wrong in acting or not acting. This is one of the strategic and ethical societal choices, similar to the choice of strengths of evidence to be used in civil or criminal court cases, that needs to be openly debated.

Acknowledge complexity when dealing with multiple effects and thresholds

The world is drawing down its natural capital through an over-reliance on fossil-fuel-based,

synthetic chemicals that are compromising the health and resilience of ecosystems and key organisms such as fish and bees, in combination with other stressors such as climate change and invasive alien species. There is also evidence that some types of genetically modified crops (and the agrochemical substances used alongside them), which are released into the environment and the food chain, present a threat to human health, some species and ecosystems, and food security. Human health is being further compromised by chemicals that threaten health from before birth, through childhood and into adulthood. (Barouki et al., 2012; EEA, 2012; Kortenkamp et al., 2011).

Such exposures appear to contribute to increases of many types of cancers, birth defects, male infertility, and cardiovascular, neurological and immunological dysfunctions and diseases. The impacts of these hazards are being supplemented by the harmful effects of unhealthy eating habits and lifestyles in many parts of the world, and resulting epidemics such as diabetes and obesity. Taken together, these multiple stressors have profound public health significance.

Growing scientific knowledge clearly shows that the causal links between stressors and harm are more complex than was previously thought and this has practical consequences for minimising harm. Much of the harm described in Volumes 1 and 2, such as cancers or species decline, is caused by several co-causal factors acting either independently or together. For example, the reduction of intelligence in children can be linked to lead in petrol, mercury and PCBs as well as to socio-economic factors; bee colony collapse can be linked to viruses, climate change and nicotinoid pesticides; and climate change itself is caused by many complex and inter-linked chemical and physical processes.

In some cases, such as foetal or fish exposures, it is the timing of the exposure to a stressor that causes the harm, not necessarily the amount; the harm may also be caused or exacerbated by other stressors acting in a particular timed sequence. In other cases, such as chemicals like BPA, low exposures can be more harmful than high exposures; and in others, such as asbestos with tobacco, and some endocrine disrupting substances, the harmful effects of mixtures can be greater than from each separate stressor. There are also varying susceptibilities to the same stressors in different people, species and ecosystems, depending on pre-existing stress levels, genetics and epigenetics. This variation can lead to differences in thresholds or tipping point exposures, above which harm becomes apparent in some exposed groups or ecosystems but not others. Indeed there are some harmful effects that occur only at the level of the system, such as a bee colony, which cannot be predicted from analysing a single part of the system, such as an individual bee.

The increased knowledge of complex biological and ecological systems has also revealed that certain harmful substances, such as PCBs and DDT can move around the world via a range of biogeochemical and physical processes and then accumulate in organisms and ecosystems many thousands of kilometres away. The practical implications of these observations are threefold. First, it is very difficult to establish very strong evidence that a single substance or stressor 'causes' harm to justify timely actions to avoid harm; in many cases only reasonable evidence of co-causality will be available. Second, a lack of consistency between research results is not a strong reason for dismissing possible causal links: inconsistency is to be expected from complexity. Third, while reducing harmful exposure to one co-causal factor may not necessarily lead to a large reduction in the overall harm caused by many other factors, in some cases the removal of just one link in the chain of multi-causality could reduce much harm.

A more holistic and multi-disciplinary systems science is needed to analyse and manage the causal complexity of the systems in which we live and to address long-term implications. For example, there would be substantial benefits from exploring, much earlier and more systematically, the multiple effects on people and ecosystems of chemical and other stressors, their cumulative effects, chemical metabolites, and their mixture effects. Exposures to low doses of contaminants and their effects, particularly in susceptible sub groups in populations, should also be more fully investigated, accompanied by more biological monitoring that would improve the detection of the precursors of disease.

Several case studies provide examples of where assertions that 'no evidence of harm' have been interpreted as 'evidence of no harm', which may not be the case if appropriate research over relevant time periods is missing. Examples include leaded petrol in the 1920s-60s, and risks to children from mobile phones before 2011, when the first study on children was published. Such authoritative but unsubstantiated assertions of safety have led to much harm, for example, in cases such as asbestos, tobacco, lead and mercury

Acknowledging both uncertainties and scientific ignorance is particularly important where the science is relatively immature, as with such emerging technologies as GM crops, mobile phones, nanotechnology and invasive alien species and where exposures are widespread. Recognising uncertainty also helps to avoid putting too much reliance on simple models of complex systems as in the cases of floods, nuclear accidents, climate change, ecosystems resilience and multi-pollutant human exposures

Uncertainty, though, can be a two-edged sword, being used as the basis for challenging both assurances of safety and evidence of a hazard. In particular, uncertainty has been misused, exaggerated, or even 'manufactured' in order to delay and undermine regulatory measures to protect health and environments. Examples include climate change, tobacco, lead, honeybees, and beryllium (Michaels, 2008; Oreskes and Conway, 2010).

There is also an asymmetry between the high levels of proof of harm demanded by proponents of a technology as sufficient to justify remedial or preventive actions compared to the level of evidence they deem sufficient to claim that their products are 'safe'. Waiting for high levels of proof of harm before acting not only leads to much harm but also to a stifling of innovation, as the case studies on asbestos, lead, mercury, PCBs, and CFCs illustrate.

Rethink and enrich environment and health research

The need for research to focus more on the potential hazards of emerging technologies in addition to research on product applications has already been noted. It would also be helpful if there were a greater focus on emerging hazards rather than on well-known risks. Recent research (Grandjean et al., 2011) indicates that much environmental health research still focuses on how well known hazards, such as lead and mercury, and tends to ignore newly emerging threats to health. The top ten substances studied are all metals such as copper, lead, zinc and cadmium. These established hazards account for approximately half of all the journal articles on impacts of chemical substances of the last ten years (Grandjean et al., 2011). This disproportion has crowded out research into other dangerous hazards and risks, such as on endocrine-disrupting substances and other hazards where less is known about their pathways and impacts (despite over 100 million euro of EU research funding on EDCs in the last decade) but where the evidence is growing of widespread impacts on humans and nature (EEA, 2012; Kortenkamp et al., 2011).

A major reason for this imbalance may relate to the prevailing regulatory science paradigm, where solid conclusions depend on replication and verification. Other likely contributing factors to scientific inertia are the effective use of costly infrastructure to ensure value for money; the desire of policymakers for more certainty from science regarding politically difficult choices; and the tendency of funding agencies to be conservative in their research strategies.

In order to identify hazards that may only appear over decades, there needs to be more long term monitoring of biological and ecological systems, focusing on 'surprise sensitive' parameters such as bees, amphibians, invertebrates, foetuses etc. Such monitoring will also be essential to evaluate the effectiveness of the precautionary and later measures to avoid harm. Monitoring can be supported in part by citizen scientists, using the latest GIS and monitoring technologies.

Several cases highlight the benefit of having lay and local knowledge alongside scientific evaluation of harm so that a broader knowledge base can support decision-making. For example, when a mother hypothesised that neurological signs observed in her son were due to exposure to mercury in her womb, this was dismissed by experts who did not question their assumption that the placenta provided protection (see Chapter 5 on Minamata disease). Patients, fishers, wives (e.g. in the sperm damaging, described in Chapter 9 on DBCP), mothers (see Chapter 5 as well as and the chapter on DES in Volume 1 (EEA, 2001, Ch. 8)), factory workers, and bee keepers, as well as clinicians and factory inspectors are amongst those non-scientists who have reliably provided early warnings in the case studies.

