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# *Health Biotechnology:*

# *Emerging Business Models and Institutional Drivers*

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# Executive Summary

This report *Health Biotechnology: Emerging Business Models and Institutional Drivers* addresses the future of firms and industry. In particular, the report focuses upon how and why firms involved in health biotechnology will evolve in the future. These firms will be diverse, ranging from the pharmaceutical firms and health service providers to specialised firms in biotechnology, bioengineering, biomedicine, and other fields at the intersections of biology, genomics and human health. Public policy faces major challenges here, because the developments in firms will depend upon a mixture of public and private incentives and organizations. The interface between the public and the private must therefore be analyzed and developed in future public policy. This matters for society, in order to stimulate growth and industrial competitiveness and in order to apply the advances of biotechnology to solve human health care issues.

Up until today, two business models have been dominant within the application of biotechnology for human health, or what is called health biotech in this report. One is the classical biotechnology model. In this model, scientific discoveries and technological inventions have been quickly developed within entrepreneurial firms, usually based upon venture capital. They compete through their specialized scientific knowledge, often sold to large companies, and they also compete through their flexibility, especially quick commercialization of new fields. The other dominant business model is that of the large, vertically integrated company. These large firms have integrated everything inside the boundaries of the firm, from research and development (R&D) to production to marketing and after sales monitoring. The ones in pharmaceuticals have competed through finding the next 'blockbuster drug' and the ones in medical devices have also competed through developing specific technologies and devices for large numbers of customers.

These two dominant models are being challenged, due to serious problems of profitability, changing technologies and medical knowledge and changing demand. Therefore many other ways of 'doing business' within health biotech are being developed. Indeed, as new business opportunities and shifts to the institutional context arise, then firms experiment with new types and new combinations of business models. This report concentrates on four institutional variables, which are helping to drive these changes within the business models of firms.

This report details a large number of alternative business models, as well as analyzing how the institutional drivers of change are likely to stimulate some specific business models rather than others. Future developments will be interesting, because new experimental business models are being developed, at the intersection between the two traditionally dominant models mentioned above. Some are a more refined version of today's business models, but where new discoveries and inventions in areas like system biology and individualized health care will form the core business. Other experimental models will be similar to ones experience in other industries which have undergone profound changes. An example of this is the pharmaceutical industry, where some firms will move from an R&D driven block-buster strategy, in order to instead concentrate upon the flow of resources, supply chains, and competing on lower prices and more direct contact with customers.

The experimentation and implementation of new business models will affect society because the industrial transformation expected through health biotech will affect firms in many sectors. The new business models will also involve different combinations of goods and services on offering, in order to deliver human health care.

Hence, this report relates the emerging business models in relation to four institutional drivers of change because these firms and also public organizations will play major roles in future

scenarios about the Bioeconomy. The firms will be highly influenced by their context, including institutional drivers, or what we can call the broader sectoral system of innovation. The reason comes back to the core of our analysis, namely the "economic model" or "business model". Many practitioners use the concept, as does the literature, to analyse how firms do business. These models specify the firm's core competencies and how they are turned into offerings for customers, so that the firms can generate sales and possibly profits.

The report argues that four institutional drivers will form a very different context to deliver human health care. Those four institutional drivers for change are 1) Scientific and technological advances; 2) Public research and the public-private interface; 3) Public policy, institutions and regulation; and 4) Demand and consumers. The major effects of each variable upon the business context are detailed in the report, with a summary below.

*The first institutional driver consists of the Scientific and technological advances*. Combined with better medical knowledge, public and private investments into R&D in health biotech will offer new and alternative ways to provide therapy for diseases and to improve the R&D process. These will lead to alternatives of therapy that can substitute for existing drugs and treatment such as surgery. Many technological advances are essential for personalised medicine and pharmacogenomics, especially in integrating and combining science and technology with medical research and practice.

Technological advances are broadly expected to provide opportunities for modifying and initiating business models through:

- Continuing the start-up of business ventures as specialised knowledge suppliers.
- Developing markets, expanding markets, and taking over market segments in pharmaceuticals and treatment through technological advances.
- Investing in R&D but demanding higher, more visible, and more immediate returns on investment.
- Combining and integrating existing and new scientific and technological competencies into bundles of goods and services.
- Developing specialised medical integrators, who combine specific sets of scientific and engineering knowledge with specific medical applications.

*The second institutional driver is public research and the public-private interface*. Universities and research institutes are crucial to the classical biotechnology business model. Public institutions will continue to pour money into medical and biology-related research and development. With 60% of the total US public R&D going into these areas, other countries will follow. The firms are dependent on the publicly funded basic and applied sciences, but they will need new techniques and management modes in order to exploit the global and local networks.

Public research and the public-private interface are expected to provide opportunities for modifying and initiating business models through:

- Creating business opportunities, through science and technological advances financed by the public research sector.
- Exploiting these public-private linkages, which implies firms need to develop key components like networks and open access.

- Linking into public research, on a global scale, which will help firms to position themselves to access, and to also sell, their specialised knowledge locally and globally.

*The third variable is public policy, institutions and regulation*. Future developments in health biotech business models will be affected by institutional and regulatory frameworks, especially for commercialisation, academic entrepreneurship, and regulation for products like pharmaceuticals and medical devices.

Public policy, institutions and regulation are expected to provide opportunities for modifying and initiating business models through:

- Modifying institutional structures and ownership for intellectual property rights and academic entrepreneurship in public research organisations.

- Differing trajectories for regulatory frameworks, and ways of working among the actors. The choices taken within the sectoral system of innovation will influence which countries "lead" in the new biotechnology.

- Developing outsourcing, fragmentation and integration across the value chain.

*The fourth institutional driver is related to demand and consumers for health care provision.* Increasing overall costs will create challenges for health care services, but demand will continue to expand, especially due to demographic and lifestyle changes. Moreover, patients will be better consumers, being better informed and more active in finding appropriate service providers and treatment; they may therefore participate more directly in the innovation process.

Demand and consumers in health care provision is broadly expected to provide opportunities for modifying and initiating business models through:

- Prioritising efficiency and efficacy at acceptable levels of treatment that can lower the costs (marginal and total) of diagnosis, prediction and treatment.

- Expanding major markets due to demographic and lifestyle changes.

- Developing pharmacogenomics, personalised medicine and P4 medicine, which will enable emerging business models focused on new bundles of unique services and goods. This also requires the integration of IT, biology and medicine.

- Developing direct interaction with individuals as "users" and "developers", which promotes new development and testing activities similar to those observed in open source software.

The above bullet points thus specify how these four institutional drivers of change are expected to affect the external context, within which firms experiment with different business models. Subsequent sections of the report analyze in detail how these major effects identified above will then get 'translated' into specific business models. Some of these business models already exist and appear robust. Others are experimental, and so whether they are viable in the longer run, or not, can only be answered in the future, with the benefit of hindsight. All these effects involve ways in which public policy and broader societal trends can influence firms and industrial development.

The overall recommendation is clearly that a main role for public policy to reach the Bioeconomy of the future is to stimulate product, process and organizational innovations.

Innovations within health biotech usually take place across boundaries of user-producers and of public-private actors. Private firms play a role, but so do public health providers. Because the institutional and market context is expected to have dramatically changed within thirty years, the implications for public policy can be discussed by analyzing and finding new ways to stimulate firms within this institutional and market context.

Public policy can help stimulate innovation to meet the future health needs by stimulating development across boundaries of public and private organizations. Examples include co-ordinating network mechanisms; stimulating R&D activities to solve sequences of problems; negotiating long-term goals; and developing responsive institutional and regulatory frameworks. While these types of recommendations may sound diffuse, they can be translated into specific actions, to help improve public policy to reach the longer-term objectives. To take the first example of public policy which can help co-ordinate network mechanisms, assume that the objective is treatment around a major disease category, like diabetes or avian flu. Co-ordinating network mechanisms would thereby imply that public policy-makers assemble stakeholders, in order to ensure that researchers, users, patient groups and those producing goods and delivering services exchange relevant information about emergent problems, new solutions, and ways of combining goods and services to best address the underlying medical-social-economic problems. Indeed, many research and innovation policies have moved in this direction during recent decades, namely stressing public-private partnerships and network effects. Still, health biotech poses particular challenges in terms of defining stakeholders, whom can be involved in innovation and contribute to databases, and how to stimulate the greatest returns to combined public and private efforts to transform human health.

Moving in this direction also implies that public policy for the Bioeconomy of the future should focus on new ways of analyzing the problems – and the solutions – for influencing firms through shifts to the institutional and market context. New thinking is needed on issues in order to lead to specific public policy recommendations. This especially includes issues of how to share costs and benefits between the private and public; why firms rely on public initiatives for resources and incentives; and how to engage individuals and stakeholders in the development process. Hence, the specific public policy recommendations and initiatives that are developed for the Bioeconomy of the future will also require parallel development of the underlying conceptual models and explanatory frameworks of how and why this sectoral system of health biotechnology functions.

# 1. Introduction

This report *Health Biotechnology: Emerging Business Models and Institutional Drivers* addresses the future of firms and industry in health biotechnology. The two main issues are: 1) How the institutional and market context influences business models and 2) What types of business models will emerge between the currently two dominant ones, which are classical biotechnology and vertically integrated firm. The analysis is based on a conceptualization of how and why business models may be changing in health biotech, due to transformation in the institutional and market context. Emergent business models will clearly challenge these two currently dominant business models, and many different firms, public organizations, and industries can be involved in future health care provision. Thus, the Bioeconomy of the future will allow many different types of firms and business models, but this requires shifts in both private and public spheres of activity in order to deliver on the new promises of human health care.

In particular, this report focuses upon how and why firms involved in health biotechnology will evolve in the future. These firms will be diverse, ranging from the pharmaceutical firms and health service providers to specialised firms in biotechnology, bioengineering, biomedicine, and other fields at the intersections of biology, genomics and human health. The interface between the public and the private must be analyzed and developed in future public policy. To take just one example, firms invest monies into research and development (R&D) due to expected financial returns, and yet the situation is somewhat more complex in that industrial R&D also tends to diffuse to other actors and in that those firms are also dependent upon public R&D. Hence, public policy faces major challenges in health biotech, because the developments in firms will depend upon a mixture of public and private incentives and organizations. Implementing and finding sustainable new business models will also require major shifts in the public-private interface, significant scientific and technological advances, and new ways of co-ordinating and delivering bundles of health care goods and services. This matters for society, in order to stimulate growth and industrial competitiveness and in order to apply the advances of biotechnology to solve human health care issues.

Up until today, two business models have been dominant within health biotechnology for human health care, or what is called health biotech in this report. One is the classical biotechnology model and other is that of the large, vertically integrated company. In the classical biotechnology model, scientific discoveries and technological inventions have been quickly developed within entrepreneurial firms, usually based upon venture capital. They compete through their specialized scientific knowledge, often sold to large companies, and also compete through their flexibility such as quick commercialization, alliances, and keeping up to date with scientific and technological break-throughs. These firms invest heavily in research and development (R&D) – but often have difficulties making money off their internal knowledge resources.

In the large, vertically integrated company business model, economies of scale and the use of integrated resources have been characteristic. These firms have integrated everything from research and development (R&D) to production to marketing and after sales monitoring. They have competed through finding the next 'blockbuster drug' in pharmaceuticals and through having large segments of the market in other industries like medical devices.

These two dominant models are being challenged, due to serious problems of profitability, changing technologies and medical knowledge and changing demand .Indeed, as new business opportunities and shifts to the institutional context arise, then existing and new firms are experimenting with new types and new combinations of business models.

This report identifies a number of emerging, experimental and possible business models. Some already exist in some form whereas others are more thought-experiments of what could happen to businesses in the future. However, it will not be easy for the firms to develop viable business models because they are dependent upon the institutional and market context. That future is uncertain – and exciting, due to the new promises of addressing human health care concerns. Because the institutional and market context will change dramatically in the coming thirty years, so too the firms and industries developing health biotechnology will also change. Major opportunities and challenges lie ahead – for health care provision overall and for the private and public providers of goods and services. These include radical shifts as well as incremental ones in health care provision.

In the more radical shifts, health care provision will change in fundamental ways, towards a system where individuals hold more responsibility, but at the same time, more effort must go into maintaining and monitoring the overall health care system. On the one hand, individuals will need to become even more active consumers, in preventing medical conditions, in monitoring biological and medical information, and in choosing among alternative treatments. In return, the promise is that the individual can obtain better health benefits. They will be offered specific, individually tailored combinations of pharmaceuticals, health care services, preventative medicine such as exercise and new diets, and so forth.

Paradoxically, this radical push towards individually tailored health care provision requires large quantities of data and new co-ordination of the overall health care systems. The radically new system will require "personalised" but also "group" medicine as well as significant scientific and technological advances through R&D. Medical researchers and professionals will therefore need information about many variables about populations, as well as deeper medical understanding of diseases, in order to reasonably predict treatments and benefits for the specific individual. That will in turn call for massive public investment into areas like pharmacogenomics, systems biology and bioinformatics, as well as new public-private compromises to access large-scale data and biological material useful as biomarkers, genomic information, and others.

In the more incremental shifts, smaller but systematic changes in health care provision are also expected, which will shift demand. For example, we can expect that health service providers will establish more stringent requirements that suppliers must meet, to reach the overall goal of providing reasonable quality services efficiently. This will put pressure on the suppliers to innovate in products, processes and organisations. Moreover, providers will have to develop new methods to evaluate alternatives ways of delivering treatment, through new routines and procedures. This will lead to changes in existing regulation, such as deciding about the treatment of a condition by evaluating diagnostic equipment, the side effects of biopharmas, and tradeoffs between these two different treatments. More incremental changes in health care provision may, over a longer period and through a number of smaller steps, lead to demand for more radical types of innovations in the longer run.

Taken together, the radical and incremental shifts to health care provision will affect demand. Changing demand will not only be in terms of increased quantity but also qualitative changes in what will be demanded in the future. Qualitative changes in demand matter a lot in this industry. Health care goals can often be achieved through a variety of combinations of procedures, operations, drugs, etc., to reach different levels of care. Since making an incremental improvement to an existing good and service is usually cheaper in the short run than making a radically new innovation, the provider may opt for the incremental one. The reason is that making a more radical change may be more costly (and less efficient) than existing treatments during the initial development phase. However, in the long run, the radical ones can provide significant benefits for health and become cheaper per treatment. Providers must make choices about whether only to provide the best care currently available at lowest cost, or to also support innovative treatments for the future, which tend to be more costly in

the short run. This implies that both public and private organizations will play key roles, not least by providing very long-term monitoring, evaluation and feedback about information relevant to these complex medical decisions, which in turn shape demand.

Hence, in the future, biotech health firms will be developing business models for a new institutional and market context, where aspects such as demand, the public-private interfaces and the sectoral systems of innovation will differ. The firms must especially understand how this future will differ along two dimensions: the types of scientific, technological and medical competencies valued, and the way in which demand will be co-ordinated among public and private actors in bundles of goods and services. These two dimensions will help determine which business models in biotech health prove more viable in the long-run.

A main role for public policy to reach the Bioeconomy of the future is to stimulate product, process and organizational innovations. Innovations within health biotech usually take place across boundaries of user-producers and of public-private actors. Private firms play a role, but so do public health providers. Because the institutional and market context is expected to have dramatically changed within thirty years, the implications for public policy can be discussed by analyzing and finding new ways to stimulate firms within this institutional and market context. Health biotech poses particular challenges in terms of defining stakeholders, whom can be involved in innovation and contribute to databases, and how to stimulate the greatest returns to combined public and private efforts to transform human health.

