Chapter 8

Policy Options for the Bioeconomy: The Way Ahead

The social and economic benefits of the bioeconomy will depend on good policy decisions. The required mix of policies is linked to the potential economic impacts of biotechnological innovations on the wider economy. Each type of innovation can have incremental, disruptive or radical effects. In many (but not all) cases incremental innovations fit well within existing economic and regulatory structures. Disruptive and radical innovations can lead to the demise of firms and industrial structures, creating greater policy challenges, but they can also result in large improvements in productivity. This chapter identifies policy options to address challenges in primary production, health and industrial biotechnology. It also looks at cross-cutting issues for intellectual property and for knowledge spillovers and integration, global challenges, and the need to develop policies over both the short and long term.

Primary production provides a diverse range of policy challenges. Examples include the need to simplify regulation, encourage the use of biotechnology to improve the nutritional content of staple crops in developing countries, ensure unhindered trade in agricultural commodities, and manage a decline in the economic viability of cool-climate forestry resources for low value commodities such as pulp and paper. The main challenges for health applications are to better align private incentives for developing health therapies with public health goals and to manage a transition to regenerative medicine and predictive and preventive medicine, both of which could disrupt current healthcare systems. Industrial biotechnology faces multiple futures due to competitive alternatives from both outside and within biotechnology. Policy needs to flexibly adapt to different outcomes and prevent "lock-in" to inferior technological solutions.

The "probable" bioeconomy of Chapter 7 is based on expected technological progress and current business models and policies. It should provide commercially valuable products and processes for primary production and industry and improved health therapies. Due to high costs, new health therapies will most likely be limited to high income countries and to better-off individuals in other countries.

However, the bioeconomy could provide much greater socio-economic benefits than those described in the "probable" bioeconomy estimate of Chapter 7. For example, in the field of health, safe and effective therapies could delay the onset of chronic disease and fall within the financial means of a large share of the global population. In a world of growing demand for natural resources, biotechnology could dramatically increase the production of food, animal feed, fibre and energy, reduce the environmental costs of increasing production, mitigate some of the harmful effects of climate change, and reduce greenhouse gas emissions.

Achieving the full promise of the bioeconomy by 2030 requires a policy framework that can address technological, economic and institutional challenges. Some of the solutions will require adjustments to policies that support public and private research and collaboration, training of scientists, capital markets, appropriate intellectual property rights, competitive product markets, regulation to minimise risk, and a dialogue with the public on the benefits of biotechnology.[1] Other areas of biotechnology will not develop their full potential without major policy interventions and new policy mechanisms.

Why should governments provide long-term policy support for an emerging bioeconomy? The main rationale is the large potential of biotechnology to create new markets and to improve productivity, health and environmental sustainability. There is also an ethical imperative to support the bioeconomy. As noted in a 1999 report by the Nuffield Council on Bioethics,[2] a lack of support for biotechnology could result in the failure to develop improved crop varieties that would benefit the world's poor. The same principle applies to health applications, where biotechnology could help develop affordable antibiotics and other pharmaceuticals with significant therapeutic advantages over existing treatments.

The required mix of policy interventions is linked to the potential impacts of each biotechnological innovation on the wider economy. As with all innovations, new biotechnological products and processes can have incremental, disruptive, or radical effects on other economic activities (see Box 8.1). Each type of effect creates a different set of challenges for policy and for business models.

Box 8.1. **Types of innovations**

Innovation involves the introduction of a novel product or process onto the market. Innovation theory has long recognised that the characteristics of an innovation can influence its effects on the market and broader economy. Depending on these characteristics, an innovation can potentially have incremental, disruptive, or radical economic effects.

Incremental innovations are based on scientific discoveries within a well understood technological paradigm. Their socio-economic effects are largely predictable. An example is the gradual increase in crop yields over the past few decades or the steady increase in survival rates for cancer due to improved diagnostics and prescribing practices.

Disruptive innovations provide entirely new ways of performing a task, such as replacing petroleum feedstock to produce polymers with biomass. These innovations require a new knowledge base and can entirely displace an existing technology, causing the disappearance of firms that are unable to fully exploit the new knowledge. The specific effects of disruptive innovations can be difficult to predict in advance, but they are likely to create economic winners and losers.

Radical innovations are infrequent and, in addition to requiring new knowledge bases, they require new infrastructures and/or new organisational structures. Once these are in place, radical innovations can boost economic productivity. Historic examples include the shift from steam power to electricity and from post, telephone, and television communication systems to the internet. Radical innovations can have substantial and far reaching impacts on society and the economy that are impossible to predict. Two radical innovations that could emerge out of the bioeconomy are predictive and preventive medicine and new microbial production systems for chemicals and fuels based on metabolic pathway engineering and synthetic biology.

The time required for each of these three types of innovation to affect the economy varies. Incremental innovations generally diffuse rapidly throughout an economy because they fit within existing production systems. Disruptive innovations can diffuse very quickly, as with radio, or much more slowly, as with recombinant DNA technology. Radical innovations usually require decades before reaching their full potential to shape economies.

Source: Based on Smith, 2008.

Incremental innovations can create policy challenges by blocking the development of alternative technologies that offer superior economic or environmental benefits. Disruptive innovations are based on new knowledge that replaces existing technologies, leading to the demise of firms and industrial networks that are unable to adapt to the new technology. One policy challenge is to craft sufficiently flexible regulations and institutions to support new technological developments. Radical innovations are built on new knowledge bases, as with disruptive innovations, but they also require

new infrastructures. A transition from one infrastructure to another can be very difficult and costly, posing further policy challenges.

Each type of innovation is also dynamic. Biotechnology was originally based on recombinant DNA techniques that modify the genetic structure of micro-organisms to produce pharmaceutical compounds or plants with novel traits. These recombinant techniques were initially disruptive because of the difficulty in acquiring the necessary knowledge and expertise to use them effectively. This threatened the business models of existing agricultural and pharmaceutical firms. These disruptive effects are now largely over. Large pharmaceutical firms developed the necessary capabilities to use this technology, while agricultural seed firms that were unable to use it to their advantage were taken over by the limited number of major seed firms that could.

Biotechnological research continues to generate new technologies with the potential for disruptive or radical effects on the economy. Table 8.1 provides examples of incremental, disruptive and radical biotechnologies that could shape the emerging bioeconomy of 2030. Radical innovations that disrupt existing businesses and call for major investments in new infrastructure or organisational forms are both infrequent and often difficult to identify in advance. Consequently, the examples in Table 8.1 of radical biotechnological innovations are only suggestive. Nevertheless, the potential of radical innovations to render both existing industrial networks obsolete and to boost future productivity warrants careful evaluation. One appropriate tool might be the further development of foresight research.

This chapter identifies eight general approaches to policy that governments can use to help maximise the benefits of the emerging bioeconomy (see Box 8.2). Many of these approaches can be applied to each type of innovation identified in Box 8.1. As noted in Chapter 5, for instance, public sector support for R&D (research subsidies) lies behind the development of all types of biotechnological innovations.

Table 8.1. **Examples of incremental, disruptive and radical innovations for the bioeconomy to 2030**

	Incremental	Disruptive	Radical
Primary production	Improved yield, product quality, stress tolerance, and pest resistance for food, feed, and fibre crops. Improved varieties of livestock, farmed fish, and beneficial insects such as bees. Inexpensive diagnostics for immediate identification in the field of a range of plant and animal diseases or invasive species in cargo or transport vehicles. Functional foods, particularly enhanced staple crops for developing countries.	Foods (nutraceuticals) tailored to genetic subgroups to reduce the risk of developing chronic diseases. GM plants or micro-organisms to provide fish protein for aquaculture. Cellulosic biofuels based on specially tailored non-food crops. Enhanced tree species for tropical and sub-tropical climates.	The integration of primary production and industrial processing based on biorefineries that produce a wide range of end products (*e.g.* food, fuel, materials, chemicals) from a range of biomass feedstocks could require new infrastructure or organisational changes.
Health	A steady stream of new small molecule drugs, biopharmaceuticals, and recombinant vaccines. Identification of harmful genetic mutations *in utero*. Diagnostics for most chronic and infectious diseases.	Pharmacogenetic information used in a large percentage of drugs and treatments. Regenerative therapies based on stem cells and tissue engineering that provide new treatments and some cures.	Preventive medicine in which risk factors for diseases can be identified years in advance and effectively treated before onset of symptoms, using predictive and preventive treatment based on validated biomarkers to track progress and identify required lifestyle changes.
Industry	Improved enzymes for industrial processing.	Environmentally sustainable methods of biofuel and chemical production using cellulosic feedstock, production of high energy-density biofuels from sugars.	Production of a wide range of chemicals and high energy-density biofuels using micro-organisms or simple plants developed through metabolic pathway engineering or synthetic biology.

Box 8.2. **Some policy approaches and tools for the emerging bioeconomy**

1. **Research subsidies**: Uses public resources to generate knowledge inputs such as private and public sector research and development and human resources through the education of researchers, scientists, technicians, etc. This could include both mission oriented research to support a specific technology and multidisciplinary research.

2. **Market creation**: Puts in place an incentive structure that could include, among other things, procurement guidelines, production subsidies, pricing incentives, trade barriers (either their establishment or removal), and competition policies.

3. **Regulations/standards**: Mandates actions concerning safety, product registration, advertising, environmental mandates (*e.g.* tradable carbon markets, life cycle assessment), etc. This can also be a tool for *market creation*.

4. **Infrastructure investment**: Creates the underlying framework for systems such as for public healthcare, collaborative science, databases, transportation, energy production and distribution, etc.

5. **Institutional changes**: Modifies the rules for collaboration, trade, knowledge market transactions, etc.

6. **Foresight research***:* Maps the links between evolving research programmes (including targeted and multidisciplinary research), regulatory frameworks, policy initiatives, and the development of new technologies.

7. **Public forums***:* Engenders public discussion, debate, and education in areas such as ethics, benefits and risks, and the utility of biotechnology.

8. **Development commitments***:* Applies financial and other support (technology transfer, collaboration between universities, etc.) to developing countries. This includes initiatives like the United Nations' Millennium Development Goals.

In some cases, however, a specific policy approach could be most effective for one specific type of innovation. Due to the infrastructure changes associated with disruptive and radical innovations, a successful transition to their use will often require more public support for *market creation*, *foresight research*, and *infrastructure investment* than for incremental innovations.

