1992-11-16

Scientific Challenges for Regulatory Decision Making. Proceedings of a Workshop, Chicago, Illinois, November 16, 1992

Great Lakes Water Quality Board

Michael Gilbertson

GREAT LAKES WATER QUALITY BOARD
REPORT TO THE
INTERNATIONAL JOINT COMMISSION

Scientific Challenges for Regulatory Decision Making

International Joint Commission
Commission mixte internationale

Great Lakes Water Quality Board
Report to the International Joint Commission

Proceedings of a Workshop

Scientific Challenges for Regulatory Decision Making

Chicago, Illinois
November 16, 1992

Compiled and edited by Michael Gilbertson
Secretary, Great Lakes Water Quality Board

ISBN 1-895085-58-6

Printed in Canada on Recycled Paper

International Joint Commission
Commission mixte internationale

Disclaimer

This report of the Great Lakes Water Quality Board is a compilation of extended abstracts of presentations made by participants at the Workshop on Scientific Challenges for Regulatory Decision Making. The views expressed in the report are those of the participants and do not necessarily represent the opinions of the Water Quality Board or of the International Joint Commission.

TABLE OF CONTENTS

Acknowledgements

The workshop was suggested initially by Dr. Michael McMullen, former Board member from the Department of Fisheries and Oceans. Funding for the workshop participants was provided by the C.S. Mott Foundation to Dr. Theodora Colborn of the World Wide Fund for Nature. Mary Ann Morin transcribed the tapes from which the extended abstracts were prepared, and Bruce Jamieson designed these proceedings.

Scientific Challenges for Regulatory Decision Making

• • • • •

Introduction

In June 1991, as part of the Workshop on a Shared Policy Vision for the Great Lakes, the Great Lakes Water Quality Board asked Dr. Theodora Colborn to make a presentation on her recent synthesis of information on chemically-induced alterations in sexual development. Dr. Colborn's presentation was influential in the formulation of the Water Quality Board's recommendations for its 1991 Biennial Report concerning the control of specific substances. These recommendations were incorporated by the International Joint Commission into its Sixth Biennial Report on Great Lakes water quality to the governments of the United States and Canada. One month later this topic was the subject of a workshop held at the Wingspread Conference Center, Racine, WI, where scientists from 17 disciplines produced a Statement of Consensus concerning the magnitude of the problem of chemically-induced alterations in sexual development. These research findings have profoundly changed the thinking of the scientific community about the significance of environmental chemicals in relation to fetal development.

Current water quality management develops and enforces objectives based on toxicity to aquatic life or on risk assessment models for human carcinogenicity. The new evidence of effects on the developing fetus poses a challenge to existing water quality policies and practice. The Water Quality Board held a Workshop on Scientific Challenges for Regulatory Decision Making to review the evidence and to determine whether this topic should be recommended to the Commission as a priority for the 1993-95 Biennial Cycle. The workshop was held on Monday, November 16, 1992 in the U.S. EPA Region V office in Chicago, Illinois.

. . . . .

Commissioner Gordon Durnil, in his opening remarks, said that the period from 1989 to 1992 had been an exciting period of progress in how the Commission and its associated boards view water quality problems in the Great Lakes. He noted the change in the words we now use to describe the problem and the statements we are prepared to make in light of the new evidence. For instance, we talk about persistent toxic substances as distinct from toxic substances, and about injury to human health and child development in addition to fish and wildlife resources. Where in the past we only talked about potential effects, we are now prepared to make cause and effect statements based on the weight-of-evidence approach. Where cancer was considered the most serious end point, the seriousness of effects on reproduction and embryo development is now included. The Commission incorporated these ideas in its Fifth and Sixth Biennial Reports, and these reports have been regarded as landmark documents by the public and by the scientific community. They have also resulted in a serious challenge to regulatory organizations in both countries to respond effectively within the limits of their legislative power and economic resources.

Part of the challenge in implementing many of the Commission's recommendations is that, in doing so, the often separate and divergent sectors of scientific research and the regulatory community must interact in intricate ways. Each part of the community is equally important. Scientists must do the research which should provide the causal statements, and the regulatory community must take appropriate action based on these and other findings. This poses questions about how much information is needed before a policymaker changes a policy, or an industry is required to change a process, or an individual changes a lifestyle.

. . . . .