This also implies that new thinking for public policy is needed about many issues. Pertain issues include how to share costs and benefits between the private and public spheres; why firms rely on public initiatives for resources and incentives; and how to engage individuals and stakeholders in the development process.

Sections 2 and 3 introduce relevant concepts and the logic of the analysis in this report, specifically linking expectations of firm business models to the institutional and market context. Section 2 begins by addressing the specific institutional drivers of change, and then examines how they influence business models in human health care and the types of firms and industries involved. Section 3 provides a background analysis of future investments into private and public research and development (R&D), given the need to stimulate innovations in the sectoral system of innovation.

Section 4 looks towards the future, in order to understand how the institutional and market context may change, in such a way as to stimulate new types of business models in health biotech. The section includes the analysis of how the specific institutional drivers of change will lead to those changes, including many illustrations of specific business models for the future. This is the main focus of sub-sections 4.1 to 4.4, with a summary of effects on business models in sub-section 4.5. Section 5 provides the conclusions, in terms of business models for the future. This section thus specifies existing business models in biotechnology and other industries, and extrapolating more fundamental shifts which can occur in the future. This section concentrates on the more abstract details of these emerging and experimental business models. Section 6 provides policy implications from this report.

# 2. The future of health biotechnology

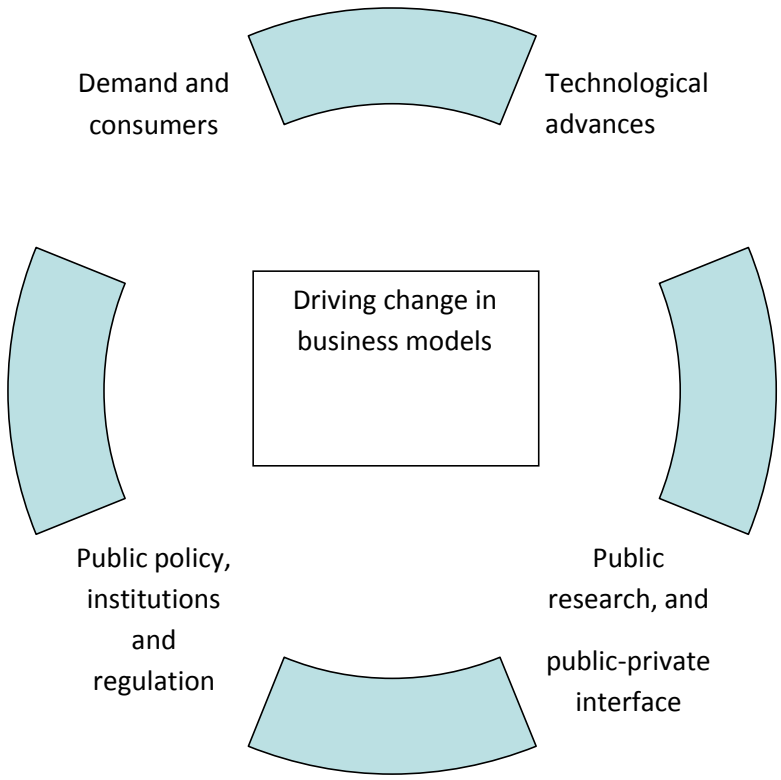
This section outlines the logic underlying this report – specifically, why the report analyses future changes in business models within companies, set in relation to shifts in the institutional and market context. The section also introduces key concepts, including business models, as well as specific characteristics of the health biotech sectoral system of innovation and institutional variables driving change.

## 2.1. Specific institutional drivers of change

Four institutional variables are identified as particularly important drivers of change to business models in health biotech. These institutional variables can help stimulate, or discourage, the development of new forms of business models, and thereby public policy has a role in influencing the development of the industry.

The four specific institutional drivers of change are: 1) Technological advances, 2) Public research and the public-private interface, 3) Public policy, institutions and regulation, and 4) Demand and consumers.

**Figure 1 - Institutional variables as drivers of change**




**Source:** Author.

Each institutional variable is briefly introduced below. Section 4 goes into detail about how and why these institutional variables will affect firms and how firms can compete, through existing and emerging business models.

*Technological advances* – New technologies help drive change. New scientific and engineering knowledge can be related to existing technologies and treatments, in that they may be a complement to them or a substitute for them; and, they may open up a new realm of scientific understanding and industrial applications. Hence, technological advances are important because they help to open up "technological opportunities", and thereby affect the choice set of biotech firms.

*Public research and public-private interface* – Health biotech is greatly affected by public research, especially in terms of public investments into research and medical provision. As a

consequence, the boundaries between the public and the private are often diffuse, with complex linkages; examples include joint ownership and dense network relationships between university researchers and academic spin-off companies.

*Public policy, institutions and regulation* – Public policy, institutions and regulations are closely related to the second variable, but here the focus is more on how and why institutions and regulations set the framework for competition. Examples are institutional frameworks for intellectual property rights and for commercialisation of university research, as well as the regulation for pharmaceuticals and medical devices.

*Demand and consumers* – The development of new business models is also clearly related to demand and consumers, including whether private and public organizations help bundle goods and services into health care provision. The way in which that demand will be expressed is likely subject to both radical and incremental shifts in health care which were outlined in the introductory section. Consumers may also play more active and direct roles, in individualised medicine.

Hence, these four institutional variables are drivers of change because they represent pressures which are external to the firm, but which help form the future institutional and market context. Firms will try to match their internal resources and processes to this external institutional and market context, usually through experimentation and trial-and-error over time.

## *2.2. How do institutional variables affect business models?*

The concept of "business model" refers to how firms do business – how they compete and make profits by using their competencies and resources to sell goods and services in the market. In other words, firms do business by combining internal resources to offer goods and services that add value to specific groups of customers (Magretta**,** 2002).

Drucker (1994) provided an early and influential definition of a business model. He defined a business model as follows: What an organisation is paid for, what an organisation considers to be meaningful results (how to make a difference) and where an organisation must excel in order to maintain leadership. This definition is broad but useful for analyzing future scenarios. It is broad in that it relates how the organisation itself perceives the internal core assets, as well as how it reacts to customers and "the market" value of the goods and services offered. The definition is useful in that it focuses attention upon how and why the firm can combine its internal assets in such a way as to compete in a market and as to survive with the institutional context.

Another way to state this is that the "business model" concept is useful here because it helps us specify how and why firms may take advantage of business opportunities. The firm reacts to business opportunities, by combining internal resources to offer goods and services that add value to specific groups of customers (including public ones), and this helps differentiate the firm from its competitors.

Hamel (2000) has a more detailed specification of a closely related idea, which he calls the "business concept innovation". He includes many aspects of strategy, where the manager can work to improve the firm's performance. The first is core strategy, which refers to aspects such as business mission, product/market scope, and the basis for differentiation. These position the firm in relation to competitors. The second component is strategic resources: these are more internal aspects such as core competencies, strategic assets and core processes. The third is customer interface, involving (*e.g.*) fulfilment and support, information and

insight, relationship dynamics and pricing structure. These thus relate the firm's offerings of goods and services to customers. Finally, the fourth component relates to interactions in the value chain, *i.e.* suppliers, partners and coalitions.

Managers often find such concepts meaningful when analysing their own firms. The reason is that the managers can pinpoint the idea of how and why the firm is using resources internally, in order to meet public and private demand. Moreover, the discussions sometimes help them shift attention from tangible products, so that they understand how they make money off of combinations of goods and services. For example, the IT boom and bust of 2000 helped popularise the business model concept especially in relation to new ways of doing business. In that period of IT hype, many so-called "new economy" firms and "e-commerce" firms set out to make money in non-traditional ways. For example, rather than just sell their goods and services, the Internet search engines like Google would offer services for searching the Internet, and the customer could thereby use specific algorithms to do so for free, as long as they were willing to allow advertising on their screen. The companies providing the search engines then made their money off of advertisements and off stocks, rather than selling directly to consumers. The IT industry has thus provided many illustrations of company business models, which were interesting because they offered a different idea of what it means to "do business" than traditional manufacturing trying to reduce costs.

The business model concept is useful here for discussing future trends in the bioeconomy because of these linkages between the firm *per se* with the institutional and market context, as specified in the variables identified above.

A main question, then, is how do institutional variables affect business models? The existing academic literature is relatively underdeveloped on this point, because most literature focuses only upon the firm. However, by taking a broader perspective of the institutional context, including economic and political aspects, this report has identified the following ways in which the four institutional variables affect business models for the biotechnology.

Institutional variables affect business models by:

- Providing resources and incentives for research, development and innovation
- Using public monies to stimulate the commercialization of new technology, instruments, models, databases, and so forth
- Setting the institutional conditions for new business opportunities
- Stimulating reform of regulations and institutions
- Influencing existing demand
- Highlighting new types of economic value (e.g. for what customers are willing to pay)
- Helping to express and form future demand
- Specifying new combinations of goods and services to address health care issues

The above list thus specifies a number of ways in which the institutional variables help drive future changes. They do so mainly by setting the broader context, within which private firms and also public organizations are active within health. They specify ways in which the ability of the firms to make money off their internal resources and market ideas will depend upon the specific market and institutional context within which they operate.

This perspective has implications for this report, especially expected future changes. The individual firm – as well as aggregations of firms within an industry – will develop and

experiment with business models within their market and institutional context. They tend to focus upon one 'main' model at a time. However, that institutional and market context will change, not least due to public policy. Over time, our expectation is therefore that the firm will experiment with different business models. As soon as they run into problems or see new business opportunities, most firms are willing to experiment. They will thus change their internal resources, their goods and services, and even their customers, in order to respond to new business opportunities and to resolve political and technological challenges.

## *2.3. What types of firms are active in health biotechnology?*

For the past thirty years, biotechnology has been considered a goldmine for business opportunities, with massive private and public investments into R&D. One relevant starting point to this report is, therefore, the debate about whether biotech has had clearly positive (or negative) impacts on business – and here, the answers differ greatly.

On the one hand, observers like Ernst and Young (2007) and IPTS (2007) argue that biotechnology is delivering real advances in areas such as medical care and pharmaceuticals. Ernst and Young (2007) argue that the global biotech industry has robust growth, including mergers and acquisitions of USD 23 billion in the United States and capital raised by global companies of USD 27.9 billion. IPTS (2007) similarly argues that biotech positively affects society, by taking a broader view of how and where the medical, scientific and technological knowledge bases are being put to use within new and existing organisations to solve health problems. The IPTS report provides many examples of areas in which biotech has influenced health, such as providing new treatments and bio-pharmaceuticals.

On the other hand, critics such as Pisano (2006) and Hopkins *et al.* (2007) argue that biotechnology is not delivering on those promises, because few biotech companies or products have succeeded in the market. Pisano (2006) argues that the revenues of all publicly held American biotech companies remain close to zero, and if the company Amgen is excluded – or private companies included – the aggregate revenues turn to losses. Hopkins *et al.* (2007), meanwhile, shows that R&D productivity has not been increased. Hence, their argument is that the basic science-oriented business model has not proved viable in the marketplace, and so biotechnology has not delivered on the great promises of the past three decades. Note that observers on both side of this debate understand that the area has huge societal implications, but they differ in their assessment of the impacts on the specific firm performance *per se.*

These two sides of the debate about whether biotech has had positive impacts on business thus use slightly different definitions of 'biotechnology'. The first ones tend to examine the broad use of the knowledge within many industries, whereas the latter tend to focus upon the small entrepreneurial firms, that is, the classical biotech model.

In this report, biotechnology is here discussed primarily in relation to its application to goods and services for human health care, regardless of industry. The OECD has for many years taken this broad view of biotechnology, as a range of scientific and engineering principles applied to goods and services, as detailed in other OECD reports.

The relevance of this broader definition of biotechnology to this report is high. In particular, the OECD definition allows us to define different types of firms and industries which develop and apply knowledge about health biotech to solve human health problems. Health biotechnology is not limited to only the small, biotech firms – which is a common delineation in many reports. Instead, the OECD definition allows the definition to be flexible over time, in order to include new types of scientific and technological knowledge and new types of

firms. As detailed further in Sections 3 and 4, modern biotech firms do many different things, and hence are not a traditional sector in the sense of selling more or less homogeneous and competing products.

Hence, this implies that biotechnology for human health is developed within many different types of firms, public organizations and stakeholders, and so the boundaries of the sector are not well-defined. There are multiple firms and industries involved, such as especially pharmaceuticals, medical technology, and health care provision and service. There are also direct and indirect types of linkages between industrial and service sectors, including pharmaceuticals, medical technology, animal health care, and health care provision and service.

# 3. Investment in R&D

This section considers factors influencing future investment in research and development (R&D). R&D is crucial for developing the product, process and organizational innovations needed to deliver human health care in the future. Investing money into R&D is not the only important aspect of stimulating innovations, due to the complexity of innovation and commercialization processes. Still, private and public R&D is highly relevant for whether, and how, the expected new types of human health care will be developed in the Bioeconomy of the future.

According to economic theory, biotech firms in human health care should invest in R&D when they judge that the future returns will be greater than their own R&D investment. The appropriability problem means that firms are likely to under-invest, due to their inability to appropriate all the economic returns to the knowledge. Governments therefore have incentives to invest – especially in basic science – because knowledge has positive externalities from which society benefits.

The empirical and theoretical story is somewhat more complex, and thereby more interesting. Modern theory about the use of knowledge in the economy has helped us understand that private and public actors have incentives to invest in both fundamental and applied R&D, even though the beneficiaries will include other organizations than those paying for, and carrying out, the research and development work. New thinking about these private and public incentives to invest in R&D, as well as the benefits, has been necessary to understand the complexity of the R&D and innovation processes. The following sub-sections therefore analyze future private and public investment into R&D, and then conclude by examining the dependencies between them within the sectoral system of innovation.

## *3.1. Private investment*

The three main factors influencing future investment by health biotech firms are expected returns to R&D, belief in R&D as core to their business model, and access to capital to make these investments.

Firms have expectations of returns to investment into R&D. According to economic theory, biotech firms in human health care should invest in R&D when they judge that the future returns will be greater than their own R&D investment. The appropriability problem means that firms are likely to under-invest, due to their inability to appropriate all the economic returns to the knowledge. These ideas hold to a large extent, as firm managers expect new products and processes from their R&D investments and as intellectual property rights help define their ability to appropriate intangibles.

Still, as compared to the above theoretical picture of public-private investment into R&D, the empirical picture is also somewhat more complicated in this sector. Many firms in the classical biotechnology model spend millions of dollars on R&D, without a product on the market. Many different types of firms in health biotech, pharmaceuticals, medical devices and services invest heavily in R&D and innovation (see review in McKelvey and Orsenigo, 2007). Possibly, firms working in health biotech are willing to invest in private money into R&D because they, in turn, gain such high levels of positive externalities from public investments into R&D.

The literature has suggested that many elements of "science" – such as R&D to sales, placing well-known scientists on boards, etc. – all have signalling effects to attract additional financiers. In order to attract star scientists, biotech firms often introduce organisational and incentive structures similar to an academic environment, such as rewards for publication (Cockburn and Henderson, 1998; McKelvey and Orsenigo 2006). This suggests that firms will continue to have incentives to invest in R&D, even though they have little information about future returns and often, too little understanding of why and how future customers are willing to pay for the R&D results. However, these signalling effects only work when venture capital and customers place a value on these types of knowledge intangibles.