This chapter evaluates some of the underlying policy issues that are raised by biotechnological innovations in health, primary production, and industrial applications and examines cross-cutting policies that could support all applications of biotechnology. For each application, the text identifies policies, drawn from the framework in Box 8.2, to address current and future challenges. The aim is to provide a toolkit of possible options for managing the emerging bioeconomy. Many of these policy approaches cover the same ground. An overarching policy framework is therefore likely to contain elements from several of the approaches in Box 8.2.

Primary production

Biotechnology for primary production includes GM and non-GM technologies (*e.g.* marker assisted selection, intragenics, gene shuffling, and directed evolution) for developing new varieties of plants and animals, diagnostics for plant and animal diseases, and a range of smaller market applications such as animal therapeutics and functional foods and nutraceuticals.

Many of the applications of biotechnology to primary production are incremental innovations, such as crop plants with improved characteristics that replace previous varieties of the same crop. Several biotechnological products could have disruptive effects on existing supply chains. These include pest resistant crops that could disrupt the business of pesticide manufacturers or GM plant-based fish feed that replaces fishery sources. Since almost all primary production biotechnologies involve improvements to existing goods, it is difficult to envisage a radical change in primary production up to 2030. However, greater integration between industrial processing and primary production could be a radical innovation as it would probably require substantial new investment in an agro-industrial infrastructure. This possibility is covered below, using the example of biomass-based biofuel production.

Incremental advances in primary production biotechnology

Plant breeding applications of biotechnology (both GM and non-GM) are a major success. The analysis in Chapter 4 of short-term trends indicates that this success will continue as new food, feed and fibre crops with improved stress tolerance, pest resistance, and quality traits reach the market over the coming decade. Policy issues for incremental innovations concern the regulation of risk, promoting research for small market crops, encouraging market incentives for crop traits that deliver greater productivity and quality, verifying the health benefits of functional foods

and nutraceuticals, and maintaining trade in primary production commodities.

Regulation

Technological development in modern societies requires regulatory frameworks that ensure safety and public acceptance of technological advances. Regulatory systems provide a framework for risk assessment and management associated with biotechnology. Approaches to regulating technological risk are founded on evidence based evaluations as well as citizen perception. Coupled with dialogue between all stakeholder groups, a continual evolution of these approaches is an essential feature to ensure the uptake of safe and effective technology breakthroughs.

The main disadvantage of the current regulatory structure for biotechnology in primary production is its cost. Current regulations require environmental and health safety studies for GM varieties, at a cost between USD 0.5 million and USD 15 million per variety. These costs reduce the economic viability of using GM technology to develop improved small market crops and are a major market barrier for small firms. Most regulatory systems, such as in Europe and Australia, focus on transgenic varieties and do not require environmental and health studies for varieties developed through non-biotechnological methods such as mutagenesis, or biotechnological methods such as intragenics that do not transfer genes across species (Russell and Sparrow, 2008). Canada is an exception, applying the same regulations to all new plant varieties with novel traits, regardless of the method used to develop the variety.

A more consistent approach would require all registrations of commercial plant and animal varieties with novel traits to meet environmental and safety regulations, with the possible exception of varieties developed using conventional breeding methods alone. However, the cost of meeting safety regulations needs to be significantly reduced so that it is financially feasible to use advanced biotechnologies to develop improved varieties of small market crops. Costs could be reduced through international agreement on safety research standards, so that research conducted in one country is readily acceptable in another country. A similar approach has been successful for chemicals, where common tools and policies for environmental and safety regulations (including an approach for mutual acceptance of safety data) amongst OECD countries result in annual savings to government and industry of over USD 65 million (OECD, 1998).[3]

Within the OECD, 14 consensus documents, which are agreed texts that set out scientific information on the components of specific crops (*e.g.* key nutrients, toxicants, anti-nutrients and allergens), have been produced. Their

value lies in their portability – they can be applied across national borders as "mutually agreed" evidence for use during the regulatory review of human food and animal feed safety, thus saving time and substantially lowering costs. Although a positive step, further harmonisation is required to reduce the regulatory costs associated with developing GM plant varieties. A reduction in regulatory costs is not, however, likely to be sufficient to encourage research into small market crops.

Small market crops

The use of GM technology to introduce a set of genes for a valuable trait into multiple varieties of plants and animals gives a competitive advantage to large firms that own elite germplasm[4] for a range of commercially valuable varieties and species (economies of scope) and lowers the cost of each transgene or intragenic event (economies of scale). This has driven mergers and acquisitions and reduced the economic viability of small firms active in major crop varieties (see Chapter 6). A policy challenge that is especially pertinent to development goals is to encourage the diffusion of genetic biotechnologies to small market crops. This could require reducing regulatory costs (as noted above), encouraging collaboration (including with regards to intellectual property) and maintaining the active involvement of the public research sector to identify markers and possibly develop varieties to the proof of concept stage. The fact that public research in GM has fallen precipitously in Europe since the late 1990s (see Box 5.2 in Chapter 5) is a highly unfavourable development that could reduce both leading-edge research in this technology and the number of graduates trained in the use of advanced agricultural biotechnologies.

Functional foods and nutraceuticals

Functional foods provide health benefits beyond basic nutrition. Nutraceuticals are food supplements, based on products isolated or purified from plants or animals, with known or assumed health benefits. Both have been available for decades, such as vitamin D fortified milk or cod liver oil. Biotechnology can play a role in both functional foods and nutraceuticals, such as developing varieties of staple crops with high levels of essential minerals or nutrients or the production of nutraceuticals such as omega-3 oils.

The main policy interest in functional foods and nutraceuticals is their possible health benefits. Well-designed clinical trials have not verified the health claims for many nutraceuticals, such as the claimed benefits of lycopene or anthocyanins in preventing cancer, glucosamine in reducing the effects of osteoarthritis (Hayden, 2008), or pro-biotics in improving general

health. Conversely, there is some evidence to support the health benefits of omega-3 oils. In many countries, including the United States, manufacturers are able to make qualified claims for these products, such as "some evidence suggests that", even when the evidence is very weak. This reduces the incentive to invest in proving health claims. In addition, the market for many functional foods and nutraceuticals is rarely large enough to support the cost of well-designed clinical trials. Advances in functional foods and nutraceuticals could depend on financial support for public research institutes to conduct trials to verify health claims.

In developing countries, using biotechnology to develop nutritionally enhanced varieties of staple crops such as cassava, maize and rice could be a cost effective method of supplying key minerals and vitamins to poor populations that cannot afford a nutritionally diverse diet.

Trade

Although not directly linked to biotechnology, unimpeded trade in agricultural commodities will be essential to the bioeconomy of 2030. India and China will run large deficits in agricultural products and will need to import food and feed, with South America and parts of Africa developing into major sources of these commodities.

Trade regulations for GM crops can close markets for exporters and increase costs for farmers and food processors in importing countries. These regulations have been a subject of serious discussion within regions that have not adopted GM crops on a large scale. There have been concerns about cost increases associated with the rejection of shipments of feed grain that contain even trace amounts of non-approved GM varieties. The problem becomes particularly acute as new varieties of GM crops are developed and cultivated without corresponding regulatory approvals in importing regions. This could increase the cost of sourcing approved livestock feed in countries or regions (such as the European Union) that limit GM technology.

Box 8.3. **Managing incremental biotechnologies for primary production**

1. **Research subsidies** and **Institutional changes**: The application of biotechnology to the development of crop varieties with small markets will probably require public support for applied research. This could include publicly funded translational research up to the proof of concept stage, research consortiums with public and private players, or policies to reduce intellectual property and regulatory costs.

2. **Research subsidies** and **Development commitments**: An effective health promotion strategy relying on functional foods and nutraceuticals will necessitate verified health benefits. In cases where clinical trials are needed to prove the veracity of health claims, public support may be required. To deliver on nutritional goals in developing countries, applied research to develop varieties of staple crops with improved nutrient levels, and the distribution of these varieties to farmers, should be supported.

3. **Market creation**: Trade in primary production commodities is and will continue to be an important tool to reduce frictions over access to resources. Policy should ensure open trade for food, feed and fibre and maintain adequate stockpiles of essential food products.

4. **Regulations/standards**: Regulations governing new plant and animal varieties may need to be modified to ensure the effective management of environmental and safety risks at minimal cost and delay. A potentially powerful tool, to this end, would be the adoption of internationally accepted protocols for establishing safety so that tests do not need to be repeated in each country. Regulatory costs for small firms (so they can compete) and for small market crops (so that new varieties are developed) could also be reduced. Another option is to implement a sliding scale for testing, with fewer tests required to establish safety for well-understood traits.

Disruptive primary production biotechnologies

Several biotechnology innovations in primary production could have disruptive economic effects by displacing other production methods: production of fish protein in GM plants or micro-organisms to replace wild fish for aquaculture, foods that reduce the risks of developing chronic diseases, enhanced varieties of trees for tropical and sub-tropical regions for producing pulp and paper or biofuels, and enhanced varieties of many feedstock crops to replace fossil fuels in chemical and plastics production.

A major environmental disadvantage of aquaculture for carnivorous species such as salmon, shrimp, tuna and cod is that they are fed fishmeal and fish oil obtained from wild fisheries. Even herbivorous fish such as tilapia and carp are fed these products to accelerate growth. Fish oils and other products for aquaculture can be produced in GM plants and micro-organisms. This disruptive innovation could replace wild fish feed with plant based products and reduce the pressure on wild fish stocks.

Predictive and preventive medicine could benefit from foods or nutraceuticals to delay or prevent chronic disease.[5] This will require good evidence for their health effects, as discussed above. If effective, it could reduce the necessity for some pharmaceutical products and reduce healthcare costs.

With adequate water, biomass production per hectare in sub-tropical[6] and tropical regions is between four and ten times the production in temperate regions, due to warmer temperatures (Larson, 2008).[7] This difference should provide a large competitive advantage to sub-tropical and tropical regions for growing low-value crops for pulp and paper, other fibres, and biofuels. Low latitude desert regions close to the ocean can be extremely productive areas for producing crops from marine species of algae. Consequently, research into these and other crops is likely to shift to varieties than can be grown in productive climatic regions. This could have serious disruptive effects on the competitiveness of forestry firms based in Northern boreal forests. These regions may need to increasingly switch to higher value wood products.

Box 8.4. **Managing disruptive and radical biotechnologies for primary production**

1. **Research subsidies** and **Market creation**: Policies may need to be diversified to support research into disruptive biotechnologies for primary production with established benefits for environmental sustainability. Support options include research and procurement subsidies and support for free trade in environmentally sustainable products.

2. **Foresight research**: Sectors facing disruptive change (fish feed for aquaculture or pulp and paper in boreal forests) should be encouraged to develop new business models and shift investment to new markets, supported by foresight research.

