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“The Bioeconomy to 2030: Designing a Policy Agenda”**

***Health Biotechnology to 2030***

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***NOTE: This document is prepared on the responsibility of the authors. The opinions expressed and arguments employed herein do not necessarily reflect the official views of the OECD or of the governments of its Member countries.***

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## Abbreviation List

AIDS	Auto immune deficiency syndrome
CRO	Clinical research organisation
DTC	Direct-to-consumer
ETC	Erosion, Technology and Concentration
FDA	Food and Drugs Administration
FQPA	Food Quality Protection Act
GM	Genetic Modification <i>or</i> Genetically Modified
ICT	Information and communications technology
IP	Intellectual property
MNC	Multinational corporation <i>or</i> Multinational company
NBF	New biotechnology firm
NGO	Nongovernmental organisation
NHC	Networked health care
NICE	National Institute for Health and Clinical Excellence
OIE	World Organisation for Animal Health
PPP	Public private partnerships
SME	Small and medium sized enterprise
SNP	Single nucleotide polymorphisms
VC	Venture capital
WEF	World Economic Forum
WTO	World Trade Organization

# 1. Baseline State of the Health Care Sector

This scenario report considers the pathways that health biotechnologies could follow, the future trajectory of the bioeconomy primarily in the context of human health<sup>1</sup> and the likely societal, economic and policy impacts of these projected outcomes, focusing on the period 2012/15 to 2030.

The impact of biotechnologies on health care has so far primarily operated through the development of drugs, either in the development of new types of molecules, in contributions to discovery, or to safety and efficacy evaluation. The starting point for development of our scenarios is thus a world health care system that, *from the perspective of potential impacts of biotechnology*, has been dominated by the innovation model of the multinational drug companies. The current economic climate for this sector is one where increasing competition has led to waves of mergers and acquisitions, leading to an ever-increasing scale of operations for multinational companies alongside the parallel trend increasingly to out-source activities related to drug discovery and development.<sup>2,3</sup>

Our scenarios consider the future of the bioeconomy to 2030 particularly from the perspectives of the following four constituencies, their interactions with one another and with the relevant trends described in the OECD's *Baseline Assumptions about Long Term Global Trends Shaping the Development of the Bioeconomy*. Across these four constituencies, some are organised systemically and some are not, and they also show varying degrees of international organisation. We use the following terminology throughout this report to identify the focus of attention at any particular point. We also use the term "health care sector" to refer to the sometimes rather chaotic and poorly organised arrangement of all these components as they contribute to public health in general.

- The **global** science and industry innovation system includes public sector organisations involved in basic discovery and in offering supporting services to the commercial sector (for example in conducting clinical trials) and also commercial companies, ranging from small and medium sized enterprises (SMEs) to some of the biggest multinational companies (MNCs).
- The **increasingly global** regulatory system where convergence of national regulatory systems, particularly those of the United States and the European Union, can be expected to be much more closely aligned by 2015.
- **National** health care delivery systems which cannot currently be regarded as internationally organised. For example the American health system differs dramatically from those of most European countries and health care systems in the south are very different from those in the north, with little evidence to suggest that they will begin to converge globally, rather than diverging in the foreseeable future.

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<sup>1</sup> We also consider animal health-related influences insofar as they are relevant to the overall evolution of the health bioeconomy. Given that health care products for animals constitute approximately 3% of the profit base of pharmaceutical companies, with a similarly low contribution to the bioeconomy as a whole (OECD data), developments in animal health care are unlikely to be major drivers of change in this sector. However, in the longer term concerns and opportunities arising in animal health care may have a more major influence on innovation in health care as a whole and also zoonoses, exacerbated by climate change, may change the focus of public and commercial funding for health-related innovation (See Box 3).

<sup>2</sup> Mitra, J. (2007), "Life Science Innovation and the Restructuring of the Pharmaceutical Industry: Merger, Acquisition and Strategic Alliance Behaviour of Large Firms," *Technology Analysis and Strategic Management*, 19(3), pp. 279-301.

<sup>3</sup> Rafferty M.A. (2007), "Managing Change in Biotech: Mergers and Acquisitions," *Nature Biotechnology*, 25(6), pp. 489-490.

- The fourth constituency in this analysis includes stakeholder and advocacy groups who, with varying degrees of legitimacy, claim to represent public or patient interests related to health care delivery. Some individual groups may operate on a **global** basis, but these groups are **not yet organised systemically**. Our scenarios will consider the circumstances under which a systemically organised advocacy coalition may arise which could have an impact on the future of the bioeconomy.<sup>4</sup>

Our scenario analyses are organised around the above four constituencies, along with the other key drivers of change identified by the OECD that are considered relevant to the health care sector – global economics, demography and human resources, climate change, security and developments in animal health, as outlined in Section 2.

Biotechnology innovation has already had a major influence on drug development. It has contributed to improving drug-related R&D processes and also to the development of new biotechnology-based drug molecules. SMEs with strong biotechnology-based drug pipelines have become a target for MNCs seeking to acquire these products to supplement their own flagging pipelines.<sup>5,6</sup> With a few early exceptions from the 1980s, such as Genentech (until recently) and Amgen, SMEs have not been able to challenge the market dominance of the MNCs. Those companies that have managed to grow and at the same time to remain relatively independent have flourished by forging close links with traditional pharmaceutical companies rather than by attempting to compete on the basis of a new innovation model.

In contrast to the health-care industries, over the past thirty years, the information and communication technology (ICT) sector has been repeatedly shaken up by new R&D models and new types of products, for example personal computers or mobile phones as hardware developments, and software-related developments by Microsoft and Google. These have, over a short space of time, transformed existing markets and created new ones, and also changed the sectoral landscape beyond recognition. Very large multinational companies have had to change their R&D models (*e.g.* IBM) or have greatly diminished in size and influence or disappeared altogether, while new companies have generated huge fortunes for their owners and shareholders. Innovation in the ICT sector has thus created a relatively rapid rate of “churn” in company and technology dominance so that the sector today bears very little comparison to the one that existed in the 1970s.<sup>7</sup>

In the 1980s, biotechnology was expected to have a similar impact on health care industries and, while it has indeed played an important role in their development, this has been mainly supportive of the prevailing model for drug discovery, rather than challenging it. Despite large scale public and private investment, the sector is still dominated by a similar set of companies (although their names may have changed) and the basic innovation model remains fundamentally unaltered.<sup>8</sup>

The most important factor contributing to this long term resilience of the drug-based innovation model, and its dominant role in the development of health care systems, is the regulatory system. The

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<sup>4</sup> Tait J., (2001), More Faust than Frankenstein: the European Debate about Risk Regulation for Genetically Modified Crops. *Journal of Risk Research*, 4(2), pp. 175-189. This paper explains how such an advocacy coalition arose around the development of GM crops and how it was able to change the development trajectory of this technology.

<sup>5</sup> Anon., (2007), “News in Brief: AstraZeneca to Acquire Medimmune in Multi-billion Dollar Deal” *Nature Reviews*, 6, p. 424.

<sup>6</sup> Kling J., (2006), “Merck Moves into Biotech”, *Nature Biotechnology*, 24(7), p. 730.

<sup>7</sup> Tait J. and Williams, R. (1999), Policy Approaches to Research and Development: Foresight, Framework and Competitiveness. *Science and Public Policy*, 26(2), pp. 101-112.

<sup>8</sup> Tait J., (2007), Systemic Interactions in Life Science Innovation. *Technology Analysis and Strategic Management*, 19(3), pp. 257-277, May 2007.

European and United States regulatory systems impose very significant constraints on the innovation system for drugs and many other health care products through the lengthy, expensive and complex sets of regulatory requirements that need to be met to bring a product to the market. In drug development, this regulatory barrier to entry is a largely ignored, but important factor in giving multinational companies their dominant role over innovative technology in health care. For example, Thomas has shown that smaller United States pharmaceutical firms suffered a devastating reduction in research productivity as a result of the US Food and Drugs Administration (FDA) adoption of the 1962 Kefauver amendments to the 1938 Food, Drug and Cosmetic Act while the largest United States firms benefited from regulation in that sales gains due to reduced competition more than offset their modest declines in productivity.<sup>9</sup> Formal regulation is also becoming an increasingly important factor in areas of health care that used to receive a much lighter regulatory touch, for example diagnostics and tissue-based therapies. This is having similar effects on the ability of small companies to operate profitably, and also the ability and willingness of all companies to respond rapidly to new ideas and scientific discoveries, particularly those that do not have a good “fit” with current regulatory systems.

Robert Powell has also pointed to the basic resilience of the drug development model over the past 40 years (although there have been major changes in discovery and marketing processes), and also to the co-dependency between industry and regulators as a source of resistance to change.<sup>10</sup> He observed that conservatism and the need for predictability in how decisions are made influence the dynamics of the relationships between the FDA and industry and that it is unlikely that industry will make changes in drug development unless the FDA also changes.

The long term resilience of this dominant pharmaceutical innovation model is now increasingly being questioned. The health care sector has become mature in the sense that treatments have been developed for all the easy targets and these products are now off-patent commodities no longer attracting high profit margins. It has become increasingly difficult to find new products that are effective enough to compete with existing product ranges, safe enough to pass the regulatory systems, and cheap enough to manufacture, hence the “drying up” of product pipelines.

Such problems in the pharmaceutical industry led analysts to expect a period of “creative destruction”, as has been the case for the ICT sector, where small start-up companies with a range of different innovation models challenge the status quo and develop products for new or un-met needs in health care or revolutionise current treatments. However, the structure of the pharmaceutical innovation sector has resisted fundamental change despite the injection of a range of potentially revolutionary biotechnologies. Biotechnology innovations have been absorbed into the industry sector and indeed have served to support its current structure, rather than undermining it. The structure of the science and industry innovation system, closely coupled to a complex interacting set of markets and regulatory systems has served public health care needs in the developed world reasonably well for the last fifty years. However, under challenge from an increasingly complex range of innovative biotechnologies (including for example stem cells and pharmacogenetics), it is beginning to appear increasingly sclerotic, to the extent that we can no longer imagine alternative futures.

Thus fundamental, rather than incremental, change becomes increasingly inevitable, but also increasingly unimaginable. Some time in the future, the science and industry innovation system may experience a “Black Swan”,<sup>11</sup> but according to Taleb, the nature and timing of the stimuli are, by

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<sup>9</sup> Thomas L.G., “Regulation and Firm Size: FDA Impacts on Innovation”, *RAND Journal of Economics*, 21(4), 1990, pp. 497-517.

<sup>10</sup> Robert Powell, FDA Office of Translational Sciences, Centre for Drug Evaluation and Research (CDER), 2007. Presentation to Innogen Executive Development Programme, 25<sup>th</sup>-27<sup>th</sup> April, 2007, Edinburgh, Scotland.

<sup>11</sup> Taleb N.N., (2007), *The Black Swan: the impact of the highly improbable*. London: Allen Lane. A “Black Swan” has the following attributes: it is an outlier; it carries an extreme impact; and it appears explainable



definition, unpredictable. Contrary to Taleb's view, one role of scenarios is to imagine the unimaginable and then to devise means to prevent catastrophe, to cope with fundamental change or, as in the second scenario in this report, to engineer fundamental change. Successful, positive engineering of fundamental change often requires the coming together of two or more visionary individuals who, perhaps because of unfamiliarity with the existing context, a lack of understanding of "What can't be done" *can* imagine alternative futures and also have the necessary skills to make them happen.

Incremental change, as discussed in the first scenario, can be the norm for a considerable period of time, with simultaneous changes taking place in science and innovation systems, regulatory systems, health care delivery systems, and stakeholder and advocacy groups. Each individual change will add to or (occasionally) subtract from the overall pressure for change, building up over time a log-jam that becomes increasingly unstable. Once the instability has reached a certain level, it only takes one small, apparently insignificant change, the removal of a single log, to break up the log jam in a process that can be chaotic and destructive.

The first scenario in this report describes the continuation of the current series of incremental changes through to 2030, with increasing build-up of pressure for change and increasing "instability of the log-jam". The second scenario describes the situation where, some time between 2015 and 2030, a combination of visionary individuals with the financial backing and the ability to engineer fundamental change, supported by a range of appropriate incremental changes in the components of the health care sector, is able to engineer a relatively rapid and non-destructive transition to a new, transformed science and industry innovation system.

The future of the health bioeconomy by 2030 thus will be determined by the interactions between the global science and industry innovation system, the increasingly global regulatory system, the increasingly divergent range of national and regional health care delivery systems and the stakeholder and advocacy groups that so far have not become systemically organised.

The changes in the bioeconomy beyond 2012 will each appear disruptive to some of the major players in such a complex context. However, we distinguish our two scenarios on the basis of the skill and adaptability with which change is managed by two of the key constituencies in the health bioeconomy, the science and industry innovation system and the regulatory system. Also, although industry and regulators will need to be the lead agents in such changes, the health care delivery systems and those who pay for health care will also need to act as intelligent consumers of innovative health care in the new bioeconomy.

The first scenario, *Muddling through*, envisages the outcome where there is resistance to change in the healthcare sector, and the key constituencies outlined above are unable to align their interests resulting in a competitive environment that is not conducive to rapid and creative biotechnology innovation, accompanied by sporadic, localised conflicts.

The second scenario *Rapid Change* will require a fortuitous sequence of changes to innovation and regulatory systems resulting in significant changes to society and the economy. This will require a willingness of industry, regulators and stakeholder groups to collaborate in ensuring a smooth transition to a set of overall healthcare systems that deliver a more equitable distribution of benefits and a more cost-effective translation of innovative developments "from bench to bedside".

The changes envisaged will help shape social and economic transformations, not just in the science and industry innovation subsystem, but also in the labour-intensive health care sectors, with the need

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and predictable after the event. Taleb's examples include the emergence of the internet, the 9/11 disaster, the sinking of the Titanic, the United States banking crisis of 1982.

for changes in professional training, for example to deliver personalised medicines. The challenges to traditional medical vested interests presented by biotechnology-related innovations will also need to be managed carefully to achieve the outcome envisaged in the first scenario.

While we cannot predict or direct the outcomes of changes in complex interacting systems such as those involved in the health care sector over long periods of time, we can ensure that policy and regulatory actions are taken with the best available knowledge of how they are likely to determine or influence the future direction of change.

## **2. Drivers of Change to 2030**

The following drivers of change, including those specified by OECD<sup>12</sup> are considered likely to contribute to the post-2012 health care scenarios.

Exogenous drivers envisaged by OECD are those which do not directly influence the biotechnology sector, for example climate change impacts and general global economic developments.

Endogenous factors include those that are directly related to developments or decisions within the health care sector, such as government policy, new developments in health care delivery systems, public and stakeholder attitudes, new business models, new funding models, new innovative developments, *i.e.* those relevant to the sub-systems and groups described above. The most important contributions to the future of the bioeconomy are expected to arise from biotechnology innovation and research, policy and regulatory changes, changes in health care delivery systems, and stakeholder and advocacy group attitudes.

Demographic change partly endogenous and partly exogenous, being driven by many factors out with the bioeconomy as well as being directly affected by it.

However, in all cases, the scenarios that emerge in future will be determined by interactions among exogenous and endogenous drivers, emphasising the importance of the timing of future developments. Synchronous change in two key drivers could have major implications for future health care systems, whereas if the same two developments are separated by a period of years, their impacts could be barely noticeable. On the other hand future developments that take place almost consecutively could cancel one another out whereas if they occur over a period of years they may have a powerful influence on the shape of the bioeconomy. These issues are discussed in more detail in Sections 4 and 5.

### **2.1 Technology and Research (the science and industry innovation system)**

Research in the biosciences, publicly and privately (including both commercially and charitably) funded, and technological innovations that emerge from this research, are likely to be the main determinants of future healthcare scenarios. Investment in bioscience and biotechnology is currently high in the developed world and can be expected to increase there and also to become a much more important feature in the economies of the new rapidly developing economies.

National governments are likely to continue to invest in fundamental discovery in this sector, partly because it is seen to be an important component of a country's international competitive position. There is also an increasing trend for governments to invest in "translational research", to take products

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<sup>12</sup> OECD (2007), *Baseline Assumptions about Long Term Global Trends Shaping the Development of the Bioeconomy*. OECD Futures Project on the Bioeconomy to 2030: Designing a Policy Agenda.

further along the development route and closer to market application, in an attempt to cover the investment gap between the end of basic research funding and demonstration of an investment opportunity for the private sector.