This implies that this sector has several interesting characteristics regarding private investment into R&D, especially that these firms have difficulties making reasonable assumptions about returns to investments in R&D. One aspect is the high degree of uncertainty, since much company R&D is essentially (basic) research rather than product development. Uncertain, entrepreneurs and management cannot know whether the R&D projects will lead to results that satisfy market demand and/or that function medically and technically in health care. Uncertainty makes it impossible to accurately calculate future returns. Another aspect is that many of these firms are entrepreneurial, and literature in this field suggests that most start-ups are systematically biased about the business. They overestimate their opportunities and future returns, and they underestimate the amount of resources and efforts necessary to achieve those goals.

Hence, a different way to consider the second factor, namely that private investment largely has to do with the relationship between R&D and the business model. For many biotech firms, R&D constitutes a major element of "what the firm is", and thereby constitutes a crucial element of the current business model. Classical biotechnology firms are primarily specialized suppliers of scientific and technological knowledge.

An example of this view of biotech firms as primarily specialised knowledge suppliers can be illustrated in the early history of biotechnology, set in relation to the pharmaceutical industry. When biotechnology first emerged commercially in the late 1970s in the United States, the early companies like Amgen and Genentech focused on specific biotech techniques and scientific knowledge. However these companies were using multiple ways of making money, or appropriating the returns. They were both selling R&D contracts to large pharmaceutical companies and trying to produce their own pharmaceutical products. Genentech developed recombinant DNA-techniques and industrial processes that enabled them to develop ways of producing both insulin and human growth hormone within genetically modified bacteria in the early 1980s (McKelvey, 1996). For insulin, they sold R&D contracts to the American pharmaceutical company Eli Lilly, and did not produce themselves. For human growth hormone, Genentech sold R&D contracts to the Swedish pharmaceutical company Kabi (later Pharmacia), but they also developed and produced their own drug for the American market. Genentech thus produced drugs and competed with traditional pharmaceutical firms as well as selling R&D contracts.

This dimension of the perceived value of scientific, technological and medical competencies remains, even when the organizational form changes. To continue the illustration, some years

later Genentech was acquired by the Swiss-German pharmaceutical company Roche-Hoffman, and so became specialised suppliers of this type of scientific competency to the multinational company. Conflicts over scientific procedure and intellectual property rights are also part of the story, *e.g.* the lawsuits between University of California, Genentech and Eli Lilly over recombinant DNA bacteria to produce insulin and human growth hormone. This illustration indicates that although biotech companies can and sometimes do sell pharmaceutical products, investment in R&D is a key component of what they do and who they are, and as such, a core component of their business model.

A third factor to consider is whether the actors will actually have access to capital, so that biotech and pharmaceutical firms can continue to spend millions of dollars on R&D. The answer is that the amounts will likely drop for both the classical biotechnology firm and for the large, vertically integrated firm, but for different reasons.

The smaller firms have been more dependent upon external sources of capital, especially venture capital and public policy initiatives for academic spin-offs. In the past, it was possible to make long-term losses. The cumulative nature and large amount of losses incurred by the smaller biotech companies suggest that financiers have in the past been willing to continue investing within long-term, basic science (Pisano, 2006). For the future, it is unlikely that venture capital and private equity will continue to invest at those levels without significant returns, and so this type of external capital will likely decline. Other external capital such as public policy initiatives and early stage financing will likely continue at about the same levels. This implies that the classical biotechnology firms will have to shift focus to demand from future customers, and put less emphasis on what they have so far perceived as the unique assets of their scientific and engineering knowledge.

The large, vertically integrated firms tend to be incumbents within specific industries, with large market shares. They have used much of their aggregate assets, including sales, stock issues, and so forth, to finance millions of dollars of R&D. Similar trends towards increasing difficulties of maintaining R&D spending are visible in related sectors, where access to financing and capital for R&D is becoming more problematic. R&D costs have been especially skyrocketing within pharmaceuticals, alongside problems of profitability and legitimacy. Strategies to address these problems include mergers and acquisitions (to access larger number of products in-pipeline) as well as purchasing and licensing intangibles for innovation from both iuniversity research and the specialised knowledge suppliers.

The three main factors influencing future investment by health biotech firms are expected returns to R&D, belief in R&D as core to their business model, and access to capital to make these investments. Taken together, our expectations for the future are that private investments into R&D will remain high, but at a steady or somewhat lower level. Those financiers of capital to classical biotech firms will also require more financial returns to R&D investment. The larger companies are already pressured towards more returns on R&D.

## *3.2. Public investment*

Governments therefore have incentives to invest – especially in basic science – because knowledge has positive externalities from which society benefits. R&D investments by the public research sector are expected to remain high in coming decades, and likely increase and become more global.

One factor is the historical and current high public investments into R&D. Indeed, one characteristic of this sector is that public research especially in the USA has long been the main institutional driver of health biotech. The United States has had the lead in terms of public research and in terms of public-private interlinkages, which help stimulate new ventures. In the past few decades the increased level of commitment to research in health is

striking. Recent figures are also relevant. American public investment into medical research at the National Institutes of Health topped USD 28 billion in 2007 (www.nih.gov), whereas the National Science Foundation asked for a 4.6% increase to USD 116 million, within molecular and cellular biosciences (MCB) (www.nsf.gov). Other countries have also increased their spending, although medical councils in many European countries are also arguing that their public spending on research is too low to compete with the American system.

Another factor influencing future public investment is the rationale for investing in research. Rather than just funding research, the idea is that funding medical research will also stimulate innovation-driven economic growth. Huge amounts of public and private money have been invested in academic spin-offs, venture capital-backed companies, and initiatives such as technology transfer to stimulate academic scientists to commercialise their results. To some extent, this will occur *de facto*. Public research will continue to open up new areas of technological opportunities, well beyond the advances currently known and identified in Section 4. To some extent, innovation for growth will be a complex process. The research advances will be diffused and further developed by other scientists and firms through a variety of research results, problem-solving, techniques, instruments, training and the like.

Finally, global issues will become more relevant to public investments in R&D, and more countries will play leading roles, within specific areas. Public research will increasingly become a global domain. An illustration from Asia is useful. China has actively worked towards developing the health biotechnology innovation system through public policy (Zhenzhen *et al.*, 2004). It was the only developing country to participate in the Human Genome Project. China set up Beijing Genomics Institute and the Chinese National Human Genome Center. Specific subfields have been targeted, including therapeutic antibodies, severe acquired respiratory syndrome (SARS), gene therapy, functional genomics and stem cells. This has also led to results in commercialisation, and in 2003 the Chinese firm Shenzhen SiBono GenTech was the first firm to obtain a drug licence for a recombinant gene therapy. Despite these successes, China shares many of the problems found in many countries, such as brain drain, safety and regulatory concerns, limited funding, and limited domestic collaboration. Hence, in the future, we can expect that a few currently leading countries (like the United States) and a few entrants to the research (like China) will dominate.

The future debates about the role, and effects, of public policy will link the second and third factors. Clearly, we can expect future debates about whether public research and public-private interactions sufficiently benefit "local" or "national" citizens. Tax-payers and policy-makers expect direct economic effects, but research and innovation are global. This discrepancy will lead to some tensions and different ways of ensuring economic returns. For an historical illustration, the US public policy debate during the 1990s argued that the United States was investing extensively into science and technology, but losing in economic competitiveness because other countries benefited as "free riders". The answer seems to be that everyone benefitted, including the USA. Hence, the ability of a specific political unit to increase and to change the focus of public investment into R&D will likely in the future have to address concerns both about economic growth and about the local-global benefits of that investment.

## *3.3. Why the combination of private and public investment into R&D stimulate certain business models within this sectoral system of innovation*

This section provides further illustrations of the currently dominant business models, set in relation to each other and to public policy. The private and public investments into R&D are closely linked in this sector, as presented in Sections 2 and 3. Due to the nature of R&D and innovation processes, boundaries between the 'private' and the 'public' are sometimes difficult to draw because they are dependent upon each other. In addition to the R&D investments, the bundles of goods and services which are delivered as human health care involve many actors. They are active within many related industries, which are directly influenced by public policy, ranging from institutions and regulation to public provision of care. This implies that a somewhat broader perspective of the sector is necessary, in order to illustrate current models here and to discuss emerging business models in Section 4.

To begin with, we can identify a diverse set of firms which are active and present within the health biotech sectoral system of innovation. That system can be broadly defined as including the relevant firms, organisations and institutions supporting R&D and innovation within an industrial sector (Malerba, 2002, 2004). Starting with the public and private organizations, the system of innovation approach can then be further developed to define the most influential knowledge, institutions, and networks. This provides insight into the economic and societal context within which the firms active in health biotech are competing.

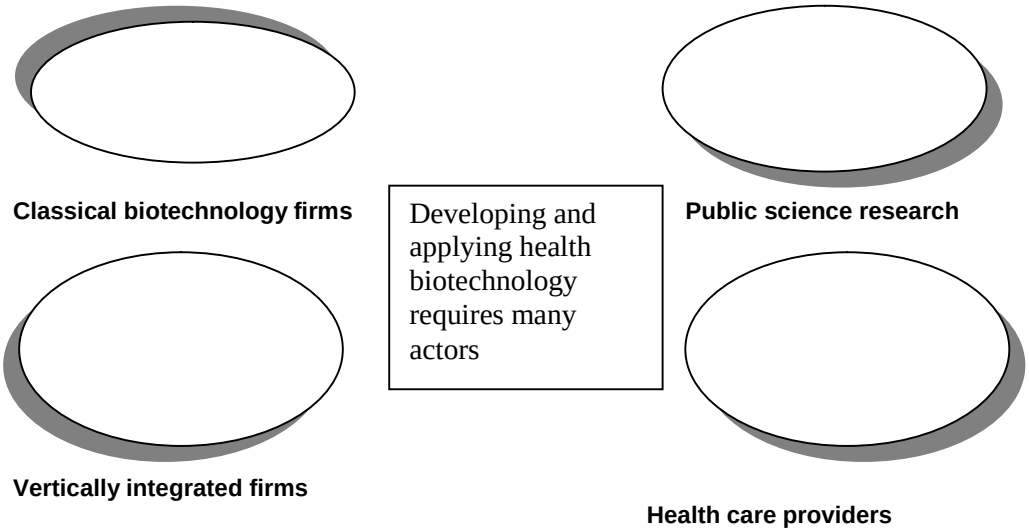
By placing the organizations in relation to each other within a sectoral system of innovation, the rationale for the two dominant business models also become more obvious, as argued and illustrated with examples below.

The reason has to do with how the new scientific and technological knowledge is developed and used in practise. Many of the new societal applications of health biotechnology are related to the interactions between medicine, biotechnology, and health care. Biotechnology has greatly impacted medical understanding during the past three decades. Technological advances and scientific results have led to new understanding, new research questions, new instruments and technologies, and new ways of working based on biologically-related scientific and engineering principles. These advances have come through public and private investments into R&D (research and development). Those advances are in turn 'translated' into socially useful goods and services, which may be delivered by private and public organizations (McKelvey and Orsenigo 2006).

Hence, the two dominant business models of classical biotechnology and large, vertically integrated firm are bar of the same sectoral system of innovation. The main characteristics of this sectoral system of innovation are relevant to this report because different types of health biotech firms compete but also collaborate with a number of different private and public actors. Figure 1 identifies four main categories of public and private organizations that are involved in financing, carrying out, and using the results of private and public R&D.[1]

[1] This section is developed from McKelvey *et al.,* 2005; McKelvey and Orsenigo, 2006.

**Figure 2 - Health biotechnology sectoral system of innovation**




**Source:** Author.

These four main categories of actors are all influenced by private and public investments into R&D. In turn, the business models are affected by the broader sectoral system of innovation linking knowledge, competition and collaboration within directly relevant areas of research, pharmaceuticals, and health care provision

The "classical biotechnology firms" provide specialised scientific and engineering knowledge, which is useful for R&D and useful in producing services and goods.

Biotech firms like Genentech and Lion can be characterised primarily as specialised suppliers of knowledge, with links respectively to University of California and to the European Molecular Biology Laboratory (EMBL). Biogen Idec, a merger in 2003 between Biogen and IDEC Pharmaceuticals, was also started by prominent scientists. In 2006, they had USD 2 billion in net revenues and USD 718 million in R&D expenditures. They are also involved in starting new companies, or corporate venturing. In 2007 they started Biogen Idec Innovation Incubator (bi3). "Bi3 is a corporate initiative designed to contribute to the company's drug development pipeline by offering entrepreneurial scientists the opportunity to rapidly convert novel biological insights into life-saving and life-changing therapies." (www.biogenidec.com).

Over time, different firms tend to turn to the newer types of specialised scientific and engineering knowledge, as these are most unique, difficult to imitate and thereby valuable. The idea with the business model is that the firm ought to focus on specialised knowledge for which customers are willing to pay – *i.e.* biomaterials, instruments, diagnostics, groups of patients, specific scientific techniques, databases, and so forth. Different biotech firms can thus see their main "internal resources" as many different types of knowledge specialisations.

Conceptualising biotech firms as specialised suppliers of knowledge also helps us understand other components of the currently dominant business model within this sector. Many firms do not sell products. Instead, they use what financing that they can obtain for additional research. Many of these firms depend heavily on venture capital and public policy initiatives for commercialisation of ideas; they must obtain additional capital to survive and continue investing in research projects. Thus, the business models of many of these firms depend on obtaining external sources of financing and on selling more immediate intangibles such as licences and joint ventures in order to invest into research with long-time horizons. In the longer run, these biotech firms may succeed in selling tangible goods and services.

Secondly, there are "vertically integrated firms" within related sectors. These are usually incumbent firms, especially pharmaceuticals, diagnostics, instruments, and medical devices. These are generally large firms within industrial sectors providing goods and services of relevance to human health care. Pfizer, for example, presents itself as "the world's largest research-based biomedical and pharmaceutical company" (www.pfizer.com). It employs close to 90 000 employees worldwide, with year 2006 revenues of USD 48 billion and actual R&D spending of USD 7.6 billion. Pfizer has products for both human and animal health. Another incumbent firm is Amersham, which is a world leader in medical diagnostics and in life sciences. "Our company is focused on enabling molecular medicine, working through three main business areas in diagnostic imaging, protein separations and discovery systems" (www.amersham.com). Headquartered in the UK, Amersham employs over 10 000 people worldwide and in 2002 had sales of GBP 1.62 billion (USD 2.54 billion) and invested GBP 184 million in R&D. The pre-merger Amersham Pharmacia was an early commercialiser of high-throughput sequencers of genetic data developed at EMBL (Harvey and McMeekin, 2007). Their current aim is to develop personalised medicine centring on diagnostic imaging agents (Amersham Health) and enabling technologies for gene and protein research, drug screening and testing, and protein separations systems (Amersham Biosciences).

These vertically integrated firms also usually control a long value chain,[2] in the sense that they own, have networks of and control flows of resources across a range of complementary assets. Much of the long value chain exists internally to the firm, but they also have strong links to external organizations. They are usually larger and older, and often more profitable than the specialised suppliers of knowledge. Many of these firms depend on the stock market and revenue streams from products, especially "blockbusters" in pharmaceuticals and dominant design products in instruments and medical devices. The leading firms within both pharmaceuticals and medical devices have merged and become giant conglomerations, with global R&D labs and global markets.

These biotech firms and large, vertically integrated incumbent firma are specialised in somewhat different knowledge areas. The large firms usually package their scientific and engineering knowledge into services and goods. This is particularly true for pharmaceuticals and, to some extent, medical devices.