Precautionary actions are justified by lower strengths of evidence than those conventionally used for establishing scientific causation, yet in their search for 'certainty' scientists are cautious in attributing causation to an agent while some scientists may sometimes be less cautious when asserting 'safety'. The case studies show that in the past there have been premature assertions of safety based on inadequate scientific methods, such as an over-reliance studies that were conducted over too short a period to reveal long-term effects for example.

Also evidence of harm has often had to reach the high standard of 'causality' as is the standard for

less complex situations, rather than precautionary strengths of evidence based on plausible association between hazards and harms. The strength of evidence chosen can range from 'a scientific suspicion' of harm to 'beyond all reasonable doubt', depending on the complexity of the system, the level of protection required and the pros and cons of being wrong in acting or not acting.

To avoid waiting for strong evidence of harm in humans and ecosystems, data from animal or other species and methods (ECVAM), should be more widely used to justify precautionary action. This is particularly needed where the potential damage is irreversible — as with some cancers, species and ecosystems losses, and reproductive or developmental effects.

Research, precaution, and exposure control also need to be applied to the substitutes or alternatives to hazardous agents. The chapters on pechloroethylene (Chapter 4), CFCs (EEA, 2001, Ch. 7), leaded petrol (Chapter 3), DDT (Chapter 11) and booster biocides (Chapter 12) as well as the chapter on MTBE in Volume 1 (EEA, 2001, Ch. 11) illustrate the hazards that some alternatives have brought in the wake of banned substances, especially when the alternatives are chemically very similar (e.g. HFCs for CFCs). Minimising the hazards of alternatives could be helped by the avoidance of such chemical characteristics as persistence, bioaccumulation, and large spatial range; by the hazard screening of alternatives; and by the greater use of the knowledge to be found in smarter and greener chemistry and technology.

Greater awareness of the complexity, interconnectedness, multi-causality and uncertainties inherent in global environmental issues underlines the need for greater humility about what science can and cannot tell us. Framing issues as purely scientific and technical inappropriately places scientific perspectives above equally valid social and ethical contributions that should be part of decision-making. A shift is needed to more explicitly integrative environmental science approaches in support of public policy, in which systemic considerations and early warnings feature strongly. This shift has started to take place in discourses but often not in practices.

The case studies in Volume 2 of *Late lessons from early warnings* also illustrate how regulatory health and environmental science is still defined in very narrow terms, which obstructs it from being able to identify the complex multifactorial stresses on environmental systems and humans. There is therefore a need for environmental science to become more attuned to the inherent complexities of socio-ecological systems by, for example, balancing a traditional disciplinary focus with more holistic cross-disciplinary scientific research, thereby complementing precision with relevance and comprehensiveness (Phoenix et al., 2012). Such science would often embrace longer timescales, more end-points, and multi-causality.

Since the first volume of *Late lessons from early warnings*, scientific approaches such as 'sustainability science', 'systems biology', or 'futures research' have continued to emerge to help deal with some of the challenges arising from the interconnections and dynamics of socio-ecological systems, focusing on analysis and interventions at the systems level. These emerging disciplines can also help build bridges between research, policy communities, other stakeholders and the public (Kates, 2011).

Last but not least, the case studies show that early warners — scientists and others — have often been harassed for their pioneering work which threatened economic interests and often challenged conventional scientific paradigms. This harassment can include bans on speaking out or publishing; loss of funding; legal or other threats; demotion; transfer to other work and character assassination in scientific and other media (McCulloch and Tweedale, 2007; Martin, 1999, 2008; UCS, 2012). Such early warners should receive better protection via the extension of 'whistle blowing' and discrimination laws; by more active support and protection from scientific societies in the case of scientists; and by awards that acknowledge the value of their work.

Improve the quality and value of risk assessments

Volume 1 stressed the differences between risk, uncertainty and scientific ignorance, and the need to acknowledge and identify all three when doing evaluations of evidence, as in formal risk assessments. Since 2001, some considerable progress has been made in characterising uncertainties in risk assessments, for example, in the food industry (EFSA, 2006, 2013), the field of emerging risks (SCENIHR, 2012), and in climate change (IPCC, 2010). This recognition of uncertainty and ignorance is particularly important where there is much reliance on modelling, as in climate change, invasive alien species, or exposure assessment.

The majority of case studies indicate that it is often inappropriate to use a narrow conception of 'risk' to manage the complex issues at hand with their inevitable features of ignorance, indeterminacy

and contingency. The increasing awareness of the complexity of biological, ecological and technological systems, calls into question the relevance and prevalence of some of the simplistic methods, models and assumptions used in risk assessments. For example, linear dose response curves can be inappropriate when low doses are more harmful than high doses, as in the BPA story; the dictum that the dose alone 'makes the poison' is inaccurate when it is the timing of the dose that makes the dose harmful, as in the TBT and DES cases; assuming uni-causality is too simplistic when multi-causality is the reality, as in the lead case study and many ecosystems such as fisheries; testing for single substances is inadequate when mixtures are present as in all cases of chemical exposures; and there can be an over-reliance on statistical significance when use of confidence limits would be more appropriate.

Simplistic assumptions are also observed in technological risk assessments. As the Fukushima Investigation Committee (NAIIC, 2012) concluded, 'the accidents present us with crucial lessons on how we should be prepared for 'incidents beyond assumptions'. With its failure to plan for the cascade effects beyond design–base accidents 'the regulatory emphasis on risk based probabilistic risk assessment has proven very limited'.

In other words, narrow risk assessment approaches are now outstripped by the realities that they cannot address, recognise and communicate. Too often this contributes to effective denial of those risks that do not fit the risk assessment frame. It is therefore urgent to transform risk assessment practices to make them broader-based, more inclusive, transparent and accountable. That should also enable more transparent communication of diverse scientific views, especially on emerging issues where the uncertainties and ignorance are high and genuine differences of scientific interpretations are likely, desirable, and defensible (Stirling, 2010).

In practice, risk assessments could be improved by including a wider range of stakeholders when framing the scientific risk agenda, through ensuring all available evidence is readily accessible, by broadening the scope and membership of risk evaluation committees, by increasing the transparency and consistency of committee approaches and methods, and by ensuring their independence of vested interests. Improvements in transparency were recently announced by EFSA, who wish all data submitted as part of the product authorisation procedure to be made publicly available, (EFSA, 2013).

The case studies on mercury, nuclear accidents, leaded petrol, mobile phones, BPA, and bees, have shown that there can be significant divergence in the evaluations of the same, or very similar, scientific evidence by different risk assessment committees. It is often not clear from their published reports why this is so. It would be helpful if each risk assessment report explained the committee's choice of paradigms, assumptions, criteria for accepting evidence, weights placed on different types of evidence, and how uncertainties were handled. This would also help reduce the confusion amongst users of such divergent risk assessments when they are faced with very different evaluations of essentially the same evidence. It would also help people to recognise the difference between 'settled fact, majority opinion, legitimate minority view, and unsubstantiated assertions' (Weiss, 2002). Moreover, it is helpful if the sources of finance for the research studies under consideration are made explicit because of the 'funding bias' that has been observed in research on issues such as tobacco, pharmaceuticals, food, BPA, GM products, and mobile phones.