Up till now, venture capital has been invested in biotechnology in the expectation of large pay-offs, albeit on a long time-scale. The expectation of large pay-offs have mainly not been borne out and venture capital investment in biotechnology is faltering, and will probably continue to do so, unless there is a fundamental change in the industry innovation system.

Companies in the health care sector can be categorised roughly as (i) large multinationals (“big pharma”), (operating globally, with candidate products in all major classes, markets in all major countries), (ii) middle-sized multinationals (operating multinationally but not necessarily globally, generally focusing on particular niche markets, often partnering with large multinationals to gain access to particular markets), (iii) companies of a wide range of sizes, including some divisions of large pharmaceutical companies, producing off-patent commodity drugs at relatively low profit margins but for larger markets, (iv) small companies developing new drugs with the aim of contributing products into the pipelines of the multinationals, either through licensing agreements or through takeover, (v) small companies providing analytical and other services to multinational companies, (vi) small tissue engineering and diagnostic companies developing products for specific niche markets and (so far) remaining relatively independent and profitable enough to permit internally generated and sustainable growth.

To an increasing extent these companies, including those developing the most innovative products as well as the commodity producers and the service providers, will be based in India and China.

Although it is not possible to predict the exact nature and timing of future innovations more than a few years in advance, it is reasonable to assume that those innovations which survive long enough to be influential will have the following types of impact:

- They will enable treatment options to be more targeted to the needs of specific groups of patients through more advanced diagnostic tests;
- They will enable more rapid responses to the emergence of new infectious diseases through the development of diagnostic devices, vaccines or antibiotics;
- They will deliver treatments for currently incurable diseases or for those that are currently ignored;
- They will enable new types of drugs or other treatments to be delivered more effectively or more cheaply, for example by speeding their passage through various stages of regulation or by developing new approaches to drug delivery or targeting;
- They will enable complex drug molecules to be synthesised more cheaply;
- They will enable long term treatments for disease to be replaced by cures;
- They will allow future susceptibility to disease to be avoided through the use of genetic testing and/or dietary supplements.

These technological developments would all be positively enabling from the point of view of contributing to better health care systems at the societal level, *i.e.* they are enabling of the progress of the bioeconomy as a whole. However, some of the companies involved in health care will be potential winners and some will be potential losers from each type of innovation, *i.e.* whether a particular biotechnology development is enabling or competing will depend on the type of company concerned. Companies will be likely to respond variably to each innovation depending on its fit with their current innovation models and markets or its potential to contribute to future competitive positions (See Box 1). For example, stem cells as treatments or cures for long term chronic diseases will not have a good fit with the innovation strategies of multinational companies developing new drugs whereas they will fit well with the strategies of smaller tissue-engineering based companies developing therapies and

potential cures for chronic and currently incurable diseases. On the other hand stem cell related developments designed to speed up efficacy and toxicity testing for new pharmaceutical developments will fit well with multinational pharmaceutical company strategies.<sup>13</sup>

#### **Box 1 - Path Breaking and Path Dependent Innovation Systems<sup>14</sup>**

For more than ten years, analysts have been claiming that, despite a series of life science-based innovations, the overall drug discovery and development model of the pharmaceutical industry sector is fundamentally unsustainable. Explanations have included failure of innovative capacity, too great a focus on incremental rather than radical innovation, excessive regulation, and lack of venture capital investment.

However, from an alternative perspective, one could say that the innovation model that has evolved in the life science industry sector has been remarkably robust compared, for example to those in information and communication technologies. Despite difficulties in markets, the emergence of a series of potentially disruptive innovations, the steady build-up of an onerous regulatory system, escalating development costs and a product development life span of up to 12 years, the underlying business model of the industry sector has remained remarkably constant, and indeed has been reinforced, over the past fifty years. The dominance of the multinational corporations (MNCs) and their prevailing block-buster drug model of innovation has until recently been unassailable.

Some of the innovative ideas that have emerged from life sciences have been “incremental”, presenting few serious challenges to the prevailing innovation model and easily accommodated within it. Others are potentially “disruptive”, stepping outside existing paradigms, leading to discontinuities in innovation pathways, to major shifts in product types and their place in the market, and even to the creation of new industry sectors or radical re-structuring of existing sectors.

Underlying at least some of the public and commercial investment in life sciences has been the assumption that the technology in question might be the “next big thing”, the innovation that will lead a company to become a multinational in its own right, with a winning strategy that is different from incumbent multinationals. More realistic investors assume that they will support a new biotechnology firm (NBF) only until it becomes large enough or successful enough to be taken over by, or to license its technology to, a multinational.

#### **Barriers to entry**

Regulators impose very significant constraints on life science innovation through the lengthy, expensive and complex set of requirements needed to bring a product to the market. This forms a barrier to entry for any new firm and is one of the most important factors giving multinational companies their dominant role in the sector. A symbiotic relationship has built up between the sectoral innovation system and regulatory bodies since the 1950s, with each change in the regulatory environment being incorporated into the innovation system in a way that reinforced the dominant position of the multinational companies.

Many analyses acknowledge a role for regulation as one factor among many in influencing sectoral innovation systems in life sciences. However, we would give it the key, controlling role in explaining the long term resilience of the current innovation model of the multinationals. By acting as such an effective barrier to entry to the sector it has ensured that, with a few early exceptions, no NBF has been able to develop an innovation strategy which challenges or would compete with those of the multinational companies.

The market context is also an important, but lesser, barrier to entry to the sector. Unlike most markets, products have not generally been sold directly to the public. Despite the increasing volume of internet sales, they are still delivered mainly through highly specialist health care networks, publicly or privately

<sup>13</sup> See Note 8.

<sup>14</sup> Tait J. (2007), Systemic Interactions in Life Science Innovation. *Technology Analysis and Strategic Management*, 19(3), pp. 257-277, May 2007.

funded. As with regulation, it is very difficult for a new entrant to break through this barrier and to market its products independently.

### ***Problems of maturity – when is a sector ripe for disruption?***

One factor to be taken into account in charting the future of the life science sector is its maturity, in the sense that products have been developed for all the easy targets and these compounds are now off-patent commodity products no longer attracting high profit margins. It has become increasingly difficult to find new products that are effective enough to compete with existing product ranges, safe enough to pass the regulatory systems, and cheap enough to manufacture. These factors, and not complacency or a failure of innovative capacity, are the main reason for the drying up of product pipelines. These problems of maturity became urgent for both agrochemical and pharmaceutical companies in the late 1980s. They are an indication of a sector that is ripe for a period of creative destruction where new companies with a range of different innovation models challenge the status quo.

Biotechnology was expected to provide this challenge but most industry-watchers point to its failure to rejuvenate product pipelines. However, there is an alternative explanation. Biotechnology may have succeeded in enabling pharmaceutical companies to ride out their maturity problems for at least another ten years, contributing to preventing major disruption of their innovation model and a slide to become mere producers of commodity chemicals.

### ***Comparing cases – degrees of disruption***

This analysis compared three case studies, the impact of GM crops on the agrochemical industry and of pharmacogenetics and stem cells on the pharmaceutical sector, to identify why some innovations fail to have the predicted disruptive impacts, while others are more disruptive than expected. An innovation that challenges a sector's internal R&D model and at the same time its regulatory and market environments is much more likely to be seriously disruptive of the sector than one which only affects one of these areas.

GM crops proved to be highly disruptive of the innovation model of the agrochemical industry because of their simultaneous impacts on company R&D (requiring a shift from chemical to biology-based development and production systems), on markets (selling seeds is a very different business from selling pesticides), and on regulatory systems (the European Union deemed it necessary to develop a new regulatory system from scratch to deal with this new product type). There are some important lessons to be learned by the pharmaceutical sector from the earlier experience of the agrochemical industry with GM crops.

With pharmacogenetics, companies have been able to exert more control over the way the innovation is being incorporated into the innovation system. They are attempting to guide market expectations and at the same time focusing on applications which will avoid potential market disruption, and they are also influencing the plans and expectations of regulators as they consider modifications to regulatory systems. Pharmacogenetics therefore seems unlikely to be disruptive for the pharmaceutical industry.

On the other hand, stem cells, as with GM crops, could have major simultaneous impacts on innovation systems, markets and regulatory systems, in a manner that is much less controllable by the multinational companies than is pharmacogenetics. For stem cells, an important difference from GM crops is that so far pharmaceutical companies are only planning to use the technology in an incremental manner, as a tool to develop new and better drugs, and not to develop products based on stem cells themselves.

### ***Regulatory – Technology Interactions***

GM crops were almost totally disruptive of agrochemical innovation systems but they would have been a much less disruptive innovation for seed companies of any size. However, once the agrochemical industry had decided to focus its future innovation system on GM crops, these other players were either bought out by agro-biotechnology companies or left the field, as for example did Unilever. One could speculate that, if GM crops had been developed by seed companies, European regulators would have been less likely to erect such an onerous regulatory system, although the products could still have been regulated effectively.

A similar situation arises for stem cells. They would be highly disruptive of pharmaceutical R&D systems, markets and possibly also regulatory systems, but largely an incremental innovation, for example for a small tissue engineering company. Whether the multinationals or the tissue engineering companies take the lead in developing stem cells as products will depend mainly on the still-evolving regulatory systems. If this becomes so onerous that it is impossible for small companies to continue to operate independently, then stem cells will be an incremental rather than a disruptive innovation for pharmaceutical companies. On the other hand if NBFs are able to develop the technology independently, then it may become externally subversive of pharmaceutical innovation systems rather than internally disruptive.

The research community and the industry have so far paid little attention to the role of regulatory systems in determining the kinds of company that are able to develop innovative technology and the nature of, and markets for, the products themselves.

### ***The future of “big pharma”***

The agro-biotechnology sector has already seen major change and radical re-structuring of its profit models, at least partly as a result of its incorporation of GM crops within its product range. Companies in this sector are now no longer divisions of joint companies with pharmaceutical companies. They are less varied, less powerful and less able to withstand disruptive shocks than they were previously.

It is conceivable that pharmaceutical multinationals could continue to survive in their present form despite the alleged unsustainability of their innovation models. However, this model is being undermined, not only from within through the problems of maturity, but also through regulatory and market challenges, with demands for cheaper drugs, regulatory changes encouraging drugs to be developed for small niche markets and an increasingly negative public image of the sector. These factors were also part of the environment that contributed to the disruption of the agro-biotechnology sector.

The pharmaceutical innovation sector is now becoming more diversified – it is still dominated by the pharmaceutical MNCs but the balance of power is slowly shifting and impacts from regulatory systems and market structures are the primary influences likely to speed up the rate of change.

If, as we propose, disruptive change in pharmaceutical innovation systems is increasingly inevitable, it will be important for the delivery of medical benefits to the public that this change is balanced and carefully managed. The key to achieving this is through evolution of the regulatory system – regulatory change needs to be accompanied by a good understanding of the subtlety and complexity of the interactions between regulation and innovation in life sciences.

Innovative biotechnologies currently being developed include synthetic genomics, pathway and systems biology, genetic databanks, cell banks and stem cell based therapies, pharmacogenetics, nano-biotechnology, new sensors and diagnostic technology, biopharmaceuticals. These developments are being facilitated through new initiatives such as translational medicine, intended to speed the passage of biotechnology related innovations in health care “from bench to bedside” through better integration of technological approaches to development and delivery of innovations in both public and commercial sectors.

Many of these currently hot topics will have become commonplace or will have disappeared from the lexicon beyond 2012, to be replaced by an even bigger range of new ideas and ambitious R&D agendas. Many of these developments are highly interdisciplinary and we are already beginning to see “convergence” of innovative strategies between biotechnology, engineering, chemistry, physics, nanotechnology and information technology in ways that are likely to transform what we currently think of as the bioeconomy. This convergence of innovation strategies is being driven by the increasing realisation in scientific communities of the benefits of interdisciplinary research in removing some of the bottlenecks that can occur through single-discipline approaches and of how

cross-disciplinary contributions can greatly speed up the delivery of fundamental research outcomes and also the translation of these outcomes to practical innovations.<sup>15</sup>

An alternative vision of *convergence*, in the societal rather than the scientific context, arises with so-called P4 Medicine, being promoted by Professor Leroy Hood – medicine that is *predictive, preventive, personalised, and participatory*. The prediction is that P4 medicine will be “cheap and available to the entire world”;<sup>16</sup> however, the basis for this expectation focuses only on the scientific possibilities and ignores the role of regulation in enabling or constraining particular types of innovation.

It is difficult to envisage which new areas of technology innovation are likely to be competitive with biotechnology between now and 2030. There will be strong competition between different areas of development within biotechnology for a decisive role in the future of the bioeconomy, but there is no apparent competitor for biotechnology-driven innovation *per se* as the key determinant of the nature of the future health care sector.

## **2.2 Government Policies and Regulation (the regulatory system)**

One of the key factors in determining the fate of all novel biotechnologies, and hence their contribution to the bioeconomy, will be the type of regulatory system chosen to determine their safety, quality and efficacy before they are registered for use. In health-related technology it is a common observation that an onerous and lengthy set of regulatory hurdles favours bigger companies (with the corollary that the range and inventiveness of new technology developed is more limited). In the context of biotechnology, this can be illustrated by the large number of small innovative companies working on diagnostics, devices and tissue-based therapies (so far relatively lightly regulated areas) with the relatively small number of long term market entrants among companies developing new drugs.

Mainly through the requirements for clinical trials, we have seen a fairly relentless increase in the regulatory burden for both small molecule and biotechnology drug development. Major changes in regulatory systems were often made in response to evidence of gaps in current provision, for example the introduction of teratogenicity testing for new drugs in response to the thalidomide tragedy. The increasing maturity of the sector has also been responsible for some of this regulatory escalation – increasingly large samples of patients and longer timescales are needed in clinical trials to demonstrate additional benefits from molecules that do not represent a radical departure from previous classes of drugs, described as “me-too” drugs.

There is also an increasing regulatory burden in areas such as diagnostics and tissue engineering where the regulatory system that has until recently been “light touch” is being brought more into line with the regulations for drugs under the jurisdictions of the FDA and the European Medicines Agency (EMA.) This extension of regulatory oversight to new types of product will potentially squeeze out small companies that were previously able to survive with relatively small profit margins but will not be able to generate sufficient profits to support a longer and more expensive development period. However, these areas of innovation will not necessarily be taken up by multinational companies, particularly if the technologies in question would lead to smaller, more segmented markets or even to the disappearance of some lucrative markets for drugs for chronic diseases. Pharmacogenetics is a

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<sup>15</sup> To give a (superficially) simple example, a stem cell scientist needed to be able to measure the oxygen balance within the cells she was culturing. She approached an engineer in a neighbouring department and within 10 days he had developed a nano-device capable of doing what she wanted.

<sup>16</sup> Kautz R., (2007), *Systems Biology and Systems Medicine: presentations by Lee Hood at the Barnett Institute of Chemical and Biological Analysis*. [www.barnett.neu.edu/BInews\\_060301/HoodSummary.htm](http://www.barnett.neu.edu/BInews_060301/HoodSummary.htm), accessed on 07/10/2007

current example of such forces at work, where the commitment of multinational companies to this area of innovation is increasingly muted, compared to the enthusiasm of research scientists and regulators.<sup>17</sup>

Although regulatory inflation has indeed been a feature of the health care area in general, there are some areas where regulatory requirements have been relaxed to encourage companies to satisfy public needs, *e.g.* for treatments for diseases which affect only small numbers of people and which would otherwise not generate a sufficiently large income to cover the costs of development. The introduction of FDA initiatives such as the Orphan Drugs Act, the Fast-Track System and the Critical Path Initiative can be seen as moves away from a “command-and-control” coercive approach towards an approach that facilitates problem solving between policy targets and policy makers.<sup>18</sup> This points to the potential of targeted regulatory change (in the direction of being more enabling and discriminating) to have a significant influence on the number of products developed and the range of innovative approaches to treatments that find their way into development pipelines.