Key uncertainties for primary production

Public acceptance of biotechnological methods for developing new varieties of plants and animals is a key uncertainty for primary production. As with computers in the 1970s,[8] public acceptance of a new technology often depends on perceived personal benefits. A common view is that public acceptance of transgenic breeding methods will increase when new products with quality benefits for the consumer reach the market, such as nutraceuticals or healthier functional foods. However, the main market for quality traits is likely to be for crop varieties with improved food processing characteristics, with low visibility for consumers.

This does not mean opposition to transgenic crops in regions such as Europe will be unending. Public opinion could change if biotechnology produces environmental benefits and is shown to help maintain or increase yields in the face of greater stresses from climate change. Such a change in public opinion has already occurred in Australia (Eureka Strategic Research, 2007), driven by public awareness of the effect of long term drought on agriculture. Acceptance of GM in many countries could improve if the public is aware of successes in developing nutrient enhanced food crops for developing countries, crop varieties that reduce the need for environmentally harmful fertilisers and pesticides, or varieties that tolerate drought or salinity, thereby increasing food security in some regions. Public opposition to transgenic and cloned animals in developed countries is likely to continue, possibly beyond 2030, due to a combination of ethical concerns and uneasiness about the idea of transgenic or cloned meat.

Other uncertainties for primary production include the factors that influence production choices. Farmers decide what to plant and where in response to fluctuations in prices and markets. Political concerns, such as recent debates focusing on food versus fuel, can also play a role. These production decisions, which are difficult to forecast more than a year in advance, will affect supply and demand conditions and influence the types of crops that are grown. This could affect the market for biotechnology over the short term (up to 2015), but over the longer term an increasing share of all new crop varieties will be developed using biotechnology. Therefore, the impact of crop prices on the market for varieties developed through biotechnology will decline.

Box 8.5. **Managing key uncertainties for primary production biotechnologies**

1. **Public forums**: Better education on the benefits of biotechnology, perhaps through the involvement of scientists, could help address public concerns over the application of biotechnology to primary production. This method has often been rejected because of concerns that a lack of understanding is not the cause of opposition to new technology. Nevertheless, opinion research (see Chapter 5) shows that public attitudes do respond to information. Public opposition to agricultural biotechnology is also based on concerns over the concentration of ownership of plant varieties in a few firms and intensive farming practices. Forums and other methods of fostering public discussion on expectations for agricultural production systems may help, in part by clarifying the roles of biotechnology and intensive farming in food production.

Health applications

This report considers several possible futures for health biotechnology in developed countries. The first is incremental change based on the annual market approval of a moderate number of new pharmaceuticals and therapies, the gradual implementation of pharmacogenetics: (first to increase safety), improved diagnostics for diseases and for genetic susceptibility to chronic disease, and several improved therapies to treat genetic diseases. This future is a continuation of the estimated supply of new therapies up to 2015 discussed in Chapter 4.

A second possible future includes the success of disruptive technologies based on regenerative medicine such as tissue engineering, stem cell treatments, and gene therapies that offer temporary or long-term cures for chronic disease. Many of these are experimental technologies that are in the research phase, with very few successful therapies having received market approval by early 2008. They are often disruptive technologies. By curing rather than treating diseases, they could replace markets for pharmaceuticals, such as insulin, that treat long-term chronic disease. In addition, their mode of delivery to patients will differ from the delivery system for pharmaceuticals, possibly disrupting how health services are provided.

A third possible future includes both a continued supply of new therapies and the introduction of regenerative medicine, along with the

implementation of radical innovations to support a predictive and preventive healthcare system. This future offers potentially significant improvements to the quality of life by reducing the number of years living with a disability. It could also add several years to the expected baseline increase in life spans of 1-1.5 years per decade.

The first future, based on incremental innovation, will develop under the current healthcare system in developed countries, although there is room for improvement. However, the second and third futures, which potentially offer greater health benefits, could require new policies to support changes in research, business models, institutions, and the infrastructure for healthcare.

Incremental advances in health biotechnology

Long before 2030, almost all pharmaceuticals, as well as therapies based on regenerative medicine, will be developed using biotechnology. Therefore, the regulatory system for all pharmaceuticals is an integral part of the policy agenda for the bioeconomy. Other regulated therapies such as medical devices are also likely to be influenced by biotechnology, though to a lesser degree. One of the main policy challenges is to improve the cost-effectiveness of new therapies. This requires a better alignment between private sector incentives and public health goals (Kaplan and Laing, 2004; Morgan *et al.*, 2006, 2008) and policies to ensure that this alignment supports disruptive and radical innovation.

Despite a number of major therapeutic advances, investment in health biotechnology has been criticised as inefficient (Ernst and Young, 2008), both in terms of the cost of developing new therapies and the aggregate therapeutic benefit obtained from private and public R&D expenditures. Policy papers on drug development costs frequently cite average private sector costs per new pharmaceutical of between USD 800 million and 1.3 billion. Although these could overestimate the actual cost,[9] drug development is clearly expensive and is partly responsible for the high prices of many new drugs. Yet expensive drugs do not always provide major therapeutic advances, as discussed in Chapter 3. Approximately two-thirds of all new drugs applications to the American FDA from 1993 to 2004 are classified as "me too" drugs that offer only small improvements over existing treatments. Furthermore, the cost-effectiveness of drug development, measured by R&D expenditure per new molecular entity (NME) submitted the FDA for approval, has been decreasing over time (GAO, 2006).

A policy agenda for health incentives

Conflicts over the cost-effectiveness of new therapies are largely responsible for the frequent disagreements between funders and pharmaceutical firms over the cost of new treatments. The goal for public health is to obtain highly effective and safe therapies at the lowest possible cost. The goal for health firms is to recover the costs of developing new therapies and earn a profit. This depends on the ratio of development and production costs to future revenues.

Several biotechnological innovations can potentially increase or decrease drug development costs:

- increase costs from the need to validate biomarkers and identify genetic and other factors that influence response to treatment;
- reduce costs from the application of pharmacogenetics and other knowledge to lower the percentage of candidate therapies that fail (OECD, forthcoming);[10]
- reduce costs from smaller and fewer clinical trials from the use of pharmacogenetics and biomarkers;
- reduce manufacturing costs through more efficient production methods.

On the other side of the ledger, several factors, not all of which are linked to biotechnology, influence the potential revenue from each new therapy:

- the potential market size for the therapy, based on the prevalence of the targeted disease;
- market losses from prescribing restrictions due to pharmacogenetics and possible losses or market gains from post market assessments of the efficacy and safety of a therapy;
- the patent life remaining before the introduction of generics, which will influence the price that can be charged;
- the price that can be charged for treatment during the time the therapy is covered by a patent and the price after patent protection ends.

Many of the current policy debates focus on one or more of these factors. The current business model of many pharmaceutical firms and the market incentive structure ensure that it is in the firm's interest to reduce development costs, increase the size of the potential market (*e.g.* through

direct to consumer advertising,[11] off-label prescribing, or seeking regulatory approval for multiple indications) and extend patent protection for as long as possible.

Several policy approaches could help to reduce the development costs for new therapies.

Increasing public support for biomedical research is one option, although each of several waves of biotechnological innovation has promised a leap of magnitude in the efficiency of pharmaceutical research and each wave has passed by and increased costs (Pisano, 2006; Hopkins *et al.*, 2007). Although scientific progress could create enormous gains in therapeutic efficiency, the fact that it has not happened so far suggests a need to search for other solutions. Other possible options include support for "translational medicine"[12] and greater collaboration to increase the speed and effectiveness of transferring knowledge from the public research sector to firms.

Another option is to reduce costs through changing the structure of clinical trials, which are estimated to account for between 30% and 58% of total drug development costs (Rawlins, 2004). Cost savings from this strategy depend on several factors. Both the size of clinical trials and their number depends on the efficacy of the drug, with more effective drugs requiring smaller trials than drugs with minor benefits over placebo. Pharmacogenetics, by identifying subgroups of patients that respond to treatment, could reduce the size of clinical trials for establishing efficacy, but larger trials would still be required to establish safety. Consequently, the impact of pharmacogenetics on reducing the size of clinical trials is likely to be highest for cancer and other fatal diseases where the benefits of treatment can be much greater than the risk of adverse effects.[13] Conversely, non-fatal diseases are likely to continue to require trials that are large enough to establish safety.

Savings in manufacturing costs are particularly relevant for many biopharmaceuticals, where the cost of production using GM micro-organisms in bioreactors is very high. Producing biopharmaceuticals in GM plants or in the milk of GM animals could potentially result in large cost savings (Frost and Sullivan, 2004). This would require regulatory systems to manage the use of GM crops and animals to produce high value non-food products and mechanisms to ensure that these products do not enter the food chain.

Other polices could increase the potential revenue from new therapies, but these need to be linked to evidence of significant improvements in therapeutic value.

An alternative method for improving the ratio of drug development costs to future earnings is to increase the effective patent life by shortening the time required to obtain marketing approval. This could be achieved by shifting some of the late stage clinical trials for safety or efficacy to the post approval stage,[14] but at a potential cost in terms of greater safety risks.[15] Regulatory systems already contain the flexibility to rapidly move promising treatments for cancer and other serious diseases from clinical trials to market approval (Dukes, 2008). Therefore, the potential impact of this method on the average effective patent life will depend on the share of all new pharmaceuticals that target potentially fatal diseases such as cancer and the degree to which higher risks of adverse effects will be accepted for drugs that target non-fatal disease.

To improve the cost-effectiveness of new therapies, policies to increase revenues must be combined with strong incentives to support the development of highly effective new drugs. Experiments with several incentive mechanisms are underway, whereas others remain theoretical and require further study. Several countries already link the level of reimbursement to health outcome measures such as Quality Adjusted Life years (QALYs). There is also greater interest in setting clear reimbursement targets for priority drugs to provide an incentive for investment. A theoretical option is to introduce a prize system, an example of which is described in the scenario "Muddling Through" (see Chapter 7), where the financial reward is based on the therapeutic advance offered by the therapy. Identifying the best treatments can also benefit from publicly funded comparative trials of different treatment options (Kaplan and Laing, 2004).

Incentives to encourage more effective therapies are likely to increase costs to health providers, although some of these higher costs could be recouped by reducing payments for marginally effective treatments. This dynamic may be temporary, however, as better financial incentives lead to more effective and consequently more expensive new therapies. The trade-off would be significant benefits for public health. In the end, the challenge for governments is how to implement and finance new incentive systems.