In her opening remarks, **Dr. Theodora Colborn** noted the challenge of translating scientific evidence into policy and regulation. As an example, she cited a paper published in 1950 by Burlington and Lindeman* from Syracuse University in which male White Leghorn chicks, exposed to DDT during hatching, failed to develop combs or to reach sexual maturity. Despite this 40-year-old knowledge of the developmental effects of DDT on avian reproduction, no action has been taken against DDT, based on developmental effects, though action was taken based on carcinogenesis. She noted that the scientists themselves were not necessarily at fault, since they are not, generally, publicists or lobbyists. The regulators are not necessarily at fault because they are frequently not given the power to address new problems. Thus a new approach is needed to translate science into a regulatory context and specifically to deal with the new evidence concerning developmental and transgenerational health effects. Since exposures to chemicals that cause these effects occur globally, she said that it is imperative to take action to protect human civilization.

. . . . .

Dr. John McLachlan, Director of Intramural Research at the National Institute of Environmental Health Sciences at Research Triangle Park, North Carolina, gave a presentation entitled "New Scientific Information on Subtle Effects of Environmental Chemicals on Fetal Development." He organized his talk around the following three issues:

a) the fetus of the developing human being or animal represents an especially sensitive target site for environmental chemicals;
b) some environmental chemicals mimic biologically important molecules such as hormones, nerve stimulating chemicals and immunological chemicals;
c) the functionally significant effects caused by these environmental chemicals are subtle and thus difficult to measure and monitor.

Dr. McLachlan briefly reviewed the history of the development of teratology, the study of birth defects. Before 1961, teratology was a small science, centred at a laboratory in Cincinnati in which the deformities induced by chemicals in the offspring of exposed mice were studied. In 1961, the relevance of teratology was heightened by the finding of the relationship between phocomelia (extreme shortening of the limbs) in infants born to mothers who had taken thalidomide during pregnancy. In 1971, the science was further transformed when transplacental carcinogenic effects were documented in post-pubertal female offspring of women who had taken the synthetic estrogen, diethylstilbestrol, during pregnancy. Transplacental exposure to environmental chemicals, and estrogens in particular, were thus shown not only to cause subtle effects such as cancer but also immunological dysfunction, neurological deficits, and long-term delayed effects. The Wingspread Conference in July 1991 further changed perspectives on the science of teratology by showing that several organochlorine and other chemicals found in fish, wildlife and human tissue samples were hormone disruptors and thus could influence fetal development.

Thirty years ago, the placenta was thought to protect the fetus from environmental chemicals in the pregnant mothers. It is now well established that a wide variety of chemicals can reach the human fetus as well as developing fetuses of wildlife. In the pregnant mother and developing fetus, a large part of the estrogens they produce are bound to an extracellular binding protein called α-fetoprotein, or are metabolized by the placenta. But in the case of diethylstilbestrol and other synthetic compounds with estrogenic activity, they do not seem to interact with these protective mechanisms of the fetus.

Knowledge is increasing on how the development of the reproductive tract and its structure and function

* Burlington, H. and V.F. Lindeman. 1950. *Effect of DDT on testes and secondary sex characteristics of White Leghorn cockerels.* Proceedings of the Society for Experimental Biology and Medicine. 74:48-51.

are physiologically controlled in mammals. For example, there is a period of time after conception, at the beginning of development of all mammalian and avian fetuses, in which both male and female reproductive systems are present. In mammals, all fetuses are destined to be females without the genetic activation from the Y chromosome (male) to make a product that turns the developing gonad into a testicle. The testicle in turn makes two other hormones, male sex hormone and a protein that causes the female reproductive system to disappear. This process of sex differentiation can be reversed by exposing the developing fetus to female sex hormones. For instance, if diethylstilbestrol or estrogen is given to a pregnant mouse, the male offspring will look normal, produce testosterone and behave like males. But they will have undescended testicles and associated epididymal tubes, which remain in the abdomen. These mice will still make male hormone and sperm, but adjacent to these structures the mouse will have the female organs as well, including the fallopian tubes, oviducts, a uterus, cervix and the upper part of the vagina. Further, male mice that have been exposed to diethylstilbestrol *in utero* have even been shown to develop uterine cancer. Estrogens and estrogen-like compounds can thus affect the process of sex differentiation or sexual development in many profound but subtle ways.