These comments on the need for more targeted and focused approaches to the regulation of health care products should not be taken to imply that the risks attached to health care products are exaggerated and that regulatory reform should automatically mean relaxation of the regulatory burden on companies. However, as outlined in Box 2, changes in the nature of the regulation, from constraining to enabling or from indiscriminate to discriminating, or even in some cases from regulations to standards, can have a powerful impact on the nature of innovative products reaching the market place and on the speed of delivery. It should also become an increasingly important part of the regulatory arsenal to consider biotechnology innovation as an alternative to regulation. For example, potentially self-replicating nano-biotechnology systems that could become part of health care arsenals by 2020 could be regulated by requiring any such product to be controllable through the incorporation of a “self-destruct” mechanism that is activated either automatically or remotely by a specific signal, rather than by using regulation to ban potentially useful developments. Likewise, where there is concern about the potential carcinogenicity of stem cell-based or genetically engineered tissue therapies, the introduction of a “suicide gene” into the cell structure could be considered as an option to guard against this outcome, rather than conducting extensive clinical trials to demonstrate total absence of this risk.

Having operated for some time with the prevailing regulatory systems of the United States and the European Union, China and India are now following these systems in setting up their own regulations, primarily with the aim of ensuring that the products of companies based in these countries will be acceptable to American and European markets as well as to their increasingly significant home markets. The advantages of this policy currently outweigh the disadvantages. However, in future these increasingly powerful components of the bioeconomy may see a competitive advantage in leading regulatory reform so as to encourage more innovative health care sectors to develop, initially for their large and increasingly wealthy home markets, and perhaps also to encourage change in the United States and European regulatory systems.

In addition to regulatory systems, government policies for the promotion of innovation are also highly relevant to the future shape of the bioeconomy. Public funding for basic bioscience in Europe and the United States has been increasing since the 1970s and this trend seems set to continue. In addition, countries in other parts of the world (including newly industrialising countries like China, Korea, Singapore and others such as India, Cuba, and Brazil) are also investing increasingly in biotechnology in order to promote their international competitiveness. Charitable funding of bioscience research has

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<sup>17</sup> See Box 1 and Note 8

<sup>18</sup> Milne C-P., J Tait, L. Cabanilla and J. Wegner (2007), Evolution along the Government-Governance Continuum: impacts of regulation on medicines innovation. (Manuscript in preparation)



also reached unprecedented levels, and organisations such as the Gates Foundation are bringing new modes of operation to the areas where they are investing (AIDS and malaria in developing countries). In parallel with this steadily increasing scale of investment there are signs of mounting frustration over the low success rate in developing useful products from the science funded by governments and charities. This has led to further public funding in areas such as translational research in an attempt to facilitate the path of innovative new products to commercial markets or to application in health services and it could also lead to a new set of voices attempting to influence the course and targets of regulatory change.

At a more general level, variation in the over-arching ethos of national governance approaches contributes to regulatory differences, for example between the United States and the European Union, which have had major implications for the development of the global bioeconomy. By 2012 we may have seen the emergence of an internationally recognised regulatory system for health care products and processes, or at least have a clear indication that it is beginning to emerge. However, it is also possible that current splits will have been reinforced and new splits will have emerged, making the realisation of a global regulatory subsystem even less likely than it is today.

Bezold and Peck<sup>19</sup> have made some detailed predictions about the future of drug regulation as influenced by innovation in biotechnology and information technology and conclude that there will be a continuing need for government regulation of pharmaceuticals, probably led by an international agency, but that this regulation will focus mainly on regulation of the quality of the knowledge base used as evidence for increasingly complex health care decisions. Their paper considers a range of interactions, including new approaches to clinical trials, the rise of combination therapies, empowered and better informed consumers with the right to decide what risks they want to take, and changes in health care delivery (more evidence-based and building on increasingly universal electronic health records). Their paper thus recognises the possibility of dramatic and unilateral regulatory reform, not necessarily carried out in collaboration with the pharmaceutical industry sector, but they do not consider the implications of such reforms for companies, health care providers, other actors and for the functioning of the bioeconomy as a whole.

## **2.3 Health Care Delivery Systems**

As noted above, health care delivery is systemic at the national, but not at the global level, and it may be unduly optimistic to expect these national systems to converge on a global model by 2030. In the developed world, biotechnology-related innovation, and the increasingly costly treatments which have characterised this area so far, are placing strains on the delivery systems of European countries which have a strong element of public provision of health care and also on those of the United States with their focus on privately funded health insurance, but with a large proportion of the population not covered by such provisions. The ideal model for a health care delivery subsystem in a developed economy may turn out to be some combination of publicly and privately-funded provision, but there is no evidence so far of such a convergence. The combined impacts of privatisation of health care systems and personalisation of care are difficult to predict.

The absorptive capacity of the health care delivery system in any country or region is very important for the success or otherwise of the bioeconomy, in that it has so far determined the fate and profitability of innovative technology developed by commercial companies, *i.e.* the size of the market for innovative products. The labour market for health workers is growing and makes up a large percentage of formally employed people (including the movement of labour around the world) as well as a growing proportion of family members who care for those with chronic illnesses and disabilities. The future shape of the health care sector will depend as much on how these professional, commercial

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<sup>19</sup> Bezold C. and J. Peck (2005), Drug Regulation 2056. *Food and Drug Law Journal*, 60(2), pp. 127-136.

and public stakeholders interact with one another and this will have an important impact on the future for biotechnology-related innovation.

There is concern among public funders of research in biotechnology about the fact that many of the resulting innovations fail to deliver any public benefit because of a lack of a commercial route to market. In addition to its role in facilitating drug development and delivery, translational medicine is expected to make an important contribution to public sector research through facilitating the introduction of such innovations directly into public or private health care systems without the need for a conventionally commercial intermediary. The existence of novel market arrangements of this type in future could play an important role in extending the contribution of biotechnology to health care systems beyond the current dominance of the pharmaceutical innovation model.

The faster uptake of biotechnology innovations in health care systems which could be part of the future bioeconomy, by either public or commercial routes to markets, will require the staff in these systems to be more technologically aware and knowledgeable and to be willing to change current systems where this creates an affordable advantage for patients.

The concept of absorptive capacity is relevant to both developed and developing countries but it has been a particular focus for analyses of health care systems in developing countries.<sup>20</sup> Countries like China and India that are attempting to scale up their biotechnology-related industry sector currently have to rely to a large extent on United States and European markets as outlets for their products. If the state of the health services in China and India and their absorptive capacity could be improved, these countries could have more freedom of action in the development of an innovative biotechnology based industry sector that is relatively independent of those of Europe and the United States. Cuba provides an interesting case where the existence of universal health care with good absorptive capacity has enabled a relatively small country to develop a successful independent biotechnology based industry sector.<sup>21</sup>

Future expectations of more direct patient involvement in health care provision, including choice of drug-based treatments, mediated through the Internet or other forms of direct-to-patient communication and advertising could further challenge the roles of national health care delivery systems. There is evidence that this could be as much a factor in, for example, India as it is in Europe or the United States, perhaps helping to move towards greater regional equality in health care delivery.<sup>22</sup>

A current move in the opposite direction is the emergence of regulatory bodies that make decisions on behalf of health care providers on the cost-benefit ratio of new biotechnology-based products and therapies. In the United Kingdom this function is provided by the National Institute for Health and Clinical Excellence (NICE). In terms of the systemic structure outlined for this report such organisations are “boundary crossing”, being based within health care delivery systems, but linking them to the science and industry innovation system, the regulatory system and also to advocacy groups representing the interests of patients.

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<sup>20</sup> ODI (2005), *Scaling up versus Absorptive Capacity: challenges and opportunities for reaching the MGDS in Africa*. London: Overseas Development Institute Briefing Paper, May 2005, ISSN 0140-8682; [www.odi.org.uk](http://www.odi.org.uk)

<sup>21</sup> H. Thorsteinsdottir (2007, in press) The Role of the Health System in Health Biotechnology in Developing Countries. *Technology Assessment and Strategic Management*, 19(5)

<sup>22</sup> This is supported by preliminary findings from a research project based in India, funded by the UK Economic and Social Research Council and the Department for International Development, based in the Centre for International Public Health Policy, University of Edinburgh.

Power structures in health care subsystems are also important factors in the uptake of innovative technology. Many current areas of medical professional expertise will be undermined by future innovative biotechnology developments and they are therefore likely to be resisted unless training and incentives are included in an overall translational medicine package.

## **2.4 Public and Stakeholder Attitudes**

The agro-biotechnology sector has shown how a relatively small number of well-organised advocacy groups, backed up by an enthusiastic press campaign, can have a major impact on the development of innovative technology, in that case, genetically modified crops. These pressures had a direct impact on companies and also on the market for genetically modified (GM) crops, but they primarily acted via policy makers to ensure that the regulatory system in Europe, in contrast to that of the United States, is so onerous as to be inhibitory of innovation even by large multinational companies. Their actions have also greatly reduced public funding for research on GM technology for agriculture.

So far, in the health care sector, pressures from advocacy groups against the development of high-tech approaches to health care such as those involving biotechnology have not been generally influential. Advocacy groups with this perspective that take an active interest in biotechnology in general, and also have explicit interests in health related biotechnology include Genewatch in the United Kingdom,<sup>23</sup> the Council for Responsible Genetics in the United States<sup>24</sup> and the Action Group on Erosion, Technology and Concentration (ETC) in Canada.<sup>25</sup> Campaign issues so far adopted by these groups include genetic databases,<sup>26</sup> genetic testing, synthetic genomics and nano-biotechnology,<sup>27</sup> discrimination through insurance policies, human cloned embryos and stem cell developments for disease treatments. Such groups generally have roots in the GM crops debates but are moving, so far on an opportunistic basis, to campaign on health-related issues.

An important tipping point in the European GM crops debate came with the development of a powerful advocacy coalition linking environmental, consumer and third world groups in a co-ordinated campaign against GM crops. However, so far challenges from advocacy groups with health-related concerns have been balanced by those of patient groups demanding faster development of biotechnology-based cures and treatments for diseases. Nevertheless, an effective coalition promoting an anti-technology campaign in the health care area could be triggered by major unpredicted and/or unregulated problems in new biotechnology-based products, actions by companies or scientists that are considered by the public to be unethical or irresponsible, and/or events that undermine the trust of patient groups in the pharmaceutical industry. A few such events have occurred recently and if many others emerge over the next 5 to 10 years, they could potentially build up in the public framing of biotechnology-based health care until they spill over into serious, co-ordinated well-organised opposition to health-related biotechnology in general.

Such an advocacy coalition<sup>28</sup> could emerge in the form of a system dedicated to opposing biotechnology-based medicine in general with a strategically co-ordinated set of campaigns on individual issues that attract press attention and are likely to further their overall aim. The most important keys to avoiding such an outcome, from the perspective of the bioeconomy as a whole, will be to ensure that the patient advocacy groups continue to be regarded as independent advocates of

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<sup>23</sup> <http://www.genewatch.org/>

<sup>24</sup> <http://www.gene-watch.org/index.html>

<sup>25</sup> <http://www.etcgroup.org/en/> (accessed 070827)

<sup>26</sup> <http://www.privacyinternational.org/article.shtml?cmd%5B347%5D=x-347-540765> (accessed 070827)

<sup>27</sup> [http://www.etcgroup.org/upload\\_publication/602/01/synbioreportweb.pdf](http://www.etcgroup.org/upload_publication/602/01/synbioreportweb.pdf) (accessed 070827)

<sup>28</sup> Sabatier P. and H. Jenkins-Smith, eds. (1993) *Policy Change and Learning: An Advocacy Coalition Approach*. Boulder, Co: Westview, pp. 290.

patient interests, that they are not perceived as having been “captured” by industry interests, and that they continue to see biotechnology-based innovation as being in the interests of their members.

## **2.5 Global Economics**

Global changes by 2030 are likely to increasingly integrate more industrialised advanced developing countries into the dominant health care system as well as to produce new models to solve the public health problems of the very poorest. Key impacts will include: big increases in affluent groups from the South; increased scientific, technological and industrial capabilities and competitiveness of the most industrialised developing countries; and, development of new finance models to solve the worst problems of global diseases of poverty.

An important impact of global economics on health-related biotechnology will arise through increased affluence and discretionary spending, enabling more people to afford expensive health care technologies to prolong life or to improve the quality of life. Particularly important will be the increasing affluence of the much more numerous middle classes in India and China, providing a market for innovative health technologies in these countries.

General globalisation-related trends, for example in international trade, are expected to continue or to increase. However other, more specific aspects of globalisation will also be relevant to the health bioeconomy, including the continuing trend to ever-larger company size in the pharmaceutical sector, along with a greater focus on out-sourcing specific company functions to the most cost-effective locations, and inexorable pressures for ever-increasing profit margins. Companies and subsidiaries in India, China and the top ten developing countries will be partners of choice in certain health care niches, both for the production of health therapies, and in the institutions that may emerge.

In the context of profit margins, numerous analysts have pointed to the relatively low profit margins associated with biotechnology’s contribution to the health economy.<sup>29</sup>.. This will continue to be a source of tension for the development of the bioeconomy and is already leading, for example, to innovative financing models for drug development in future, for example royalty streams, clinical research organisation (CRO) -linked financing and collaborative development financing.<sup>30</sup>

Public private partnerships (PPPs), often involving major charitable organisations such as the Gates Foundation, are another increasingly influential approach to supporting biotechnology-related initiatives that are unlikely to be funded through venture capital or multinational company investment. At present, the main focus of attention is the development of new models for the top “neglected” diseases of poverty. However, if public-private models are developed successfully, they could become a more general feature in the translation of new products and processes into therapies and well-being. In the future globalised economy, large companies in India and China are likely to become competitive with, and comparable in size to, European and American multinationals well before 2030.<sup>31</sup> Increasingly they will achieve this on the basis of innovative performance as their cost-of-labour advantage will probably not extend much beyond 2015. Per capita incomes in general are expected to increase in these countries by 3.1% per annum and the rate of increase is likely to be greater in the professional classes most involved in the bioeconomy.

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<sup>29</sup> Pisano G.P., (2006), Can Science be a Business? Lessons from Biotech. *Harvard Business Review*, October 2006, [www.hbr.org](http://www.hbr.org) (accessed 7<sup>th</sup> December 2006).

<sup>30</sup> Kessel M. and Frank, F. (2007), A better prescription for drug development financing. *Nature Biotechnology*, 25(8), pp. 859-866.

<sup>31</sup> Wield D., J. Chataway and D. Kale (2007), “Frameworks for Pharmaceutical Innovation in Developing Countries: the Indian Case”, Special Issue *Technology Assessment and Strategic Management*, 19 (5).

## 2.6 Demography and Human Resources

World population is expected to continue to increase up to 2030, mainly in developing countries, with slow or even declining growth in the more advanced economies. The steadily increasing life expectancy in all countries is largely related to improved health care, although AIDS-related infections could reverse this trend in some countries that are not able to implement effective treatment regimes. Currently unknown diseases that are expected to emerge in future could have similar impacts on life expectancy to that of AIDS today.

In all countries these larger populations are also expected to be better educated, resulting in more discriminating consumers of health-related technologies and also more skilled workforces.

## 2.7 Climate Change

An important direct impact of climate change on health care systems is likely to be through encouraging the emergence of new diseases or the spread of existing diseases to new areas. New diseases can emerge as zoonoses where people come into contact with animal disease hosts to which they have not previously been exposed, or diseases can spread to new areas through movement of insect vectors in response to warmer or wetter climates. Where climate change leads to water shortages and crop failures, the movement of large numbers of people as refugees can increase the incidence of life-threatening diseases and spread them to new areas, in addition to the impacts of such changes on the economy in general.

A race is being perceived by health policy makers between disease development and the development of biotechnology-based solutions to these problems, which is providing a major spur to innovation in diagnostic technology, antibiotics and vaccines.<sup>32</sup>

## 2.8 Security

National security considerations are most likely to impact on the health bioeconomy through increased investment in infectious disease detection, prevention and treatment, stimulated by expectations of terrorist attacks. Such investments in the next ten years will begin to deliver successful technological innovations by 2015.