Two technical advances will probably help improve the cost-effectiveness of new therapies: pharmacogenetics and the use of bioinformatics to construct databases of the prescribing histories and long-term health outcomes for millions of individuals.[16] Furthermore, these technologies are fundamental to the development of predictive and preventive medicine. Both of these technical advances, as well as emerging business models to take advantage of opportunities created by pharmacogenetics and predictive and preventive medicine (see Chapter 6), could help support a better alignment between incentives and public health goals.[17]

Finally, facilitating the use of pharmacogenetics and biomarkers will support preventive medicine, through an increase in the number of diagnostic tests for disease risk factors. This in turn could encourage people to make lifestyle changes or receive treatment that could prevent or delay the onset of disease. These tests will need to be reliable. A false positive diagnosis could create anxiety while a false negative diagnosis could result in failure to provide treatment. Furthermore, the widespread use of tests to identify very rare diseases or very low risk factors for chronic diseases could drive up healthcare costs without significantly improving health benefits. These and other concerns over the clinical validity, regulation, and advertising of diagnostic tests are currently being addressed by many governments (OECD, 2001a, 2007).

Box 8.6. **Managing incremental biotechnologies for health**

1. **Regulations/standards**: Policies to improve the ability of pharmaceutical and other health technology firms to recover high R&D costs should better align private sector incentives with public health goals. Care is required to ensure that incentives and regulatory systems also support the future development of beneficial disruptive and radical innovations, such as predictive and preventive medicine or the production of biopharmaceuticals in plants.

2. **Foresight research**: Policy research should urgently explore methods to improve the incentive structure for effective breakthrough therapies and to reduce drug development costs. Options for the former include setting clear reimbursement targets for diseases that lack adequate treatments or setting prices based on health outcomes. Options for the latter include translational medicine and changes to regulatory systems that do not conflict with the public health interest in safety and efficacy.

3. **Foresight research**: Further research is required into the effect on total healthcare costs of financial incentives to improve the therapeutic value of new healthcare treatments and on the willingness of taxpayers or insurers to pay for these costs. Higher therapeutic costs, for example, could be compensated for by a decline in other healthcare costs. Alternatively, higher costs for therapeutics could be acceptable to the taxpaying public if there is a noticeable improvement in health benefits.

4. **Foresight research**: Testing for future disease risks raises a number of potential challenges for healthcare, including the management of tests for genetic risk factors *in utero*, the detection of risk factors for chronic diseases that may or may not develop, and the accuracy of such tests. Further research is required into the ethical, cost, and psychological effects of genetic testing and the types of policy actions that might help to reduce potential risks.

Disruptive and radical health biotechnology

Regenerative medicine could have several disruptive effects. Its use to replace damaged tissue, teeth or bone could significantly reduce pharmaceutical markets for several chronic diseases, including Type 1 diabetes, rheumatoid arthritis, and neurological and cardiovascular diseases. Furthermore, some types of regenerative medicine could also disrupt current business models in the health sector.

The patentability of regenerative medicine poses several policy issues. The development and diffusion of regenerative medicine might be delayed if laboratory techniques or methods of differentiating cells that are important to all regenerative medicine applications are given broad patent rights and only licensed at high cost (or not at all). The opposite problem might develop for regenerative medicine based on autologous cells. Even if these cells are patentable, intellectual property rights might fail to provide an incentive for investment in this technology. With personalised treatment, it would be difficult for patent owners to determine if their patent was infringed, for instance by patients seeking lower cost treatment in countries where infringement is difficult to detect.

Predictive and preventive medicine is a potentially radical innovation that could seriously affect the business models of healthcare firms and healthcare delivery services. Several organisations such as Kaiser Permanente have already established some of the basic requirements for predictive and preventive medicine, such as an electronic data infrastructure for linking medical records on treatments, outcomes, and genetic and environmental risk factors over an entire lifetime. Despite potential benefits, this can create concerns over privacy and the release of confidential information to insurers and employers (OECD, 2001a, 2008a; Hempel *et al.*, 2008). Other aspects of predictive and preventive medicine will require changes to how healthcare is provided. Doctors will need to scrupulously follow best-practice recommendations for diagnostics, prescribing, and treatment. This will involve a major shift away from the current "medicine as art" approach of many medical practitioners, in which, recent evidence shows, there is widespread failure to follow best-practice rules[18] and extensive off-label prescribing. Future best-practice methods will be identified through long-term analysis of integrated data records, comparative clinical trials, and experimentation with doses. This is a proven strategy that has been verified for childhood cancers.[19] In order to discourage inappropriate prescribing and ensure that both doctors and patients comply with best practice, this approach to medicine is likely to require stricter rules on advertising and on advertising claims.

Due to high costs and a poor fit with current business models, predictive and preventive medicine is unlikely to reach its potential without public funding for research, including long-term trials to identify best practice. This should build on the model of the very successful research programmes into treatments for childhood cancer and for heart attacks.

Box 8.7. **Managing disruptive and radical biotechnologies for health**

1. **Research subsidies** and **infrastructure investment**: Predictive and preventive medicine could require further targeted investment to support infrastructure for integrated databases and extensive long-term public support for research due to high costs and long lead times required to obtain results.

2. **Foresight research**: Research is required into the effect of regenerative and predictive and preventive medicine on the provision of healthcare services and their implications for data confidentiality, physician training, and human resource needs.

3. **Foresight research**: Current business models are based on earning revenues from selling products such as tissue scaffolds or drugs, or from licensing patented knowledge. This model could fail to provide sufficient revenues to fund private investment in regenerative and predictive and preventive medicine. Private sector success in both of these new approaches may require shifting business models towards earning revenue from providing personalised services. A thorough evaluation of the implications of both biotechnologies on the ability of private sector firms to profit from R&D investments, and possible changes to policy to support such investment is required.

4. **Foresight research***:* Public healthcare systems separate the private supply of drugs and other therapies from the public provision of healthcare services. This could affect the introduction of regenerative and predictive and preventive medicine. Research is required into how public healthcare systems might need to adapt to take advantage of these emerging approaches to medicine.

Key uncertainties for health biotechnology

In addition to the scientific and technical hurdles facing health biotechnology, there are two important uncertainties that need to be examined.

Longevity

A key uncertainty is the effect of advances in health biotechnology (and other factors) on longevity and the quality of extra years of life. The baseline forecast by the US Census Bureau estimates that average life expectancy in the United States will increase by 1.3 years per decade, giving an average life expectancy of 80.5 years in 2030 (Sonnega, 2006). Average life expectancies in many European countries, Japan and Australia could reach 84 to 86 years by 2030. Advances in healthcare due to biotechnology could increase longevity above these baseline estimates.

A common concern is that longer life spans could substantially increase total healthcare costs, especially if the extra years of life are spent in poor health or suffering from dementia (see for example BBC News, 2008). New healthcare technologies employed to meet these challenges are also likely to increase costs further exacerbating the problem (OECD, 2006). These combined effects could place enormous financial stress on both the healthcare and the pension systems. Some disagree with this assessment however. At least one positive "win-win" scenario, developed by SRI Business Intelligence (2008), sees health biotechnology leading to both longer and healthier lives. This would engender a fall in the share of GDP spent on healthcare, although this is an exception to most research, which finds that new healthcare technology increases costs.

Elements of the positive scenario are supported by research showing that the elderly are healthier than in the past, thus reducing the expected increase in healthcare costs (Romanov, 2002). Furthermore, it is not clear if the number of years with dementia has been increasing with longer life spans. One study reported both a decline in the prevalence of dementia over time and in the number of years with dementia (Langa, 2008). Other research finds an increase over time in the number of years with dementia for men but a decline for women (Sauvaget *et al.*, 1999).

Longer life spans could require a shift in the distribution of income from working age populations to retired populations, triggering changes to a wide range of social policies and practices. Advances in biotechnology that increase life spans may however be balanced by advances that increase the number of years of life without serious disability. Pension systems could adjust to greater longevity if people remain healthy into old age and if there is a commensurate increase in the percentage of older people that remain in the work force. If health in old age does not improve, an increase in the average lifespan will increase healthcare and pension costs without a proportionate increase in the quality of life. This imbalance in the costs and benefits of medical advances could create intergenerational conflict over the

costs as well as widespread fear over ageing, with a reduction in the quality of life for many people.

Developing countries

A second unknown is the future role of major developing countries such as China, India and Brazil as regulators, producers, and markets for health biotechnology products.

China and India, as with other major developing countries, currently have weak regulatory systems for pharmaceuticals. Yet both countries are moving towards a stronger regulatory system that is similar to that in Europe. This is because regulatory improvements in China and India are not only driven by domestic demand to improve the quality of domestically manufactured healthcare products,[20] but also by an interest in accessing the world's largest markets for health therapies. The EMEA and Canadian regulatory systems are currently favoured by the BRIC countries. One of the perceived disadvantages of emulating these two systems is that both, compared to the American system managed by the FDA, limit public access to data that could be used to improve health research (Vitry *et al.*, 2008). Fundamental improvements have already been made in China, with the regulatory system moving towards international standards on marketing approval, licensing of manufacturing plants, and detection of counterfeit drugs (Dukes 2008).

Developing countries offer growing markets that could provide new revenues for pharmaceutical firms, possibly offsetting a decline in revenues in OECD countries from smaller markets for new drugs. Between 2002 and 2006, the pharmaceutical markets in India grew at an annual rate of 7.3% and in China by 17%. Neither growth rate is likely to be sustainable to 2030, but China is already expected to be the world's seventh largest pharmaceutical market by 2010 (Pharma Futures, 2007).

However, several factors could limit the market potential of developing countries. Average income in both countries in 2030 will be substantially less than in developed countries, limiting the ability of individuals to pay for costly therapies. China could also strengthen its public healthcare system and place limits on the level of reimbursement for drugs. Domestic demand could also be increasingly met by domestic firms with low production costs. By 2030, research intensive Chinese and Indian pharmaceutical and medical device firms, which are already involved in R&D outsourcing, are likely to be competing globally and could drive down pharmaceutical prices in OECD countries.

Box 8.8. Managing key uncertainties for health biotechnology

1. **Foresight research**: Research is required into the social, ethical, and economic consequences of possible increases in longevity. There is a strong public interest in supporting health research that improves the quality of life and minimises the years spent with major disabilities.

2. **Public forums**: In all OECD countries, including the United States, publicly funded institutions are the major source of finance for healthcare and often for health research as well. Consequently the public should participate in a discussion on what they want from healthcare. What are their views on longevity versus long-term disability? What level of health benefits would they be willing to pay for?