The timing of exposure to these hormones and biomolecules will determine the outcome in predictable ways. Specific genes are activated and deactivated at specific times to start and end these processes. If the process described above is interrupted with estrogen, it will irreversibly preserve hermaphroditic structures. The endocrine system integrates the development and functioning of many organs, including the brain, the nervous system and the immune system. These systems can therefore be irreversibly compromised by what happens during development through exposures to environmental chemicals. Because the effects during fetal development are irreversible and persist long after the estrogen-like substances or other molecules that caused the effect have disappeared, it is difficult to establish a causal relationship through chemical analytical techniques.

When given to adult males, estrogen and estrogenic compounds cause breast enlargement, shrinkage of the testicles and decrease in sperm count and libido. A recent publication*, reviewing 61 different publications on sperm counts and quality in men in the Western world, showed a decrease in sperm over the past 40 years. An accompanying editorial raised the possibility that this might be consistent with an increase in environmental chemicals that act as hormones. The editorial also suggest that *in utero* exposure to environmental estrogens such as PCBs or DDT may have inhibited full development of the sperm-producing organs in men worldwide.

Many chemicals in our environment mimic biological molecules. Some chlorinated hydrocarbons such as DDT, PCB and dioxin show estrogenic activity and function like weak diethylstilbestrol molecules by reversing the process of male sexual differentiation in embryos of birds, mammals and turtles. They are ubiquitous, persistent and bioconcentrated to levels associated with the subtle effects. In addition, many different kinds of plants make their own female hormones. Environmental estrogens can cause hormonal effects on mammals that eat them. Assay methods have been developed to measure estrogenic activity of chemicals, based on the ability of an estrogen receptor molecule to recognize estrogen-like substances. Some PCBs have been tested in this assay and have been shown to be recognized by the estrogen receptor.

In the research area, we need to find biomarkers that can indicate the genes and their products that are irreversibly affected. When we understand the biological mechanisms of action of the molecules, we may be able to prevent damage. For instance, diethylstilbestrol has been used as a metaphor of how certain molecules can affect fetal development. The same principles are being established for the effects of environmental chemicals on the nervous system, the immune system and on the skin. For example, pregnant mice given a carcinogen that induces skin cancer have offspring that do not exhibit skin cancer. But if these offspring are subsequently exposed to a promoter, they all get skin cancer. *In utero* exposure to the carcinogen affected the molecular programming of the skin cells to predispose them to being susceptible to the second chemical.

---

* Carlsen, E., A. Giwercman, N. Keiding and N.E. Skakkebaek. 1992. *Evidence of decreasing quality of semen during past 50 years.* British Medical Journal. 305:609-613.

. . . . .

Dr. Andrew Gilman, Chief of the Great Lakes Health Effects Program of Health and Welfare Canada in Ottawa, Ontario, gave an overview entitled "The Effects of Contaminants on Human Health: The Old and the New." He prefaced his remarks by noting that the recent integration of knowledge, as outlined by Dr. Colborn and Dr. McLachlan, has brought new insight into the significance of exposures to environmental chemicals. It is extraordinarily difficulty, however, to communicate information to the public in a credible way. In addition, the public expects that science is going to deliver the required evidence, but it has proved difficult to detect attributable effects in human populations exposed to environmental chemicals, because of confounding factors. Government action to control environmental chemicals does not have to wait, however, until everything is known about the substances.

Dr. Gilman compared current and new health endpoints. Cancer, birth defects and organ toxicity such as kidney or lung disease, and liver dysfunction have been useful measures of health for a long time. Neurotoxic effects such as brain and nerve damage have been demonstrated for exposures to various drugs and contaminants through behavior testing. More sensitive neurotoxic effects can be measured, such as delayed effects in adults through somatosensory testing and developmental neuropathy in infants, through measuring attention span, learning and pattern discrimination. Traditional measures of reproductive toxicity have included fertilization and implantation rates as well as embryo and fetal toxicity. Newer reproductive measures include the incidence of sexual dysfunction, changes in hormone regulation, changes in the age of onset of menstruation and of menopause, and changes in birth characteristics such as gestational age, birth weight, length and head circumference. Various aspects of genetic toxicity of compounds have also been measured, including embryo death associated with genetic alterations, miscarriages and various syndromes. Immunotoxicity is a rapidly expanding field with assays being developed on an international basis to measure immune impairment or imbalance. Some immune response in the population seems to be expressed as a general increase in hypersensitivity, allergy, asthma and low-level morbidity. Because health is also considered to be the start of well-being as well as an absence of disease, there has been a growing interest in social impacts of contaminants on altered lifestyles. Examples of measures of psycho-social health include exercise opportunities in urban centers related to space and ground level pollution, willingness to commute longer distances between jobs and a preferred living space, alterations in diet to improve health and reduce contaminant exposure, socio-economic and cultural impacts on communities from pollutants, urban odours and the incidence of depression.