Security issues may also lead to international imbalances in regulatory approaches, making it more difficult to harmonise regulations to create an equitable innovation environment. There are indications that researchers and policy makers in the United States are more concerned about the security implications of synthetic genomics than are similar groups in Europe, although this situation could change rapidly at any time over the next ten years. The extent of regulation in the name of security will be an important driver of this and other areas of biotechnology innovation, as will the nature of that regulation – some forms of regulation will be more inhibitory than others. To give an example from synthetic genomics, because of the security implications, it is unlikely that light-touch or self regulation, as is being advocated by many of those involved in this area, will be the chosen pattern of regulation. A regulatory system driven by homeland security considerations may inhibit many potential health care benefits (*e.g.* the ability to synthesise new complex drug molecules more cheaply or the ability to develop vaccines and antibiotics targeted to new diseases more rapidly). So far the European Union position on the regulation of synthetic genomics is more focused on product safety

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<sup>32</sup> Brownlie J., C. Peckham, J. Waage, M. Woolhouse, C. Lyall, L. Meagher, J. Tait, M. Baylis, A. Nicoll, (2006), *Foresight. Infectious Diseases: Preparing for the Future. Future Threats*. Office of Science and Innovation, London.  
[http://www.foresight.gov.uk/Previous Projects/Detection and Identification of Infectious Diseases/Reports and Publications/Final Reports/T/t1.pdf](http://www.foresight.gov.uk/Previous%20Projects/Detection%20and%20Identification%20of%20Infectious%20Diseases/Reports%20and%20Publications/Final%20Reports/T/t1.pdf) (accessed 061106)

regulation rather than homeland security, but even here there is no guarantee that the regulatory system chosen will avoid unnecessary inhibition of innovation (See Box 2).

Restrictions on the flow of information in the interests of security could be just as potentially inhibiting of innovation in biotechnology as are regulatory initiatives.

## **2.9 Developments in Animal Health Drivers and their Interactions with Human Health Care Systems.**

Box 3 outlines some potential biotechnology-related drivers of animal health, the implications of these developments for animal health itself and, where relevant, the interactions with, and impacts on, human health care systems. Commercial activity in this area is currently approximately 3% of that related to human health, but some biotechnology related developments in animal health care and also the development of new diseases in animals and their potential transmission to humans could result in a much increased emphasis on animal health care per se and also its interaction with human health care systems.

## **3. Health Care Scenarios: Interactions among Drivers in Determining the Rate and Direction of Change in the Health Related Bioeconomy.**

Closely coupled interacting systems like the health care sector with its intimate inter-twining of companies, markets and regulatory systems can be very robust and resistant to change. However, when change does come it can take place dramatically and surprisingly rapidly if it happens unexpectedly, particularly if changes occur simultaneously, within companies, in markets and in regulatory systems.<sup>33</sup> The pressures for change are indeed building up in all three areas, but for the moment they are aligned in different directions, in many cases so as to inhibit technological innovation in some key areas and also to restrain the development of some new markets.

Large pharmaceutical companies are currently the dominant players in the bioeconomy, although not in areas of health care delivery that do not relate to biotechnology. However, the overall sustainability of this dominance is increasingly being called into question.<sup>34</sup> The scenarios developed for this report presume that this instability will continue to be problematic beyond 2015 and that between then and 2030 we will see either a continuation of the current mixed and somewhat dysfunctional “muddling through” or a “rapid change” involving a managed transition in the health-related bioeconomy.

These scenarios are a tool to achieve the project goals – to maximise the desirable features of the bioeconomy and to minimise negative outcomes or missed technological opportunities. Previous research has shown that perceptions of desirability in outcomes can vary across different constituencies – what is seen as desirable from the point of view of actors involved in health care delivery may be different from the perceptions of managers in large multinational companies and this will differ again from the perceptions of managers in SMEs, and so on. These variations in perceptions among key actors in the scenarios, and how they are translated into future behaviours will have important impacts on the eventual smoothness of the transitions envisaged.

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<sup>33</sup> See Note 8.

<sup>34</sup> See for example the latest in a long series of similar articles in Nature Journals: Anon (2007) “Time for a Medical: the pharmaceutical industry is struggling to adapt to a harsher political environment” *Nature*, 447, pp. 507-8.

Attempting to predict future technology, policy and other developments and their influence on complex systems is a highly uncertain exercise beyond the timescale of a few years. Many of the trends and bottlenecks which will determine the future of the health-related bioeconomy are evident today, but there will be others which we cannot predict. In addition, as noted at the beginning of Section 2, interactions among drivers will determine the future of the bioeconomy and it is unlikely that any single factor will have a dominant influence. It is also important to consider the timing of emergence of changes in drivers – changes that occur simultaneously can have a powerful mutually reinforcing effect or alternatively could cancel one another out; likewise changes that are separated by a period of years can build one on the other in a synergistic manner or alternatively the time lapse may mean that the opportunity for an impact has been missed.

The following scenarios explore possible directions for change up to 2030 and the influence of these changes on the bioeconomy as a whole. The nature, extent and rapidity of change in the health-related bioeconomy will depend on all the drivers outlined above, and also on:

- new technological developments, how they interact with one another and with prevailing health care systems;
- the regulatory systems that evolve to ensure safety, quality and efficacy of new developments; and
- the responses of markets, consumers, key actors in a range of settings, and health care related advocacy groups.

The first scenario, *Muddling Through*, assumes that tensions among key actors are exacerbated by narrowly focused thinking and insufficient attention to the tensions and interactions in the system as a whole, leading to an outcome which is different from that of today but is also sub-optimal and locally dysfunctional. The second scenario, *Rapid Change*, assumes that the key actors in the system are able to reach a broad, common understanding of the factors driving change and of the range of options open to them, and collaborate in ensuring a transition to a new health-related bioeconomy which is radically different from that of today.

To facilitate thinking about these future events, the scenarios are presented first from the perspectives of the three key systems outlined in the introduction: the global science and industry innovation system; policy and regulatory systems; and national health care delivery systems; along with key stakeholder and advocacy groups which may in future become systemically organised. Finally the scenarios consider how interactions among these groups will determine the eventual outcomes for the future of the bioeconomy.

## **4. Health Care Scenario – “Muddling Through”**

### **4.1 Introduction**

This section describes the outcome in 2030 for a health care sector which, as seems most likely today, remains dominated by highly competitive actors seeking to maximise the short term advantages to their own organisations arising from biotechnology-based innovation. In normal circumstances these are admirable survival tactics for commercial companies. However, they are not conducive to radical, systemic change. And the failure to take up opportunities for radical change when the timing is ripe is likely to mean that, when the inevitable change does take place, it is more disruptive for all concerned than it would otherwise have been.

By 2015, this scenario envisages a health care innovation sector that has managed to avoid serious or major disruption and is even more dominated than today by a much reduced set of very large, globally significant multinational companies.



It is also characterised by a range of features that suggest a potentially failing set of organisations:

- there are continually increasing difficulties in finding innovative products to fill product development pipelines;
- there is a lack of funding for new technology;
- the sector consists increasingly of pharmaceutical commodity producers with a diminished R&D component in company strategies;
- there have been numerous missed technology-based opportunities and there is dysfunctional competition between and within companies;
- company relationships with regulators tend to be adversarial rather than collaborative; and
- legal actions by health care providers and patients against companies and regulators are increasing in number and in cost.

Many people within companies and regulatory agencies had seen the need for change, but none of these was in senior enough positions for long enough to make a difference - many were made redundant or side-lined because they had promoted initiatives that were not seen as being in the interests of their organisation.

Despite the failure to initiate major systemic change, there had been many small and even relatively large initiatives that were moderately successful locally. However, these were one-off developments, not followed up and not globally integrated and so did not achieve their full potential benefit. Local fiefdoms, nationally, within and between companies and among regulators, had prevented such potentially useful developments from having a wider influence.

To take stem cell technologies as an example, early expectations in Europe and the United States for stem cell based therapies and even cures for major diseases had not materialised. The slow progress towards the development of successful therapies, combined with low returns from the relatively small markets for these products, had seriously inhibited public and private investment. On the other hand, the use of stem cells to facilitate drug development had become the dominant innovation mode for this biotechnology, given that companies and venture capitalists were willing to invest in that area. Technological difficulties in developing therapies had contributed to this change of emphasis, but the major influencing factor was the increasingly lengthy and stringent regulatory system that was built up from 2007 in these countries for stem cell-based therapies.

By 2015, Chinese and Indian pharmaceutical companies had grown along with their home markets and had continued to penetrate United States and European markets for commodity products. This was particularly the case for Chinese companies, given that China had been much more successful than India in developing a widely available, publicly funded health care delivery system. However, even by 2015, the pharmaceutical industries in these countries had not been able to develop sufficiently robust R&D pipelines to cover the costs of failed products and to overcome the hurdles controlling entry to R&D based drug development in these markets. Given that Chinese and Indian regulators had continued to follow the Western regulatory models of the EMEA and FDA, and that their cost of labour advantage had been considerably eroded by that time, pharmaceutical companies in these countries had little comparative advantage over companies based in Europe and the United States and some of the key companies were now owned by European and United States companies.

Unlike pharmaceuticals, in the case of stem cell based therapies, China had developed a much more permissive regulatory system than those of the European Union and the United States. Since the risks that had been predicted for these therapies (*e.g.* cancer and zoonotic disease transmission [arising from the use of animal products in the early stages of stem cell development]) did not emerge with these more permissive regimes, this had been greatly to the advantage of the Chinese. China also maintained



a very generous level of public investment in the science, with the result that such therapies were widely and affordably available in China and there was a flourishing health tourism sector.

These two examples, pharmaceuticals and stem cells were characteristic of the health related bioeconomy by 2015. The pharmaceutical sector, globally, remained resistant to fundamental change, with a continuation of current trends towards increased costs of drug development along with a declining rate of emergence of new approved products. This situation was reinforced by the increasingly global reach, and unreformed nature of the regulatory systems that were dominated by the FDA and EMEA. Likewise, for stem cells and other non-drug related developments, the European Union and the United States continued to place increasingly onerous regulatory hurdles in the path of innovative therapies, following the earlier pattern for pharmaceuticals. However, the emerging economies of the world in China, India and South America had developed their own approach to regulation and as a result had much more flourishing sectors in these niche areas.

This section explores the outcomes from 2015 to 2030 for a health care sector that has remained resistant to change, and dominated by the pharmaceutical sector, at least in Europe and the United States.

## ***4.2 Science and Industry Innovation Systems – resistance to change***

### **4.2.1 The economic context**

From 2015 the product portfolios of European and American multinational companies became increasingly reliant on commodity products. R&D based activity continued, and high value-added products were still developed for relatively smaller but high value markets. However, the high cost of meeting regulatory requirements meant that the price of each product was still high enough to severely limit the number of such markets that were viable.

These circumstances applied equally to Indian and Chinese pharmaceutical companies so that they were also not able to progress to become R&D-based companies producing high value-added products as had once been their ambition. The large populations of these countries, the emergence of a large middle class sector and the increasing availability of public sector health care for the poor did give Indian and Chinese companies some competitive advantage in their development of commodity drugs, but were not sufficient to create more than a small number of viable markets for patented products. The very large size of the markets in these countries did give some competitive advantage to locally based companies, but they were still subject to competition from United States and European companies and, despite progress in both publicly and privately funded health care provision, limitations on willingness and ability to pay were still a major constraining factor.

The availability of venture capital funding for SMEs from 2015 continued the declining trend that had been apparent since the beginning of the century. There was increasing competition from more lucrative, less long term and less uncertain investment opportunities. Also, data on the relatively poor historic performance of investment in life sciences was being increasingly widely emphasised<sup>35</sup> and confidence in the sector was being eroded. There were thus fewer SMEs contributing to drug development, resulting in an increasingly impoverished innovation environment.

This trend continued despite the increase in public sector investment in translational medicine that had been intended to bridge the venture capital (VC) funding gap. Public sector investment in translational medicine for products other than pharmaceuticals, had been relatively successful. However, attempts

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<sup>35</sup> See note 29, Pisano, 2006.

to use public funding to take pharmaceutical products further along the development path where they would then be taken up by the commercial sector had been largely unsuccessful.

#### **4.2.2 The industry structure**

The trend to outsource early stage R&D activities that had begun in the 1990s also continued unabated through 2015 so that the primary expectations of any new SME in this sector were unchanged – success for them would constitute licensing out viable products to a multinational company or being taken over by it. However this increasing reliance of pharmaceutical companies on external sources of innovative products coincided, as noted in the previous paragraph, with a reduction in the number of available SMEs, leaving the multinationals increasingly short of new innovative products to take to the market.

By around 2020, this situation was leading multinationals to begin to re-invest in in-house R&D divisions and also to invest externally in earlier stage research within SMEs, but this is a long term strategy under any circumstances and it becomes increasingly difficult when funding is constrained. By 2030, the trend to ever-increasing costs of R&D, combined with reduced numbers of new products appearing on the market and lower profit margins was still continuing. During the period 2015 to 2030, following a trend that had first become apparent in agro-biotechnology companies in the early 2000s, several of the major pharmaceutical companies stopped conducting R&D for new drug development and became producers of commodity chemicals, alongside the relatively new commodity-based, generic pharmaceutical companies.

This highly competitive, operating environment for the pharmaceutical industry also accelerated the trend in acquisitions and mergers.<sup>36</sup> There were fewer large multinational companies but the potential increase in size of the merged companies was offset by the persistent erosion of profit margins and regular downsizing of the merged companies.

Up till around 2010 an important component of the pharmaceutical sector had been the middle-sized pharmaceutical companies. Although multinational, they focused on a narrower range of products than the large multinationals, often concentrating exclusively on, for example, cancer therapies, vaccines or central nervous system treatments. Given their structure and innovation models, these companies would have been able to cope more effectively than large multinationals with the smaller, niche markets that were becoming the most common outlet for the sector. However, beyond 2010, almost all of these companies had been taken over by multinationals, in some cases in competitive financial deals which were described at the time as extravagant.

#### **4.2.3 The role of innovative technologies**

By 2015, several innovative technologies were indeed contributing on a routine basis to drug development. As noted in Section 1, biotechnology continued to have a similar role to that observed in the 1990s and 2000s, where it enabled the multinational pharmaceutical companies to remain profitable (and unassailable by alternative approaches) on the basis of an innovation model that was widely seen as fundamentally flawed.

The time to market from initial discovery was reduced to an average of around ten years and the number of molecules rejected in later stage clinical trials declined and this offset to some extent the continuing challenges to the viability of the pharmaceutical sector through to 2030. However, it was not alone sufficient to free up the sectoral innovation system in a manner

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<sup>36</sup> See note 2, Mittra, 2007.

which was truly path-breaking, as described in the second scenario. Several technologies contributed to drug development in this way:

- synthetic genomics contributed to the affordable manufacture of complex drug molecules, meaning that some drugs which would otherwise have been rejected from pipelines because they were too expensive or difficult to manufacture were taken through to market approval;
- synthetic genomics also contributed to the more rapid development of effective vaccines, enabling companies to respond to public sector demands for effective treatments for new and emerging diseases;
- pathway and systems biology enabled the more rapid and accurate identification of druggable targets;
- stem cell technology was used to identify at an early stage molecules that were likely to give rise to toxicity problems or to be less effective than expected if used as therapies, resulting in fewer rejected products during clinical trials;
- the use of biomarkers at the cellular level also enabled better identification of effective and safe products in advance of the setting up of clinical trials.

Pharmacogenetics is not included in this list. By 2015 and beyond, it was still the subject of protracted negotiations and discussions between drug companies and regulators. The companies were concerned about the ability of this technology to reduce the size of their markets below what would be viable for a large multinational, and increasingly (for the reasons outlined above in this section) their views were not challenged by companies with an alternative perspective.

#### **4.2.4 Interactions with regulatory systems**

Up to 2015, there had been signs of a change in the mind set of regulators to recognise the co-dependency between regulators and the drug industry and to attempt to be initiators of change, rather than merely regulators of drugs.<sup>37</sup> However, the visionary regulators willing to contemplate such a change were relatively few in number and the resistance of the large multinationals to such changes was able to limit their effectiveness.

Regulatory systems for new drugs thus remained reactive to technological innovation, rather than collaborating with the science and industry innovation system as a whole in the faster and more effective delivery of public benefits from new drugs. In Europe and the United States, the pace and scale of development of non-drug based innovations was also affected by the rigidity of the regulatory systems. For example tissue-based therapies and diagnostics that had previously been relatively lightly regulated had been subject to new regulatory approaches that were similar to those applied to drugs (see Box 2). The outcome of these moves was that no small company could afford to take a diagnostic or tissue therapy based product through all stages of the regulatory system. In most cases these products also did not fit with the strategies of multinational companies (see Box 1) and so were not developed. Thus many potentially innovative areas of scientific development which had received considerable support from public funding were not developed for health care markets.