3. **Development commitments**: Countries with robust regulatory systems should continue to assist developing countries to craft appropriate systems, but the wider goal should be to improve all regulatory systems. One approach involves greater transparency. This could require increasing access to some clinical trials results. While this might reduce development costs and provide support to further research into improving health outcomes, there are significant hurdles to be overcome in order to reach a consensus on how to move forward on opening up clinical trial data. Some options are discussed below.

Industrial applications

Industrial biotechnology faces multiple futures: from providing a limited number of incremental improvements to major changes in how products are produced and delivered. Industrial biotechnology has the potential to significantly reduce the environmental impacts of chemical and fuel production, but in some cases other technologies for achieving the same ends could be superior. The extent to which industrial biotechnology will be used by 2030 will depend on policy choices, private investment decisions, infrastructure development, technological breakthroughs and the competitiveness of biotechnological solutions compared to other alternatives.

Incremental advances in industrial biotechnology

Industrial biotechnology can provide substantial benefits such as lower operating costs and a reduced environmental footprint (OECD, 2001b), but

it must compete with alternative production technologies. The main challenges for industrial biotechnology are scaling up biobased production to an industrial scale and ensuring a secure supply of biomass feedstock of a known and consistent quality. Successes have been realised however, particularly in areas where industrial biotechnologies provide a significant yield or efficiency advantage or where government support has driven investment.

An example of the former is industrial enzymes, which are widely used in the production of food, animal feed, textiles, and detergents. The production of fine chemicals, including vitamins and pharmaceutical precursors, is another example where efficient biobased production using micro-organisms in bioreactors is often the preferred method. The use of biotechnology to produce enzymes and fine chemicals should continue to grow to 2030.

Biotechnology has been used less frequently to produce bulk low-value chemicals. None the less, steady technological progress has expanded the range of specialty and bulk chemicals that can be produced with the assistance of biotechnology. Further use will depend on high prices for fossil based feed stocks, experience in scaling up production, and policy interventions to create and sustain markets for biochemicals.

The production volume of biopolymers continues to increase, but they currently only have a very small share of the global polymer market. Rapid growth is expected in niche areas such as biodegradable plastics for consumer and food packaging. Other types of biopolymers will increase more slowly and require the development of new processes. Remaining challenges for biopolymer uptake include meeting performance criteria, security of feedstock supply and measurement of sustainability.

Governments currently support biofuels via subsidies, mandates, and trade restrictions (OECD, 2008b). In the absence of past support or a continuation of these policies, very little ethanol or biodiesel would currently be produced from food or feed crops (with the exception of sugarcane ethanol), and only very small volumes of biodiesel from animal fats and waste cooking oils. Not only is the cost of producing biofuel higher than petroleum-derived fuel, but crop-based biofuel is subject to the vagaries of the weather and other forces affecting crop yields and competes with crops for food and feed.

Due to their disadvantages, the future of bioethanol or biodiesel from food or feed plants will be limited to countries with ample supplies of low cost vegetable oil or sugars. Incremental developments in industrial biotechnology will focus on improving fermentation processes and will be coupled with the development of new biofuel crop varieties with improved

yields. In other regions bioethanol and biodiesel from food or feed plants are likely to only be a short-term solution and will be replaced by higher energy-density biofuels, or from biofuels made from non-food sources. These have the potential to substantially reduce dependence on fossil fuels for transport and are consequently discussed in the next section.

Due to strong price competition from other technologies, the financial viability of biorefineries will depend on improved economies of scale and flexible production, where a variety of end products can be manufactured in a single facility. Ethanol biorefineries already produce animal feed as a by-product, but novel by-products could increase the value added of the final product mix. For instance, recent research has found ways of converting glycerol, a by-product of biodiesel production, into plastics.

There is a high potential for the use of modern biotechnology in environmental services. Both biosensors and bioremediation could play a major role in ensuring human and environmental safety. For example, real-time biosensors are a powerful tool for identifying invasive species in cargo. While carefully selected micro-organisms could be used in bioremediation, genetically modified organisms are likely to be more efficient and can be more quickly adapted to site specific conditions. The drawback to their use is high regulatory costs that are in the millions of dollars combined with relatively small markets. The future use of biotechnology for environmental services is likely to be highly dependent on policies to create and sustain markets and on the design of regulations.

Box 8.9. **Managing incremental biotechnologies for industry**

1. **Research subsidies**: Public R&D funding for industrial biotechnology is very low compared to agricultural and health biotechnologies and could be increased to take advantage of the potential of many industrial biotechnology applications to reduce pollution and energy consumption. Research is particularly needed to develop reliable feedstock from non-food crops.

2. **Research subsidies**, **Market creation**, and **Regulations/standards**: The development and application of promising industrial biotechnologies for environmental remediation and biosensors are hindered by the combination of high R&D costs and small markets. Subsidies and procurement policies to create demand and reductions in regulatory costs could be based on their potential for environmental benefits.

Disruptive and radical industrial biotechnologies

Several industrial processes based on biotechnology could have disruptive effects on economies by replacing production systems based on petroleum feedstock. Other processes might have radical effects, such as the use of micro-organisms or simple plants developed through metabolic pathway engineering. This could disrupt current methods of producing chemicals and require new infrastructure for large scale chemical production. The latter might also produce unimaginable new chemicals with possible disruptive effects on other economic sectors.

Biofuel production is a good example of the potential of industrial biotechnology to result in either disruptive or radical innovation. The main difference between biofuel as a disruptive or radical innovation is possibly the scale of production. Large scale production, either through the use of biomass or through direct production in micro-organisms, would need substantial investment in new knowledge and infrastructure. For example, the former would require investment in new crop varieties to provide an adequate supply of biomass, technical solutions to reduce the cost of transporting biomass to biorefineries, new biomass transportation infrastructure, and possibly (if based on ethanol) specialised pipelines or tankers to distribute the biofuel to markets. Greater integration between agriculture and industrial processing would also be necessary, creating an "agro-industrial" economic sector.

The evolution of developments in industrial biotechnology is often hard to ascertain due to a lack of data. However, due to recent interest, a great deal of new information has been collected for biofuels. This provides an opportunity to examine what changes may be radical and disruptive. Some of the issues discussed below, such as the potential for tensions between new production methods, will also be applicable to the production of other chemicals and biomaterials. In other areas of industrial biotechnology, such as environmental services and resource extraction, radical changes are not foreseen.

There are two competing technological approaches to industrial biotechnology, both of which will disrupt supply chains and production methods for chemicals and fuels based on petroleum feedstocks. The main difference between the two approaches is the source of energy and carbon to produce compounds such as biofuels, bioplastics and bulk organic chemicals. The first approach uses biorefineries in which micro-organisms such as yeast convert biomass into useful products, drawing energy, carbon and nutrients from the biomass itself. The second approach uses enhanced micro-organisms or plants to produce a similar range of products, but draws energy from sunlight and carbon from the atmosphere. Nutrients can be

added artificially or obtained from the soil or from animal or human wastes. In each approach, transgenic, intragenic, directed evolution, gene shuffling or synthetic biology techniques could be used to produce enhanced varieties of plants or micro-organisms.

These two technological approaches are potential competitors. Given technological breakthroughs, biofuels and many other bulk chemicals could be produced more cheaply using the second approach than through the two-step processes that are currently in use or under development for biorefineries. There is a possibility of a future clash of business models and a loss of capital investments in the infrastructure for biorefineries. Alternatively, the two solutions could complement each other. Biorefineries could be competitive in humid sub-tropical and tropical regions with ample biomass resources and with high biomass production rates per hectare. The direct production of biofuels from marine algae or synthetic micro-organisms could be the dominant production method in regions with a lack of low-cost biomass resources, such as Japan, or in low latitude desert areas with ample sunlight and access to brackish or salt water, such as the South Western United States, Northern Mexico, Australia, Eastern India, Spain, North Africa, and the Middle East.

For environmental, food security, and technical reasons, a shift in biofuel production from the current focus on bioethanol to cellulosic fermentation of biofuels with higher energy-densities and ultimately, in suitable regions, to direct production of high energy-density biofuels by algae or micro-organisms, is preferable. In addition to concerns over the effect of bioethanol on the environment and on food security, bioethanol is only a short-term solution because it is an inferior fuel. It provides only 65% of the energy per volume as petrol and is also miscible in water, which makes it difficult to transport in pipelines. It is primarily used in low-percentage blends with petrol (around 10%). Higher ethanol concentrations, of more than 30%, require modifications to vehicle engines (OECD, 2008b). For these reasons, it is unlikely to be able to compete with improved biofuels, such as high energy-density fuels made from sugar cane or cellulosic crops.[21]

The future competitiveness of cellulosic biorefineries for both biofuels and biochemicals depends on solving difficult technical and organisational challenges. A biorefinery needs to flexibly use different biomass feedstocks and produce different products, depending on input and output prices. Due to high transport costs, feedstock is likely to be obtained from high yielding GM tree, grass, or shrub varieties that are sourced from an area relatively close to the plant. This will limit the volume of feedstock and require efficient small or medium sized biorefineries. Similarly, the efficient production of biofuels or other products from micro-organisms or algae

requires solutions to the issues of scaling up production and preventing contamination by undesirable organisms.

Large firms are likely to dominate biorefineries because of high capital costs and the need for familiarity with complex production plants. SMEs active in industrial biotechnology face several barriers, including access to finance and to proprietary and tacit knowledge on scaling up production plants. For both reasons SME involvement in biorefineries is likely to be based on collaboration with large firms. Greater opportunities for SMEs exist in synthetic biology, particularly for obtaining venture capital, which could be attracted by faster rates of return than in pharmaceuticals (a 5-8 year development time *versus* 12-14 years) (Podtschaske and Mannhardt, 2008).

Over the long term (and possibly well before 2030), it will not be possible to reduce significantly GHG production with biofuels unless they are produced directly by micro-organisms or algae. In the absence of this technology, a shift towards electric vehicles powered by solar, wind, geothermal, tidal, or nuclear energy could be a preferable option. The potential production volume of biofuels from biomass crops is constrained by global limits on the supply of low cost biomass and low output levels per hectare.

The highest observed yields for bioethanol are from sugar cane, which can produce 5 200 litres of petrol equivalent fuel per year per hectare.[22] To meet 100% of the predicted global demand for liquid fuels in 2030 would require almost 10% of the global land area (excluding Antarctica) to be used for sugar cane or other high yield bioethanol crops. This is approximately equal to all land currently under cultivation worldwide. In contrast, microalgal production of high energy-density biofuels, using marine species adapted to salt or brackish water, could theoretically provide enough liquid fuel to meet global demand in 2030 on 0.9% of the global land area (excluding Antarctica) and it would preferentially use semi-desert or desert lands instead of high quality farmland.[23] A radical shift to algal production would require pre-treatment of salt water to remove competitors or the development of algal varieties that can thrive in water that contains other species.