The case studies on bees, lead, BPA, and nuclear accident risks have shown that the scope and membership of some risk assessment committees have been too narrow, and they have sometimes been dominated by one discipline or paradigm with shared assumptions which are not therefore questioned. Risk assessments can be made more reliable if they embrace all relevant scientific knowledge and approaches. For example endocrinology currently brings new insights into hormonally active biological systems that complement conventional toxicology. Toxicity test methods and risk assessments can benefit from more recent yet reliable scientific knowledge emerging from academic research fields.

The case studies also show that toxicity tests designed for acute effects are unlikely to be relevant to chronic effects, and that novel technologies, such as systemic pesticides that replace sprayed pesticides or new chemical compounds replacing earlier ones, usually need novel risk assessments.

The value of being transparent about what is known and not known and about uncertainties and disagreements is equally pertinent. Scientific conclusions should not be portrayed as if there is consensus when there is not. Science by its nature progresses by building on critical appraisal. Several cases show that disagreement can be helpful to decision-makers with a broader picture of the

alternative directions and options available before making a decision.

The whole process of risk analysis which includes risk assessments, risk management and risk communication, would benefit from the involvement of stakeholders, particularly when framing the risk assessment and identifying options for risk management. This is illustrated in Ch. 27 on the precautionary principle.

Foster cooperation between business, government and citizens

An element that is often missing from innovation policies and practice is the recognition that innovation should be considered as a means, not an end in itself, and desirable to the extent that it improves human health and well-being while maintaining ecological resilience. Policy formulation should start from these premises and from a broader concept that includes not only technological innovation but also non-technological, social, institutional, organisational and behavioural innovation (van den Hove et al., 2012).

In this framework, governments have at least three roles: first, providing direction by putting in place smart regulations and consistent market signals; second, ensuring that the distributional consequences of innovations are balanced between risks and rewards across society; and third, fostering a diversity of innovations so that the wider interests of society take precedence over narrower interests.

Numerous case studies show that decisions to act without precaution often come from businesses. There are, however, several impediments to businesses acting in a precautionary manner, including a fundamental economic focus on creating and increasing short-term economic value for shareholders. There are also a number of psychological factors involved that lead to a so-called 'ethical blindness' or a 'self-serving bias' whereby people largely (and often unconsciously) tend to interpret ambiguous situations in their own interests.

This report reveals interesting parallels between older case studies and fast emerging issues such as nanotechnologies, genetically modified crops, new chemicals, and the possible link between brain tumours and non-ionising radiation from mobile phones. For example, only a very small number of actors were involved in making strategic decisions about lead in petrol in the USA in 1925 yet the technology spread all around the world before being phased out some 60 years later. With issues such as GMOs in food and energy options for a low carbon future, only a relatively few actors are involved in choosing innovation pathways that will shape the future of agriculture and energy supply and use for many decades.

Governments and businesses could collaborate more with citizens and civil society on publicly disclosing and analysing the potential value conflicts entailed in acting on early warning signals. Public disclosure and a culture of transparency and open discussion can in turn promote positive business attitudes and innovations. As stressed above, in many cases, accurate determination of risk is difficult and open to disagreement, making engagement, openness and transparency all the more important.

Involving the public can also help in choosing between those innovation pathways to the future (WBCSD, 2010; EC, 2011; WBGU, 2012); identifying and prioritising relevant public research (e.g. Diedrich et al., 2011); providing data and information from other knowledge holders — including NGOs, lay observers and citizens — in support of monitoring and early warnings; improving risk assessments; identifying and considering both alternatives to potentially hazardous agents and the unintended consequences of both actions and inactions on such agents; striking appropriate trade-offs between innovations and plausible health and environmental harms; and, making decisions about risk-risk trade-offs, such as the health benefits of consuming fish which contains mercury and PCBs. In particular, a feature of the studies is the top-down nature of innovations — the history of antibiotics in animal feed and lead in petrol, for example, show how a very small number of people can take decisions which have a major impact on millions. The public should help shape the future, including helping to choose strategic innovation pathways, for example, to sustainable agriculture and low impact renewable energy systems, by 2050.

The case studies also illustrate that there is often a lack of public accountability and access to the private research on which public protection authorities rely. Such access would help to increase independent verification of data submitted for licensing and would increase public trust in the regulatory authorities at a time when such trust in elites is very low.

Information and communications technologies (ICT) and their role in transforming social behaviour can help to engage the public on these issues. ICT has spawned a wide range of new collaborative

tools and approaches, which, as we saw above, are already transforming the dynamics of governance and innovation, fostering two-way interactions, and which can be used to support a more diverse approach to engaging with citizens. Less positively, ICT developments and access to knowledge may be building barriers to collaboration by fostering more hectic interactions and competition in the pursuit of enhanced productivity, less face-to-face contact, and less space for thinking through possible solutions to complex realities. Creating the space for more deliberative thinking and innovation could contribute to more collaborative problem solving.

For public engagement to be effective there needs to be adequate procedures for identifying and including the relevant stakeholders and public interest groups and for the provision of adequate educational and financial resources to enable such groups to play an effective role. Public engagement can be encouraged and supported by substantially improved and simpler access to relevant data and information, building on the provisions of the Aarhus Convention and national freedom of information laws. Business concerns about confidentiality and competitiveness can be overcome through judicious use of information technologies to manage access rights while maintaining transparency on how such information has been used and the insights drawn.

Today there are large imbalances within publicly financed research between product development and the study of potential hazards, an imbalance that seems to repeat the histories of better-known hazards. In Europe for example, in the period 2002–2013, about 1 % of the total amount that the EU Framework Programmes of Research and Development allocated to developing products from nanotechnologies, biotechnologies and ICT was spent researching their potential hazards. Research carried out by private industry may well show a similar imbalance, but data is not easy to obtain.

Correcting this imbalance between researching innovations and their applications, and anticipatory researching of potential hazards posed throughout their life cycle (production, use, recycling and disposal) can help avoid unequal distribution of costs and benefits further down the line and support a better public acceptability of such technologies.

Correcting market failures using the polluter pays and prevention principles

When evidence of initial harm emerges, the costs of such harm need to be internalised into the prices of polluting products, via taxes and charges, in line with the polluter pays principle. The revenues could be devoted partly to stimulating research into less hazardous alternatives, as was the case in the US with CFCs, and partly to reducing taxes and charges on labour.

The pollution taxes/charges would rise or fall in line with knowledge about increasing/decreasing harm and this would help to level the market playing field for innovative alternatives to the harmful products that are otherwise subsidised by the external costs of their pollution. Tax shifts from labour to pollution and inefficient use of resources bring other benefits such as increased employment, a stimulus to innovation and a more efficient tax system (EEA, 2011b and 2011c).

More realistic market prices, that reflect the true economic, environmental and social costs, can help encourage more sustainable behaviours by governments, businesses and citizens. More broadly, firms and governments need to extend their accounting systems beyond economic and financial capital considerations to incorporate the full human and natural capital impacts of their activities, building on developing practices worldwide (UN, 2012; EEA, 2011d; Puma, 2011)

Many case studies also demonstrate the long time lags between evidence of harm and the additional injustice and time of forcing victims to pursue their case through civil compensation claims. In the case of Minamata this took over 50 years. Prompt and anticipatory no-fault compensation schemes for victims of harm and damage to ecosystems could be set up and financed in advance of potential harm by the industries that are producing novel and large-scale technologies, thereby helping to correct this market failure. These schemes increase incentives for innovating companies to carry out more *a priori* research into the identification and elimination of hazards.