However, for these diagnostic products and tissue-based therapies, as noted above, India and China did not follow the Western regulatory path, and these countries became global leaders in the development of these technologies, profiting greatly from health tourism.

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<sup>37</sup> See note 10, Robert Powell, 2007.

Several large public/private partnerships (PPPs) had been developed before 2015 with the intention of enabling drug development for poorer countries and neglected diseases, *e.g.* the Gates/Buffer/Clinton initiatives, together with major financing tools such as the International Financing Mechanism for Innovation in Medicines. These initiatives did create some momentum but the investment was also much less productive than it might have been because of continued restrictions on developments arising from regulatory constraints, the lack of venture capital investment in other areas of medical innovation, and the relatively impoverished innovation environment surrounding the multinational drug companies.

### **4.3 The Regulatory System**

The vital role played by regulators and insurers either in enabling or in blocking the development of highly innovative products in life sciences is clear in this scenario. Regulatory agencies played an increasingly important role in the evolution of the pharmaceutical industry from the 1960s, particularly in acting as a barrier to entry for new potential entrants to the sector, in addition to their primary aim of safeguarding the safety, quality and efficacy of new products. The parallel role of regulators in enabling the relatively unconstrained build-up of these very large and highly profitable multinational companies had been, until around 2000, beneficial for society as well as for the industry. It had allowed the development of block-buster drug markets and generated the revenue for further investment in health care R&D on a scale that could never have been supported by public funds.<sup>38</sup>

However, beyond 2000, it became increasingly clear that the dominant regulatory systems in the United States and European Union, were beginning to inhibit innovation, particularly in the new biotechnology-based sciences, and at the same time were failing to ensure that products which were approved for marketing were not subsequently subject to costly withdrawals or, worse, expensive litigation. This situation prevailed well beyond 2015 because of the simplistic assumption by all concerned that the only way to prevent post-marketing drug withdrawals and all the attendant costs to a company and its insurers was to increase the stringency of regulation. As suggested in the next scenario, a more imaginative and free-thinking approach to regulation, alongside a more positive approach to some kinds of innovation, could free up drug development processes while maintaining acceptable levels of safety.

In this scenario, as noted in section 4.2.4, regulators had begun to think about regulatory reform well before 2015. However, expected benefits arising from pharmacogenetics or personalised healthcare had been slow to emerge, partly because large multinational companies had influenced regulatory agencies to ensure that any changes to facilitate the passage of products based on pharmacogenetics remained voluntary. This was part of a general pattern where regulatory reform was not given a high profile in regulatory agencies, the staff assigned to the task were constantly moved to other projects, and the whole process continued to be undermined by the opposition of influential senior managers in pharmaceutical companies who were aware of the potential impact of a less stringent regulatory system on their company's competitive position (see second scenario).

This relative rigidity in regulatory agencies was a classic case of reluctance or inability to see the opportunities that were being presented to those that were able and willing to embrace systemic change, to become part of the new, more collaborative global innovation environment, and to work with new partners to stimulate innovation. Embarking on such a route presented career risks to those in senior positions, another important factor discouraging change.

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<sup>38</sup> See note 8

In this scenario, the regulatory agencies were thus unwilling to take the lead in reforming health care innovation systems, perhaps reinforced by a desire to extend their power so that they become the automatic regulators of choice for any innovative product in the health care sector. By 2015 they had reached a position where, at least for Western nations, all new regulations for innovative products in life sciences were built on the now-reinforced precedent of the drugs regulatory system with its extended and expensive series of clinical trials. The result was that only products and processes that fitted with and reinforced the drugs-based profit-model of the pharmaceutical companies could be developed, and those SMEs that remained active in the sector, as at present, saw no alternative future other than delivering services, or selling intellectual property (IP), to multinationals.

#### **Box 2 - Regulatory Systems and their Impacts on Innovation<sup>39</sup>**

To say that regulation has an important impact on the kinds of product that are developed by an industry sector is a statement of the obvious. In the pharmaceutical industry for example, regulation is designed to ensure that products for the treatment of diseases are safe, effective and of high quality. However, regulatory systems can, by a series of incremental changes over a long period, become increasingly dysfunctional and out of step with innovation in the technologies they regulate. Also, as a regulatory system builds up in this way it becomes increasingly complex and a change or addition to one set of regulations can have unpredicted implications, for example for new products in development or for companies outside the range of the regulations themselves.

Two different types of interaction between regulation and innovation, at the macro and the micro levels are particularly relevant to the health bioeconomy.

##### ***Impact of regulation on the structure of the pharmaceutical industry***

The lengthy and demanding nature of the regulatory system as a whole, as it has been applied to the pharmaceutical industry, has been a major contributor to the overall shape of the sector itself, including the so far unchallengeable dominance of the multinational companies. The very high costs and long delays entailed in taking a new product through the regulatory system ensure that only large MNCs have the necessary resources to operate throughout the whole innovation cycle. This barrier to entry for small companies has shaped the structure of the industry sector, leaving the MNCs in an unassailable position and insulating them from challenges to their supremacy by smaller innovative companies with a high growth potential. Small companies either rely on MNCs to take their products through to market, or alternatively they need to make themselves an attractive acquisition target, which in both cases means that they tailor their innovation strategies to match, rather than to challenge, those of MNCs.

Scientific discoveries in biotechnology have begun to lead to new types of products, such as stem cell-based therapies, for which there is no clear regulatory precedent and the typical response in such cases is to look for a pre-existing regulatory framework into which the new type of product can be fitted. An alternative option in such cases would be to design a new regulatory framework tailored to the specific needs of the new technology. However, the most notable precedent for this approach, the

<sup>39</sup> This summary paper is based on a series of research projects carried out by Joyce Tait, Joanna Chataway and David Wield, beginning in the 1980s. The most recent papers based on this research are:

Tait J. (2007), Systemic Interactions in Life Science Innovation. *Technology Analysis and Strategic Management*, 19(3), pp. 257-277, May 2007.

Tait J. and C. Chataway (2007), The Governance of Corporations, technological change and risk: Examining industrial perspectives on the development of genetically modified crops. *Environment and Planning – C: Government and Policy*, 25, pp. 21-37.

Chataway J., J. Tait and D. Wield (2006), The governance of agro- and pharmaceutical biotechnology innovation: public policy and industrial strategy. *Technology Analysis and Strategic Management*, 18(2), pp. 1-17.

Milne C-P., J. Tait, L. Cabanilla, J. Wegner (2007), Evolution along the Government-Governance Continuum: impacts of regulation on medicines innovation. (Manuscript in preparation)

regulatory system adopted for GM crops in Europe, is unlikely to spawn imitators in other technology areas. FDA and EMEA seem increasingly likely to take on the role of overarching regulatory bodies for health care-related governance.

Because of their influence on the power balance between MNCs and other companies in the health care sector this gives these regulatory agencies a particularly important place in shaping the health care industry sector (or sectors) of the future, whether through major structural reforms of the regulatory system or through more targeted approaches to particular technologies.

#### ***Impact of specific types of regulation on products and companies - pesticides***

In our research on agro-biotechnology, we were able to identify specific pesticide regulatory initiatives that had had either positive or negative impacts on innovation processes and which could form a useful starting point for thinking about similar issues in developments related to pharmaceuticals. We distinguished among regulatory instruments on the basis of whether (i) they were perceived as ***enabling*** or ***constraining*** by industry managers and (ii) whether they were ***indiscriminate*** or ***discriminating*** among products (or in some cases whether they discriminate on a basis which is inappropriate to the overall policy aim). Two examples can be used to illustrate these distinctions.

##### ***Enabling and discriminating regulation.***

The US Food Quality Protection Act (FQPA) 1996 offered a “fast track” approach to regulation for pesticides that could demonstrate a better health or environmental safety profile than products currently on the market. This selectively enabled some companies with societally desirable products to gain an advantage over others and rapidly began to change the behaviour of some companies in the agro-biotechnology sector. Some managers described a situation where the large number of candidate products with these desirable properties was making it difficult to register a pesticide without these benefits in an economically viable time scale. Our industry interviewees thus saw this legislation *enabling* them to compete more effectively to get certain products through to the market place faster, by *discriminating* in favour of such products. Of course it was not enabling for companies that did not have such products in their pipelines, although it would stimulate them to move their R&D in this direction in the longer run.

##### ***Constraining and indiscriminate regulation.***

In contrast to the FQPA the European Drinking Water Directive (80/778/EEC), at the time of our research, set a low limit on the permitted level of contamination of drinking water by pesticides with no discrimination among pesticides related to environmental damage or toxicity to people. As a result, agrochemical company screening systems would automatically reject a chemical with a likelihood of appearing in drinking water, *e.g.* because of its mobility in soils. In our categorisation, this legislation was thus *indiscriminate* and acted as a *constraint* rather than a positive incentive as in the FQPA.

Zeneca Agrochemicals gave an example of how these two regulatory instruments operated in practice. One of their strobilurin fungicides, widely regarded as very safe products from both health and environmental points of view, was the first product to be registered under the FQPA fast track system, but this class of chemicals narrowly escaped being rejected from the pesticide pipeline at an early stage because of their mobility in soils and hence the risk of falling foul of the EC Drinking Water Directive.

The general lessons that we drew from our pesticide-based research included the following:

- Some regulatory initiatives can have major, rapid and positive influences on innovation processes and it is more to learn more about how knowledge of such influences can be used constructively to help design or re-design the regulatory systems of the future.
- Regulations appropriate to one policy area often have unexpected negative impacts when applied in other areas, particularly when regulators are not aware of potentially useful but vulnerable new products and processes under development.
- A regulatory policy which *enables* positive change in industry and that *discriminates* among products on the basis of societally relevant criteria, is likely to be more effective and efficient than one which is *indiscriminate* and attempts to *constrain* undesirable behaviour.
- The *enabling* criterion will affect the speed with which a particular regulatory policy is able to

exert its influence, while the extent and appropriateness of its *discrimination* among products or processes will determine its effectiveness in guiding product development in particular directions.

***Impact of specific types of regulation on products and companies – health care***

In the pharmaceuticals sector, some initiatives have discriminated among particular products with the intention of enabling innovation in particular directions, for example the US FDA Fast Track and the Orphan Drugs Act but, as in agrochemicals, such changes are rare. The general pattern in these sectors has been one of gradual accretion of regulatory constraints on the development of innovative products for health care and hence reinforcement of the current pharmaceutical innovation model.

Two particularly challenging areas, in the policy sense, are the development of regulatory systems tailored to the needs of pharmacogenetics-based innovation, and the development of stem cell based therapeutic products (ignoring for the moment the use of stem cells to support pharmaceutical R&D) (see Box 1). Both these areas are currently the subject of regulatory as well as technological innovation, and the outcome could be an opening up of many new innovative opportunities for SMEs.

To support innovation in these areas of the health bioeconomy an agency could usefully focus on the extent to which a proposed regulatory approach is able to *discriminate* between different types of product and the appropriateness of this discrimination. For example, the more a regulatory process for stem cell-based therapies is able to recognise the distinctions between them and pharmaceutical products, and to tailor the regulatory instruments to their specific needs, the more this will stimulate their development by new or existing tissue engineering companies.

## **4.4 Health Care Delivery Systems**

There was considerable demand in health care systems and among individual patients for the promised benefits from the “life science revolution” and absorptive capacity had indeed been built up in most industrialised countries in expectation that this would begin to be significant after 2010. However, given the numerous failures of the research and innovation communities to deliver on extravagant promises, disillusionment had become widespread. Public and charitable funding of basic science and of early stage translational medicine began to be withdrawn from such areas in favour of approaches to health care that were more based on personal fitness and diet. This coincided with an increasingly vocal campaign from advocacy groups that now felt they could achieve public and press support for their long-held views that investment in the expensive, high-tech bioeconomy was an inappropriate use of public money.

New biotechnology-based, non-pharmaceutical, developments for health care were being marketed to wealthy patients who could afford to pay for them, often by travelling to India or China to receive treatments. However, there was a vicious cycle of interactions whereby the high cost of innovative developments limited the market to small numbers of wealthy patients; while the small markets for such products did not provide sufficient profits to fund the next generation of innovative products, resulting in an overall slowing down of the innovation cycle.

There were many local and regional initiatives, often involving collaboration with life science and ICT based companies, and including significant venture capital investment, that were reasonably successful. However there was no clear route to capitalise more generally on such initiatives, no long term build-up from a series of small initiatives to something bigger and most such initiatives failed to become part of anything resembling a “new bioeconomy trajectory”.

This situation caused resentment in the majority of patients in wealthy countries for whom such products were not available. In poorer parts of the world, financial constraints in the science and innovation sector meant that research and development on the promised products for neglected diseases were severely cut back. It had become clear that the charities and PPPs working in this area did not have the skills themselves to bring new products to market, the large pharmaceutical

companies lost interest in such products as their profits were ever more tightly squeezed beyond 2015, and the smaller companies (SMEs and middle-sized pharmaceutical companies) with whom they might have collaborated in such a venture had largely been bought out by the large MNCs. The feeling became widespread among Third World health care specialists that the enormous investment from charitable bodies in solving the healthcare problems of the poorer groups in society had had disappointing results and that this was partially due to failure of co-operation from multinational drug companies.

Direct-to-consumer (DTC) advertising and sales of drugs and other health care products had become much more widespread and had greatly increased sales of, and profits from, commodity drugs with corresponding advantages to generic producers. However, the outcomes of DTC sales had been more mixed for patented products, further limiting the funding available for future R&D. DTC sales had also increased the problem of counterfeit drugs, particularly for the more expensive patented products, damaging the industry's reputation.

As noted above, lack of regulatory change had meant that personalised healthcare did not deliver on its initial promise and this also set in place a pessimistic pattern of expectations of benefits from the bioeconomy in health care systems in general.

The continuing high cost of patented products that is an inevitable outcome of this scenario strengthened the hand of healthcare based regulators (such as NICE in the United Kingdom), leading to continuing refusals to accept new, expensive treatments for patients in publicly funded health services. However, this trend was not restricted to publicly funded areas – private health care systems, including those in the United States, also increasingly began to ration health care options for their patients. As a result, relations between health care providers and companies developing innovative products became increasingly acrimonious.

## **4.5 Stakeholders and Advocacy Groups**

Interactions between patient groups, pharmaceutical companies and other health technology providers had generally been mutually helpful and constructive up to 2015. However, the patient groups began to distance themselves from commercial companies as they were increasingly accused of being manipulated by them, and these moves were reinforced by the increasing tendency of companies, as they came under pressure from a wide range of sources, to assume uncritically that their interests coincided with those of patient groups. It is a common feature of companies under stress from an increasingly complex set of sources that they lose the ability to identify, to support, and to work with their friends, while responding in an increasingly *ad hoc* way to the pressures they face. They are too busy responding in to each challenge as it arises to be able to develop a systemic approach to the company's future.

In this scenario, "Third World" advocacy organisations, including many powerful NGOs and charities that campaigned on behalf of poor people with inadequate diets and water supplies, and little access to medicines, also became increasingly influential. Their campaign message was that, despite the promises given, biotechnology had failed to deliver any benefits for the poor people of the world.

Thus the general impression among governments and members of the public that listened to these groups was that biotechnology based innovation had failed to deliver benefits to the poor of the world and had severely fallen down on its promises to deliver benefits to the wealthy. Both sets of stakeholders became increasingly strident in their demands; they mounted very effective media campaigns, were openly critical of the pharmaceutical industry and took every opportunity to expose what they felt was unacceptable behaviour.



Patient groups wanted reform of the health care delivery system as a whole – they realised it was seriously dysfunctional but they had no clear ideas on what needed to be done. They were not against biotechnology-based innovation for health care but they wanted to see it developed through a system was more innovative and that could deliver benefits more rapidly and more cost effectively to wider groups of patients than the system prevailing in this scenario.

Many of the Third World NGOs had an agenda that was similar to the patient groups, but some were much more radical and questioned the need for, and the benefits of, continual improvements in health care through biotechnology-based innovation.