Dr. Gilman noted the widespread misperception about what realistically could be detected from studying human exposures to chemicals. He reviewed the advantages and disadvantages of studying laboratory animals, wildlife and humans to detect environmental impacts on human populations. Though direct causal statements can be made about effects of specific substances on laboratory animals, the information must be extrapolated for use in humans. Causal statements about the effects of pollution on wildlife species are indirect and of a correlative nature, yet they reflect the real world exposures to mixtures of environmental pollutants. The results from wildlife studies also must be extrapolated for use on humans. Though information on the effects of chemicals on humans is correlative and thus subject to potential confounding factors, no extrapolation between species is required to interpret the information. Most endpoints are easily measured in laboratory animals and many are also measurable in wildlife, but it is difficult to obtain many kinds of data on humans, particularly those concerning some aspects of reproduction and genetic toxicity and delayed neurotoxic effects. Experimentation with individuals or populations is generally unethical and gathering data from individuals is subject to misreporting, and gathering samples is too invasive.

In assessing the risks posed by contaminants, regulatory agencies have applied a weight-of-evidence approach to obtain information on all routes of exposure, congruity between studies, reliability, consistency of outcome, and biological plausibility. In synthesizing an overall assessment, information concerning laboratory animals, wildlife and human populations is now being combined, whereas previously, only information on wildlife and laboratory animals or on laboratory animals and human population was used. It is essential in making decisions on

chemicals, that a sound scientific basis be used, because any irrelevant or frivolous regulation can end up in court. By using a sound scientific basis for decision making, a preventive approach can be initiated based on what is known now, even while further research is undertaken. Science cannot answer - or would take too long to answer - all the questions if regulations are to be based on complete knowledge. Rather regulatory action must be based on the best available knowledge.

A balance between the traditional and the new research studies is needed. For instance, some classic 90-day toxicity studies still must be undertaken for a range of individual chemicals. New studies also must be undertaken on delayed neurotoxicity, the effects of hormone mimics on reproductive outcomes, and the effects of mixtures of contaminants found in food such as in Great Lakes fish on several generations. In epidemiology, there must be classic case control studies as well as newer approaches to preparing atlases of cancer and congenital anomalies for hypothesis generation. Surveillance activities must continue to document human exposure to contaminants by monitoring breast milk, blood, food, air and water. In addition, new studies on reproductive effects are needed to monitor levels of pollutants in follicular fluid that bathes the ovum in the female and influences egg cleavage. New initiatives are needed to store tissue samples for retrospective analysis of samples through tissue banking for contaminants and microbiological agents. Knowledge about these and other advances have been shared between scientists at conferences but it is increasingly important to bring together scientists from several countries for direct consultation on research planning and evaluation of specific issues. In addition to classical public opinion polls, site visits and community consultation are increasingly used to find out what people are really concerned about. U.S. and Canadian scientists have traditionally worked together in partnerships, but joint projects must also be undertaken with other nations or communities, especially in Europe. Innovative sources of funding, in partnership with health, fisheries and wildlife researchers, anthropologists, sociologists, psychologists, economists and others may evolve from this expanded consultative process.

Levels of persistent organochlorine chemicals declined rapidly in the Great Lakes up until about 1983. Since the mid-1980s levels of most persistent toxic substances have not decreased very rapidly, primarily as a result of environmental cycling of substances. As levels have declined, more sensitive techniques have been developed to detect effects. Some techniques that measure endpoints such as neurological development, somatosensory effects, neurotransmitter effects and hormonal dysfunction, have low specificity for the causes and thus there is potential for confounding factors to give specious associations.

. . . . .