However, changes are expected. The profitability of the incumbents and the ability to innovate have become increasingly difficult to achieve in recent years, in both industries but especially in pharmaceuticals. Meeting the standards required by regulation is costly, and many have argued that regulation presents disincentives for innovation. A key issue affecting these firms is the ever-increasing costs of R&D. To reduce the cost of internal R&D, many incumbent firms have been purchasing and using biotechnology from outside suppliers. They access external sources of biotech competencies through many mechanisms, such as purchasing licences and intellectual property rights (IPR), acquiring companies, entering into collaborative agreements with universities, and so forth.

A third major set of actors are "health care providers"; these can include a variety of public, private, and public-private organisations.

Health care provision will not be a main subject here, but it does represent an institutional variable in that it influences demand and consumers. Illustrations from different countries point to great diversity. Public health care has traditionally either covered specific groups in

[2] Some biotech firms as specialised suppliers of knowledge develop specialised products and goods for these sectors, but they differ from larger incumbent firms in that they rarely assemble the many components into a long value chain.

society, such as Medicaid and Medicare in the United States, or else provided basic care for the whole population, such as the traditional European welfare states. Many countries, like Australia, have a mixed system, with both public and private health care providers working in parallel. Private health care can be delivered by small organisations running one business place, as less expensive services within retailers such as Wal-Mart and by massive health care service companies such as Kaiser Permanente in the United States. Moreover, health care provision relies on different types of co-ordination, reimbursement and management-driven measures of efficiency within the national institutional and regulatory frameworks. As such, health care providers represent demand but also provide incentives and pressures for change, due to impact on another institutional variable, namely public policy, institutions and regulation.

Finally, "public science research" refers to organisations engaging in public scientific research, which play a major role in this sectoral system of innovation.

Clearly, public investment in basic research in medicine and related areas of science and engineering provides an enormous resource for society, such as research supported by the National Institutes of Health in the United States (www.nih.gov). As a science-based business, public research plays an important role not only for the development of research *per se*, but also for the generation of new specialised supplier firms, intellectual property, clinical testing, and so on.

The sectoral system of innovation analysis, as presented in this section, provides an opportunity for illustrating specific business models which usually link private and public R&D as well as business opportunities. This discussion has also provided a broad framework, which will be useful for understanding how and why some types of emerging business models are more likely to succeed than others, as the actors, knowledge and processes co-evolve in the system over time. This sectoral system of innovation approach also helps explain how future business models will tend to differ along two dimensions: the types of scientific, technological and medical competencies valued, and the way in which demand will be co-ordinated among public and private actors in bundles of goods and services.

# 4. How institutional drivers of change will influence emerging business models in OECD countries

The Bioeconomy of the future will be influenced by the four specific drivers of change. This section thus provides insight about the future in relation to the two main issues of this report, namely: 1) How the institutional and market context influences business models and 2) What types of business models will emerge between the currently two dominant ones, which are classical biotechnology and vertically integrated firm.

Clearly, for the future, the two dominant business models in health biotechnology will be modified and will also have to move over for emerging business models. Illustrations of specific firms and business models are given throughout the text.

Section 2 argued that by taking a broader perspective of the institutional context, including economic and political aspects, this report has identified many ways in which the four institutional variables affect business models for the biotechnology. This section therefore focuses upon specific ways in which the ability of the firms to make money off their internal resources and market ideas will depend upon the future institutional and market context within which they operate.

Some of the shifts in the context have to do with serious problems with existing business models and fundamental problems within existing industries. An example here is the

pharmaceutical industry, where the returns to R&D investment have dropped due to difficulties of finding a block-buster drug. Other shifts have to do with new organizing mechanisms, such as when new types of public-private partnerships co-ordinate public and private actors to tackle major medical problems. An example here is the Gates Foundation, which not only provides significant financial resources but also leadership and organizational focus for other organizations to tackle some developing country diseases. Yet other shifts allow the development of new business opportunities. An example here is the company which focuses upon coordination and packaging of goods and services to provide treatment more effectively for an aging population.

This section thus focuses on how institutional drivers for change will lead to problems, new organizing mechanisms, new business opportunities, and so forth which will lead to new types of business models. The focus here is upon future developments and illustrations of how those business models would work, while these current, emerging and possible business models is found in the conclusions, Section 5.

## *4.1. Technological advances*

Technological advances represent a key institutional variable driving changes in business models, because new techniques and technologies build on scientific, medical and engineering knowledge in order to solve health care-related problems. This section looks more closely at the types of technological advances that are expected, and then moves into more details and illustrations of how firms will be pressured by, and can react to, to such changes.

Table 1 lists major areas of technological advance that can use biotech knowledge. Biotech firms must continually renew their scientific and engineering competencies, due to the rapid and diverse range of these advances. Indeed, the long list of possible ideas and technologies underlines a crucial point about this sector, namely renewal of business opportunities through science and technological advances.

Areas listed and defined within Table 1 include: antisense and RNA interference (RNA-i)-based therapies, cell-based therapies, biologics and biosimilars, bioinformatics, functional genomics, gene therapy, microarrays, nanomedicine, pharmacogenomics, proteomics, stem cells and therapeutic vaccines. These technological advances will affect human health care in different ways. Some, for example, will be directly useful in goods and services; others will improve the R&D process. Some will lead to new bio-based pharmaceuticals, whether completely new or biosimilars that provide similar drugs but on a different biological basis. Others will offer a new approach to treating patients individually through detailed data, such as pharmacogenomics. Yet other technological advances are what we can call enabling technologies, components, and analytical tools, like bioinformatics. For these types of advances, major impacts are often on research and company R&D rather than stand-alone products.

Technological advances are broadly expected to provide opportunities for modifying and initiating business models through:

- *Continuing the start-up of business ventures as specialised knowledge suppliers*

Firms could be started in any of the scientific technological areas listed in Table 1. These firms will have access to specialised personnel, resources, techniques and knowledge within newly developed areas of scientific and engineering knowledge. Their knowledge competencies will be narrow, specialised, and difficult to imitate. At least for some period, value-creation will be possible, by delivering a unique R&D service.

**Table 1 - Technological advances**

| Name | Application, definitions, impacts |
|---|---|
| Antisense and RNA interference (RNA-i)-based therapies. | Potential uses as therapeutics. Inhibits gene expression and production of proteins. |
| Cell-based therapies | Use of cells, structures, biomolecules, etc. to regenerate diseased tissues and organs. Applications for tissue, organs as well as therapy. |
| Biologics and biosimilars | Complex medicines, manufactured using living organisms (microorganisms, plant cell, animal cell). Related to "generics" discussion in pharmaceuticals. |
| Biodata and bioinformatics | Digital repositories of information, generated through different techniques. For some uses, paired with biobanks with tissue samples. |
| Functional genomics | Used in modern drug discovery to prioritise the potential drug targets (using genomics information) and to translate that knowledge into rational and reliable drug discovery. From there, approaches that have been applied to drug discovery include RNA profiling, proteomics, antisense and RNA interference, model organisms and high-throughput, genome-wide overexpression or knockdowns. |
| Gene therapy | Tried in various therapies. Means introduce genes into existing cell, to treat. Applications to some narrow conditions. |
| Microarrays | Measurements of target proteins and study of protein-protein and protein-DNA interactions. |
| Nanomedicine | Used to deliver specific therapies, means nano-scale and nano-structured materials. Applications such as drug delivery, in vitro diagnostics, in vivo imaging, and biomaterials. |
| Pharmacogenomics | Used for disease management and diagnostics. Study of genetic variation on inter-individual differences in response to therapy. Applications can be used by firms in drug discovery and development. |
| Proteomics | Used for analysis. Means large-scale study of proteins, especially the structural and functional properties of proteins and their expression.<br>Relies on a variety of techniques, including microarrays and biomarkers. |
| Stem cells | Used in clinical applications, cancer, cardiovascular and neurodegenerative, etc. Means use non-specialised cells. |
| Therapeutic vaccines | Used to prevent infectious diseases but also hoped to use to treat diseases. Means use disease-specific proteins and sometimes cell-based approaches. Applications to infectious and autoimmune diseases as well as neurodegenerative ones. |

**Source:** IPTS, 2007; OECD, 2007; www.bio.org; Kramer and Cohen, 2004; Jain, 2004; Harvey and McMeekin, 2007.

These firms can turn their specialised knowledge into value through several of the business models listed above, especially: the classic biotech firm focused on science; the fully integrated pharmaceutical model focused on the discovery process; the information model focused on systematic information; and the service provider model with specialised B2B services for health care. Indeed many firms have already been started, such as those providing a specific technique within nanomedicine and using algorithms to optimise data mining within large-scale datasets. This is similar to historical business ventures, but most will absorb much R&D resources without producing positive financial results.

In the future, we do not expect these new ventures to survive as independent firms. Instead, we see an intensification of another trend, namely that these specialised knowledge suppliers are acquired by other firms requiring their competencies. Amir-Aslani and Negassi (2006) report that companies like Celera Genomics aim to combine genomics with (especially) bioinformatics and proteomics to provide diagnostics and treatment – but to do so, Celera needed new competences. They therefore purchased Axys Pharmaceuticals, in order to obtain specialised competencies in oncology-focused drug discovery, medicinal chemistry, high-throughput screening, and pharmacology. Other examples of acquisitions of new business ventures for their value as specialised knowledge suppliers include, in 2002, the OSI purchase of Cell pathway, Sequenom's purchase of Axiom biotechnologies, and Incyte genomics' acquisition of Maxia pharmaceuticals.

One reason for this acceleration of mergers and acquisitions (M&A) is fragmentation; another is that both the newly started and existing firms enter a kind of technological race, which leads many to fail and is highly costly. At each and every period, certain new types of scientific and technological competencies will become "valuable", often because they are relatively scarce and widely applicable. Over time, however, many of these competencies become less valuable because they become "generic competencies", in the sense of widely spread among students, competitors and so on.

The problem for the firms already in business is that they usually must devote many resources to monitoring and building up a scientific and technological competence internally, and to network relationships. They may find six months later that they can purchase or develop similar competencies much more cheaply or that the competencies are not directly relevant to their product. Despite the financial risks, health biotech firms must keep up with these developments and will therefore increasingly turn to mergers and acquisitions to obtain these specialised competencies. Supporting specialist skills and services related to M&A will be in great demand, such as lawyers and financial specialists to evaluate companies.

- *Developing markets, expanding markets, and taking over market segments in pharmaceuticals and treatment through technological advances*

Firms can develop markets in pharmaceuticals and treatment, because technological advances offer treatment for medical conditions that were previously not treatable or for which few patients could be treated (for some reason). These firms can create a market – or greatly expand a small market – if they can apply technological advances to meet these needs, and also create a supply and a demand expressed through market transactions.[3] However, the buyers' perceptions of costs (total and average) help determine whether customers will actually use biotech especially as substitutes and complements – and thereby affect demand.

[3]Moreover, because some advances are "generic technologies" or "general purpose", they can often open up new opportunities for goods and services, for uses and market segments that were not originally envisioned.

The firms can have business models primarily in the classic biotech and in the fully integrated pharmaceutical industry, as the emphasis is on pharmaceuticals and competition with incumbent firms. These types of business opportunities have been around for many years. The early biopharmaceutical products developed in the 1980s were insulin and human growth hormone, partly because existing supplies were limited and sometimes unreliable. More recently, the issue has been how to show that biotechnology products are reasonable substitutes or complements, given the difficulties of comparison. These developments would enable the firms to follow the market maker model by introducing a treatment that did not previously exist, such as combining pharmaceuticals, lifestyle changes and preventive treatment. The FDA is aware of these trends. The FDA Critical Path Initiative identifies pharmacogenomics as an opportunity for product development and personalised medicine.

To illustrate the importance of these issues, let us look how the American biotech industry association, Bio (Bio.org) has been active in debates to specify costs and clarify standards for comparison. One report commissioned by Bio focused on pharmaceuticals and found that "innovative therapies" (biotech pharmaceutical products) would not create large cost burdens in aggregate in the future despite being more costly per patient/treatment (Pyenson and Murphy-Barron, 2007). The reason was that despite costing more than USD 5 000 to USD 20 000 per person per year, innovative therapies would be used on a small number of patients. Moreover, the majority of claim costs would be related to hospital and other medical costs (not prescription drugs). Bio org has also been active in the debate on "comparative effectiveness". The term implies a range of characteristics that differentiate it from traditional double-blind pharmaceutical clinical trials. Comparative effectiveness trials means that: one treatment is compared to one or more treatments; the treatments are not limited to medicines; risks and benefits are included; and sometimes there is evidence from "real world" health care, not randomised and controlled trials (Buckley, 2007). The Bio org report mainly outlines the complexity of the concept of comparative effectiveness. Few standards currently exist, but the development of standardised modules and interfaces would help promote diffusion.

In the future, a major problem for the health biotech firms will be how to demonstrate that their goods and service product can offer advantages in the long run, in order to expand their market, when they offer a different type of treatment. Current regulation means that this problem applies to biosimilars as well as to more innovative treatments. Strategies for getting around the problem include working closely with preferred customers, using extreme cases to try out new techniques, and investing own resources on data for long-term monitoring for proof of treatment. Public-private partnerships like the initiatives by deCODE, FDA and the Gates Foundation will lead to new systemic bioinformatics infrastructures, but in other cases the firms must develop or obtain access to specialised information about medical records, genomics, and other aspects of bioinformatics.

- *Investing in R&D but demanding higher, more visible, and more immediate returns on investment*

As Pisano and others are arguing, venture capital is no longer willing to finance very long-term research efforts. This will pressure biotech firms to modify their existing business model, to focus more on applications and less on the basic science.

This type of pressure is relevant to all the business models listed in Section 4.1, and represents a fundamental shift in attitude about the value of internal resources. Technological advances developed by the firm must be usefully applied to goods and services, which can be sold in the short run future. Hence, existing and new business ventures that intend to sell specialised knowledge relevant to these technological advances must be able to demonstrate that they can package and apply their unique competencies to solve immediate problems.

They must demonstrate much more visible returns than many firms were required to so in the past.

A related outcome will be modification of business models, in order to more explicitly demonstrate how these economic returns to R&D investment are obtained, or appropriated, at the firm level. Hence in the future, we need to consider whether, and how, specific ways to appropriate the returns to R&D work. Let us take the example of licensing, using data from a study of biopharmaceutical companies (Kollmer and Dowling, 2004). They found that 360 North American biopharmaceutical companies were identified as licensors, and a sample of 70 firms was used. Twenty-six per cent of the firms were fully integrated, in the sense of having the multiple steps in the pharmaceutical value chain of research, pre-clinical development, clinical trials, regulatory expertise and marketing and sales. Seventy-four per cent were not fully integrated. Unlike many other industries, pharmaceuticals out-license during research and development rather than market introduction, and their results confirm this finding for both sets of firms. For the integrated firms, they tend to decide to out-license when the IPR does not fit with the company strategy, and thereby tend to accrue similar benefits as the non-integrated firms. Similar results can be found for the Netherlands medical biotechnology firms, where product firms also use short-term revenue generating activities like contract research (14.2%), out-licensing (4.8%) and selling research products (14.2%) (Willemstein, van der Valk and Meeus, 2007). These empirical findings suggest that firms will continue to use short-term revenue-generating activities to appropriate returns to their R&D expenditures.