Precedents exist for such schemes in some countries, for example for nuclear accidents, oil spills, some radiation exposures, and some environmental liability laws, including contamination by GM crops of adjacent non-GM farms. Within the schemes there needs to be provision for penalising gross negligence, which under a tort system justifies punitive damages. Consideration also needs to be given to the use of anticipatory liability bonds by innovating companies so as to increase their incentive to minimise hazards and to provide adequate funds to compensate those who may suffer from any harm that may arise from their

products. Re-insurance schemes are also playing a role in helping to anticipate long tail liabilities from emerging technologies.

Attributing responsibility and sometimes negligence to corporations and others active in the history of hazards has relied mainly upon evidence uncovered by the legal processes of document discovery in civil compensation cases. The further use and development of freedom of information laws and the Aarhus Convention could provide a speedier means of accessing documented history. This will be even more necessary if no-fault administrative schemes replace some civil compensation cases.

Governance of innovation and innovation in governance

This chapter opens with a picture of unprecedented global change and interdependence. Such change provides many benefits to societies but also exposes them to more shocks and surprises. Scientific and technological innovations proceed apace, more often than not on trajectories that exacerbate risks and threats. At the same time, those researching and developing technological innovations often fail to acquire relevant existing knowledge from other disciplines. Governments tend to use structures and methods from the past to monitor the potential hazards of future technologies, rather than implementing more advanced, flexible and relevant approaches.

Failures, such as those presented in the two volumes of *Late lessons from early warnings*, provide numerous valuable insights, yet it appears that memories fade quickly. Typically, a hazardous event generates a sense of urgency and enthusiasm for strengthening preparedness systems, initiating research and implementing long-term monitoring, and heavy expenditure often follows. In the aftermath of an event, relevant authorities elaborate ambitious plans and launch works, but lessons are soon forgotten. After some time without adverse events, willingness to invest in risk research, long-term monitoring, etc. decreases sharply and projects are downscaled or suspended. Chernobyl and Fukushima are cases in point.

This cycle of events is termed the 'hydro-illogical cycle' in the case study on floods but could perhaps be called the 'homo-illogical cycle' as it seems to be a recurrent pattern for humankind, which is found across many cultural, political, social and economic systems. Despite its prevalence, this pattern need not be inescapable. Humans can learn, change and transform and there is enormous potential in human creativity and its capacity to inspire cultural, social, political, institutional, organisational and behavioural innovation, beyond 'mere' technological innovation. If, as Plato said, necessity is the mother of invention, then the crises we are facing create a level of necessity that will hopefully engender the needed innovations.

Crucially, governance systems also need to better recognise the value conflicts that are underpinning all societal and environmental issues. They are unavoidable and are even desirable as they are constitutive of the human condition. What is often missing is the institutional space to have a much more systematic, and non-judgmental, analysis of such conflicts so that they can be made explicit, enabling policymakers and other actors to start working together on the problems along the lines described in this chapter.

Of course such analysis already takes place (in part) in some quarters — examples include some parliamentary commissions and non-governmental organisations — but it is not sufficiently systematic and does not always focus on value conflicts. There could be merit in establishing a place in formal institutional frameworks where such value conflicts (and consequent conflicts of interests) could be analysed and proposals offered for their resolution.

The ideas for the governance of innovation and innovations in governance presented in this chapter will remain at the level of good intentions unless they are translated into institutional arrangements and practices. This is the task that lies ahead.

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Annex 2 — An overview of *Late lessons from early warnings: the precautionary principle 1896–2000 vol. 1*

Volume 1 of *Late lessons from early warnings* was published in 2001. The rationale behind the report was that science's growing powers of innovation seem to be outstripping its ability to predict the consequences of its applications, while the scale of human interventions in nature increases the chances that any hazardous impacts could be serious and global. The report therefore aimed to take stock of past experiences and identify lessons on how we can adapt to these changes, particularly in terms of providing information and identifying early warnings.

The lessons of history have rarely been used in trying to manage current and future risks. In volume 1 of *Late lessons from early warnings*, fourteen case studies were chosen where sufficient is now known about their impacts to draw conclusions about how well they were addressed by governments and civil society. Such conclusions were based on 'the spirit of the times' and not on the luxury of hindsight. The authors, all experts in their particular field of environmental, occupational and consumer hazards, were asked to identify the dates of early warnings, to analyse how the information was used or not used in reducing hazards, and to describe the resulting costs, benefits and lessons for the future.

This annex summarises the fourteen cases studies included in *Late lessons from early warnings: the precautionary principle 1896–2000*. The full report is available at: http://www.eea.europa.eu/publications/late-lessons-2001. A free printed copy can be ordered from the EU Bookshop: http://bookshop.europa.eu.

Table A2.1 Case studies in *Late lessons from early warnings: the precautionary principle 1896–2000*

Case study	Date of first early warning	Date of effective risk reduction action	Years of substantial inaction
Fisheries: taking stock	1376	1995–2008 'responsible' management (which is not very effective)	Hundreds
Radiation: early warnings, late effects	1896	1961–1996 UK and other countries, then EU laws.	65
Benzene: occupational setting	1897	1978 benzene voluntarily withdrawn from most US consumer products.	81
Asbestos: from 'magic' to malevolent material	1898	1999 EU ban by 2005	101
PCBs and the precautionary principle	1899	1970–1980s: EU and US restrictions, phase out by 2010	c. 100
Halocarbons, the ozone layer and the precautionary principle	1974	1987–2010 global ban on CFCs and other ozone depleters	10–30
DES: long-term consequences of pre-natal exposure	1938	1971–1985 US, EU, global ban	30–50
Antimicrobials as growth promoters: resistance to common sense	1969	1999 EU ban	30
SO_2: from protection of human lungs to remote lake restoration	1952 (lung) 1968 (lakes)	1979–2001 increasing EU and other restrictions leading to c. 90 % reduction on 1975 levels by 2010	25–55
MTBE in petrol as a substitute for lead	1960 taste/ odour/ persistence in water	2000 undesirable in Denmark and California, permitted elsewhere	40+
Great Lakes contamination	1962/1963	1970s DDT banned in North America and the EU. Debates continue about persistent health damaging pollution	45+
TBT antifoulants: a tale of ships, snails and imposex	1976–1981 French oyster beds collapse	1982–1987 French, UK then north-east Atlantic ban; 2008 global ban	5–30
Beef hormones as growth promotors	1972/1973 oestrogen effects on wildlife	1988 EU ban, US continues	16+
Mad cow disease — reassurances undermined precaution	1979–1986	1989 partial; 1996 total ban	10–17

Source: Gee, 2009.

Fisheries: taking stock

Malcolm MacGarvin

Measures to secure sustainable fishing have been known for centuries. However, when industrial fishing intensified in the second half of the 20th century pressure on fish stocks increased dramatically. Necessary safety margins were underestimated, bringing, for example, North Sea herring to the brink of collapse by the 1970s.

The chapter analyses different approaches to managing stocks in Canada, the US and the EU. It also evaluated the implications of international documents introducing the term 'precautionary approach' to fisheries.