Dr. Larry Reiter, Laboratory Director of the U.S. EPA Health Effects Research Laboratory, Research Triangle Park, North Carolina outlined three major changes that have been instituted in his laboratories to respond to the new information concerning subtle effects of environmental chemicals. The first change is in context. U.S. EPA is a regulatory agency and research therefore must be mission oriented. The new evidence of subtle effects, however, suggests that U.S. EPA should reorient some of its work to solving specific environmental health problems. To this end, U.S. EPA has extended the use of the 1983 risk assessment paradigm developed by the National Academy of Sciences as a conceptual framework to consider different environmental health problems and priorize those that pose the greatest risk. This has brought about the second change which is in terms of organization. The laboratory is now structured according to scientific as well as regulatory programs to ensure scientific excellence and program relevance. The objective is to improve communication between those responsible for setting standards and maintaining regulatory programs, and those responsible for scientific leadership and direction to the research program. The third organizational change has been in terms of function, by instituting a multidisciplinary approach that uses a variety of health endpoints such as growth, development and immune competence as well as a multidimensional approach that spans toxicology, clinical research and epidemiology. These changes are needed to address contemporary environmental health issues.
The general context in which U.S. EPA performs contaminants research is to understand the health effects resulting from exposure to environmental

chemicals and, as a regulatory agency, to control these exposures. There is a series of intervening events between human exposure and the manifestation of health effects. These events include absorption of the dose, dose to the target organ, and the consequent biological effect resulting in a health effect. Frequently information on these pharmacokinetic processes is inadequate to build a predictive model to understand these relationships. Many newly recognized subtle effects that result from perinatal exposures to chemicals do not manifest themselves until later in the life of the organism. Thus there is a temporal disconnect between the exposure and the resulting health effect, which poses further complexity in understanding the relationship between exposure, absorbed dose, target dose, biological effect and adverse outcome. A second difficulty arises from the specificity of the mechanism of action for some compounds. A compound that affects a hormone receptor can express its action at a concentration far below the concentration that would interfere with the basic metabolic processes in cells.

There are three distinct, but interrelated, activities that the U.S. EPA undertakes to focus regulatory decisions on the appropriate risks. These include:

a) scientific research to generate the data on the determinants of environmental health effects;

b) risk assessment to interpret the data or hazard, dose-response and exposure to estimate the likelihood and magnitude of the human health risks; and

c) risk management to apply the data to decide which risks are unacceptable and how they should be addressed through public information, standards, technology or regulatory prohibitions.

In performing risk assessments and discussing risk management it frequently becomes clear what significant information is still required, thus it is important that information about these research needs and data gaps is given to those involved in the scientific research. In this regard U.S. EPA has identified the following three generic areas of research to support risk assessment:

a) state of the science biological assays;

b) predictive models; and

c) chemical specific data.

For instance, in the assessment of the risks of perinatal exposure to potential neurotoxic agents, in addition to the general need for biological assays, there is a specific need to investigate the long-term developmental implications for the nervous system of fetal exposures to organophosphates and carbamates, which cause acetyl cholinesterase inhibition, on learning and memory. Similarly, specific biomarkers are needed to evaluate exposure and interaction with target tissue for carcinogens. In the regulatory decision making process, the time when the agency could rely completely on data on effects on laboratory organisms has passed and thus there is a need for predictive models. The development of quantitative risk assessment models will require an understanding of the underlying biological processes, particularly as it relates to pharmacokinetics. For instance, in the re-evaluation of the risks posed by dioxins and mixtures of dioxin-like PCBs, advances have been made through understanding the mechanism of action and the relationship between the toxicological potencies of the compounds and their binding affinities to the Ah receptor.

The U.S. EPA Health Effects Research Laboratory is structured to address not only the major health endpoints ranging from neurotoxicity, pulmonary, developmental, immunologic, genetic, carcinogenic to pharmacokinetic endpoints, but also the different levels of biological organization ranging from molecular, cellular and tissue through organ systems, whole organisms, to the population level. Both these multidimensional and multidisciplinary approaches are required to develop information needed to assess risks relevant to U.S. EPA regulatory programs for air, water, toxics, pesticides and hazardous wastes.