In the future, we can expect a polarisation across different business models, but also within the same firm and public research organisation over time. On the one hand, developments will continue as they have in the past. Some firms will be mainly concerned with protecting intellectual property rights, especially patents and licensing. Firms will also use other strategies like first mover advantage and secrecy to protect the competitive advantage gained from their unique knowledge competencies. On the other hand, we can expect more radical developments. Some firms will develop an open innovation and open source software model, where they allow access to intellectual property in return for community involvement in problem solving and testing. How this polarisation plays out will depend on the strategies of actors.

Historical evidence suggests that the actors pushing for ownership and closed access are not always firms, and those pushing for open access are not always public research institutes. Harvey and McMeekin (2007) provide detailed evidence about the competition and conflicts over how genomics information shaped the strategies for patenting, disclosure, public deposits, etc. between major pharmaceutical companies like Merck, universities like the University of Washington, start-up companies like Celera Genomics, and public research organisations like the National Institutes of Health. Merck, for example, deposited EST sequences into Genbank, whereas NIH applied for patents. Their historical case studies as well as developments in other industries such as software suggest that the boundaries between public and private knowledge will remain fuzzy in the future. In addition to traditional roles, some large commercial actors will promote open access and some public research organisations will promote closed structures and ownership of intellectual property. Different solutions are possible. Co-ordination will be more costly, and this implies that firms must develop more sophisticated techniques to determine and negotiate information rights of the underlying science and technology, in order to demonstrate the value added to their own R&D.

- *Combining and integrating existing and new scientific and technological competencies into bundles of goods and services*

Because technological advances lead to multiple types of new knowledge, techniques, areas of application, etc., combining and integrating knowledge into functioning medical and life science systems is increasingly complex. Two main issues for health biotech firms are to choose which technological advances are core internal resources, and to develop methods and processes to combine and integrate those competencies to deliver goods and services to buyers.

Pressures for modifications will cause firms to change all the business models, as they also become more strategic about their ways of combining and integrating knowledge. The ones most likely to gain value are firms in the information model, hybrid technology model, horizontal non-exclusive model, and the pure tool and component model. These four business models rely especially on the technological component of the firm's internal resources. They will need to "modularise" or package their knowledge into standardised units that either can be sold or used reliably within internal processes. Clearly the smaller knowledge suppliers can develop niches within the overall network, but they must be prepared to adapt to pressures within that network.

New business models can also be developed in health biotech. Firms can start to develop the systems integrator model by specialising in combining and integrating competencies, both for themselves and for other firms. They will develop competencies similar to large engineering firms with complex product systems, where firms use a modularity approach for organizing complex products and processes efficiently and where firms increasingly profit from services rather than goods. Modularity involves decomposing complex tasks into similar units, which may be more or less standardised and customised, and which are later rearranged (or integrated) into a product architecture (Baldwin and Clark, 1997). One reason that systems integration will become particularly relevant to health biotech is that many of the expected technological advances require large-scale and multiple sources of data, and the integration of goods and services within complex products.

Possible developments for the future in pharmacogenomics can be seen by analysing biomarkers as the integration of epidemiology and biology with other fields. Diagnostic and prognostic biomarkers have so far failed to emerge at the pace expected from advances in genomics, despite their key importance for new types of health care (Porta, Hernández-Aguado, Lumbreras and Crous-Bou, 2007). More issues need to be resolved at the public-private interface.

One key issue for that interface is clearly the need to discover and validate biomarkers. It is not clear who will undertake this necessary research. Translational research between scientists and clinicians is necessary in order to link biomarkers to pharmacological effects, to estimate dose ranges, to determine efficacy, and to determine differentiation from existing treatments (Sultana, Roblin and O'Connell, 2007). Different phases require different actors (Porta, Hernández-Aguado, Lumbreras and Crous-Bou, 2007). Discovery leads to a list of candidate biomarkers, standardisation of analytical procedures and analysis of biological variability and this phase requires laboratory scientists and (often) small samples. Moving to the validation phase requires integration with other types of knowledge and medical practice, in order to collect samples (of genetic information, tissues and so on) relevant for clinical and prognostic purposes. Samples are rarely complete, due to "selection biases". Selection bias occurs because samples exclude eligible patients and relevant information for many reasons: individuals chose not to be included; only patients receiving treatment are included; medical records are incomplete, etc. This means that validation of those biomarkers and their "usefulness" for medical practice will depend on decisions made when collecting samples, such as whether to collect from all individuals at high risk for a disease, or only those with symptoms, or only those receiving treatment. Validation of the biomarkers phase will thus require the involvement of medical experts from different fields, as well as likely large companies and public organisations able to access the biological material.

It is unlikely that any one firm or public organisation can develop internal competencies relevant for the whole range of knowledge necessary. Co-ordination of the system towards common goals and R&D efforts could be made through a centralised actor, such as a public agency, to systematise, collect, analyse and use the material. There have been developments along these lines in countries, like Canada and Sweden, with nationalised health care. However, these systems will require high-level commitment to succeed, because at the same time, they are struggling with rising total costs for health care provision; these longer-term goals may be in conflict with the immediate goal of providing reasonable and reasonably priced care today.

A main issue is to establish who will provide the guidelines and databases for biomarkers. If technological advances are analysed as a modular product system, then it is clear that these guidelines could function in a similar way to technical standards in software and the telecommunication industry, in providing well-defined interfaces between components. This has already worked in health biotech, namely through the human genome project and global databases such as those of GenBank, EMBL and NDJB (Harvey and McMeekin, 2007). Public-private initiatives are also needed in pharmacogenomics, including biomarkers, to develop guidelines as well as large databases for both the discovery and validation phases. For example, the FDA Critical Path Initiative has developed initiatives for guidance and voluntary submission of exploratory pharmacogenomics information – such as best-practice documents, the VGDS and VXDS systems, and a tool called ArrayTrack – to manage, analyse and interpret multiple types of data (Tong *et al.* 2007). These initiatives run on voluntary contributions and hence, like open source software systems, they need to attract enough participants in the community to contribute samples and development work, propose solutions, and test and interpret the data and overall system. Likely, an international standards-setting body – likely based on FDA and NIH standards – will be developed.

- *Developing specialised medical integrators, who combine specific sets of scientific and engineering knowledge with specific medical applications*

Technological advances will also enable firms to specialise as integrators of science with medical applications. The idea is similar to the business models of systems integrator and orchestrator model, in that the firm must make a complex set of knowledge and interactions function. The combinatorial and integrative dimensions of this business model are similar to the above discussion.

Still, this represents a new type of business model, because integration is linked to the specific medical application. Health biotech firms would have to specialise in integrating technological advances with very specific knowledge of an area of medicine; that knowledge would have to cover treatment, conditions, medical practice and alternative forms of health care provision. Similar large-scale, quantitative understanding will be necessary to deliver on the promises of personalised and P4 medicine (see further Section 4.5), although so far only one company seems to be succeeding with this strategy.

deCODE is an American firm located in Iceland that develops drugs based on gene discovery work in common diseases (www.decode.com). Many common diseases are complex, and involve interactions between inherited and environmental factors. deCODE uses combinations of many types of scientific and medical knowledge – use genetic factors, population approaches, protein and targets, and biological pathways of diseases – for treatment discovery. Much debate has centred on a key feature of their business model, namely that they have developed a national computerised medical record database for public health authorities in Iceland, while also creating a parallel commercial genetics research database called “Genealogy Genotype Phenotype Resource” (Merz, McGee and Sankar, 2004). The company thus has unique access to comprehensive data about medical history as

well as genomics information, in an isolated, homogeneous population with excellent historical data. deCODE has worked with Roche since 1998, on treatments for a range of common diseases like stroke, schizophrenia, osteoporosis, obesity and type 2 diabetes (www.decode.com). More recently, deCODE has developed what they call "Information Rich Clinical Trials" (IRCT) to use the genetics information to better select and analyse trials, working in connection with Merck. Hence, deCODE is now using their core competencies to address one of the key problems underlying the rising costs and decreasing R&D productivity of pharmaceuticals, namely better and more effective clinical trials.

Many other companies as well as public organisations understand the need to integrate components to achieve the promises of pharmacogenomics. Everyone, however, is wondering how to reach these new goals, who will pay, and who will innovate. Clearly, access to large-scale, reliable data is key, as is the possibility to interpret results relative to specific diseases. deCODE can exploit their whole-population advantages by focusing on common diseases, but other databases will probably be concerned with specific diseases. Given the need for reasonably large samples, such databases will likely succeed when the collecting and analysing organisation has specialised clinical activities, such as large teaching hospitals in the United States. Another element necessary for success will have to do with handling the sheer scale of analysis and data required. Millions of SNPs (single nucleotide polymorphisms) must be identified and analysed to determine involvement in drug response, and genetic variation across populations with different characteristics must be determined. This requires either centralised actors or co-ordination across multiple actors; public agencies and private companies are therefore developing accessible bioinformatic infrastructures, such as the American initiatives VXDS, MAQC, and ArrayTrack (Tong *et al.* 2007). Other issues have to do with delivery at the health care provider, because they will need retraining for pharmacogenomics. Techniques will also change, as protein microarrays will need to become useful tools in the doctor's office for diagnostics. The public-private interface will therefore need to develop incentives, competencies and network interactions to deal with specific problems requiring solutions and to upgrade skills in this move towards a radically different system.

In the long run, integration of knowledge with medical practice should have other implications as well, due to new types of supply and demand from health care based on different principles. Many developing country firms will enter through an innovation-driven and blockbuster approach. Many others will enter the market through a range of other approaches, including generic drugs, biosimilars, and alternatives such as Chinese medicine. Competition from generics from, say, Indian firms will matter most to those industrialised firms with products going off-patent and without new blockbusters. In contrast, the degree to which traditional Chinese medicine represents competition instead depends on whether medical professionals and individual consumers really identify these as alternatives to the FDA-approved type of drugs.

## *4.2. Public research and public-private interface*

Public research and public-private interactions will continue to help drive the development of health biotech. The central role of basic and applied research thus relates the discussion of how and why this institutional variable will drive change with the discussion in Section 3, which addresses future investment in private and public R&D.

In this report, public research and the public-private interface are expected to provide opportunities for modifying and initiating business models through:

- *Creating business opportunities, through science and technological advances financed by the public research sector*

A defining feature of health biotech, as introduced in Section 2, is the crucial role and importance of public research, public actors and public-private interlinkages in this sectoral system of innovation. Public dimensions of health biotech help stimulate innovation, promote additional private R&D, and enable firms to commercialise science and technological advances. In other words, business opportunities are created, enabled and facilitated by public research and public-private networks, including informal social networks. The future will likely see a continuing high investment into public, and publicly funded, R&D.

The future effects on business models have already been explored in Section 4.2. Firms with classic biotech models will continue to be started, based on these business opportunities. Firms in the platform, the hybrid technology, the horizontal non-exclusive, and the pure tool and component models will also draw benefit, because their models depend crucially on technologies that in turn are developed by investments in private and public R&D.

These future trends and required strategic decisions are related to classical decisions within manufacturing that will affect the firm's position in the sectoral system of innovation. The health biotech firms must choose which elements of existing and new competencies to keep in-house and which to outsource to partners in their network. These choices are known as "make or buy" (Teece, 1986). Health biotech has long worked with multiple sources of knowledge, but biotech firms will increasingly use – and be judged on – quantifiable measures to identify and track the performance of network partners.

Pressures to change business models along these lines will to some extent reinforce the existing sectoral system of innovation. This means that biotech firms will continue to benefit from network relationships and positive externalities. They may do so through bringing previously external competencies into the firm, such as through organic growth, mergers and acquisitions, and developing their own bioinformatics department. They may also do so through external networks, *e.g.* outsourcing risks and collaborative agreements with universities and firms.

An additional effect to consider is what happens when (and if) public research plays a less central role for firms in future business models. The reason is that health biotech, and especially the business models of the biotech firms, are being pushed to become more directly relevant to applications and more immediately profitable. Hence, this offers some possibilities for the development of the orchestrator model to provide unique, valuable services to identify valuable partners, because all firms will need to be more selective about not only the quality but also the type of public science with which they are linked.

- *Exploiting these public-private linkages, which implies that firms need to develop key components like networks and open access*

Exploiting public-private linkages hence requires the firm to be more selective about their networks. It is well-known that health biotech is characterised by multiple public-private linkages (Powell, Koput and Smith-Doerr, 1996). Health biotech networks between public research and specific firms have been identified in many OECD member countries; there are a huge number of studies available in the social scientific literature. An interesting point made by Harvey and McMeekin (2007), and also found in McKelvey (2006) for earlier cases, is that within biotech, the boundaries of what is considered public and what is considered private have to be negotiated among actors, and that these boundaries will change over time, during the co-evolution of knowledge, actors, and institutional and regulatory frameworks.

As introduced above, business models based on orchestrator model will therefore be developed in the future to define and manage boundaries. Those firms will specialise in facilitating relationships and the co-ordination of information within these complex, global

knowledge networks. Hence, they will facilitate the search of incumbent firms in related industries and of biotech firms to find appropriate partners. To do so, they will use qualitative measures such as informal networks and scientific standing, as well as quantitative methods such as network techniques based on graph theory and scientific citations.

However, these firms will have difficulties in developing a sustainable business model, because the incumbent and biotech firms will be reluctant to pay repeatedly and so their customers will instead quickly move to integrate these competencies in-house. The most viable business model here would therefore further develop the orchestrator model into an orchestrator of information, not of relationships. Within IT and technology, firms like Forrester Research provide a host of services related to research, tools, access to analysts, etc.; they provide contacts and insights from other industry leaders, as well as up to date information (www.forrester.com). This type of firm should be further developed within life sciences.

Note that the component of public-private linkages does not in itself guarantee that the business model is working successfully, in such a way as to make money from ideas. Recent research has suggested that these networks function different for differently types of firms. Firms involved with early stage product development benefit from networks with universities. Firms concerned with later stage product development and on services and products for sale generally do not do benefit from alliances or networks to the same extent (Mangematin *et al.* 2003; Niosi, 2003; Baum, Calabrese and Silverman, 2000). Their networks should be more oriented towards buyers and suppliers.

- *Linking into public research on a global scale, which will help firms to position themselves to access, and also to sell, their specialised knowledge locally and globally*

Health biotech firms need to access quality and relevant research, without the constraint of territorial boundaries; we nevertheless expect an intensification of global pressures and local advantages.

The pressures to become global will increase, and they are relevant to all the business models because science, technological advances and markets are increasingly global. Many other firms will be "born globally", by opening up R&D labs, sales offices and contract research labs in other countries. Biotech firms are also often acquired by international companies, and sign R&D and licensing contracts with them. Australian biotech firms in Queensland and in New South Wales, for example, can access venture capital in the United States. This strategy requires dedicated production and knowledge network relationships to be visible with reliable partners, in order to overcome the tendency for venture capital to invest in activities in close proximity, or what is known as the asymmetrical information problem.

Paradoxically, some firms will be able to benefit from public policy set in specific areas that allow access to global developments, an issue also addressed in Section 4.4. Fifty per cent of Canadian biotech firms are in Toronto and Montreal, municipalities that host multinational pharmaceutical companies like Pfizer, Eli Lilly, and Novartis; universities and research hospitals like University of Toronto and McGill; and many other actors, like venture capital and clinical research organisations (Niosi and Bas, 2002). Co-location, externalities, regional innovation systems and learning are considered to give positive feedback loops, promoting specialisation within the regions (Cooke, 2002). Firms may gain higher externalities from co-located partners, due to factors such as tacit knowledge and learning effects sourced in intense interactions.