Table A2.2 Fisheries — early warnings and actions

Early fisheries in the United Kingdom	
1376–1377	Setting up a committee is the answer of the English parliament to a call for precautionary actions in fishing by controlling the mesh of the nets
1866–1893	Following uncertainty about the consequences of fisheries growth official enquiries take place, but no action is taken
Sardine fisheries in California	
Mid-1920s	Californian sardine fisheries scientists call for precaution and research
1942	Continuous inaction leads to the collapse of the sardine stock (signs of recovery only in mid-1980s)
Northern cod fisheries in Canada	
Late 1970s	Canada starts managing the northern cod fisheries up to 200 nautical miles, claiming it is doing so precautiously
1986	Keats Report commissioned by inshore fishers indicates severe underestimation of the fishing pressure
1988	Alverson Report, prepared by fishery scientists, states that consistent overestimation of the stock size leads to overfishing
1989	A new government assessment recommends that the offshore catch should be halved
1990	A new independent assessment, the Harris Report, confirms overfishing
1992	The stock collapses and a moratorium is imposed
1999	Restart of the northern cod fisheries at low levels, but dissidents state it is not low enough
General fisheries	
1990s	The ecosystem approach slowly settles in fisheries management procedures
1995	FAO Code of Conduct for Responsible Fisheries and the UN Agreement on Straddling Fish Stocks and Highly Migratory Fish Stocks are negotiated and published
2001	European Commission Green Paper on the future of the Common Fisheries Policy
2001	Positive changes are occurring, but are they happening fast enough to avoid further collapses?

Radiation: early warnings; late effects

Barrie Lambert

This case study analyses the development of radiation and radium protection over more than 100 years. Although injuries and fatalities caused by radiation were acknowledged as early as 1896, the serious consequences of widespread use of radiation were not recognised. Absence of an agreed unit to measure radiation made the introduction of effective standards of protection difficult. In the 1930s–1950s there were still many examples of ill-conceived use of radiation e.g. for fitting children's shoes, the treatment of ringworm and removal of hair.

In the 1950s Alice Stewart was instrumental in collecting evidence linking radiology during pregnancy to leukaemia in children. Although controversial at first, her work along with that of other researchers eventually lead the way for the principles of justification, optimisation and dose limitations aimed at protecting patients as well as radiologists. Similar concerns are now being expressed at the frequent over-exposure to radiation from CT scans.

Table A2.3 Radiation — early warnings and actions

1896	Injuries from exposure to X-rays noted by Edison, Tesla and Grubbe
1899	John Dennis, New York journalist, campaigns for licensing of radiologists and warns of harm from X-rays
1904	Death of Edison's assistant from complications arising from severe X-ray radiodermatitis
1904	William Rollins, Harvard dentist/doctor, publishes many warnings on X-ray hazards, and recommendations on prevention for radiologists and patients, including pregnant women
1913	First published rules of voluntary radiological protection by German Radiological Society
1924	New York dentist, Theodore Blum, identifies 'radium jaw' in radium dial painters: but wrongly attributes this to phosphorous
1925–1929	Harrison Martland, New Jersey pathologist, identifies radium as the cause of the jawbone cancers in the dial painters studied
1928	Establishment of the International X-ray and Radium Protection Committee: which later became the International Committee on Radiological Protection (ICRP)
1934	Reports by Colwell and Russ, on the death of more than 200 radiologists from radiation-induced cancers
1949	ICRP concludes that there is no dose threshold for radiation-induced cancer and optimisation of all exposures is crucial
1958	Alice Stewart reports that 'low dose' X-rays to pregnant women can cause leukaemia in their children. Not generally accepted until the 1970s
1961	The United Kingdom publishes regulations covering the use of radioactive substances
1977	ICRP updates its radiation protection recommendations and links dose limits to risk
1988	Regulations covering radiation doses to patients produced in the United Kingdom
1990–1997	NRPB reports 20 % of medical X-rays are probably clinically unhelpful; that 50 % of the collective dose to patients could be avoided; and that individual doses for the same X-ray vary by 100x between hospitals
1990	ICRP concludes in Publication 60 that the risk of radiation-induced cancer is 4–5 times greater than estimated in 1977 — reduces the occupational dose limit to 20mSv per year
1996	EU Directive on Ionising Radiations based on ICRP 60 which will be mandatory on Member States

Benzene: an historical perspective on the American and European occupational setting

Peter F. Infante

Despite early knowledge that benzene is poisonous to bone marrow, it was used as a solvent in the rubber industry from 1910 and later expanded into many other industries. This was accompanied by reports of benzene-induced leukaemia as well as other cancers and non-cancer diseases. Exposure recommendations were set slowly and remained at high levels for many years. From the 1970s the benzene industry began to attack the science demonstrating its harm. This contributed to delays in government action and in identifying safer threshold limit values on occupational exposures.

Table A2.4 Benzene — early warnings and actions

1897	Santessen report on observed aplastic anaemia in Sweden and other reports show that benzene is a powerful bone marrow poison
1926	Greenburg and colleagues observe abnormally low white blood cell counts in benzene workers
1928	Dolore and Borgomano publish the first case of benzene-induced leukaemia
1939	A number of investigators recommend the substitution of benzene with other solvents, but this was not implemented
1946	American Conference of Governmental Industrial Hygienists (ACGIH) recommends a limit of 100 ppm for benzene exposure, even though some cases of benzene poisoning were associated with levels of 25 ppm and 10 ppm
1947	Recommended value reduced to 50 ppm
1948	Further reduced to 35 ppm
1948	American Petroleum Institute (API) concludes that the only absolutely safe level is zero, but recommends 50 ppm or less
1957	ACGIH lowers recommended exposure to 25 ppm
1950s–1960s	Obvious lack of precaution for workers exposed to benzene in many parts of the world with fatal consequences
1977	Infante et al. publish the first cohort study of workers linking benzene exposure directly to leukaemia
1977	Based on these results, the US Department of Labor wants to reduce exposure to 1 ppm, but is challenged in the courts by API
1978	Benzene was voluntarily withdrawn from consumer products in the United States of America
1980	US Supreme Court issues the Benzene Decision severely limiting regulatory actions
1987	New benzene standard of 1 ppm. This 10-year delay caused more than 200 deaths in the United States
1996	Studies showing benzene-related diseases from 1 ppm level of exposure
2001	Petrol contains benzene, giving public exposure risk

Asbestos: from 'magic' to malevolent mineral

David Gee and Morris Greenberg

Asbestos became increasingly popular among manufacturers and builders in the late 19th century because of its sound absorption and its resistance to fire, heat, electrical and chemical damage. A severe downside, however, was the risk for workers in the mining and production industries, as exposure to asbestos dust proved to cause the lung disease asbestosis and cancer. With an average latent period of 20–40 years from first exposure to cancer outbreak, it took a long time before the seriousness of the problems were recognised, although inspectors had warned about the risks as early as 1898.

From 1959 a third asbestos-induced disease, mesothelioma cancer, was identified. It is this cancer that is now causing the bulk of current and future harm from asbestos, including some 400 000 expected deaths in Europe over the next three decades.