Dr. Reiter gave an overview of the research on ozone and on non-cancer health effects to illustrate how the agency has been coordinating research using toxicology, clinical studies and epidemiology approaches. About 90 million people in the U.S. live in areas that are not in compliance with ozone standards. Research on the health effects of ozone has changed from acute effects to those effects resulting from chronic exposures. This change reflects the amendments to the Clean Air Act that address the issue of non-attainment of the standards. Several research questions exist concerning exposure scenarios, dose-response relationships, cross-species extrapolation, pulmonary functioning and cumulative effects of acute episodes

versus chronic low level exposure. Through interagency meetings between U.S. EPA, the California Air Resources Board and the National Institute of Environmental Health Sciences, a coordinated research program has evolved to undertake the needed toxicological, clinical and epidemiologic studies.

The second example concerns the U.S. EPA dioxin re-evaluation. It has recently become clear that although current risk assessments are based on cancer, several studies suggest that reproduction and development are more sensitive endpoints than cancer. U.S. EPA has set up a multidisciplinary program to replicate and extend the various observations. Researchers will study the multiple health effects of perinatal exposure to TCDD, including effects on male and female reproduction, and neurobehavioral and immune responses. These studies will be compared with information on the target dose derived from pharmacokinetic modelling to investigate whether there are critical periods of exposure for different kinds of health effects. It may be possible to extend these studies to obtain generalized findings from a variety of laboratory animal species, and to extend these findings not only to the dioxin-like PCBs but also to the non dioxin-like PCBs. Understanding the mechanisms of action is emphasized for which there will be a need for further development of methods.

. . . . .

Dr. Jim Donald, Acting Chief of the Reproductive Toxicology Unit of the California EPA, gave a presentation on the reorganization that has taken place in California State Government. He explained how California established an Environmental Protection Agency in July 1991 to consolidate many of the different environmental regulatory functions that were spread between various disparate agencies. One of the half-dozen boards and departments that were brought together or created was the Office of Environmental Health Hazard Assessment(OEHHA). This is now the primary department in California government for risk assessment, and uses the risk assessment model developed by the National Academy of Sciences as the basis for its regulatory framework.

A copy of the Wingspread statement was referred to Dr. Donald's Unit for review. The result of the review was that there was a need for a re-evaluation of the capability of scientific departments of the state for risk assessment for subtle ecological effects, as opposed to human health effects. OEHHA formed a working group to identify California departments and programs involved in ecological risk assessment. In essence there are two agencies in California that have this capability and mandate; the California Environmental Protection Agency, and the Resources Agency. Dr. Donald reviewed the several parts of these organizations that have this responsibility.

California has a fairly large number of scientists and extensive expertise spread across a variety of different groups and organizations. There is a need to integrate the expertise to formulate the best plan and best methods available for ecotoxicological risk assessment. Through the OEHHA working group, departments, particularly in the same agency, have an understanding of each others work. The working group is preparing an overview plan to review what research has and has not been done. For example, some gross endpoints such as lethality and congenital abnormalities in birds have been adequately addressed, but further work is needed on the subtle endpoints such as disruption of the endocrine, immune or nervous system. Through the preparation of a long-term plan, the working group will propose a coordinated approach to ecotoxicological risk assessment in California.

. . . . .

Dr. Gerald Pollock, Acting Chief of the Fish and Sediment Contamination Evaluation Unit of the California EPA, described the activities being undertaken to document chemical contamination of fish, the Bay Protection and Toxic Cleanup Program, and on the opportunities for institutional adaptation in the area of ecotoxicology.

Several studies have been undertaken in California to document chemical contamination of marine fish. Twenty-four sites and many fish species were sampled from Santa Monica Bay and the Los Angeles Bight. A companion study was undertaken in Monterey Bay, which generally found low levels of contamination. An assessment of dioxin contamination of fish below a pulp mill on the Sacramento River also was conducted, where trout and bottom-dwelling fish were found to have high levels of

dioxins and furans. As a result, a risk assessment map was prepared and a consumption advisory issued to sport anglers.

Two years ago, the Governor of California signed a bill to establish The Bay Protection and Toxic Cleanup Program. Under this bill, the Office of Environmental Health Hazard Assessment and the Department of Fish and Game are mandated to assist the State Water Resources Control Board to establish sediment quality objectives based on protection of human health and aquatic life. A strategy is being prepared to address persistent toxic substances that contaminate sediments and biomagnify in food chains, resulting in high exposures to fish-eating wildlife and humans.