A transition to biofuels has both advantages and disadvantages as compared to other non-fossil fuel based transport systems. Widespread use of ethanol and other comparable low energy-density biofuels, is likely to have relatively high infrastructure cost requirements. This is due to the potential need for dedicated shipping pipelines and, if ethanol rises to above 20% or so in the fuel blend, the need for special "flex fuel" motors and refurbishment of filling stations (Yacobucci and Schnepf, 2007). Higher

density biofuels will avoid many of these costs, but they will need new production facilities that could be located in areas that will require some new infrastructures to gather the fuel and distribute it to consumers. Other alternatives to current fossil fuel-based transportation systems, such as electric cars or electric-fuel hybrids, would also require new infrastructure for recharging vehicles. If reducing GHG is part of the goal, new high-voltage transmission lines would be needed to link geographically dispersed solar, wind, geothermal, and tidal plants. Nuclear energy production would fit more easily into existing electrical grids.

Biofuels face a classic transition problem for a new technology. Today's fossil-fuel based transportation systems have been put in place over the last century and the shift to biofuels and other energy sources that have the potential to reduce GHG emissions could require expensive new infrastructure. Some of the past research into minimising the costs of producing and distributing fossil fuels will favour biofuels (NIC, 2008). However, any serious transition will still be very costly and is likely to necessitate public involvement. Private investment in biofuels will not proceed without a niche market willing to pay high prices, or a reduction in the risks of competition, either through Government subsidies for biofuels, as has been the preferred method to date, or an increase in fossil fuel costs. In the long term, biofuels will not be competitive without subsidies unless the cost of producing biofuels falls. This requires long-term investment in both research *and* in solving problems of scaling up production.

Within the IEA countries, publicly funded research spending on biofuels accounted for 3% of all public expenditures on energy research in 2006,[24] with more public spending on fossil fuel research than for all renewable sources of energy combined. Venture capital investment in clean energy has been increasing rapidly, from USD 279 million in 1999 to USD 5.99 billion in 2007,[25] although the data do not differentiate between biofuel and other sources of low carbon energy. The promise of high energy-density biofuels is unlikely to be met without an increase in both public and private investment in research into high yielding plant or algal varieties and into solving problems of scaling up production.

Box 8.10. **Managing disruptive and radical biotechnologies for industry**

1. **Research subsidies** and **Foresight research**: Research support programmes need to address both current bottlenecks and long term possibilities. Well-designed support for research into biomass fuels based on cellulosic, sugar, and starch crops should continue as these products will play a role in reducing GHGs and promoting energy security over the next decade. Research to reduce the high transport costs for biomass are required, possibly by improving the characteristics of feedstock plants for biofuels or chemical production. For the longer term future, research incentives should be directed towards biofuels that meet three criteria: high energy-density, minimal environmental impacts and a high compatibility with existing infrastructure designed for fossil fuels.

2. **Research subsidies** and **Market creation**: A major technical problem for all types of bioproducts is scaling up from prototype plants to full-scale commercial production. There is a role for greater public sector research into the core technologies for bioproducts, with the results made available to all firms. Firms could then compete on their abilities to scale up production at low cost. Public funding for prototype plants may also be needed, but it should be available for all firms. Otherwise, subsidies for prototype plants could be anti-competitive.

3. **Market creation** and **Regulations/standards**: "Green" production of biofuels and other bioproducts produced in biorefineries will not be effective or sustainable unless there are: *(1)* standards and enforcement methods to prevent displacing rainforest, peat bogs and other carbon sinks with tree plantations, food or feed crops and *(2)* market mechanisms to support the competitiveness of bioproducts. The former will require performance standards, based on a robust life cycle analysis (LCA) methodology, to assess the level of GHGs and other pollutants from biotechnological and other methods of producing chemicals, plastics and fuels. Mandates or incentives are required to create a market for bioproducts with favourable LCA scores. Carbon will need to be priced high enough to maintain the competitiveness of low GHG energy in the face of inevitable declines in fossil fuel prices from a fall in demand.

4. **Market creation** and **Infrastructure investment:** Government subsidies or mandated targets for biofuels or other bioproducts should be designed to prevent lock-in into sub-optimum fuels or expensive infrastructure that only support one product. This could be a major roadblock to the future adoption of superior technologies.

Key uncertainties for industrial biotechnology

The main uncertainty is the economic competitiveness of industrial biotechnology to produce bioproducts compared to alternative technologies. Biofuels fit easily into existing transport infrastructures and therefore have an initial advantage over other low GHG transport fuels. This advantage could be eroded if problems of energy storage and costs for electrical vehicles are solved. These types of advances could limit the biofuel market to air transport and heavy vehicles.

It is also possible that biorefineries are neither the most economically nor environmentally beneficial solution for the production of many bulk chemicals. The global chemical industry, with sales of USD 1 300 billion in 2004, only used approximately 4% of global petroleum consumption. Using petroleum feedstock combined with efficient recycling could be a more economical and environmentally responsible method of producing many bulk chemicals. Only full life cycle analysis can identify the most environmentally sustainable options.

Box 8.11. **Managing key uncertainties for industrial biotechnology**

1. **Research subsidies** and **Market creation**: Targeted policy support for biotechnological solutions for renewable energy or chemical production at some time will need to become technology neutral, with research and other support granted on a competitive basis to the most promising solutions. Until then, life cycle analysis can help identify the most sustainable technologies.

Cross-cutting issues

Several policy issues are relevant to all applications of biotechnology and to incremental, disruptive and radical innovations. These issues include intellectual property, collaboration, and integration across applications. Intellectual property issues are closely linked to collaboration and consequently these two topics are evaluated together.

Intellectual property and collaboration

Firms will not invest in innovation unless there is a reasonable probability that they will be able to recover, or appropriate, their

investments in the cost of developing new products and processes. Intellectual property rights such as patents, trademarks, trade secrecy, and copyright provide mechanisms for firms to protect their investments in innovation from competitors. These methods are often combined with other appropriation strategies such as building lead time advantages over competitors (Arundel, 2001; Cohen, 1995).

In jurisdictions with functioning intellectual property rights, patents are possibly the most useful form of intellectual property for biotechnology firms because they can be used to buy, sell and trade knowledge. These characteristics can facilitate mechanisms such as licensing (OECD, 2002; Herder and Gold, 2008), collaboration and knowledge markets for sharing knowledge between firms. The main challenge is to facilitate the efficient dissemination of intellectual property to potential users and reduce R&D costs.

In health, creating knowledge markets for proprietary information on failed or abandoned pharmaceutical projects, toxicology data (usually kept secret), or intellectual property that is not part of a firm's core activities can reduce research replication and therefore costs. In addition, many types of collaborative models exist in all applications where intellectual property rights can be used to encourage knowledge sharing and reduce research costs. They include research consortiums that minimise transaction and licensing costs for their members, collaborative networks of researchers to develop technologies for targeted problems, patent pools where several firms agree to share their patents, and open source models that follow rules on intellectual property established by the open software community.

The public research sector is a major contributor to the pool of biotechnology patents, accounting for 21.5% of all biotechnology PCT patents originating in OECD countries between 1996 and 2005 inclusive.[26] The justification for patenting inventions from universities or government research institutes, instead of putting the information in the public domain at no cost to firms, is that firms will be unwilling to invest in developing an invention to the commercial stage without exclusive patent rights that prevent competitors from developing the same invention. However, over half of university licenses are non-exclusive,[27] with some patents licensed to hundreds of firms. These non-exclusive licenses earn revenue for the university, but they do not provide an incentive for innovation, since the same invention can be licensed to many competing firms. In other cases poor granting of exclusive rights could result in a failure for the invention to be adequately developed. In recognition of these problems, the University of California has introduced patent guidelines to support the social goals of faster and less expensive innovation.[28] Changes in patenting practices that

reduce the cost of access to biotechnology inventions could increase the uptake and diffusion of knowledge.

Intellectual property, as it relates to biotechnology, is a particularly contentious issue.[29] Governments will need to find a common agreement on how to manage intellectual property in a way that protects and compensates innovation, while encouraging the diffusion of biotechnologies with potentially large socioeconomic benefits.

Box 8.12. **Managing intellectual property for the bioeconomy**

1. **Institutional changes**: There is a strong policy interest in promoting knowledge markets and collaborative mechanisms such as networks, research consortiums, patent pools and open source models that could reduce research costs, prevent replication and bring knowledge quickly to a large number of potential users. These mechanisms will evolve with changes in competition and regulatory policies.

2. **Institutional changes**: Publicly-funded universities should be encouraged to adopt patenting guidelines that incorporate the public interest in rapid innovation, as when enabling and platform technologies are made broadly available. One option is to encourage public universities to limit exclusivity unless it is necessary to attract follow-on investment and to require the licensee to commit to "diligent development" of the invention.

Knowledge spillovers and integration

Biotechnology is based on a generic knowledge base. Knowledge of how to sequence genomes and determine the function of genes can be applied in primary production, industry and health. The benefits of biotechnological research will therefore be magnified if knowledge produced for one application "spills over" and is adopted by researchers working in a different application.

The integration of two biotechnology applications could create entirely new economic benefits that would not otherwise be obtainable. An example is the integration of primary production with industrial processing to produce chemicals, plastics and biofuels. The economic competitiveness of these products will depend on both the application of biotechnology to improve the characteristics of biomass feedstocks *and* the application of biotechnology to develop more efficient industrial processes that use

biomass. In this case researchers working on modifying plant varieties need to collaborate closely with researchers working on industrial processes.

Both knowledge spillovers and integration across applications would magnify the private and social returns from investment in biotechnology by increasing the size of future markets. As noted in Chapter 7, biotechnology has potential applications in sectors that account for between 6% and 8% of the GDP of OECD countries. Knowledge spillovers and integration to create new applications, along with emerging trade opportunities that expand markets, could further increase the economic potential of biotechnology to more than 8% of OECD GDP.

Box 8.13. **Managing knowledge spillovers and integration**

1. **Institutional changes**: Knowledge spillovers and integration will affect government ministries responsible for research, education, agriculture, industry, health and the environment. Policy coordination across these ministries can help promote greater integration and consequently maximise the potential economic and environmental benefits of biotechnology.

2. **Foresight research**: Integrative applications of biotechnology could disrupt existing processes and value-added chains, creating economic losers. Foresight research can help to identify potential opportunities for entrant firms into new value-added chains and determine if there is a role for policy in reducing barriers to integration.