Table A2.5 Asbestos — early warnings and actions

1898	UK Factory Inspector Lucy Deane warns of harmful and 'evil' effects of asbestos dust
1906	French factory report of 50 deaths in female asbestos textile workers and recommendation of controls
1911	'Reasonable grounds' for suspicion, from experiments with rats, that asbestos dust is harmful
1911 and 1917	UK Factory Department finds insufficient evidence to justify further actions
1918	US insurers refuse cover to asbestos workers due to assumptions about injurious conditions in the industry
1930	UK Merewether Report finds 66 % of long-term workers in Rochdale factory with asbestosis
1931	UK Asbestos Regulations specify dust control in manufacturing only and compensation for asbestosis, but this is poorly implemented
1935–1949	Lung cancer cases reported in asbestos manufacturing workers
1955	Doll establishes high lung cancer risk in Rochdale asbestos workers
1959–1960	Mesothelioma cancer in workers and public identified in South Africa
1962/1964	Mesothelioma cancer identified in asbestos workers, in neighbourhood 'bystanders' and in relatives, in the United Kingdom and the United States, amongst others
1969	UK Asbestos Regulations improve controls, but ignore users and cancers
1982–1989	UK media, trade union and other pressure provokes tightening of asbestos controls on users and producers, and stimulates substitutes
1998–1999	EU and France ban all forms of asbestos
2000–2001	WTO upholds EU/French bans against Canadian appeal

PCBs and the precautionary principle

Janna G. Koppe and Jane Keys

PCBs were primarily used in the electrical industry where they facilitated smaller, lighter, and what were thought to be safer, equipment. Use subsequently expanded to many other industries. Within the electrical industry, adverse effects on workers such as a painful disfiguring skin disease, chloracne, and severe liver damage, were already well known in the 1930s. From the 1960s findings emerged of PCBs in the tissues of wildlife causing infertility and severe damage to animals. Later PCB contamination of human breast milk was found and studies showed effects of endocrine disruption. Prohibition only happened gradually with each government action taken on the basis of a high level of scientific proof.

Table A2.6 PCB — early warnings and actions

1899	Chloracne identified in workers in chlorinated organic industry
1929	Mass production of PCBs for commercial use begins
1936	More workers affected by chloracne and liver damage
1937	Chloracne and liver damage observed in experiments with rats. Results did not gain attention from policymakers but both labour regulators and manufacturers were made aware of the concerns surrounding PCBs
1966	Jensen discovers unknown molecules in sea eagles in Sweden — only in 1969 was he able to demonstrate that they were PCBs
1968	Poisoning of 1 800 people who had ingested PCB-contaminated rice oil in Japan gives rise to a new Japanese word: Yusho — rice oil disease, and to the first well-publicised warning that PCBs are harmful to humans
1970s	High levels of PCBs found in infertile seals of three different species
1972	Sweden bans 'open' uses of PCBs
1976	Toxic Substances Control Act (United States) — PCBs to be used only in a 'totally enclosed manner'
1979	2 000 people again poisoned, in Taiwan, by polluted rice oil. Follow-up research showed that 25 % of children born of poisoned mothers died before the age of four years
1980s	Evidence of PCB contamination of breast milk
1990s	PCBs associated with IQ and brain effects in children exposed in utero to mothers' PCB-contaminated diets. Fetotoxicity represents a new paradigm for toxicology
1996	EU directive to eliminate PCBs, with phase-out by 2010
1999	Chicken food contaminated with PCBs is found in Belgium

Halocarbons, the ozone layer and the precautionary principle

Joe Farman

CFCs came into industrial use in the 1930s as refrigerants and their use increased during the Second World War when widespread use of aerosol sprays commenced. The ozone layer had been discovered at that time and variations in the amount of ozone measured. Concerns linking human activities to the ozone layer did not arise before the 1970s. Five reports from the World Meteorological Organization published in the period 1985–1999 concluded that halocarbons were beyond reasonable doubt responsible for damage to the ozone layer. When phasing out CFCs they were largely replaced by HCFCs (ozone depleting substances, but less harmful that CFCs) and HFCs (with zero ozone depletion but powerful greenhouse gases). The political process failed to stimulate more radical changes towards halocarbon-free and energy-efficient technology.

Table A2.7 Halocarbons — early warnings and actions

1907	Laboratory experiments by Weigert on the decomposition of ozone photosensitised by chlorine
1934	Ditto by Norrish and Neville
1973	Global survey of CFCs by Lovelock et al. showing their distribution in the atmosphere worldwide
1974	Molina and Rowland publish their theoretical arguments that CFCs would be destroying the ozone layer
1977	United States bans CFCs in aerosols based on 'reasonable expectation' of damage, followed by Canada, Norway and Sweden
1977	Research-oriented 'world plan of action on the ozone layer' agreed, overseen by UNEP
1980	European decision restricting use of CFCs in aerosols, but rising use in refrigerators, etc. marginalises this restriction
1985	UNEP Vienna Convention for the protection of the ozone layer agrees research, monitoring, information exchange and restrictions if and when justified
1985	Farman, Gardiner and Shanklin publish results showing hole in ozone layer over Antartica
1987	Montreal Protocol on protection of the ozone layer is signed, with phasing out of ozone depleting substances for both developed and developing countries within different timescales
1990s	Increasing finance to developing countries to help them reduce their dependence on ozone depleting substances
1997	Amendments to the Montreal Protocol in order to restore levels of chlorine by 2050–2060
1999	Beijing Declaration calling for efforts to stop illegal trade in ozone depleting substances

The DES story: long-term consequences of prenatal exposure

Dolores Ibarreta and Shanna H. Swan

In 1970 seven young women were diagnosed with a rare vaginal cancer in the US. Studies in the following years linked these and other cases to consumption of DES (a synthetic oestrogen diethylstilboestrol) by the patients' mothers during pregnancy. DES had been prescribed to pregnant women from 1947 in the belief that it prevented miscarriages. Prescription continued even though trials in the 1950s established the ineffectiveness of DES in preventing miscarriages. The cancer findings forced scientists to abandon their commonly held view of the foetal environment as a safe place, protected by the placental 'barrier' and replace it with an understanding of the extreme vulnerability of the developing foetus.

Table A2.8 DES — early warnings and actions

1938	DES synthesised
1938	First report of increased cancer incidence in animals after DES administration
1939	First report of DES administered to patients
1942	Approval of DES by the American Council of Pharmacy and Chemistry
1942	First report of DES used for prevention of abortion
1947	US Food and Drug Administration (FDA) approves DES for the treatment of threatened or habitual abortion
1948	Use of DES increases following publication of large-scale study in the US
1953	First large placebo-controlled randomised trial shows DES ineffective in the prevention of miscarriage
1970	Published report of seven cases of vaginal clear-cell adenocarcinoma in young women
April 1971	Prenatal DES exposure is linked to vaginal clear-cell adenocarcinoma
November 1971	FDA withdraws approval of DES for use by pregnant women
1972	Registry of Clear-Cell Adenocarcinoma of the Genital Tract in Young Females is established
1978	Reanalysis of 1953 Dieckmann data shows that DES actually increased the risk of miscarriage and other adverse pregnancy outcomes
1985	Last reported use of DES by pregnant women world-wide

Antimicrobials as growth promoters: resistance to common sense

Lars-Erik Edqvist and Knud Børge Pedersen

Antimicrobials are defined as substances of natural, semisynthetic or synthetic origin that kill or inhibit the growth of microorganisms. Growth promoting properties of antimicrobial agents in farm animals were discovered in the late 1940s, resulting in e.g. faster growth of chicken, improved egg production in laying hens and increased milk yields in dairy cows. Bacteria exposed to antimicrobials can, however, develop resistance to them with possible effects on human health. The number of independent scientific studies of this issue was relatively small compared to the number of studies supported by the pharmaceutical industry. The number of independent studies only increased when the resistance associated with using additives in animal feed was made clear.