The juxtaposition of the development of sediment quality objectives for protection of aquatic life and for human health has been a significant institutional adaptation. In addition to conducting acute toxicity studies, the Department of Fish and Game is developing bioassays to determine the toxicity of these compounds to early larval forms. Particular attention will be given to subtle endocrine effects, particularly as it relates to reproductive toxicity. Much of the resources for this initiative is going into this ecotoxicological research rather than into human health. However, sediment objectives will involve an interagency collaboration rather than on the basis of a single narrow mandate, which is an innovative development.

. . . . .

Mr. Jim Armstrong, Chief of Controls Division of the Commercial Chemicals Branch of Environment Canada, described the assessment and control processes under the 1988 Canadian Environmental Protection Act. The purpose of the presentation was to show how new information, such as that on subtle developmental effects, would be incorporated into the assessment and regulatory processes. The Canadian Environmental Protection Act is the principal piece of Canadian federal environmental protection legislation and the toxic substances part is central to this act. The act's definition of toxic substances is broad and comprehensive, and relates to substances that enter or may enter the environment in a quantity or concentration or under conditions that:

a) have a harmful effect on the environment; or

b) present or can present a danger to the environment on which human health depends; or

c) present a danger to human life or health.

Mr. Armstrong explained the process of preparing a list of priority substances for detailed assessment. The assessment is based on supportable science to determine whether the priority substance is toxic based on a weight-of-evidence approach. If the Minister of the Environment and the Minister of National Health and Welfare decide that a substance is toxic, they must publish what regulatory controls they intend to implement. After a socioeconomic assessment has been made, the ministers may approve and promulgate the regulations.

Mr. Armstrong noted the regulations that were promulgated since 1977 on the import, manufacture, distribution, sale and release of polychlorinated biphenyls, terphenyls, polybrominated biphenyls and mirex and on the manufacture and use of chloroflurocarbons. The next real challenges are regulations for polychlorinated dibenzo-*p*-dioxins and dibenzofurans from pentachlorophenol manufacture, chemical treatment and preservation of wood, municipal incinerators, and pulp and paper mills using chlorine bleach. The adsorbable organically bound chlorine (AOX) in pulp and paper mills was thought to be a causal agent in the toxicity of mill effluents. However, the situation is more complex and regulation of pulp and paper mills based on AOX does not seem to be a viable option.

In summary, he stated that the act and the definitions under the act are sufficiently broad and comprehensive to accommodate consideration of the substances causing the subtle effects previously described. The substances must be added to the list of priority substances to be assessed in detail, using supportable science to persuade the people who must make the decisions about whether and how to regulate the substances.

Discussion

• • • • •

There was extensive discussion after the presentations. The following are some of the topics addressed.

The traditional concern has been with substances that are persistent, toxic and bioconcentrated. Several substances such as PCB, dioxin and DDT that have these characteristics can cause subtle effects on the developing fetus. However, because there are short, critical periods during development, maternal exposure, to non persistent, toxic substances that are not bioconcentrated, can result in irreversible subtle damage to the developing fetus. Of particular concern are the effects of maternal exposures to organophosphates and carbamates on fetal neurological development.

Groups of organisms and subpopulations of humans are highly exposed because of the food they eat. Some aboriginal people eat foods at the end of long and complex food chains. Some eat predators such as seals, whales, wolves, cougar and wildcat. The resulting contamination by persistent toxic substances can be seen most dramatically in analyses of breast milk samples from northern communities. Those that live on food from terrestrial sources have levels that are appreciably lower than those dependent on marine ecosystems. Since certain wildlife species are generally more contaminated than humans, ambient environmental quality standards to protect and restore affected wildlife may need to be more stringent than for protection of human health.

Wildlife have been useful indicators of environmental quality in relation to persistent toxic substances. The early observations and research on congenital anomalies and embryo mortality in wildlife were slow to influence researchers of reproduction and development in humans. Even now, the wildlife and health communities still undertake their work without sufficient consultation with each other. Many more measurements, which have traditionally been undertaken on laboratory animals or on humans, could be applied to understanding toxicological problems in wildlife.

In the future, there will likely be much more research oriented to understanding mechanisms of action in order to predict the toxicological characteristics of chemicals. With improved knowledge of biological processes and the mechanism of toxic action, testing strategies can be developed including more effective *in vitro* assay systems to undertake quantitative risk assessment.