The global challenge

Biotechnology can offer solutions to numerous global challenges, such as climate change, healthcare, energy supply, food security and clean water. In some cases these challenges can be met by national policies, but in other cases either regional agreements or wider international collaboration among governments might be necessary.[30]

National actions by both governments and firms have taken large strides towards finding solutions to some of these problems. Denmark and Brazil have, respectively, become the global leaders in industrial enzymes (used in environmentally sustainable chemical production) and bioethanol, partly due to policies that helped domestic firms build on national strengths. American

and European firms are world leaders in agricultural biotechnology, selling improved crop varieties on several continents.

Solving other challenges would benefit from regional agreements that create sufficient economic and political clout to establish powerful *de facto* environmental standards, based on life cycle analysis, for specific goods such as bioplastics or agricultural products. Another example is the ongoing harmonisation of pharmaceutical regulations by the American, European and Japanese drug regulatory agencies. This could provide a model for global regulatory standards for the safety and efficacy of pharmaceuticals.[31]

The rate at which the bioeconomy moves forward would benefit from greater global collaboration on research. The public sector in many countries is a major participant in biotechnology research. Developing improved crop varieties for developing countries or new drugs for antibiotic resistance or neglected diseases would benefit from greater research funding, strategies to build international networks of scientists, and improved access to research outcomes. There are many innovative options here, such as creating an international pool of research funds, with contributions based on per capita GDP,[32] or private-public research partnerships. Another option is to assist universities and research centres in developing countries to take part in collaborative international research networks. These options should improve the research capabilities of both developed and developing countries and increase the global pool of highly skilled scientists using biotechnology. Examples include the Drugs for Neglected Diseases initiative (DNDi)[33] which created a virtual network of researchers, the international AIDS Vaccine Initiative (IAVI), and the Noordwijk Medicines Agenda (NMA) to develop and deliver medicines, vaccines and diagnostics for neglected and emerging diseases.[34]

International collaboration (at a minimum between the major economies) could be essential in four areas of relevance to the bioeconomy: to reduce GHG production, prevent disease pandemics in animals and humans, reduce trade frictions that would stifle the emerging bioeconomy, and to manage endangered biological resources.

National and regional policies can encourage investment in low GHG energy such as biofuels. Yet these policies would be more effective if combined with international agreements on GHG production, performance standards for environmentally sustainable biofuels, and source-of-origin rules to prevent unwanted side effects such as deforestation. In the longer term, agreement by the major GHG producing countries on a mechanism to price carbon is essential. Otherwise, a shift towards low GHG energy sources will reduce demand for fossil fuels, driving the price of oil down, and undercutting the competitiveness of low GHG energy.

In health, global collaboration is essential to maintaining the surveillance system for infectious diseases in animals and humans as a first line of defence against pandemics. This system will benefit from research into DNA microarrays that can detect pathogens.

The emerging bioeconomy for primary production and industry would benefit from unhindered trade to prevent frictions over access to resources and to support the development of competitive markets. The global community of nations will also need to insure against the threat of hoarding, which will exacerbate disputes over food or fuel shortages, by building up reserves. In 2008, cereal stocks declined to the lowest level in 25 years (FAO, 2008).

Genetic fingerprinting, a biotechnology which can identify specific species through genetic markers, can be used to identify the source of origin of rainforest timber, wild fish stocks of tuna or cod, or other endangered living resources. Fingerprinting could prevent the sale of illegally harvested goods, but it requires international agreement on its use and the active enforcement of restrictions. As an example, without effective global enforcement, most commercial stocks of ocean fish species could collapse by 2050.

Box 8.14. **Managing challenges at the global level**

1. **Institutional changes** and **Development commitments**: Governments should support mechanisms to develop the capabilities of scientists in developing countries to conduct basic and applied research in biotechnology. This could be supplemented by institutional arrangements to promote the sharing of research results.

2. **Institutional changes***:* Continue pursuing consensus within relevant international fora (*e.g.* World Trade Organization, Biological Weapons Convention, etc.) to ensure that the socioeconomic benefits of biotechnology are realised.

3. **Public forums** and **Development commitments**: Forums could promote regional and international agreements that act as an incentive for investment in biotechnology. These include agreements on greenhouse gases (GHGs), Life Cycle Analysis (LCA) methodologies and performance standards, protection of endangered species and habitats, and trade in biotechnology products.

Timing

Some of the challenges facing the bioeconomy are sequential, with solutions required to one set of problems in order to clear the way for future applications. Policies can therefore be divided into two groups: those that need to be implemented reasonably quickly (within five years) in order to pave the way for future applications of biotechnology, and those that can be implemented later. The second group includes some policies that will need to be in place over the long term, possibly up to 2030.

Over the short haul (over five years)

In primary production, the application of biotechnologies to developing improved plant and animal varieties is constrained by public opposition in some regions, a lack of low cost access to enabling technologies, and the concentration of expertise in a few major firms. These barriers to the full application of biotechnology need to be overcome, particularly in developing countries which are the largest market for primary production biotechnologies.

In health, the technologies to create and analyse integrated "cradle to grave" health records are already available and promise significant improvements in healthcare treatments. However, it may be difficult to fully implement these technologies without a solution to confidentiality issues, modifications to regulatory structures, and funding for post-marketing trials and long-term comparative trials of different therapies to identify the most effective treatments. Once a supporting regulatory, research funding, and health record system are in place, the cost of developing personalised and preventive medicine may fall to a level conducive to rapid improvements in healthcare.

The development of many biotechnology applications in industry is likely to require government support for the creation of markets, for instance through economic instruments such as mandates, environmental taxes, or subsidies. The cost to consumers or taxpayers of these instruments will be difficult to justify without good evidence for environmental benefits. The latter is constrained by a lack of environmental performance standards for bioproducts. Agreement on life cycle methodologies and a mechanism to link economic instruments to the results of life cycle analyses could be essential for maximising the uptake and environmental benefits of many bioproducts.

Over the long haul (up to 2030)

In primary production, long-term international agreements will be required to protect living resources such as forests, ocean fisheries and arable land. Biotechnology can be applied to each of these areas, such as the use of genetic fingerprinting to protect fish stocks. Free trade in primary production products, particularly food and feed, must be maintained to prevent friction over resources.

In health, governments need to analyse the long-term structural effects of regenerative and personalised medicine on healthcare, including data confidentiality, new models for healthcare delivery such as home healthcare, new relationships between patients and doctors, the robotic administration of drugs, etc. There will be a need for long-term planning to provide the necessary human resources and infrastructures for regenerative and personalised medicine. In countries with public healthcare systems, governments should examine the possible effects of regenerative and personalised medicine on the provision of public healthcare services. Research into the social, ethical and physical consequences of longer life spans is also required.

Many bioproducts and biofuels will not be competitive with petroleum feedstocks without long term support. This could require mandates or carbon to be priced at a high enough level to cover its environmental costs. At some time in the future, direct subsidies or mandates should be withdrawn, for instance when the production of high-energy density biofuels produced from cellulose or by algae approaches competitiveness with petroleum products. Maintaining subsidies and mandates as a result of competition from other low carbon energy sources would however probably decrease the probability of achieving goals for reduced GHG emissions.

For all applications, drawing developing countries into a global research network for biotechnology will increase the benefits of the emerging bioeconomy. The ability of developing countries to benefit from biotechnology will partly depend on the choices made by their firms and governments to invest in biotechnology research and to collaborate in international research networks, for example to develop new antibiotics, other necessary drugs, or crop varieties. Developed countries can play an active role by meeting their commitments to capacity development, Millennium Development Goals, and free trade, especially in sub-Saharan Africa, southeast Asia, and less developed regions of South America.

The complex policy context

The emerging bioeconomy will be based on a mix of incremental, disruptive, and radical innovations in three major applications fields. This will require both short term policies and long-term policy approaches that can prepare for future needs. Not surprisingly, this creates a complex set of policies to support the emerging bioeconomy. Many incremental innovations can be managed with adjustments to current policies. Conversely, other goals, such as using biotechnology to improve health or address climate change, will require policies to manage disruptive or radical innovations.

Policy support for radical innovations (and some disruptive innovations) in biotechnology will require a broad mix of the eight types of policy actions discussed above. These include using foresight research to identify opportunities and risks, substantial resource mobilisation through research subsidies, commitment to biotechnology during its uncompetitive phase by creating markets through procurement and pricing incentives, the management of risk and uncertainty through regulations and standards, sustained problem solving through collaborative invention, creation and support of new infrastructures and institutions, public forums to help integrate public and business sector commitments, and international collaboration to support the emerging global bioeconomy.[35]

The interdisciplinary nature of many challenges associated with the use of disruptive and radical technologies will require the active participation of various government ministries and agencies. This adds complexity to the already difficult task of determining which government ministries should take the lead in implementing government policy. Governments should recognise this from the outset and dedicate resources early on to setting up effective management structures to design policies for the bioeconomy that include all relevant actors.

The policy options described in this chapter should help governments to maximise the public benefits from a wide range of different types of biotechnology. The implementation of multiple policy actions will need to be carefully crafted. While some actions can be undertaken in parallel, others will need to be developed in sequence. For instance, a government decision to commit resources to building infrastructure for the deployment of one technology could hinder the development of another. Indeed, many of the policies to support incremental innovations are required to lay the ground work for future disruptive and radical innovations. Facilitating a transition to predictive and preventive medicine – a radical innovation - could require a shift in the incentive structure for developing incremental

pharmaceutical innovations. These time sensitive interactions need to be considered in detail when developing policy.

The next chapter summarises the main messages of this report.

Notes

1. See, for example, the policy recommendations by European Commission (2002) and Canadian Biotechnology Advisory Committee (2006).
2. See paragraphs 8.48 to 8.49 of Nuffield Council on Bioethics (1999).
3. The yearly savings estimate is based on information for 1995 to 1996. It was converted from French Francs to USD using the official exchange rate of 1 Euro = 6.55957 French Francs and 1 EUR = USD 1.34, which is the average of monthly exchange rates from June 2005 to September 2008. An updated savings estimate due to the OECD's work on chemical safety is currently being prepared, but was not available at the time of writing.
4. Elite germplasm refers to crop varieties that are optimised for local or regional conditions.
5. This is by no means a new idea. Examples include low cholesterol diets or special foods for diabetics.
6. Much of the south-eastern United States is within the sub-tropical climatic region.
7. See Figure 10 of Larson (2008).
8. It is frequently forgotten today, but in the 1970s there was widespread opposition to the use of computers at work, due to concerns over exposure to radiation from video display terminals (VDTs) and the risk of repetitive strain injuries. This opposition rapidly withered away after the introduction and market take-off of home computers in the early 1980s, which brought the benefits of computers to individual users.
9. Many of these estimates are based on updating drug cost estimates by DiMasi *et al.* (2003). The study estimated total average development costs of USD 802 million in 2000 dollars for 68 drugs that received marketing approval between 1994 and 2001. Two factors could lead to an

overestimate of costs. First, the drugs evaluated by DiMasi *et al.* may not have been representative of all drugs, with a high average number of clinical trial patients per drug in the DiMasi *et al.* study. Second, almost half (49.8%) of the DiMasi *et al.* estimate is due to opportunity costs that assume an annual discount rate of 11%. This equals the average return on capital invested in the stock market during the 1990s. As average stock market prices, using the S&P 500 have changed little during the past decade, opportunity costs during the 2000s would be markedly lower than in the 1990s and approximately equal average dividends of between 3% and 4% per annum.