Regions and nations can develop public policy to access these developments, by stimulating, for example, international training, global networks and labour mobility between private and

public actors. As an illustration, Singapore has explicitly developed their health biotech by stimulating international mobility – such as the government paying for education and training abroad in exchange for later working in Singapore – and by stimulating linkages among companies and researchers. Health biotech in Singapore should be seen as part of a complex set of government policies to stimulate science, technology and innovation for economic growth (Koh and Wong, 2005). For example, the government set up a USD 1 billion fund to invest in venture capital, and the total gross expenditure on R&D has increased from 0.2% in 1978 to 2.1% in 2001. Hence this broader push for an innovation-based economy sets a public policy context in Singapore that has led to specific health biotech and biomedical initiatives like the Biomedical Research Council, the Tuas Biomedical Park, Biopolis, and expansion of research funding at the National University of Singapore. The National University of Singapore has changed its strategy and outcomes in terms of internationalisation, commercialisation, patents, and entrepreneurial spin-offs, in co-evolution with the institutional structure and public policy context (Wong, Ho and Singh, 2007). This suggests that specific nations and regions can stimulate regional innovation systems; however, it should be remembered that this example involves a country that has reoriented a complex set of institutional structures, public policy, and incentives towards innovation-driven economic development.

Firms can also develop other niches within the global value chain. For example, firms linked primarily to the local and regional innovation system are more likely to become suppliers to regionally-based incumbent firms. Moreover, research has shown that many of the especially scientific networks of health biotech firms are primarily local and national, as measured by informal collaboration and co-publications. Sweden, for example, has a concentration of biotech firms in the major metropolitan centres, with pharmaceutical-related biotech and protein engineering in Stockholm-Uppsala, biomaterials in Gothenburg, and a mix of biotech in Lund-Malmö and the Östersund region (McKelvey, Alm and Riccaboni, 2003). These Swedish firms have scientific networks that are, in descending order of importance, national, towards the United States and United Kingdom, towards Europe and towards the rest of the world. However, given the rapid rate at which new research results are questioning accepted wisdom in biology, we expect that firms need to monitor public research on a broad global scale, even if their specific competitive advantage comes from dense, close proximity to co-located actors.

## *4.3. Public policy, institutions and regulation*

Health biotech firms work within an environment largely shaped by public policy, institutions and regulations. Given the dependency on public research discussed above, expected changes to ownership of intellectual property rights and corresponding changes in the behaviour of public research organisations will affect these firms. Moreover, the framework of regulation should ensure desirable outcomes such as quality, safety, efficacy, and reasonable standards of treatment for health care provision. Changes there will affect the viability of business models and sectoral systems of innovation.

In this report, public policy, institutions and regulation are expected to provide opportunities for modifying and initiating business models through:

- *Modifying institutional structures and ownership for intellectual property rights and academic entrepreneurship in public research organisations*

Modifying institutional structures and ownership issues related to science and technological advances will influence the future, given that health biotech firms have traditionally relied on a science-driven business model. Many firms have benefitted from positive externalities, trained labour and open exchanges of information. However, universities and research

institutes have already become keener to protect their intellectual property rights (IPR), and this trend will intensify.

These changes will have particular effects on the platform, hybrid technology, horizontal non-exclusive, pure tool and component, and open innovation models. The reason is that these firms rely on types of technology and technical knowledge that are subject to intellectual property rights. IPR will likely continue to extend to areas previously thought exempted, and so will also affect firms based on the business models linked to the technological advances identified in Section 4.1.

Feldman and Brenitz (2008, forthcoming) identified multiple forms of university-based support structures, including sponsored research, invention disclosures, patents and licensing, university-based spin-offs, science parks and incubators. Specific universities as well as countries have also been shown to differ in terms of the timing, and types, of support structures and policy in place to stimulate, or hinder, entrepreneurship from academic science. Hence, specific firms could choose to "relocate" to more favourable environments and also to engage in university collaborations in regions elsewhere in the world. The illustration from Singapore above also indicates that many Asian countries have been moving towards a science-driven economic model.

Many OECD member countries have been changing institutional structures and property rights, in imitation of an American model of academic entrepreneurship. This is true in many fields but especially medicine and health biotech. The Bayh-Dole Act of 1980 in the United States, which allowed patents for publicly funded research results, has been at the centre of many debates around the world over whether or not to imitate and stimulate an American-style academic entrepreneurship. European countries have done so, even if Mowery and Sampat (2001) argue that the rise in patenting was due to a number of historical factors, and that in fact the upswing in this type of patenting can be dated before Bayh-Dole. Whereas Denmark removed the "professor's privilege" in the early 2000s and thereby transferred property rights from the individual researcher to the university or institute, Italy made a decision to introduce the professor's privilege around the same time, and thereby transferred property rights from the organisation to the individual.

These shifts to public science arenas will affect health biotech greatly. Firms will face additional pressures to modify their business models because the behaviour of universities and public research organisations will change to match these institutional changes. *Ad hoc* evidence suggests that as universities become managed more like knowledge businesses and less like social institutions, they are also more aggressively pursuing IPR and monitoring infringement. Thus, the nature of the public-private linkages will change in the future, and we can expect additional and escalating conflicts over IPR and access to biological materials.

- *Differing trajectories for regulatory frameworks, and ways of working among the actors. The choices taken within the sectoral system of innovation will influence which countries "lead" in the new biotechnology*

Business models within health biotech depend on the regulatory frameworks and ways of working among actors in the sectoral system. Regulatory systems are lagging behind technological advances, for example for pharmacogenetics-based innovation and for stem cell-based therapeutic products (OECD, 2007, p. 31). Therefore, the "trajectory" or rate and direction of change will affect which countries develop positive externalities and institutional conditions, to develop and attract quality actors into their localised sectoral system of innovation.

The regulatory system for pharmaceuticals is quite complex, with demands of careful documentation of each result and each step. Getting a target molecule through this process

requires a great deal of resources and much time, and potential pharmaceuticals can fail at any point during the stages, as described in Amir-Aslani and Negassi (2006). DiMasi, Hansen and Grabowski (2003) attributed rising costs to the FDA developing risk-averse requirements for approval. Recent estimations are that it takes 12.5years for product development to turn into a drug candidate, and it costs USD 500-800 million to develop a new pharmaceutical drug. Of that, 75% of costs represent risks associated with products that fail (DiMasi, Hansen and Grabowski, 2003; Bains, 2004; Amir-Aslani and Negassi, 2006). Although the regulatory system has been blamed for rising costs and decreasing productivity of R&D, it is clear that mergers and acquisitions have also been associated with the decreasing productivity of R&D.

Pfizer is one, if not the, largest company in pharmaceuticals. For example, it spent more than USD 21 billion on R&D in the early part of 2000 and went through two mega-mergers, with Pharmacia Corporation in 2003 and with the Warner-Lambert Company in 2000. Amir-Aslani and Negassi (2006) claim that despite these M&A and R&D expenditures, the large pharmaceuticals have not solved their R&D productivity problem, and that few blockbusters have emerged. However, if we take the Pfizer example, the Pfizer website in 2007 lists a number of new drugs launched for areas as diverse as diabetes type 1 and 2, tumours and infections. They also list other initiatives such as the Infectious Diseases Institute in Uganda and "Pfizer Helpful Answers", an initiative to allow the American uninsured to access Pfizer medicines. This suggests that pharmaceutical companies are becoming involved in, and co-ordinating, larger public-private initiatives for their treatments, rather than simply focusing on R&D.

Fundamental changes to the regulatory system can in the future shift power among actors in the sectoral system of innovation. Examples are whether firms developing drugs will face new, post-marketing types of monitoring and regulations or whether medical devices, diagnostics, and therapeutics face similar stringent and long-term pharmaceutical-type regulation. Clearly the latter development is very likely, given that products such as diagnostics and medical devices have recently seen an increase in regulation.

The OECD has outlined different scenarios for regulation in relation to the future of health care (OECD, 2007). In the scenario "Muddling Through", the regulatory agencies apply the pharmaceutical model to other products and increase the stringency of regulation. The outcome of this scenario is that the incumbent firms, especially the multinationals in pharmaceuticals, are able to continue their strategy of pursuing blockbuster drugs to generate new revenue for R&D. The health biotech firms would here primarily remain specialised suppliers of knowledge. In the scenario 'Rapid Change', regulators shift to a more proactive stance, to stimulate innovation and promote relevant new health care outcomes. The regulators also encourage firms to use pharmacogenetics, in order to develop personalised health care. These scenarios thus illustrate how choices can lead to different trajectories, which stimulate modifications to certain business models.

Such choices about regulation will especially affect firms developing those business models that rely on selling goods and services to patients or to incumbent firms, like the fully integrated pharmaceutical, contract research, and service-provider model. But the effects are in fact broader and will affect other health biotech firms. The "Rapid Change" scenario implies that the costs of regulation and large-scale clinical trials would decrease. Smaller and younger firms working under resource constraints could thus bring their own products to market, rather than develop drug targets for the incumbent pharmaceutical and medical device firms. Additional business models will also become more viable, especially the platform technology, the information, and the hybrid technology models. The reason is that regulation for personalised and P4 medicine requires combining and integrating IT and specialised medical knowledge about health care applications, in order to develop ongoing and post-treatment monitoring through biomarkers in large populations of patients.

- *Developing outsourcing, fragmentation and integration across the value chain*

The value chain in pharmaceuticals and medical devices will become more fragmented and also more integrated into networks in the future (Drews, 2003). Trends in regulation and industrial structure suggest that compared to historical trends, incumbent firms in the pharmaceutical and medical devices industries will become less vertically integrated. For example, the industries have long outsourced some R&D and innovation, which has enabled the classic biotech model to sell their research and results. Other examples of fragmentation of the vertically integrated firms are the increasing importance of CRO (clinical research organisations) for testing and of outside engineering consultants for IT and monitoring quality in operations and production.

In the long run we would expect more reliance on the systems integrator and the orchestrator models, as well as the development of completely new business models to deliver specific value to the global value chain. This would be part of more fundamental changes to the industries. Lessons from other industries can be valuable to predict future changes. For example, the automobile industry remains to some extent a vertically integrated industry, with giant corporations producing millions of cars annually – in 2006, General Motors and Toyota each produced more than 8 million units (OICA, 2006). At the same time, this industry has many specialised producers and complex global networks. Automobile makers primarily keep in-house design and assembly, but they must also rely on technological joint ventures and on long supply chains to source components. Similar trends are likely in the future in the pharmaceutical and medical device industries, such that incumbent and larger firms will primarily play roles as suppliers, integrators and co-ordinators of information, people, and resources.

Hence, more radical changes in the strategies of different firms will occur and affect the system of innovation. We expect these changes to affect the types of partners, networks and value chains that the health biotech firms are willing and able to engage in the future. Our expectation is that the pharmaceutical, medical devices and health care provision industries will become similar to large engineering and manufacturing industries like automobiles, with specific techniques to manage networks such as supply chain management and optimisation of operation.

Using cases from construction and shipbuilding, Hameri and Paetela (2005) outline the pressures that affect supplier networks, in terms of network structure, location, information technology and organisational structure.

Table 2 thus illustrates a range of pressures and types of management techniques that health biotech firms will face, for both tangible supply networks and intangible knowledge networks. For example, the pressures towards connectivity, proximity and quality in the network will require new management techniques to decide and monitor outcomes.

Co-ordination of the system is therefore more likely through co-ordination measures across the network. Large companies and public organisations will use more management techniques to promote connectivity, integration of IT, local suppliers and the like, to maintain high levels of interaction among actors and to develop common visions of the future, including the key problems to be solved next. Modular knowledge and interfaces would become the norm, so that actors could specialise in, for example, discovery phase or validation for one group of patients.

**Table 2 - Pressures for changes within supplier networks**

| Pressure | Towards tier-structure | For expansion and contraction | For management procedures across firm boundaries |
|---|---|---|---|
| **Network structure** | Cost efficiency<br>Multiple value networks<br>Outsourcing<br>Modular product design<br>Life cycle services | Relocation of operations<br>Higher value offerings<br>Technical specialty<br>Alternating customer demand | Quality<br>More complex products<br>Reverse logistics<br>Life cycle services |
| **Location** | Global operations<br>Industrial parks<br>Channel management<br>Quick integration | Low-cost production<br>Cost pressures<br>Standardised routines | Proximity<br>Production cycles<br>Network planning |
| **Information technology** | Simple interfaces<br>Connectivity<br>Supplier-oriented | Packaged solutions<br>Implementation | Exchange of data<br>Shared responsibility |
| **Organisational structures** | Outsourcing<br>Network effects | Access to technology and know-how<br>Access to customers | New positions<br>Emphasis on suppliers and customer integration |

**Source:** Adapted from Hameri and Paetela, 2005.

Thus, smaller firms could adopt the orchestrator and pure tool and component models, which help the vertically integrated incumbents provide the final goods and services to health care providers. These requirements could thus lead to the development of new types of business models devoted to integrating production, delivery and monitoring of complementary assets across supply networks and value chains.

Regulation will help drive these changes towards managing network integration. The regulatory processes in pharmaceuticals is characterised by many (and increasing) stringent demands on the companies to monitor large quantities of data. Many of these data address modular elements like the technical specifications of manufacturing processes and complex medical processes like treatment and side effects. Similar trends towards increasing regulation and standardising processes are visible within medical technology and health care provision. These trends require that the firm has access to high levels of competencies to manage, for example, operations, knowledge management, regulatory interactions and process control. Many of these activities can be outsourced.

For developing countries, the disintegration of the pharmaceutical and health care provision systems into suppliers, modules and interlinkages suggests that firms will play more central roles within global value chains. They may produce fairly standardised components (such as reagents) but they may also enter into the high-value, high-risk science-driven model (such as gene therapy). As the above illustrations from China and Singapore suggest, these countries are moving into a model of economic growth based on extensive science and innovation. Hence it would be a major mistake to consider developing countries as primarily low-cost

countries for production in the future while OECD countries remain the primary knowledge producers. Firms and public organisations in developing countries will further build up their classical biotech and other models, and thereby enter the global market for integrating and outsourcing innovation into the value chain.

## 4.4. Demand and Consumers

This section discusses the fourth institutional variable, in order to identify major demand and market opportunities that may emerge in the future; the main focus here is on broad changes expected in biotech as relevant to health care provision because it is a key area of demand.[4] It also constitutes a key form of organisation to link patients, health care providers, and firms delivering components and final services and goods within the sectoral system of innovation.

Significant shifts are expected in coming years in health care provision, both in the short run of five years and in the long-run horizon of twenty years (OECD, 2007). Areas where changes are expected in the developed countries include the organisation, governance forms and financial contributions between public and private provision of health, shifts in demand due to major demographic changes, and new types of medicine and other therapies.

Health care services can be delivered in many different organisational forms, with different levels of coverage and quality for the population. OECD countries at each end of the spectrum seem to be pushing towards the middle. On the one hand, private health care and public-private arrangements are increasingly being developed in many of the countries (previously) dominated by nationalised public health. Among others, reasons include that many consumers have a demand that is unmet by public health due to, *e.g.*, queues, lack of specialists or lack of access to certain treatments. On the other hand, countries like the United States with a primarily private health care system have a lively debate over the need for public health to provide care for the huge number of uninsured, and to make health care "affordable". Such changes are relevant, but outside the scope of this report.

Still, different types of system to provide health care affect the health biotech firms. Whether the biotech firm sells pharmaceuticals, diagnostics or other services and goods, they must usually reach their final customers through the health care providers. This report will address the implications to business models of common challenges, especially of rising costs and of stimulating innovations, as well as new opportunities such as P4 medicine.