For biological research undertaken for regulatory purposes, as well as advances in toxicology and epidemiology, there must be improvements in information sciences. Advances in computers and other electronic technology, such as virtual reality, may be used together with the intuitive senses of some brilliant minds to bring about progress in estimating risks, particularly from exposures to multiple chemicals. Too frequently in research for regulatory purposes, there is not enough time to sit and think about the data and to try to fit the pieces of evidence together, not only to develop conclusions but also to put forward new hypotheses.

Risk assessment has been undertaken to determine priorities. There is, however, a difference between the priorities derived from this method and the priorities that the public perceives. Public perception of the risks from multiple chemical sensitivity, indoor air and electromagnetic radiation fields are the primary motivation behind the involvement of U.S. EPA and other agencies in these issues.

Many forces drive the research, regulatory and political agendas on persistent toxic substances. The challenge is to avoid merely responding to whatever pollutant happens to be topical. In 1989, Canadian officials developed a Priority Substances List of 44 chemicals or mixtures of chemicals to be assessed in detail under the Canadian Environmental Protection Act. The list was compiled in consultation with industry and the public and is primarily based on scientific evidence. The Priority Substances List is not designed to directly influence the research agenda, but information gaps identified in the individual assessments are being picked up by federal agencies and other research organizations. In addition, a substance that has been newly identified as a concern can be assessed in detail without being placed on the Priority Substances List. There are, of course, concerns about how to address observed biological effects for which there are no specific

chemicals that have been identified. Since many of the chemicals that have been identified as disrupting the endocrine systems are pesticides, a systematic process is needed to evaluate new pesticides and re-evaluate existing pesticides for these kinds of effects.

Elaborate processes in both countries seek to build consensus on whether a substance should be assessed in detail and whether it should be regulated. More information from laboratory experimentation, human epidemiology and wildlife epizootiology is being integrated. To obtain this level of integration some jurisdictions have even reorganized or instituted a new agency. Some decision making processes have even been shared between existing agencies. In one jurisdiction, regulatory decisions can be swiftly influenced through the provision of new information. Mechanisms are well established in both countries to appeal or challenge a proposed regulation or ruling.

The assessment process, though it relies on scientific evidence from many sources and disciplines, necessarily must use a weight-of-evidence approach. There are uncertainties implicit in this process and challenges, not only in building consensus for action but also in communicating policy despite these uncertainties. Occasionally, past policy has been set based on political exigency, and scientists and the regulatory community have been directed to prepare the science to support the policy decision.

. . . . .

Based on the presentations and on the discussion that followed, the Board made the following conclusion and recommendations:

The Board concludes that there is a need for improvement in the integration of research findings and information on human, fish and wildlife health effects caused by endocrine disruptors.

The Board recommends that the Parties undertake improvements in institutional mechanisms, including: holding multidisciplinary workshops on specific biological effects; publishing integrated research findings in a manner that is comprehensible for regulatory action; establishing the requisite authority as well as responsibility, if necessary through legislation and allocation of suitable resources.

The Water Quality Board recommends that the International Joint Commission hold workshops during the 1993-95 Biennial Cycle on the effects of chemicals on embryo development. The following subjects might be considered:

1) ***Definition of information needs for regulatory decision making on existing chemicals and the application to a weight-of-evidence approach;***

2) ***The role of persistent toxic substances in the demise and recovery failure of Great Lakes lake trout (possibly to be undertaken in conjunction with the Great Lakes Fishery Commission);***

3) ***Recent advances in embryo neurotoxicity and immunotoxicity;***

4) ***Application of new information technology to the integration of information on chemicals that cause subtle effects on development of vertebrates;***

5) ***Improvements in knowledge of biological processes and mechanisms of action for prediction of the toxicological action of chemicals.***

The Great Lakes Water Quality Board recommends that the Parties include the factor of the ability of substances to disrupt endocrine systems, particularly for embryos, in the evaluation of new pesticides and re-evaluation of existing pesticides.

International Joint Commission offices:

100 Metcalfe Street, 18th Floor
Ottawa, Ontario
K1P 5M1

1250 23rd Street, NW
Suite 100
Washington, D.C.
20440

100 Ouellette Avenue, 8th Floor
Windsor, Ontario
N9A 6T3

or

P.O. Box 32869
Detroit, Michigan
48232