10. Herceptin, developed by Genentech, originally failed in clinical trials. It was rescued after post-failure analysis determined that it was effective in a group of patients with the HER-2 receptor (PwC, 2005).

11. The effectiveness of direct to consumer advertising in increasing revenues is emphasised in a study to assist investors in the pharmaceutical sector (Pharma Futures, 2007).

12. Translational medicine refers to methods of rapidly "translating" discoveries in the public research sector to commercial applications.

13. The regulatory system for drug approval evaluates safety on a risk-benefit basis. Higher safety risks are accepted for drugs that treat fatal diseases than for drugs to treat non-fatal diseases such as mild depression or arthritic pain (Dukes, 2008).

14. This is sometimes described as a "living license". Policy documents from the private sector, governments and academics have supported this concept (PwC, 2007; DG Enterprise, 2007; Tait *et al.*, 2008).

15. Safety risks take time to identify. A study by Giezen *et al.* (2008) found that the probability of a biological drug receiving a safety warning by up to three and ten years after marketing approval was 14% and 29% respectively, for biologicals that received marketing approval in either the United States or Europe between 1995 and June 2007. Biologicals that were first in their class had a higher probability of a safety warning and all biologicals appear to have a higher probability than small molecule drugs.

16. As noted in Chapter 4, these large databases permit researchers to identify adverse drug reactions, drug interactions, and the most effective treatments.

17. A few of the regulatory options under discussion to improve public health are the adoption of a life-long approach to the risks and benefits of treatment, strong regulatory authority before and after market approval, support for comparative clinical trials, and restrictions on consumer

advertising of new drugs until sufficient safety data are available. These options are supported by the Institute of Medicine (2006). The private pressure group FasterCures supports both faster approval processes and stronger requirements for post marketing follow-up (Simon, 2006).

18. Stolk (2008) reports large differences between the prescribing habits of doctors in seven EU countries and national best-practice prescribing guidelines.

19. The large fall in childhood mortality rates from 100% in 1950 to 25% in 2000 from acute lymphoblastic leukaemia (ALL) was due to careful experimentation with drug dosages and treatment regimes, with no new pharmaceuticals available over the past three decades. Further improvement will require new drugs and better diagnostics (Kruger, 2007). Research by Yang *et al.* (2009) indicates that genetic differences account for some of the variation in response to treatment, opening up the possibility of personalising treatment through genetic testing.

20. Counterfeiting and poor product quality is a problem in India, partly due to inadequate enforcement. An examination of the situation in one Indian State for the World Bank by Dukes (2008) found that the State Inspectorate routinely inspected four drug manufacturing plants of fair but not distinguished standing. However, eight other manufacturing firms in the same city existed, none of which was registered with the inspectorate.

21. Of note, the environmental advantages of cellulosic biofuel crops compared to food biofuel crops would be substantially reduced if cellulosic demand led to deforestation (OECD, 2008b).

22. Bioethanol production from sugar cane ranging from 6 800 to 8 000 litres per hectare exceeds estimates for cellulosic production from switchgrass (3 100 to 7 600 litres per hectare) or poplar (3 700–6 000 litres per hectare) (Marris, 2006; Sanderson, 2006).

23. This assumes production rates of 50 000 litres of biodiesel per hectare per year and a global demand for oil (in diesel equivalents) in 2030 of 6 trillion litres (5 575 Mtoe), based on IEA (2007). The maximum production rate for algal biodiesel is one-third of the maximum estimated by Sheehan *et al.*, (1998). Estimates of land requirements are from Briggs (2004).

24. Total expenditures were USD 8.93 billion, of which USD 3.45 billion was spent on nuclear research (both fission and fusion), USD 1.01 billion on fossil fuels, USD 889 million on all renewables, and USD 255 million on biofuels (IEA, 2007).

25. By the second quarter of 2008, there was USD 3.34 billion VC investments in clean energy technologies (Cleantech, 2008).

26. PCT (Patent Cooperation Treaty) patents are filed in multiple countries and therefore are taken out on inventions that have a high expected economic value. The public research sector includes patenting by universities and government, with the latter largely due to government research institutes. The share of public research sector patents is higher in the United States, at 26.4%. Hélène Dernis of the Economic Analysis and Statistics division of the OECD kindly provided the data on university biotechnology patents.

27. According to the AUTM, in the United States in 2006, 61% of licenses from universities and 72% of licenses from hospitals and research institutions were provided on a non-exclusive basis. However, there are no data on the percentage of inventions that are licensed on an exclusive basis. (AUTM, 2006).

28. See also relevant recommendations by Gold *et al.* (2008).

29. Detailed information on some of these debates can be found in the background documents to *The Bioeconomy to 2030* project at www.oecd.org/futures/bioeconomy.

30. Many of these challenges would benefit from both national and international strategies to promote innovation. The OECD has pioneered innovation studies since the 1980s. These studies relate growth to innovation in the economy and focus on areas such as biotechnology and ICT. For instance, see *www.oecd.org/innovation/strategy* and (OECD, 2005a, 2005b, 2005c, 2008a).

31. The International Conference on the Harmonisation of Technical Requirements for the Registration of Pharmaceuticals for Human Use (ICH) has been working since 1990 to improve harmonisation. The ICH includes representatives from the pharmaceutical industry and the regulators from Europe, the United States and Japan. The ICH also collaborates with the World Health Organization (WHO) to set standards in a larger group of countries, such as for clinical trials. See *www.ich.org/cache/compo/276-254-1.html*.

32. The literature on prizes as an incentive for health research provides many examples of possible solutions to global governance issues (Love and Hubbard, 2007).

33. See *www.dndi.org*.

34. See *www.oecd.org/document/45/0.3343.en_2649_34537_39163757_1_1_1_1.00.html*.

35. For an example of the role of policy to support a radical transition to low carbon energy, see Smith (2008).

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Abbreviations and Acronyms

ADR	adverse drug reaction
AG	agronomic trait
AIDS	acquired immunodeficiency syndrome
ALL	acute lymphoblastic leukaemia
APHIS	Animal and Plant Health Inspection Service
BP	British Petroleum
BRIC	Brazil, Russia, India and China
BSE	bovine spongiform encephalopathy
CDER	Center for Drug Evaluation and Research
CGAP	Cancer Genome Anatomy Project
CGIAR	Consultative Group on International Agricultural Research
CSIRO	Commonwealth Scientific and Industrial Research Organisation
DBF	dedicated biotechnology firm
DDT	dichlorodiphenyltrichloroethane
DHA	Department of Health and Aging (Australia)
DHHS	Department of Health and Human Services (United States)
DNA	deoxyribonucleic acid
DNDi	Drugs for Neglected Diseases Initiative
DOE	Department of Energy (United States)
EEC	European Economic Community
ELISA	enzyme-linked immunosorbent assay
EMEA	European Medicines Agency
EU KLEMS	European Union Capital (K) Labour (L) Energy (E) Materials (M) Service Inputs (S) Database
FAO	Food and Agriculture Organization of the United Nations
FDA	Food and Drug Administration (United States)
FFN	functional foods and nutraceuticals
GAO	Government Accountability Office (United States)
GBOARD	government budget outlays and appropriations for research and development

GDP	gross domestic product
GHG	greenhouse gas
GM	genetically modified *or* genetic modification
GVA	gross value added
HAS	*Haute Autorité de Santé*
HIV	human immunodeficiency virus
HR	human resources
HT	herbicide tolerance
HT-IR	combined herbicide tolerance and insect resistance
IAVI	International AIDS Vaccine Initiative
IB	industrial biotechnology
ICH	International Conference on Harmonisation
ICT	information and communication technology
IEA	International Energy Agency
IMSR	improvement of medical service rendered
IPCC	Intergovernmental Panel on Climate Change
IPO	initial public offering
ISAAA	International Service for the Acquisition of Agri-biotech Applications
ISO	International Organization for Standardization
IT	information technology
IVD	*in vitro* diagnostic
IVF	*in vitro* fertilisation
LCA	life cycle analysis
M&A	mergers and acquisitions
mAb	monoclonal antibody
MAS	market-assisted selection
MEOR	microbial enhanced oil recovery
MSR	medical service rendered
Mtoe	million tons of oil equivalent
NAFTA	North American Free Trade Agreement
NCE	new chemical entity
NGO	non-governmental organisation
NICE	National Institute for Clinical Excellence
NIH	National Institutes of Health (United States)
NMA	*Noordwijk* Medicines Agenda
NME	new molecular entity
OECD	Organisation for Economic Co-operation and Development
OIE	World Organisation for Animal Health
PCR	polymerase chain reaction
PCT	Patent Cooperation Treaty
PDO	polydioxanone

PGD	preimplementation genetic diagnosis
PHA	polyhydroxyalkanoates
PHB	polyhydroxybutyrate
PPP	purchasing power parity
PQ	product quality
PVC	polyvinyl chloride
QALY	quality adjusted life years
R&D	research and development
RFA	Renewable Fuels Association
RNA	ribonucleic acid
RNAi	RNA interference
SARS	severe acute respiratory syndrome
SM	small molecule
SME	small- and medium-sized enterprise
SNP	single nucleotide polymorphisms
Synbio	synthetic biology
TB	tuberculosis
TRIPS	Trade-Related Aspects of Intellectual Property Rights (WTO)
UN	United Nations
UNU-MERIT	United Nations University Maastricht Economic and Social Research and Training Centre on Innovation and Technology
USDA	United States Department of Agriculture
USITC	United States International Trade Commission
USPTO	United States Patent and Trademark Office
VC	venture capital
WHO	World Health Organization
WTO	World Trade Organization

Table of Contents

List of tables

List of figures

List of boxes