Table A2.9 Antimicrobials as growth promoters — early warnings and actions

1945	Alexander Flemming warns against misuse of penicillin as 'microbes are educated to resist'
1950s	Antibiotic resistance widely recognised — vertical transmission
1960s	Horizontal transmission recognised
1969	Swann Committee recommends severe restrictions on antimicrobials in animal feed
1970s	Most Swann recommendations initially implemented in the United Kingdom and EU
1975	Swann recommendations are relaxed: tolysin and spiramycin still permitted as growth promoters as human equivalents; vancomycin comes into use
1977	Swedish Agriculture Board considers potential risk of antibiotic resistance, but concludes it is negligible
1984	Swedish farmers ask for government ban on antimicrobials in animal feed because of health and consumer concerns
1985	Swedish ban on grounds of antibiotic resistance in animals and 'uncertain' long-term effects
1997	Swedish report concludes that risk of antibiotic resistance in humans is 'far from negligible'
1997	WHO scientific meeting concludes that it is 'essential to replace growth promoting antimicrobials'
1998	EU bans four antimcirobials in animal feed as 'precautionary' measure
1999	EU Scientific Steering Committee recommends phase-out of antimicrobials that may be used in human/animal therapy
1999	Pharmaceutical industry opposes EU bans and takes EU to the European Court; judgement expected end 2001 (*)
2000	WHO recommends ban on antimicrobials as growth promoters if used in human therapy and in absence of risk-based evaluation

Note: (*) EU won the case against Pfizer Animal Health (Pfizer Animal Health SA v Council of the European Union, judgment available at: http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=CELEX:61999A0013:EN:HTML.

Sulphur dioxide: from protection of human lungs to remote lake restoration

Arne Semb

Dense smog over London in 1952 and 1962 drew attention to air pollution and its severe health impacts. Measures were slowly taken to reduce the emission of sulphur dioxide (SO_2) but increasing energy consumption in the 1960s resulted in large emission increases. Studies of precipitation introduced the concept of 'acid rain' and determined the long-range impact of emissions. Its harmful effects on forests and fish drew attention to the need for transnational cooperation. In Europe, this was extremely difficult during the Cold War period but progress in reducing SO_2 emissions were achieved during the 1980s and 90s.

Table A2.10 Sulphur dioxide — early warnings and actions

1952	A dense smog kills more than 2 000 people in London
1952	The Beaver Report prepared by a parliamentary commission proposes modest remedies
1962	Second smog incident kills 800 people in London
1968	Acidification of precipitation and rivers in Sweden is linked to sulphur dioxide emissions in other countries
Late 1960s	An OECD Air Management Sector Group is set up, contributing to solving air problems
1972	Further evidence of acidification of Swedish lakes presented to the UN environment conference, Stockholm
1972	OECD acid rain study is launched
1972	OECD programme on long-range transport of air pollutants is launched
1977	OECD report is published, determining the relationship between emissions and depositions of sulphur compounds
1979	Convention on Long-range Transboundary Air Pollution (LRTAP Convention) is agreed
1979	WHO recommends air quality guidelines, setting a standard for the pollution abatement work in Europe
1980s	Forest death from 'acid rain' in Germany, Poland, Czechoslovakia and North America
1985	LRTAP Convention protocol agrees 30 % reduction in sulphur emissions
1988	The EU directive on large combustion plants is published, and amended in 1988. These were very efficiently used by Germany against the British opposition to emission controls
1994	Second sulphur protocol, based on the critical load concept that had already been mapped all over Europe

MTBE in petrol as a substitute for lead

Martin Krayer von Krauss and Poul Harremoës

The toxic effects of lead have been well-known for centuries (as noted in Chapter 3 on lead in petrol). Following debate about the hazards of using lead as an anti-knocking agent in petrol in the 1960s, the petrochemical industry chose MTBE as a substitute. In around 1990 concerns arose as studies identified MTBE contamination of groundwater, which rendered large water reserves useless and thereby put pressure on supplies in many areas. Suspicions were also raised that MTBE causes asthma, cancer and endocrine disruption.

The chapter examines the extent to which it would have been possible to foresee undesirable properties of MTBE at the time of its introduction.

Table A2.11 MTBE in petrol — early warnings and actions

1954	First scientific paper demonstrates low biodegradability of the ether family in water
1960	Information about taste and odour in water and low biodegradability available in textbook
1990	First indications of the potential for groundwater pollution with MTBE at laboratory scale
1990	Significant increase in use of MTBE in the United States due to amendments to the Clean Air Act
1990	Comprehensive investigations of carcinogenicity initiated in the 1990s
1995	MTBE detected in wells that supplied drinking water in Santa Monica, California. These had to be closed and the city lost 71 % of its local water supply
1996	Concerns become widespread following a US Geological Survey report
1997	Field studies demonstrate that MTBE is highly soluble, mobile and persistent and therefore a potential risk to groundwater
1998	A Danish EPA report acknowledges that the government was informed in 1990 that MTBE might give rise to groundwater problems and presents an action plan for MTBE remediation and risk reduction
1999	California recommends removal of MTBE from petrol as soon as possible, but not later than end 2002
2000	Indications that MTBE might be linked to asthma in some US cities
2000	Indications that MTBE might be an endocrine disrupter
2000	US EPA announces that steps will be taken to significantly reduce or eliminate MTBE as a petrol additive
2000	Danish EPA places MTBE on its list of undesirable substances
2001	EU reports on analysis of risks and risk reduction related to MTBE. European Chemicals Bureau decides that MTBE should not be classified as a carcinogen
2001	The debate goes on

The precautionary principle and early warnings of chemical contamination of the Great Lakes

Michael Gilbertson

The Great Lakes on the border between the US and Canada have been subject to comprehensive pollution for decades. In 1972, the two governments responded to findings of organochlorine compounds in wildlife with the Great Lakes Water Quality Agreement and prohibitions of DDT and other substances. In the 1980s, however, the political climate changed and statements about the effects of persistent toxic substances on wildlife and humans were met with scepticism and demands for proof of a causal relationship before appropriating funds for remedial works. Decades later the efforts to clean up the area continue.

Table A2.12 Great Lakes contamination — early warnings and actions

1962	*Silent spring* by Rachel Carson is the significant early warning of the effects of organochlorine pesticides on fish and wildlife as well as the threat of cancer in humans
1963	First observation of changes in eggshell quality on Pigeon Island in Lake Ontario
1966	Hickey et al. publish the first analytical results of the presence of organochlorine compounds in organisms in the Great Lakes
1969	DDT and related pesticides are banned in Canada
1972	DDT is banned in the United States (dieldrin is banned in 1973) and gradual improvements in wildlife begin in the Great Lakes
1974	Concerns of possible effects of organochlorine compounds on human health
1978	Association of incidence of diseases (high rates of birth defects, miscarriages, cancers, etc.) in Love Canal, Niagara Falls with the disposal of toxic wastes (including dioxin) denied by Hooker Chemical Company
1978	Renegotiation of the Great Lakes Water Quality Agreement, including a precautionary policy, but it is not properly implemented
1980	President's Emergency Declaration moves 900 families from the hazardous Love Canal area
1984	Studies show that, at birth, infants exposed to high levels of PCBs (maternal consumption of Lake Michigan contaminated fish) weighed less and had smaller heads
1996	Studies of Lake Ontario affected children published that observed same behavioural effects as in affected children from Lake Michigan
2000	The specific relationship between behavioural anomalies and prenatal exposures to the highly chlorinated biphenyls is determined
2000	Reluctance to undertake costly remedial actions even after causal relationship is proven

Tributyltin (TBT) antifoulants: a tale of ships, snails and imposex

David Santillo, Paul Johnston and William J. Langston

Preventing plants and animals from growing on and fouling hulls has a huge effect on the fuel consumption of boats. TBT marine paint was introduced in the late 1960s and the first incidents of imposex in gastropods were discovered in France in 1970. It was not until early 1980s, however, that analytical techniques were sensitive enough to identify TBT as the agent responsible for sex reversals in oysters and snails caused by disruption to the endocrine system. This case study analyses the process leading up to the prohibition of TBT for vessels under 25 metres and subsequently for all vessels.