The demand and consumers variable in health care provision is broadly expected to provide opportunities for modifying and initiating business models through:

- *Prioritising efficiency and efficacy at acceptable levels of treatment, which can lower the costs (marginal and total) of diagnosis, prediction and treatment*

Health care providers will put pressure on firms to increase the efficiency and efficacy effects of their goods and services. They will face increasing demands, in terms of providing lower cost and better goods and services at acceptable levels of treatment. The pharmaceutical industry has been facing these shifts in demand for several years, which has squeezed profitability. This has of course directly and indirectly affected the health biotech firms and

[4] Defining market competition within health biotech depends on the type of service and products. The reason is that biotech refers to knowledge, and while a market for these specialised suppliers of knowledge does exist, scientific and engineering competencies are also relevant to many related industries. As such, the market competition can vary greatly in terms of industrial structure, main buyers and rate of innovation. For the purposes of this report, therefore, demand and consumers are primarily addressed in terms of health care provision.

the pressure for better, cheaper care should accelerate in the future. Moreover, private and nationalised health care systems will also demand that firms can meet a new combination of efficiency (current treatment, better at lower cost) and of innovation (future treatment).

Firms in the business models of classic biotech and the fully integrated pharmaceutical model will be, respectively, indirectly and directly affected. The classic biotech firms will be affected through the pharmaceutical firms, which often fund and license their research. The fully integrated pharmaceutical firms will be directly affected, as they aim to sell their pharmaceuticals to the health care providers.

These pressures on the business models towards efficiency and efficacy can also be linked to much broader shifts in organisation, governance forms, and payments of costs for health care provision. The rising costs of health care are well documented, and all countries grapple with the problem of escalating costs for health care. Public health care usually covers some costs but requires co-payment of others. A major issue with innovative treatments is that they usually have high marginal costs, at least initially, so the questions are, who should pay for the future, and which treatments will be available, to whom and at what price. The answers to these questions will affect the ability of health biotech firms to determine the types of goods and services that are likely to be demanded in the future.

Such pressures can thereby affect firms developing all the business models discussed in Section 4.1, but these shifts will provide conflicting pressures, business opportunities, and types of products and goods demanded. Most OECD countries experiment with various degrees of public-private provision of health care, as a way to balance the demands of different groups of citizens. Some countries like Sweden are primarily public health oriented, whereas other countries like the United Kingdom and Italy have mixed and parallel public and private systems. Most European countries, including Italy, the United Kingdom, Denmark and Sweden, also allow contributions to private health care alongside the public system. Private health care may be paid by individuals and households (personal) or by businesses and employers (private commercial payer). These different national institutional agreements will provide different sets of incentives to change the system, when facing political challenges such as increasing total costs and high marginal costs of specific health biotech treatments.

This has implications for the types of goods and services likely to be demanded within their future business models. Market developments may go in opposite directions. Countries moving from nationalised towards mixed public-private help will probably develop demand for niche and unique services and goods. In contrast, other OECD countries moving from private towards nationalised health care will develop new demand for more mass market type of provision, as more patients should be covered.

Note that this does not necessarily mean convergence, or the development of an international health care provision. Instead, the outcome will likely be increasing divergence, as each country experiments with governance forms in an attempt to solve its own perceived problems. Different scenarios for the future are possible, such that some countries may restrict the use of high-priced biotech-based treatments whereas others may mandate universal coverage and negotiate lower prices for higher volume. Of course, this illustration of the diversity of nationalised health care forms in (especially) Europe also gives some insight into why health biotech firms must devote resources to learn the rules of the game of somewhat different markets in each country – or else choose to develop local/regional markets.

More demand in developing countries means an increasing market for a range of services and goods, as well as the United States no longer being the main market in the future. It is hard to predict whether that shift will occur before 2030. Demand in developing countries is expected to rise rapidly, not only due to the existence of needs but also to the increasing ability to pay. The evolution of the middle class and the upper middle class in countries like China, India,

and Russia are rapidly expanding the demand, not only in their home country but also that of global specialists. Many of the wealthy individuals from developing countries fly to countries like London to obtain health care by specialists.

However, a main characteristic of developing countries is the differential ability to pay due to skewed wealth and income. This affects not only demand, but also the types of treatment needed by the population. The poorest segment of the population usually has a different disease and medical conditions profile than the richest segment of the population. Hence, the population in developing countries also needs some types of health care and treatments that are rare in developed countries, such as for malaria and severe malnutrition. Recent initiatives for these neglected categories of disease have often involved public-private partnerships, such as the Gates Foundation. The firms must have clear ideas about their customers, and also are likely move into post-purchasing agreements for services.

- *Expanding major markets due to demographic and lifestyle changes*

Firms in health biotech and related industries have identified growing future demand, due to demographic changes and lifestyle changes. The firms can shift their business market to target pharmaceuticals as well as other aspects such as services, R&D techniques and technological platforms that address the needs of these groups of consumers.

One such group can be identified through demographics, where the ageing population and longer life expectancies in developed countries have shifted expected markets. This affects overall health care costs, because people above 80 years of age tend to consume a high percentage of health care resources. They have specific needs, such as combining multiple medicines and treatments. Other groups of consumers can be seen through lifestyle changes. Some of these consumers exist due to the "rich country syndromes", such as the increasing prevalence of diseases like obesity and diabetes. Other consumers demand positive lifestyle changes, available through "feel good" drugs such as Viagra and "look good" interventions such as cosmetic surgery and luxury skin products.

Firms using different types of business models may be affected. The ones with classic biotech, fully integrated pharmaceutical and service-provider can develop directly for the consumers. To move into these types of expanding markets, health biotech firms would have to specifically target disease classes but also groups of consumers, as their needs and demands will differ greatly. The bundles of goods and services demanded will likewise vary, and understanding such differences is clearly necessary for firms working under the business models of platform, contract research, service-provider, hybrid technology, horizontal non-exclusive, and pure tool and component models.

A major issue for the firms will then become how to price services. This becomes very relevant if new approaches to health care are to provide new combinations of services, goods, prevention and alternative treatment. In the automobile industry, the definition of the product service system PSS is "a system of products, services, supporting networks and infrastructure that is designed to be competitive, satisfy customer needs and have a lower environmental impact than traditional business models" (Williams, 2007).[5]

Table 3 provides an overview of different service-based alternatives from the automobile industry, which can also be relevant to human health.

[5] This concept is similar to the sectoral system of innovation concept in the range of relevant actors, but PSS is more focused on particular processes and outcomes of the industrial sector.

**Table 3 - Types of services in the product service system (PSS)**

| Category | Specification | Characteristics |
|---|---|---|
| **Product-oriented services** | Product-related services | Provider sells product as well as services needed during use phase (like maintenance) |
| | Advice and consultancy | Provider gives advice on most efficient use of product |
| **Use-oriented services** | Product lease | Single user; provider retains ownership of product |
| | Product renting or sharing | Multiple users; provider retains ownership of product |
| | Product pooling | Multiple users; provider retains ownership of product |
| **Result-oriented services** | Pay per service unit | User buys output of product according to level of use; product forms basis of PSS model |
| | Functional result | Provider and user agree upon end result, without specifying how the result is delivered |

**Source:** Williams, 2007.

For the move to services in health biotech, the more interesting aspect of PSS in automobiles is the identification of a variety of ways in which businesses are paid for providing services.

In the future, demographic and lifestyle changes could lead to an increase in diseases that could be treated either in a traditional approach or through new combinations of therapies. The business model to meet expanding demand could be built on a traditional approach in pharmaceuticals, namely to develop a drug for treatment of identifiable medical conditions and hence build on classic biotech and fully integrated pharmaceutical models. However, the more radical development of the business model would be to develop, co-ordinate and deliver new combinations of goods and services to combine prevention, prognosis and treatment. The over-80 population, for example, could benefit from more sophisticated IT-based monitoring systems for side effects, multiple medications, and specialised dosages in relation to specific medical conditions. Moreover, Scandinavian countries allow medical practitioners to prescribe physical exercise instead of drugs for some conditions. These latter developments lead us to predict the emergence of new types of business models, which bundle goods and services to deliver complex treatments.

Moreover, several developing countries have moved into the market for lifestyle health care in the "feel good" and "look good" areas identified above. Thailand, for example, offers a range of "fly-in" treatments in areas ranging from dental and beauty operations to more basic health. The more patients are willing to fly around the world for the best treatment, the less health care providers are limited by the characteristics of service as a deliverable provided at a particular time and place. As long as the potential patients (demand) are willing to move around the globe, specialisation and economics of scale become possible in services as well.

This would enable firms pursuing a service-provider model to specialise, at high levels of volume, through global customers.

- *Developing pharmacogenomics, personalised medicine and P4 medicine will enable emerging business models focused on new bundles of unique services and goods. This also requires the integration of IT, biology and medicine*

Pharmacogenomics is the study of how an individual's genetic inheritance affects the body's response to drugs (www.genomics.energy.gov). P4, as mentioned earlier, refers to medicine that is predictive, preventive, personalised and participatory (OECD, 2007).[6] Providing this type of health care requires many of the technological advances outlined in previous sections as well as the more active participation of individuals. P4 and personalised medicine rely on combining and integrating existing and new knowledge, so that individual data can be interpreted in relation to population data and to a more detailed understanding of when and why diseases occur.

Completely new business models must be developed that draw on new combinations of internal resources and new identification of the main issues facing health care providers. The exact dimensions of these emerging business models are still unclear, and so we will instead consider the required shift in focus.

These shifts have fundamental implications for the future business models, in terms of knowledge, integration and the role of consumers. In terms of knowledge, technological advances have been covered in Section 4.2, and multiple advances and integration of results must be achieved. One aspect is the development and use of large-scale databases, including biomarkers that are predictive as well as real-time monitors of effects. Systems biology is needed, to identify indicators of genetic risk as well as interpret individual health histories. Many other technological advances within IT, diagnostics, genetic sequencing and proteomics are also key to realising this fundamental shift in health care provision. Hence, areas such as mathematics, system engineering, system biology and bioinformatics are necessary and will become increasingly valuable to develop and interpret the data collected.

In terms of integration, technological advances need to combine science and medicine with (especially) IT and information systems, in order to store and find the required information. Specific algorithms for data mining, for example, will have great value in P4 medicine, and thereby provide business opportunities for health biotech firms able to develop relevant, robust and powerful search engines. Hence, P4 medicine requires that the firm business model has more integrative foci, to understand the circumstances when information is "valuable" to address a medical issue.

In terms of the role of consumers, the health biotech firms must develop more direct interactions with individual patients. The contacts to obtain and provide relevant information need to go directly through the patient, to ensure up-to-date prediction, diagnostics and treatment. As in the software industry, the most likely outcome is that health biotech firms must learn to differentiate and tailor specific sets of products and relationships to B2B business as opposed to those for direct use by consumers.

[6] The implications for health care provision are huge, and have been addressed in other OECD reports (OECD, 2007). Realising personalised and P4 medicine will require shifts in regulatory practice, collaboration between actors, governance of health care provision, a shift of focus within science and technology systems, and availability of data at the individual and population levels.

- *Developing direct interaction with individuals as "users" and "developers" promotes new development and testing activities, similar to those observed in open source software*

Active consumers are inherent in the shift to P4 medicine discussed above, but also represent a broader future shift in health care provision. As with many areas of society, the individual is increasingly better educated and better able to find information about alternatives – in this case about potential treatments, risks and alternative outcomes. Use of the Internet and other IT tools enables the individual to access information and to question the opinions of the "medical expert". These active consumers are making demands on the care provided by the health system, in addition to contributing the "information" that each individual can potentially provide to large-scale databases on genomics, proteomics, medical conditions and the like.

These pressures can lead to completely new business models similar to the P4 medicine case discussed above, where firms treat individuals as active consumers rather than as passive consumers.

These pressures can also encourage open innovation and open source software models of development, where individuals act as "developers" or "problem-solvers" for the firms. A series of open source initiatives for biotechnology are being developed in Cambia, an Australian institute financed by various foundations and supporting the BIOS initiative (www.bios.net). They are working to develop open source in biotechnology in different ways, such as toolkits (for seeds), collaborative research platforms (www.bioforge.net) and a search of patent databases in the life sciences, called Patent Lens. Clearly, open source models in life sciences will differ in fundamental ways from those in software, especially when it comes to confidentiality of information, reliability and validity of biological materials, and the organisational form of delivering health care.

Our expectation is that in the longer run, this will lead to major shifts in the orientation of the business model and the sectoral system of innovation. At the extreme it implies a shift in the overall sectoral system of innovation, in which health biotech firms stop acting primarily as subcontractors of R&D to large incumbent firms and start focusing on individuals. New actors would have to be included, such as individuals, stakeholders and advocacy groups, as well as new means of co-ordination and incentives.

## *4.5. Summary*

This section has addressed how these four institutional drivers for change can likely affect the institutional and market context for firms, and thereby business models. These four institutional variables are: 1) Scientific and technological advances; 2) Public research and the public-private interface; 3) Public policy, institutions and regulation; and 4) Demand and consumers. The focus has been upon illustrations and expected future effects on business opportunities for firms and industry, as summarized below.

Technological advances are broadly expected to provide opportunities for modifying and initiating business models through:

- *Continuing the start-up of business ventures as specialised knowledge suppliers.*

- *Developing markets, expanding markets, and taking over market segments in pharmaceuticals and treatment through technological advances.*

- *Investing in R&D but demanding higher, more visible, and more immediate returns on investment.*

- *Combining and integrating existing and new scientific and technological competencies into bundles of goods and services.*

- *Developing specialised medical integrators, who combine specific sets of scientific and engineering knowledge with specific medical applications.*

Public research and the public-private interface are expected to provide opportunities for modifying and initiating business models through:

- *Creating business opportunities, through science and technological advances financed by the public research sector.*

- *Exploiting these public-private linkages, which implies firms need to develop key components like networks and open access.*

- *Linking into public research, on a global scale, which will help firms to position themselves to access, and to also sell, their specialised knowledge locally and globally.*

Public policy, institutions and regulation are expected to provide opportunities for modifying and initiating business models through:

- *Modifying institutional structures and ownership for intellectual property rights and academic entrepreneurship in public research organisations.*

- *Differing trajectories for regulatory frameworks, and ways of working among the actors. The choices taken within the sectoral system of innovation will influence which countries "lead" in the new biotechnology.*

- *Developing outsourcing, fragmentation and integration across the value chain.*

Demand and consumers in health care provision is broadly expected to provide opportunities for modifying and initiating business models through:

- *Prioritising efficiency and efficacy at acceptable levels of treatment that can lower the costs (marginal and total) of diagnosis, prediction and treatment.*

- *Expanding major markets due to demographic and lifestyle changes.*

- *Developing pharmacogenomics, personalised medicine and P4 medicine, which will enable emerging business models focused on new bundles of unique services and goods. This also requires the integration of IT, biology and medicine.*

- *Developing direct interaction with individuals as "users" and "developers", which promotes new development and testing activities similar to those observed in open source software.*

# 5. Conclusions: Effects upon business models in health biotech

This section concludes, by returning to the two issues posed in the introductory section, namely 1) how the institutional and market context influences business models and 2) what types of business models will emerge between the currently two dominant ones of classical biotechnology and vertically integrated firm. It furthers the analysis conducted above in Section 4, by considering a range of existing, experimental and potential business models for the future. Section 4 has already structured the analysis, by providing details on how the four specific institutional drivers of change will influence the institutional and market context. Extensive examples and illustrations of firms and of trends have been given in Section 4. Therefore, this section focuses upon first defining the more abstract and general types of business models. This section includes a discussion of the more likely outcomes, but also more speculative thoughts, when extrapolating more fundamental shifts which could occur in the future. These conclusions then led to the policy implications in Section 6.