Despite the divergence in their long term aims, these two sets of advocacy groups formed a coalition in 2020 to lobby for change. The groups were very clear about what they were against, mainly the pharmaceutical industry. They were much less clear about what they were in favour of and if they had explored this in detail they would probably have disagreed about their aims. The focus was entirely on the pharmaceutical industry as being in need of reform with no parallel recognition of the need for reform in regulatory agencies. The stakeholder and advocacy groups thus became very much a “loose cannon” in the health care sector.

## ***4.6 Interactions and their Timing***

The relative failure of biotechnology to contribute to the health related bioeconomy in this scenario arose from one or two unfortunate gaps or missed opportunities in timing of initiatives, and differences in the stand taken by key influential individuals in the regulatory and industry sectors at different times. Since well before 2012 small groups of people in companies and in regulatory agencies had been thinking about reform of their own organisations, often coming up with novel and radical ideas for change, none of which were implemented before the group concerned was broken up. Small think tanks were set up, influential articles were written in the business press, keynote speeches were given at major conferences but there was no overarching vision to which these individual initiatives could contribute. Despite the clearly recognised need for such a vision, no influential individuals or groups were able to get the right combination of expertise and influence around the table at the same time and to orchestrate the development of a vision which was attractive to enough of the major players to take off.

The pressure for change had not gone by 2030. Indeed it had been increasingly steadily since 2015. However, unlike other areas of the bioeconomy, healthcare was not achieving its potential. It is difficult to discuss the impact of potentially beneficial interactions which fail to take place, as was the case in this scenario. However, the next scenario discusses this important aspect of the process of achieving fundamental change in more detail in a positive context.

## ***4.7 Outcome for the Bioeconomy***

As noted in Section 1, the impact of biotechnologies on health care has so far been almost entirely delivered through pharmaceutical developments and what is possible in terms of biotechnology-based patient treatment had, up till 2015, been almost entirely determined by the multinational pharmaceutical companies, hence the major focus on the pharmaceutical sector and its regulatory system in this scenario.

Even up to 2030, the health care sector was still dominated by a set of complex, rigid, long-established systems that were resistant to fundamental change, but willing to undertake piecemeal, non-strategic, incremental change when it fitted with their overall vision of the status quo as being the preferred future for their organisations.

However, as noted in Section 4.1, a crack in this dominance began to emerge in the period 2015 to 2030, when India and China did not follow Western regulatory precedents for diagnostics and tissue-based therapies. This was possible partly because of more permissive public attitudes to risk in these countries and, given that most of the risks that Western regulatory systems had been designed to prevent did not emerge, it was a successful strategy. It gave these countries a strong lead in the development of these technologies, and the extent to which Western patients were prepared to travel to receive treatments was an indication that the risk aversion of European and American patients was perhaps more apparent than real.

The overall outcome in this scenario is not disastrous – it is merely seriously sub-optimal. It is characterised overall by conservatism, by increasingly aggressive competition between multinational companies and assertion of influence by big pharma (an outcome of resistance to change in that sector), continuing resistance to change in regulatory systems, mounting frustration in health care systems and increasingly concerted action against technology based innovation in general, and the pharmaceutical industry in particular, among advocacy and patient groups.

An important factor in the maintenance of the status quo was the continued hegemony of the multinational pharmaceutical companies. Despite the financial pressures which they faced they were able to maintain a united front, particularly in their dealings with the regulatory system and with governments. This contrasts with the situation faced by agro-biotechnology companies where an important factor inhibiting their ability to deal with the challenges they faced from GM crops in the 1990s was the break-up of the previous hegemony and the emergence of serious, public disagreements between companies.

By 2030, the sector was pervaded by a general atmosphere of low-level aggression and bad temper, and a pervasive concern that this could erupt rapidly into very damaging levels of conflict, with no clear strategy for preventing it.

The health care sector had long been expected to be the lead contributor to the bioeconomy up to 2030. However, in this scenario, its contributions are much less than predicted. The pharmaceutical sector was no longer seen a dominant driver of the economy as a whole in Europe and the United States, and was ceasing to be given special attention by governments.

The difficulty in finding profitable enough markets for high-value R&D-based products was leading to continued shrinkage in the overall size of companies and hence of the sector as a whole.

Governments were continuing to fund research and early stage development of products and processes that were likely to lead to public benefits. However, they now recognised that such products were unlikely to be delivered through the pharmaceutical sector (see section 4.2.1). They increasingly focused on translation, either taking place entirely within the public sector or alternatively involving collaboration with SMEs. In this context there was a thriving SME sector, but because of the micro-scale nature of many such markets, the companies involved were likely to remain small players and not to contribute greatly to the bioeconomy.

Much of the hype about increased longevity arising from biotechnology-based innovation had disappeared and the rate of increase in lifespan had moderated. Many people, supported by modest improvements in health care and lifestyles, were living longer healthier lives, and were continuing to remain for longer in active employment, mitigating the expected crisis in pension provision. However, a considerable proportion of society continued to have an unhealthy life-style, counteracting the more positive trend.

## 5. Health Care Scenario – “Rapid Change”

### 5.1 Introduction

This scenario discusses the key factors and interactions that will shape the evolution of health care systems beyond 2015, assuming that the interactions are well managed so as to resolve the tensions that are inherent in the current health care system and to ensure an effective, if sometimes difficult, transition to a global bioeconomy that supports biotechnology innovation in the delivery of both public and private benefits, and to enable a better global distribution of health care benefits than that of the early 21<sup>st</sup> century.

The future health scenario we envisage here had the following characteristics, as outlined in more detail in the following sections:

- the contributions of biotechnology extended well beyond the predominantly drug-related developments of today;
- it required 5 years or less, rather than the previous 10 to 15 years, to take a new product or process through all the stages needed for approval for use on patients;
- the size distribution and specialisms of companies involved in health care were greatly extended, for example with many more middle-sized companies serving more niche markets, and a more robust SME sector with company strategies that were more long-term and more independent of the needs of MNCs;
- developments that emerged from public sector research institutions could more easily be taken further down the route to application within the public sector and could in many cases be taken all the way through to application within health care delivery systems, in addition to the previously well-worn innovation path via licensing or selling the technology to a MNC.

Health care had become predominantly a service industry,<sup>40</sup> its main business being to link the delivery of new and existing products and services to patients by coordinating the activities of a range of public and private sector providers delivering drugs, information and other health care-related products, services and treatments. This service industry was now led, or perhaps coordinated is a better term, by a new type of company that was able to harness a wider range of global networks, bringing together new technology, new types of expertise, surmounting regulatory barriers to innovation, and embracing new competition models.<sup>41</sup> As nanotechnology, information technology and biotechnology become increasingly convergent at the scientific discovery level and as technologies, so did their business models also begin to converge, enabling new insights to be combined to deliver better health care faster. It was not a foregone conclusion that the leaders in this new health bioeconomy would emerge from the current set of multinational pharmaceutical companies. However, as we discuss, it was also possible that they could transform themselves and take on this role.

The following sections outline the factors that led to the managed evolution of such a scenario, arising from the baseline state of the health care sector outlined in Section 1, in response to the change drivers outlined in Section 2.

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<sup>40</sup> Anon. (2006) *100-in-1: a Vision of Our Industry in 2015*. DVD, Version 2.0, Information Transforms

<sup>41</sup> World Economic Forum (2007) Inaugural Meeting of the New Champions: Briefing Material. Dalian, Peoples Republic of China, 6-8 September 2007  
[http://www.knowledgeconcierge.com/WEFPublic/PDFs/Dalian2007/Briefings\\_EN.pdf](http://www.knowledgeconcierge.com/WEFPublic/PDFs/Dalian2007/Briefings_EN.pdf) (accessed on 070906)

## **5.2 Science and Industry Innovation System: New Strategies and Business Models**

### **5.2.1 Changes in industry structures and new innovation models**

Since well before 2015, a complex set of changes had been emerging in scientific research and industry innovation systems, beginning around 2007, stimulated by the perception of a changing balance of power, with innovative thinking about new business models being led by the World Economic Forum (WEF). A WEF meeting in September 2007 focused on “The New Champions” and “The Shifting Power Equation”, referring to a new class of leaders and innovators, the growing prominence of emerging economies and the increasing power of individuals, small groups and consumers over large institutions and producers. Advice on “making business strategies more global” was hardly needed by companies in the life science sector, but they nevertheless found it more difficult than some other sectors to respond to these opportunities, particular blockages being the overcoming of regulatory inertia, cumbersome R&D portfolios, and resolving the tensions between public and private health care providers, direct to consumer marketing, and developed and developing world health care systems. However, from 2015 to 2030 this new form of thinking began to deliver real benefits to the bioeconomy.

One factor which facilitated this change to a new form of organisation in the health care sector was the decision in 2010 by senior management in three of the large multinational pharmaceutical companies, partly stimulated by the WEF “New Champions” initiative, to begin discussions about the development of a radically new structure for the health care sector. Meetings included representatives from all regions actively involved in pharmaceutical and biotechnology innovation, companies of all sizes and specialisms active in the health care sector, public and private health services, medical and health care charities, regulators, the insurance industry, and patient representatives. Managers from the ICT sector were also included in these meetings, initially to enable participants to learn from their experience of operating in a more open, collaborative, networked environment with more direct and active collaboration with consumers.

As these discussions began to bear real fruit in the form of new business strategies, including the envisioning of an alternative range of potentially attractive profit models, additional multinational companies joined the discussions, and participation was elevated to CEO level for both pharmaceutical and ICT companies in some meetings. In 2015 one of the largest pharmaceutical companies decided to form a joint company (PATC) with a major ICT firm in order to gain “first mover” advantage in what they by then perceived was “the way forward” for the health bioeconomy. It took several years from the formation of PATC to develop the beginnings of an effective model for the new co-ordinated mode of operation which became known as Networked Health Care (NHC).

The backing of the two parent companies, with their considerable financial clout was reinforced by the support and active participation of two other major financial players, the private health care insurance industry, particularly in the United States, and the re-insurance industry. Other key supporters that were actively involved in the shaping of the NHC approach included the regulators (FDA and EMEA), the major charities funding health care research and development, and a Patient Group Consortium that had been formed in 2012 to promote innovative change in the health care sector and had mounted a campaign in 2015 to encourage the more rapid development and uptake of biotechnology-based innovation.

Several elements were crucial to this successful, if sometimes difficult, transformation, fundamentally affecting the health care sector as a whole, in a relatively short space of time. These are summarised below and in some cases are expanded in the following sections of this scenario.

1. Particularly important were the changes that had been taking place in regulatory systems since around 2005, starting with relatively small scale initiatives but progressing to become the dominant regulatory mode of operation by 2015. These changes were designed to support innovation in the development of drugs and other biotechnology-based innovations and to encourage the participation of a wider range of companies throughout the entire development pipeline (see Section 5.3).
2. Of equal importance was the coming together of two visionary CEOs in the pharmaceutical and ICT companies. This is not such an unlikely occurrence as might be imagined. The pharmaceutical CEO was one of several in the industry who could foresee the gradual drift to commodity company status described in the first scenario, who wanted the company to become part of an alternative process with a more technology focused future and who was able to persuade the company's main board to support that vision. The CEO of the ICT company was one of those restless individuals who liked a challenge and who was looking for a new outlet for their talents. PACT was built from a combination of the pharmaceutical company along with a very major investment from the ICT company, with the director of the ICT company as CEO of the combined company and a main board that included directors from both companies. The expertise of staff from the ICT partner was crucial in developing the hardware and software for the basic information network that was essential to the new style of operation. This new model also proved highly attractive to venture capital companies who, as outlined in the first scenario, had become increasingly disillusioned with the prospects of major profits being generated from health-related biotechnology.
3. The third important element necessary to the success of this scenario was biotechnology itself. As indicated in Section 4.3.2, a range of biotechnologies is poised to speed up significantly the rate of development of drugs and other innovative technologies through to application to patients, and also to reduce the cost of the process. In this scenario, pharmacogenetics is included in this list and has a crucial role to play in the new networked health care system. Its propensity to increase the cost of individual products is offset to some extent by its ability greatly to reduce the number of rejected drugs in Stage 3 clinical trials. This results in a considerable increase in the number of new drugs on the market, each with a smaller market and hence a lower profit margin. However, since PACT's profit model relies only partly on the sale of drugs this is not such a significant obstacle as it would have been for a purely pharmaceutical company.
4. Another factor which led to the "softening up" of the environment for this kind of innovative step change was the new mind-set that had become increasingly prevalent in health care delivery systems (see Section 4.4). In the period up to 2015, public and private health care providers in developed and developing countries had increasingly begun to realise that technological innovation, including biotechnology, could provide better health care more cheaply than before if well managed. Major education initiatives had been set up in all countries with advanced health care systems to ensure that the health care sector was well prepared to deliver these benefits and to collaborate in ensuring that resulting innovations were fit for purpose. In developing countries, charitable organisations and PPPs were active in equivalent educational initiatives. Patient support groups had also had an important role in encouraging these educational developments.

By 2020, PATC had two competitors, each with slightly different modes of operation, but built on similar principles. One was led by a consortium of Indian pharmaceutical and ICT companies and the other was more similar to PATC. By 2025 these three companies dominated health care provision in the bioeconomy and the remaining companies in the pharmaceutical sector increasingly operated through these companies to reach their markets more efficiently. The new approach to drug development, based on pharmacogenetics and a range of biotechnology-based innovations to facilitate

drug development, along with the new regulatory regimes meant that, from 2015, companies that were involved in drug development were increasingly obliged to operate through the NHC model. Those that resisted change either became targets for take-over by the more successful NHC based group of companies, or concentrated increasingly on commodity drug markets.

An important aspect of the NHC approach was the involvement of a much wider range of types of company and product within the same organisation. Up till 2015, the pharmaceutical sector had outsourced to SMEs many of its early and mid-stage R&D activities or had bought in from SMEs products in early to mid-stages of development. The NHC approach took the flexible kind of organisation that the pharmaceutical sector had developed for early stage drug development and extended it (i) to the whole development pipeline, through to delivery to patients, and (ii) to a much wider range of products such as the tissue-based therapies, diagnostics and devices that we can envisage today along with totally novel approaches to health care emerging between today and 2030. The difference from the situation up to 2015, and the key to the NHC profit model, was that the most powerful industry sector was no longer acting as a technology gate-keeper, inhibiting the development of innovations that did not contribute to a drug-based approach to health care. While the profit base of any individual item in the portfolio of a NHC-based company was not comparable to that of a blockbuster drug, the co-ordination of a range of drugs and therapies, each with a more modest profit based, proved to be a much more viable and resilient approach overall.

In the development of new drugs there was still a wide variety of types of relationship between the NHC-based companies, the now-smaller pharmaceutical multinationals and among the smaller companies themselves. Mergers between SMEs and middle sized pharmaceutical companies, and also between two or more SMEs became increasingly common. Mergers and acquisitions were still common but the motivation was more usually common benefits from the linking of complementary technologies, rather than straightforward purchase of inputs to a flagging pipeline as was more usually the case up to 2015.

The fact that the main route to market for health care products was increasingly mediated and brokered via the NHC-based companies meant that contributing companies, small and medium sized, could succeed financially with a much wider range of innovation strategies than was the case in 2015. Drug development no longer dominated the bioeconomy, and the fruits of public and private investment in life sciences began to emerge in new and often-unexpected ways, stimulated by new types of partnership bringing together companies and individuals with biochemical, chemical, IT, physics and engineering expertise.

The NHC innovation approach proved very attractive to Indian and Chinese companies working in both pharmaceuticals and ICT. Pharmaceutical companies in particular were able to adapt more easily and rapidly to this way of working than companies based in Europe and the United States. This became the factor most responsible for the increasing global importance of Indian and Chinese companies, taking a lead role in several of the new NHC based companies and being much in demand as partners in others.

The NHC based companies were also much more able to work constructively with the large charitable foundations and PPPs, with particular successes beginning to emerge by 2020 in developing countries. Thus, by 2030, in line with experience in other industry sectors, the long term winners were clearly the companies that, faced with a need for creative change, had been able to re-structure their innovation models, even if it meant making many current products and processes redundant. Companies that aggressively defended the status quo in a rapidly changing environment did gain in the short term but did not retain their dominance in the long run.