Table A2.13 TBT — early warnings and actions

Early 1970s	Rapid increase in the use of TBT antifouling paints on vessels of all sizes and first reports of imposex in marine snails (Blaber, 1970; Smith, 1971)
1976–81	Repeated failure of larval settlement leads to near collapse of oyster fishery, Arcachon Bay, France
1982	France introduces legislation prohibiting the use of TBT paints on small vessels
1985	First controls introduced in United Kingdom limiting concentrations of TBT in paints
1986	Bryan et al. (1986) report widespread imposex in dogwhelks on southern coast of United Kingdom, linked to TBT
January 1987	United Kingdom announces further restrictions on TBT content of applied antifouling paint
May 1987	United Kingdom introduces ban on retail sale of TBT paint for use on vessels < 25 m and on fish cages
June 1987	PARCOM Recommendation 87/1 calls for similar ban over entire convention area (Northeast Atlantic)
1988	United States introduces restrictions. Waldock et al. (1988) highlight significance of inputs from shipyards
1989	Restrictions introduced in Canada, Australia and New Zealand
1991	Harmonised ban on retail sale of TBT paint introduced at European Union level
1994	Early reports of imposex in whelks from offshore areas of North Sea linked to shipping activity
1995	Ministerial declaration of fourth North Sea conference (Esbjerg) commits to working for global phase-out of TBT paint within IMO
1997	Concept of global phase out of organotin containing paints agreed at MEPC's 40th session
1998	Draft mandatory regulations aimed at such a phase-out adopted. OSPAR (Convention for the Protection of the Marine Environment of the Northeast Atlantic) prioritises organotins for action to cease all releases. Cessation of all releases of organotins to marine environment, under OSPAR's hazardous substances strategy in 2020
November 1999	Deadlines for phase-out adopted under IMO Assembly Resolution A.895(21)
2001	Text of International Convention on the Control of Harmful Anti-fouling Systems to be finalised. In 2003 worldwide prohibition on new application of organotin antifoulants to all vessels and in 2008 the existing organotin antifouling coatings will be replaced on all vessels worldwide

Hormones as growth promoters: the precautionary principle or a political risk assessment?

Jim W. Bridges and Olga Bridges

Oestrogen and androgen hormones have been used as growth promoters to increase meat production since the 1940s, with diethylstilboestrol (DES) being the favoured growth promoter for cattle, sheep and poultry in many countries. In the early 1970s concerns about safety were raised as DES was confirmed to be a human carcinogen. Although expert scientific committees concluded that growth hormones were safe to use, the EU banned several hormones as growth promoters within Member States in 1988 and later extended this to imports as well. This can be seen as an early example of application of the precautionary principle.

The case study discusses the approach of the European Commission and the legal and financial implications of the trade restrictions in the World Trade Organization context.

Table A2.14 Hormones as growth promoters — early warnings and actions

1970s	Concerns about growth promoters' safety, as DES confirmed a human carcinogen
1972	Peakal publishes that DES likely to affect a wide range of species in the environment (wildlife) but this was ignored until the late 1980s
1972	DES banned as a hormone growth promoter in the United States
1974	Use of DES reinstated in the United States
1976	US Food and Drug Administration (FDA) sets the minimum detectable level of DES
1979	DES banned again on the grounds of the impossibility of identifying levels below which it would not be carcinogenic
1982	EU expert working group (Lamming Committee) concludes that some growth promoters are safe
1985	First EU ban is adopted, ignoring results from the Lamming Committee because the scope of their assessments had not been broad enough
1987	Lamming Committee disbanded by EU and their results were not published
1988	Ban of several growth promoters throughout the EU based on uncertainty of their effects on humans
1988	WHO/FAO Joint Expert Committee on Food, using standard risk assessments, reaches same conclusions as Lamming Committee
1989	EU ban extended to other growth promoters and to imports from third world countries
1989	Pimenta Report finds illegal use of growth promoters in some Member States
1989–1996	USA takes unilateral retaliatory measures on EC exports
1995	European Commission organises an international conference on growth promoters and meat production where uncertainties remain regarding effects on the immune system, endocrine system and cancer
1999	The EU Scientific Committee on Veterinary Measures Relating to Public Health publishes a report concluding that no threshold levels can be defined for six growth promoters
2000	International workshop on hormones and endocrine disrupters in food and water confirms impacts on the environment (wildlife) of veterinary drugs
2001	EU still suffers from sanction to its exports of around EUR 160 million per year

Mad cow disease 1980s–2000: how reassurances undermined precaution

Patrick van Zwanenberg and Erik Millstone

With the first case of an infected animal acknowledged in 1986, BSE (popularly known as mad cow disease) evolved into a serious crisis in the United Kingdom. The source of the epidemic was suspected to be animal slaughterhouse wastes recycled in animal feed, which was infected with scrapie. A decade later, suspicions that BSE might transmit to humans in the form of Creutzfeld-Jakob disease were confirmed.

This case study analyses the decisions of action and inaction taken by policymakers when weighing human health and financial consequences. The lack of precautionary measures and information to the public about the risks contributed to prolonging the crisis and the collapse of public trust in scientists and governments.

Table A2.15 Mad cow disease — early warnings and actions

Mid-1970s	The United States of America bans scrapie-infected sheep and goat meats from cattle food chain
1979	UK Royal Commission on Environmental Pollution recognises risks of pathogens in animal feed and recommends minimum processing standards in rendering industries
1986	First cases of bovine spongiform encephalopathy (BSE) are officially acknowledged
1988	First documented official acknowledgement that BSE may be transmissible to humans
1988	Southwood Committee is set up and recommends that clinically affected cattle should not go into human and animal food
1989	Ruminant feed ban, slaughter and destruction of affected cattle and specified bovine offal (SBO) ban
1995	Almost 50 % of the abattoirs checked are found to be failing to comply with the SBO ban
1995	Evidence that BSE may cause Creutzfeldt-Jakob disease (CJD)
1996	At last, experiments start to see whether cattle fed on rations deliberately infected with scrapie would get BSE
1996	BSE crisis, after a new variant of CJD emerged in the United Kingdom and consuming BSE contaminated food was considered the most probable cause
1998–2000	The Phillips Inquiry takes place and its 16-volume report is published. Its conclusions do not seem sufficiently rigorous on judging government actions over time. These conclusions state that appropriate policy decisions had been taken, although not always timely, or adequately implemented or enforced

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