The new NHC-based companies were increasingly acting as brokers and systemic co-ordinators for health care systems as a whole. ICT was now in the driving seat, with leaner and more disaggregated

production systems and more sophisticated supply chain management. The pharmaceutical companies that joined with ICT based companies to develop the NHC model of health care provision were focused on a much broader range of products sourced from a wide range of companies. They were no longer directly linked to the pharmaceutical companies in existence in 2030; these had become middle-sized multinational companies, serving middle-sized or commodity markets, generally via the NHC-based companies. Most often the drugs they developed were part of an integrated package of products for more sophisticated health care needs.

Companies operating outside the NHC-based system thus competed or collaborated with a much wider range of companies and health care deliverers than was the case in 2015. They were competing on a more equal basis and there was a greater variety of roles and responsibilities for smaller companies. Pure pharmaceutical companies, other than those that had collaborated in the NHC system, no longer had the profit margins they enjoyed in the 1990s and the early 21<sup>st</sup> century but the resulting closer and more equal collaboration among companies had allowed many more small companies to grow and develop independent innovation strategies. Following the patterns observed in other industry sectors, this greater variety of opportunity had led to an increase in the overall innovativeness of the health related bioeconomy, encouraging further investment in biotechnology.

### 5.2.2 Changes in innovative technology

Despite the initially sceptical assessment of the prospects for drug development arising from pharmacogenetics,<sup>42</sup> by 2015 this had become the basis for the dominant model of innovation in the drugs industry, linked to a genetically based, targeted approach to life style changes to accompany drug-related therapies. The smaller more specialised markets that result from pharmacogenetics-related innovation were now the mainstay of the new healthcare delivery system and biotechnology was continuing to open up new frontiers.

One innovation-related factor that made it possible to develop such niche markets on a profitable basis was the development of new approaches to the synthesis of complex biological and chemical molecules. Many potential products had been rejected from drug development pipelines in the past because they could not be synthesised at an affordable cost, even if they could be proven to be safe and effective. Synthetic genomics had an important impact in this area, as did the use of GM plants, animals and microorganisms.

Gene sequencing plus synthetic genomics is an example of a convergent technology, combining chemistry, physics, engineering, biotechnology and information technology to develop health care diagnostic and delivery systems operating at the nano scale. Such developments were facilitated by the existence of the new NHC based companies that could organise the collaborations across different disciplines required to bring such products to market.

Research on stem cells had by 2020 resulted in successful and affordable therapies, based on both adult and human embryonic stem cells. They had reduced drug bills and done away with some important drug markets. However, they had also created a new range of niche markets for products needed to support tissue engineering therapies, either in the culture of tissues for therapeutic purposes, the running of stem cell banks, or to deliver cell-based therapies directly to patients. The companies operating in this market were the descendents of earlier SMEs delivering products related to bone marrow transplants or skin grafts and many had grown to be significant operators on a global scale, although there was also a thriving body of new SMEs emerging to exploit the introduction of new, innovative therapies arising from stem cells. The successful development of stem cell therapies had been crucially dependent on the willingness of regulators to tailor the regulatory systems for these

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<sup>42</sup> Nightingale P. and P. Martin (2004), The Myth of the Biotech Revolution. *Trends in Biotechnology*, 22(11), pp. 564-569.

novel therapies to the needs of SMEs operating in this area, rather than to model the regulatory systems on those already in existence for drugs in the early 2000s.

The translational medicine approach to facilitating the development of innovative technologies for health care, begun around 2005, proved moderately successful between then and 2015. However, it really began to achieve its full potential with the arrival of the NHC –based approach to delivery of products and services for health care. Indeed, previous experience with translational medicine up to 2015 proved invaluable in the subsequent development of the NHC model.

### **5.2.3 New kinds of markets**

The development of innovative products specifically tailored to the needs of individual patients or groups of patients had meant that, although some drugs were still sold for very large markets, by 2015 these were mainly off-patent commodities that no longer attracted high profit margins. Commodity markets had increased dramatically in size with the increase in affluence in newly developed markets such as China, India and Brazil and many of the new companies serving these markets were based in these countries. Charitable schemes to extend affordable health care to those parts of the world that were still relatively poor were further increasing the profits of the commodity pharmaceutical companies.

Under the HNC approach, biotechnology innovation had led to the development of many more markets than before for new, patented, generally biotechnology-based, drugs able to generate attractive profit margins. However, the scale of these markets was smaller than for the block-buster drugs that were previously the mainstay of the pharmaceutical industry. By 2020, with the dominance of the NHC innovation model, these drugs were produced by middle-sized or small companies with specialised portfolios, companies that could work more closely and effectively with their markets and with other health care providers.

A new market was created in 2015 by large MNCs, that contributed to the growth of the bioeconomy. To help boost flagging profit margins, many companies moved to sell property rights and information related to drugs which they had previously rejected from development pipelines, perhaps because they did not fit with their market strategies at the time. This formed a small but significant contribution to revenues of these companies and it also had a very beneficial effect on the bioeconomy by stimulating the development of more affordable new products by SMEs or middle sized pharmaceutical companies.

## **5.3 The Regulatory System**

### **5.3.1 Stimuli for change in regulatory systems**

The above strategic changes in the science and industry innovation system could not have taken place without equally fundamental changes in the nature of regulatory systems for the health care related industries. The regulators involved in the discussions that began in 2015 (see Section 5.2.1), came mainly from the FDA and EMEA. From around 2005, regulators had begun to think constructively about their vital role in determining the future of the health care industry sector based on the regulatory routes to market that they devised and the nature of the regulatory systems involved (See Box 2). They had begun to make modest changes, initially of a voluntary nature, to stimulate innovation and encourage companies to develop personalised health care products arising from pharmacogenetics. An example of this kind of initiative was the FDA Critical Path Initiative. These modest beginnings had initially been resisted by some of the major pharmaceutical MNCs, but they had been embraced by others who had begun to think constructively (and at that stage only internally) about a future that was not dominated by blockbuster drug markets.



Earlier successful precedents for this kind of approach had been the Orphan Drugs Act and the Fast Track, designed to make new drugs available more rapidly for rare and/or life threatening diseases for which there were no effective treatments available.<sup>43</sup>

Regulators had generally seen their role as being limited to that of framing regulations to deal with potential safety and efficacy issues, and ensuring compliance with these regulations. Around 2007, instead of seeing themselves as passive responders to events, regulators began to see their role in a much more proactive way. In line with “new governance” agendas<sup>44</sup> and linked to globalisation initiatives, discussions began to take place within regulatory bodies about their role in stimulating changes in the processes and outcomes of health care innovation.

The process of priming regulatory systems to see the need for change had thus begun before 2015, but until then these changes were piecemeal and incremental rather than systemic. The stimulus for the systemic revision of regulatory systems, required to enable the changes outlined in Section 5.2, was the series of discussions involving the ICT industry sector that started in 2015. The experience of the ICT sector in standard setting as a mode of governance of their industry that is enabling rather than constraining of innovation, was seen as one that might be applicable with some modifications to the health care sector.

A series of creative think-tanks was set up, initially involving a restricted set of participants from the full range of life science companies, ICT companies, regulators, and insurance industry representatives. As discussions progressed and concrete proposals began to be formalised, discussion fora were widened to include patient groups and other stakeholders.

The challenge addressed was to ensure the continued safety, quality and efficacy of new drugs but to do this within a system that was responsive to the new challenges being presented by life science innovation. There was a profound shift in the perceived nature of the problem of the failure rate of new drugs in Phase 2 and particularly Phase 3 clinical trials. This had been seen as a failure of industry innovation models but began to be seen more as a mismatch between:

- the nature of new biotechnology innovations;
- the nature of the companies that could best exploit these innovations;
- public and patient expectations of new drugs and treatments; and
- regulatory systems that were designed around 20<sup>th</sup> century models of drug development.

The new regulatory approach that began to emerge required creative and constructive thinking from senior managers, regulators and analysts in life science and ICT industries, along with an enthusiasm for collaboration across non-traditional boundaries. Initially this group was self-selected and not representative of mainstream thinking in companies or regulatory systems. However as the strains in the 20<sup>th</sup> century pharmaceutical innovation model persisted and became more severe, new approaches to regulation (as with new innovation systems) began to seem, not just more attractive, but inevitable. The key to actual change was showing how it could be done, not merely recognising that it was needed. And the key to achieving change came from interaction with the ICT sector that freed up thinking about health care policy and regulation in a way that was seen as non-threatening by those involved from the pharmaceutical industry, even although it did involve very radical change.

An additional feature that facilitated change was the involvement of Indian and Chinese companies and regulators. Their innovation and regulatory systems did not have the well-entrenched position of

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<sup>43</sup> See Milne *et al.*, note 17.

<sup>44</sup> Lyall C. and J. Tait, (2005), *New Modes of Governance: Developing an Integrated Policy Approach to Science, Technology, Risk and the Environment*. Aldershot: Ashgate Publishing.

those in the United States and the European Union, and their regulatory systems were still evolving, initially to conform with the 20<sup>th</sup> century models then in existence but increasingly to support a shift to a new regulatory model more in tune with the needs of the 21<sup>st</sup> century. This move was facilitated in both China and India by their pre-existing expertise in ICT industry sectors and enabled companies in these countries to move to a more equal competitive position with companies in the United States and the European Union, and even in some cases to overtake them in global competitiveness.

### **5.3.2 New approaches to phase 3 clinical trials and beyond**

As part of the new regulatory system, there was a revision of the approach to Phase 3 clinical trials, referred to by some as the “living license”. Rather than double blind controlled clinical trials, this involved patients who volunteered to take part in the trial with the risks and benefits of the treatment and effects on a range of vital systems being monitored centrally throughout the trial by the regulators as well as by local medical practitioners, using a range of IT-related innovations. In this situation, individuals thus formed their own controls, with real time monitoring of the effects of drugs on a range of biomarkers. One major benefit of this approach was the reduction in numbers of patients required for expensive Phase 3 clinical trials. Another benefit was the earlier rejection of defective drugs from clinical trials, again saving money. However, combined with pharmacogenetics, this approach also led to a significant increase in the number of new innovative drugs on the market, also stimulating a new round of basic research into new druggable targets.

Another major benefit came with new non-drug based therapies arising from biotechnology-based innovation, such as stem cell therapies and nano-biotechnology based systemic treatments. In the early stages of development of these technologies, approaches to regulation were being built around modifications of drug-related regulation and this was proving to be extremely inhibiting of innovation. The new “living license” approach had a dramatic impact on the rate of expansion of innovation in such areas, with many more products emerging from a range of small companies operating novel convergent innovation models that brought together information technology and biotechnology, often operating at the nano scale (see Box 2).

### **5.3.3 The shape of the new policy and regulatory systems**

Regulators’ increasing understanding of the complex interactions that bound them to the pharmaceutical industry sector, along with new alliances with the ICT sector, enabled them to set about trying to find innovative ways to deliver safe medicines to the public faster at less cost, using new biotechnologies and information technology to achieve this. These new policy and regulatory approaches opened up new opportunities for innovative SMEs to build up sustainable profit models. The role of the large pharmaceutical MNCs began to change from that of innovation controller to innovation facilitator. This approach was highly successful and by 2030, the average time to take a new drug or treatment through the regulatory system was five years.

The new regulatory systems were more effectively coordinated internationally than their predecessors, but there were still significant differences between the United States, the European Union and other major players such as India and China. These differences reflected the different political systems in these regions, differences in health care delivery systems, and differences in public and patient needs and expectations.

The new regulatory systems were fully in place by 2020, but their benefits in speeding up the scale and rate of biotechnology innovation had been apparent since 2015, as a series of co-ordinated changes began to be implemented. This had an important impact on public policy makers involved in science and innovation funding who had begun to question the wisdom of investing so much public money in life sciences, given the poor record in the translation of fundamental science into effective health care innovations. Funding strategies were reviewed and money continued to flow into basic life

science but the previous trend to direct such funding to interdisciplinary areas was now reinforced. There was also a dramatic impact on the flow of venture capital into the health care sector, given that there were more rapid and direct routes to market for innovative products and profits began to accrue more directly to the SMEs that were funded by venture capital.

## **5.4 Health Care Delivery Systems**

### **5.4.1 New health care delivery systems**

The “*Rapid Change*” scenario requires as much fundamental change in health care delivery systems as in regulatory systems. In order to become intelligent customers for innovative technology the health care sector had to embrace change; to cope with shifting hierarchies as new specialisms become key to health care delivery; and to develop a flexible, more technologically literate workforce. In parallel with these pressures, patients had continued to become better informed about diseases which may affect them and to be more demanding about the treatment they received.

This had been a bigger challenge in some countries than in others. For example technological approaches to health care were previously better developed in the United States than in some European countries, but this did not necessarily correlate with the public or private nature of health care provision – other aspects of national politics seemed to be just as influential in facilitating uptake of innovations. Electronic health care records were planned to form the basis for the NHC approach and the early investments in this area, particularly in the United States private health care system and some European Union countries, proved invaluable in the initial stages of the development of the NHC approach. This also gave those countries with advanced systems an earlier and easier route to benefit from the new approach.

The Rapid Change scenario, up to 2030, envisages that there had been a convergence in developed countries in the scale and nature of public and private health care provision with most countries operating a mixed health care economy. There was much less disparity than before 2015 in the quality of public and private provision of health care. There still was not equality, but the differences were no longer so great as to lead to resentment among less privileged patients.

### **5.4.2 New health care markets**

Markets for innovative products in the new health care sector were generally smaller and smarter, alongside ever-larger markets for commodity products which were now much more widely available than before, globally. The drugs and other products developed under the new NHC system could not be claimed to be cheap but they were more affordable than previous generations of products and were developed more rapidly thanks to the revised regulatory arrangements. In addition, because of the links with the ICT sector, health care products that were combined in innovative ways with standard home computing equipment began to be available, developing mass market IT-based innovations which were able to reduce further the cost of health care products. Health care based regulatory bodies like NICE began to collaborate more enthusiastically with companies and regulators in realising what they saw as an attractive and more affordable future for health care.

As health care systems had become more technologically sophisticated themselves, there had been an increasing tendency for biotechnology related innovations to emerge directly from the medical profession and other health care workers. Thus the health care systems themselves became important innovators, creating new markets which spread directly from one health care provider to another, requiring new approaches to intellectual property protection and revenue generation. Alternatively a health care provider with an innovative idea was able to link up with a SME to develop it further and disseminate it more widely. The beginnings of this kind of thinking were apparent before 2015 (for example the slogan for translational medicine – “From bench to bedside and back again”) but it did not become a reality in the commercial sector till after 2015 through the NHC approach, when the staff

of health care delivery systems had become as familiar with the demands of innovative technology as they were with the more routine delivery of health care.

This change was greatly facilitated by the emergence of the new type of company represented by PATC which could cope with much more flexible and collaborative arrangements between companies and public sector actors. It also would not have been possible without the changes in regulatory systems described in Section 5.3. Indeed the “living license” approach, which engaged more constructively than before with medical professionals in the conduct of clinical trials, also began to stimulate innovative approaches to drug development and delivery arising from the health care system itself. This included combined convergent technology-based therapies which were much less likely to emerge from any other source that did not have the direct experience of interacting with patients.

### **5.4.3 Emergence of new diseases**

One factor that greatly facilitated funding and support for new diagnostic treatments and development of antibiotics was the emergence of new epidemic and potentially pandemic diseases. Relevant factors here included:

- farm animals, or perhaps even family pets living in close proximity with humans, that could transmit new and potentially very serious diseases to the human population (see Box 3);
- climate change that enabled insect vectors to colonise new areas or (through drought or food shortages) stimulated mass migrations that concentrated large numbers of people in insanitary conditions; and
- increasingly rapid global movements of large numbers of people for business or tourism.

The need for health care systems to respond rapidly to such emergencies was one of the stimuli that contributed to positive support for the changes to innovation and regulatory systems outlined in Sections 5.2 and 5.3.

## **5.5 Stakeholders and Advocacy Groups**

A dramatic change in overall stakeholder attitudes was seen at an early stage in the development of this scenario, once news of the new NHC approach to health care began to leak into the public domain. This fitted well with the setting up of the Patient Group Consortium that had already been set up (see Section 5.1).

Collaboration with the ICT sector, and the speeding up of delivery of innovations through the new regulatory approaches, defused the “anti-big pharma” public mindset that had become such an important component of the first scenario. Likewise, some patient groups had become increasingly frustrated by the slow progress of biotechnology-related innovation, and were also becoming increasingly critical of the pharmaceutical MNCs.

The perception that “something important was happening”, with big potential changes to a system seen increasingly as dysfunctional, meant that patient groups and most members of the public who took an interest in such things became increasingly positive collaborators in the development of the new systems.

This shift in public and stakeholder attitudes was a particularly important factor in facilitating the introduction of the new approach to Phase 3 clinical trials which required a much more active form of patient participation than had previously been the case. This shift was reinforced when the relevant public and patient groups were brought into discussions about the implementation of the NHC approach, once the early, necessarily confidential negotiations had been completed.

The advocacy groups opposed to the development of health care systems based on advanced technologies had not changed their views as a result of the new developments, but the extent of their influence was much less than it would otherwise have been.

### **Box 3 - Animal health: its role in the evolution of human health care systems and the bioeconomy<sup>45</sup>**

Animal health is considered here mainly in the context of its relationship to future human health scenarios, in particular zoonotic diseases. The following factors (some, such as the use of RNAi, are more speculative than others) relate to animal health itself and are also relevant to the evolution of the scenarios explored in this report.

- Availability of rapid, automated disease diagnostic techniques
- Availability of improved vaccines for use in animals
- Non-availability of new antibiotics for use in animals due to concerns about developing resistant strains of bacteria
- Limitations on the availability of existing animal-use antibiotics and anthelmintics due to increased resistance
- Availability of cheap and rapid genotyping, allowing the use of genomic technologies (including genome-wide selection) to breed animals with increased resistance to specific diseases
- Use of genetic modification of animals that can express RNAi to prevent multiplication of a small number of key infectious diseases
- Improved and better co-ordinated management techniques for controlling the spread of infectious diseases
- Decreased interest in products for animal health care by pharmaceutical multinational companies
- Shifting of animal production to different parts of the world resulting in resurgence of familiar zoonotic diseases (such as Brucellosis and TB) or development of new zoonoses.
- Introduction of existing zoonotic diseases to new parts of the world as a result of global warming
- Potential shortages of animal protein, locally or globally, leading to weakened immune systems and increasing vulnerability to disease
- The emergence of a new, serious zoonotic disease transmitted by cats or dogs posing a serious public health issue, given the close proximity between humans and companion animals.
- The introduction of changes to rural farming systems in, for example, South East Asia so that small farmers and their families no longer live in close proximity with their pigs, chickens and other farm animals (these changes were imposed by governments in these countries to reduce the risk of zoonoses emerging from these sources and having global impacts)

## **Future Animal Production and Health Care Systems – 2015-2030**

### ***Managed Change - Optimally Developed Systems***

Animal production is organised in large industrial units of pig, poultry and some dairy production, in integrated production systems with food processors and supermarkets. These large units are surrounded by a sea of extensive production of beef, sheep and some dairy producers. This is the case in Northern countries and also those in the South that have the capabilities for large-scale intensive production (e.g. Brazil and Thailand).

Management of intensive pig and poultry units is highly technically dependent. Disease control has been achieved by excellent biosecurity with production units segmented so that if an outbreak of disease is identified, individual sections of the production unit can be closed off extremely quickly. Rapid, automated diagnostic techniques have made it easy to detect diseases at an early stage. Animals have also been bred for disease resistance for a few key diseases and, due to the cheapness and rapidity of genotyping, genome wide selection techniques are used.

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<sup>45</sup> With thanks to Chris Warkup (Genesis Faraday Partnership) and Professor Steve Bishop (Roslin Institute) for stimulating discussions

Whenever there is a disease outbreak, survivors are used to identify the 20,000 or so Single Nucleotide Polymorphisms (SNPs) that are associated with resistance to that disease. These SNPs are then used for subsequent selection of resistant animals.

Many animals have been genetically modified to express RNAis to prevent multiplication of a small number of key infectious viral diseases, particularly those that are potential zoonoses. Expression of the RNAi is triggered by a factor in the animals' water and this trigger can be implemented without humans being in contact with the animals themselves.

Thus an infectious disease is identified quickly; affected animals are sealed-off from other animals; and a "fire-break" of genetically modified animals induced to express RNAi by a change in their water supply further reduces potential spread.

Intensive units are carefully managed for the particular breeds and strains of animals produced so that the incidence of metabolic diseases is much reduced with consequential benefit for animal welfare. The use of much improved vaccines has also helped to control infectious diseases.

Disease control in the surrounding extensive cattle and sheep units is predicated on the principle of living with the disease but mitigating its spread by keeping animals at low densities to reduce contact with other animals and by using mixed genotypes with varying resistance characteristics. The maintenance of this system requires high levels of skill and management and a high degree of co-operation between units. As a result, animal production is only allowed by licence and is subject to planning permission to control the areas in which production may take place.

One result is a pleasant countryside that is managed for aesthetic and environmental effect, except in areas where intensive production units are situated.

### ***Disruptive Change - Sub-optimal Systems***

#### ***Developing country changes***

Developing countries, particularly in Africa, continue to struggle with periodic outbreaks of serious disease in farm animal populations. The continual pressure for increased productivity to feed a burgeoning population, together with pressure on land and particularly water resources, have resulted in stressed animals and poor management. Together these factors have made disease outbreaks more likely. However, the eradication of rinderpest and the availability of better disease control through improved diagnostics and vaccines have meant that parts of Africa have become competitive with South America in terms of animal production.

#### ***Health care products for animals***

The number of companies producing veterinary products has decreased due to increased competition and continuing difficulties in finding new candidate products. As pharmaceutical MNCs continue to experience problems in the innovation pipeline they have become less interested in animal health although most animal health products are still developed by, or in association with, these companies. It is no longer acceptable to use antibiotics for treatment of animals and most existing antibiotics and anthelmintics are no longer effective due to increasing resistance. The control of worms in sheep has become so difficult that all sheep production has to be in mixed farming systems carefully managed to control worm burdens.

The livestock sector of the veterinary profession has changed its function. As improved diagnostic techniques have become available, vets have become less in demand to diagnose disease. Also, as antibiotics and other chemicals have become less available, vets are required less for treating disease. Instead they have become key to managing and planning for animal health and hold key roles in companies that produce large numbers of animals as well as co-operatives of smaller-scale farmers.

#### ***Global Climate Change***

Global warming has resulted in serious shortages of water with large negative effects on dairy

production, particularly in Australia and New Zealand.

A new tick borne disease has emerged in animals and has spread widely as a result of climate change. Unfortunately this disease can be transmitted to humans where it has serious consequences. Recreation in the countryside is now considered risky except in a few tick-free areas.

#### ***New Zoonoses - “Man’s” best friend?***

A new zoonotic disease has emerged with a similar transmission route to foot and mouth disease. It is carried in farm animals but has little effect on them. However it is easily transmitted to cats and dogs that come into contact with farm animals. The diseases not only have serious consequences for the cats and dogs but these animals can also readily transmit the disease to humans where it has a high mortality and morbidity rate. Large numbers of pet animals are being abandoned by their owners. Vaccination of pets can act to control the disease to some extent but there are long waiting lists for vaccines.

#### ***New Diseases of Farm Animals***

A new disease affecting dairy cattle has appeared and unfortunately the Holstein Friesian population that provides most of the world’s milk proved to be highly susceptible to this disease. The poor genetic diversity in the Holstein population resulted in almost all of the animals succumbing to the disease. There was a sudden and dramatic shortage of milk which caused not inconsiderable public consternation and seriously reduced the supply of milk for processing (e.g. for yoghurt and cheese). Milk production is now based on a much wider range of genotypes.

There has been a massive increase in dairy production in China and India. However, this has allowed brucellosis, and in particular TB, to become major diseases of concern. A catastrophic outbreak of African Swine Fever in Asia has killed 95% of the pig population in affected areas. In combination with the increasing use of land for production of energy crop production, the result has been serious food shortages and consequent riots. The outbreak of a hitherto unknown enteric disease in pigs in the North has further disrupted the supply of pig meat. Delays in development of vaccines and unavailability of antibiotics have prevented effective treatment of this enteric disease.

Also, the breakdown of a rationally attenuated live virus vaccine for chickens was not noticed until a large number of birds were affected and egg production was seriously disrupted which further reduced supplies of animal protein.

The WTO’s Sanitary and Phytosanitary restrictions, implemented under recommendation from the World Organisation for Animal Health (OIE), used to control animal diseases through reduction of international traffic in meat and live animals. However, these restrictions have proved increasingly difficult to implement in a less well managed international trading environment. Diseases that were previously controlled have become endemic in Argentina and Brazil, resulting in shortages of meat production. Initially, this shortfall was compensated for by increased production in Russia and China but as the diseases became more widespread the tensions within the WTO increased with serious conflict between North and South resulting in major challenges to the regulatory structures. Many diseases have now become endemic worldwide.

## ***5.6 Interactions and Their Timing***

Achieving major change in large scale entrenched systems like the pharmaceutical industry or regulatory agencies has been described as “turning round an oil tanker”. However, even once you have turned the oil tanker round, it is still an oil tanker. The challenge in this case was equivalent to converting the oil tanker into a smaller, more multifunctional mother ship in charge of a fleet of smaller faster vessels capable of taking off in many directions while remaining well connected with one another.

The outcome described in this scenario was dependent on a great deal of good judgement by key thinkers in companies and regulatory agencies backed up a considerable amount of good luck. Perhaps

even more than good judgement, these changes required contributors who were open minded and able to think creatively across disciplinary and sectoral boundaries, who had the foresight abilities to recognise the need for systemic change and to appreciate the advantages that would accrue to the first movers in making this change, and the authority (as a group) to implement the required changes.

However, good luck and good judgement are not sufficient. Any number of unforeseen events, in addition to the lack of the right kind of talent in key players, could have prevented the necessary elements of the new NHC systems from coming together in the right places, in the right proportions, and in the right order, particularly in the early formative stages of the new initiatives.

Regulators played a crucial role particularly in their willingness, primed by experience since the 1990s, to consider innovative approaches to health care product regulation. Following closely behind in timing and importance, the willingness of one or two small groups of senior managers in the pharmaceutical industry sector to come together to discuss such issues in an open-minded environment was vital. And following closely behind this factor was the willingness of one or two key players in the ICT sector to take up the opportunity to engage in such discussions. If only one of these elements had been missing, the scenario described in this section would have been much less likely to emerge. Likewise, if one of these players had attempted to dominate the outcome, the chances of an optimal resolution would have been much less.

## ***5.7 Outcome for the Bioeconomy***

In the health care sector as a whole, a broader range of biotechnologies was able to contribute more positively to health care than in the first scenario. By 2030, the pharmaceutical company sector was mainly identifiable in the form of a larger number than before of companies producing commodity drugs. The innovative component of the health care sector could no longer be described as based on pharmaceuticals, far less dominated by pharmaceutical multinationals. One of the results was a wider, more broadly based set of products being delivered by a group of companies that had as much in common with the ICT industry sector as with pharmaceuticals.

Through training programmes set up well before 2015, the health professionals who were the main market for these innovations had developed a better understanding of the demands and benefits of innovative health care products. They also were more willing to work collaboratively with other professionals at all levels in health care delivery systems, and even more important they had a positive approach to innovative technology. Achieving this transformation had not been easy, given the sometimes rigid hierarchies in the medical profession. However, it had been facilitated by the clearer benefits to be derived from the NHC approach, and also by the increasingly frequent arrival in their clinics of well informed and more demanding patients.

Under this scenario, biotechnology was able to make a much more positive contribution to the health bioeconomy than in the first scenario, making a much wider range of contributions to health care than was possible with a drug-focused approach. However, the link-up with ICT companies and with a range of other convergent technologies meant that it was increasingly impossible to allocate particular advances or sources of profit solely to biotechnology. This difficulty had already been apparent in 2007 and between then and 2030, the notion of a distinguishable separate “bioeconomy” became increasingly irrelevant to the reality of the economy as a whole.

Nevertheless, the success of the NHC initiative and the companies it spawned in delivering health benefits to populations in developed and developing economies was a major influence on governments in continuing to provide financial support to encourage bioscience related discoveries.



The new NHC sector of the economy became a major source of national prosperity in those countries that embraced this approach and led to numerous spin-out products and initiatives in other sectors of the economy.

There is a widely accepted expectation that an ageing population and a declining labour force will cause problems in developed economies - predictions are for a less healthy but longer lived population with a higher demand for expensive health care technologies, but a lower ability to pay for these through pensions, health insurance or publicly funded health services. The received wisdom is that demographic trends will increase the demand for biotechnology-based health care but only if the population has access to treatments through public health services or can afford to pay for them.

An alternative projection could be that biotechnology-based innovation (along with better diets and more exercise) may enable the ageing population to remain fit and active (including economically active) for much longer than before so that the expected demand for disease treatments does not escalate beyond the ability of governments and individuals to satisfy it.<sup>46</sup> This outcome would have a link to economic systems by placing fewer demands on health services and also on pension systems (“Live longer; Work longer.”). However, the societal benefits of this outcome would not be realised if large scale unemployment were to become a feature of these economies.

The most likely outcome is a balance somewhere between these two trends – a longer-lived population which is less healthy and places greater demands on health services and a healthier population, living longer and working longer and placing fewer demands on health services. The position of this balance will depend on societal trends such as willingness to take control of one’s health profile through life-style changes, and also on the nature of the biotechnology-related innovations that emerge and reach the market place between now and 2030. However, the “Rapid Change” scenario would appear to be likely to contribute to a positive societal and economic outcome along these lines.

If many more people remain in active employment for a longer period than in the earlier part of the 21<sup>st</sup> century, this could reduce the tendency for governments to worry about falling birth rates and thus to promote increases in birth rates because of concerns about the need to support an ageing (and presumed infirm) population. Over time, this acceptance of declining birth rates, and hence declining global populations, could have a major impact on a wider range of factors including food security, the use of scarce natural resources, global climate change and international conflict.

## 6. Overview of the Scenarios

The scenarios presented in Sections 4 and 5 can be seen as two sides of the same coin. On the one side there is the remarkable burgeoning of innovation, profit generation and customer satisfaction that is possible, given the right combination of circumstances and individuals. On the flip side is the situation that arises when an increasingly dysfunctional set of systems continues as it has always done because it cannot envisage a different future.

Radical organisational innovation as described in the second scenario requires a particular combination of people and events:

- key influential thinkers, senior in their organisation and able to implement change if necessary

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<sup>46</sup> Manton K.G., G.R. Lowrimore, A.D. Ullian, X. Gu and H.D. Tolley (2007), *Proc. Natl. Acad. Sci. USA*, 104, 10802-10807. (Quoted in Cairncross, F. (2007) Age, Health and Wealth. *Nature*, 448, pp. 875-876.)

- representation of such thinkers from the most important categories of organisation, in this case multinational pharmaceutical companies and regulatory agencies in Europe and the United States
- the presence of an apparently non-threatening outsider (in this case the ICT sector) with relevant experience to contribute the design of new types of organisation but who is not seen (at least initially) as a competitor for any of the organisations involved
- a determination from the beginning that the outcomes of the discussions and negotiations will be implemented and a clear route to implementation

The **potential** contribution of innovation in life sciences to the bioeconomy is enormous, but achieving its full potential will not be straightforward. Ideally the pharmaceutical industry sector and the regulatory bodies need to take part jointly and equally. Willingness to change on the part of either the pharmaceutical industry or the regulatory system acting alone is unlikely to have a sufficiently major impact on the future of the health care bioeconomy to initiate major change.

This raises the point introduced at the beginning of Section 2 on the importance of the sequence of timing of events in achieving major change. The changes envisaged in the “Rapid Change” scenario (Section 5) did not emerge from a vacuum – they depended on the existence of several developments that had been taking place prior to 2015, particularly in the pharmaceutical sector and regulatory systems. As a result of discussions initiated by regulators with the aim of speeding up drug development and making it simpler, mainly with the interests of pharmaceutical multinational companies in mind, by 2015 the regulatory systems had changed so as to make it easier and faster to bring a drug to market. By 2015, this had not reached the stage of enabling a SME to take a drug all the way through to market without any intermediation from a multinational company but it had opened up the field sufficiently for this to become an aspiration. This was the basis around which it was possible to develop the proposal for the setting up of PATC and the NHC approach and it demonstrates the pivotal role of regulatory systems in this process.

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