## *5.1 How institutional drivers of change will affect business models*

The first issue is how the institutional and market context of the future will influence business models. The report is interested in future developments, including ones which have differential potential to become viable – including currently dominant, existing, quite likely, experimental and speculative business models.

These results can be analyzed in terms of more general ways in which the institutional and market context affects business models, by placing the firm in a broader perspective. This report thus also contributes to the more general understanding, because the existing academic literature focuses primarily upon the firm.

As identified in this report, institutional variables mainly affect business models by:

- Providing resources and incentives for research, development and innovation
- Using public monies to stimulate the commercialization of new technology, instruments, models, databases, and so forth
- Setting the institutional conditions for new business opportunities
- Stimulating reform of regulations and institutions
- Influencing existing demand
- Highlighting new types of economic value (e.g. for what customers are willing to pay)
- Helping to express and form future demand
- Specifying new combinations of goods and services to address health care issues

The above list of ways in which public policy initiatives can influence business models are defined primarily in terms of setting the broader context, within which private firms and public organizations are active within health. Hence, public policy has a new role for defining the visions and goals for how the Bioeconomy of the future will improve human health, given the interactions across the public-private and the economic-health-political spheres. The reason that public policy can play a role is that the ability of the firms to make money off their internal resources and market ideas will depend upon the specific market and institutional context within which they operate.

These factors often interact. One clear implication of these results for public policy is that a systemic view of policy is needed. Initiatives across different Ministries may be required, to stimulate and give incentives to the main private and public actors within the sectoral system of innovation.

In other words, one result of this report is to be able to specify how public policy initiatives (defined broadly) can directly and indirect the decisions of private firms, when conceptualized as business models. Some initiatives relate to R&D and innovation, some to regulation, and yet others to demand. This systemic view of the interlinking influences of R&D, innovation, regulation and demand thus imply that public policy will play a crucial role in determining what type of Bioeconomy of the future is developed.

## *5.2 Business models in health biotech: Dominant, experimental and speculative*

Another result of this report is providing definitions of different models. Health biotech offers a number of business models at present and in the short-run future.

Current debate and analysis is highly concentrated to two dominant models, namely:

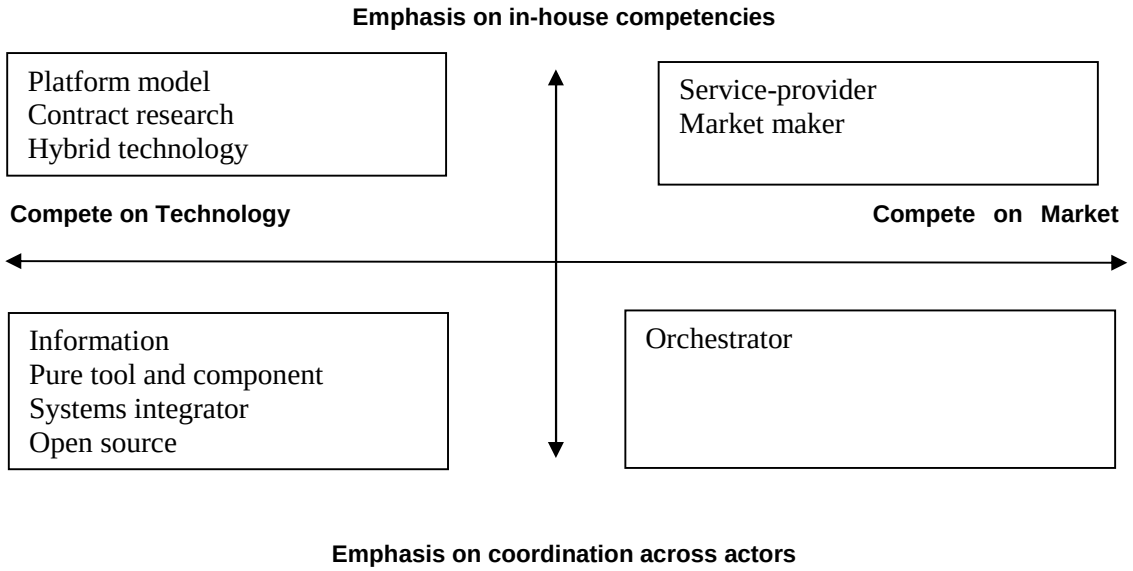
***Currently dominant models:***

- *Classical biotech model* – Firms in the classical biotech model rely on long-term, basic research, with only tenuous links to applications in goods and services ready for sale. This has so far enabled biotech firms to be specialised suppliers of knowledge and to obtain financing through stock, venture capital, R&D contracts, licensing and the like. Their business models rely heavily on positive externalities of knowledge and innovation in the sectoral system of innovation, specifically the extensive private investment into R&D, collaboration with the *public* sector, and network relationships with incumbent firms in related industries.

- *Vertically integrated model* – These firms remain oriented towards holding assets in house, and the common example is the pharmaceutical industry. Pharmaceutical firms are primarily concerned with the discovery process for pharmaceuticals; they then develop the necessary complementary assets to manufacture, produce and sell the pharmaceutical. Similar types of firms can be found as incumbents in other industries, such as medical devices and animal health care.

This report has identified a large number of emerging and speculative business models, as found in Section 4. Figure 4 places the ones identified, relative to each other. This is done along the two dimensions of ‘emphasis on in-house or emphasis on coordination across actors’ and of ‘compete on technology or compete on makets’.

**Figure 3 - Differentiating the Emerging Business Models**




**Source:** Author.

Figure 4 thus summarizes the main differences amongst the models, using these two dimensions. These different types of emerging and possible ones have been identified through the analysis found in Section 4 and through a review of existing literature.[7] The business models differ in terms of the three elements identified by Drucker (1994) – namely, what an organisation is paid for, what an organisation considers meaningful results, and where an organisation must excel in order to maintain leadership. The discussion first examines experimental models where the firms primarily compete on technology or on markets. Several speculative business models are also identified, and they are speculative in the sense that they do not appear to exist at the moment, but could be developed in the future.

***Experimental business models where the firms compete primarily on technology (and therefore depend upon public research):***

- *Platform model* – Platform technology firms develop specific technologies, usually ones to improve the R&D process in drug discovery. They are centred on incremental improvements and out-licensing their technologies, and thereby require internal knowledge competencies. Their products can add value to the R&D process of other firms, by decreasing costs, quickly sorting out drugs that may fail at later stages, organising large-scale information, and so forth.

- *Contract research model* – The contract research firm (sometimes called service firm) primarily sells research results of direct interest to clients. They are less focused on basic science than the classic biotech firm and do more "applied" research such as cloning and sequencing for other firms. They generally have trained personnel,

[7] A large number of possible business models were identified, and these ones selected. They are based on a number of sources, and several specific ones can be found in more detailed references. Formela (1998) identified the horizontal, nonexclusive model; the pure tool/component model; systems integration; and the fully integrated pharmaceutical company. Schweizer (2006) identified the integrated model; orchestrator model; layer player model; market maker model, all based on a conceptual discussion of the general literature on business models. There are two dimensions of his matrix: business logic (old game versus new game) and value chain (existing versus innovating). Willemstein, van der Valk and Meeus (2007) also provide an overview, as has Ernst and Young (2007) and Nosella, Petroni and Verbano (2005). Moreover, www.thebiotechclub.org provided inspiration for some of the models.

informal contacts with universities and specialised instruments, so that they can meet their targets relatively efficiently.

- *Information model* – Firms in the information model sell primarily systematised information and databases. These may contain genomics information with biobanks holding human genomics information and tissue samples for specific populations. They may also contain other types of information, such as validated biomarkers and the results from long-term clinical trials and monitoring of drug prescriptions. They use advanced mathematical competencies, to develop algorithms for optimisation and data-mining. Important issues for them include access to relevant biological information, reliability and confidentiality.

- *Hybrid technology model* – Hybrid technology firms are ones that sell combinations of technological platforms, services and goods. Relevant examples are diagnostics, including hardware, software, and training. The firms develop different scientific and engineering competencies, of which some are licensed to obtain short-term financing and others are developed internally for longer-term product development.[8]

- *Pure tool and component model* – Firms in the pure tool and component model also rely on technological competencies of the firm, but this time by defining a standard within a specific application. This model resembles the IT industry in terms of standard-setting providing advantages to certain firms. These firms need to be leaders within their "technological race" if they are to remain competitive; they succeed by combining internal competencies and external knowledge networks.

***Experimental business models where the firms compete primarily on market and customers (and therefore depend upon private and public health care providers and other firms):***

- *Service-provider model* – Firms following the service-provider model sell primarily services to health care providers, but the model could also develop services for individual patients. Examples can include provision of components of pharmacogenomics, specialised tissue engineering, and disease management. They have thus moved from specialised suppliers of knowledge to become specialised suppliers of services, usually sold to health care providers.

- *Market maker model* – Firms in the market maker model are less oriented towards technological competencies, and more towards market ones. They innovate by trying to introduce new business logic; in particular, they offer something that previously did not exist to a new market. An example within health biotech is to create a localised market for personalised and P4 medicine (which is not only personalised but also predictive, preventive and participatory**)**, by providing better but lower-cost health treatment to specific individuals who agree to include their biological material within larger databases. Hence, in this example a pharmaceutical firm can create new types of markets for P4 medicine by integrating health care service provision into the company, and can develop and offer lower cost drugs to certain patient groups in exchange for the rights to retain and analyse biological material. Implementing this business model would later require elements of many of the other models.

[8] Another model is very similar**.** *Horizontal non-exclusive model* – Firms in the horizontal, non-exclusive model use their specialised technological competencies to sell specialised technology. They thus provide unique technological solutions for customers. They use their unique technological competencies and understanding of the needs of clients to make revenue, especially by remaining dominant content provider and front-line specialists.

***Speculative business models:***

- *Systems integrator model* – Firms in the systems integrator model focus on using extensive internal resources and some network relationships for integrating components into a working whole. These firms place much more emphasis on integrating goods and services than previous business models. Their business logic would be similar to large engineering and manufacturing companies that use concepts such as modularity, supply chain management and complex product systems in order to integrate components within a complex, fragmented value chain. Many of the internal resources go towards managing interfaces and flows, including services. This type of business model could be developed within the pharmaceutical and medical device industries as it further develops some of the tendencies within the fully integrated pharmaceutical model, but also for health care providers.

- *Orchestrator model* – Firms in the orchestrator model are primarily oriented towards helping other firms develop the desired collaboration and co-ordination effects within specific production and knowledge networks. They hold few internal resources but instead help to orchestrate the whole system, especially in terms of alliances and information. The push towards a global value chain in health biotech, but with a parallel push towards innovative localised clusters, will increase the value of finding and maintaining specific types of partners in a network. Examples are finding a scientist to deliver specialised knowledge and a firm to do contract manufacturing. These firms also use outsourcing and collaboration, like the systems integrator model, but are more focused on adding value to other actors in the network.

- *Open source model* – Firms in the open innovation and open source software models would have to develop new ways of interacting with individuals, as active consumers and as "developers" and "problem-solvers" of puzzles in R&D. These more "open" standards usually demand that information previously considered as intellectual property rights is made publicly available, in exchange for a community potentially willing to test and propose solutions. Some firms will use explicit open source software models, where they can license proprietary tools such as database management systems for health care. Key problems will involve managing confidentiality issues, due to the use of biological information for individuals.

Hence, this above list identifies different categories of business models. This is primarily presented as a list of alternative ways of 'doing business', with an implicit assumption that a specific firm could fall into one category or another.

The models are grouped into categories. Two models are currently dominant, namely the classical biotechnology and the vertically integrated company. Many experimental business models are primarily focused upon exploited scientific and technological assets. This implies that those firms will be largely dependent upon internal R&D and competencies but also the external research, especially those resulting from public investment into R&D. A few experimental business models are primarily focused upon the market and consumers. They are therefore particularly influenced by public regulation and by health care providers. Likely, more business models which focus upon this are needed in the future. Finally, several speculative business models are also identified above, which have been extrapolated from trends in other industries and by rather vague indications that similar developments could happen here. They should be seen primarily as thought experiments – but one should also ask the deeper question of whether and how they need to be stimulated, to help meet the needs of industry and public policy issues for the future.

## 5.3 Future trends in business models

A final result of this report is to identify – and also speculate about – many different ways in which business may be conducted in the future. This is related to the second issue, namely what types of business models will emerge between the currently two dominant ones of classical biotechnology and vertically integrated firm.

To do so, we must consider the development of completely new business models and speculative ones but also to consider that the individual firm will likely change their business models, over time. The literature suggests that the individual health biotech firm changes its business model over time, and hence move between different types (Willemstein, van der Valk and Meeus, 2007; McKelvey and Brink, 2008 forthcoming). One reason for that is the complexity of ways in which how 'knowledge' can be turned into 'value' in these sectors. Health biotech can be commercialised through a variety of mechanisms, such as selling licenses, collaborating to access complementary assets, selling services, etc. To survive, the firm needs often to change foci. Recent literature suggests that health biotech firms must concentrate less on the classic biotech model, with its emphasis on biotech research *per se*, and more on creating value through integration, serving customers, and the like.

One set of expected changes comes from those emerging business models that will arise as new and existing firms make changes in the two currently dominant models. Changing those business models will in turn entail modifications of the relationships between different types of firms in the sectoral system of innovation.

*Classical biotech model* – The expectation is that this model will become less popular, in that a lower percentage of all health biotech firms will follow this model. Many existing firms following this model will have increasing difficulties with finding venture capital, which is becoming impatient with financing such long-term research without market returns. The best of those firms will be bought up by vertically integrated firms, because they represent specialized suppliers of new knowledge and ideas for future innovations. Some existing biotech firms may try to become more vertically integrated pharmaceutical firms, so that rather than licensing to the large incumbent pharmaceutical companies, the biotech firms would start selling products to final consumers (patients). However, the model is not dead! New firms following this model will also started, since scientific and technological advances make certain types of knowledge extremely valuable (for a period).

*Vertically integrated model* – The expectation is that these firms will continue to exist and have large market shares in their industries – but that they will become less vertically integrated in the future. In the pharmaceutical industry, these firms also face great difficulties, both with financing their R&D and with selling products and services. Here, we expect more out-licensing of R&D and innovation to biotech firms (as specialized suppliers of knowledge). We also expect more focus upon production, regulation and marketing as the core assets of the firm. Possibly, the pharmaceutical industry could become like the automobile one – with a clear concentration on production, with limited supplier networks, and with a combined internal-external competence for design and innovation. In other industries like medical devices and health care provision, these firms so far seem able to exploit economies of scale. We expect them to continue to interact with suppliers, users, and so forth for access to resources and ideas, but to remain essentially vertically integrated companies. These firms could also move into closely related business models, such as the integrated model, the product model, early drug developers, and late stage drug developers (see further below).

Another set of expected changes will come through pressures from the specific institutional and market context, developed in the future. Table 4 below summarizes how the analysis found in Section 4 translates into more opportunities for certain types of business models.

Hence, Table 4 indicates how the four specific institutional variables can help stimulate certain business models. On the whole, in the future we expect to see more firms specializing with specific activities in the long value chain, because of the new business opportunities. More firms can be more specialized, even to the point of primarily offering network contacts and structured information. Fewer will be offering final products to consumers (patients).

**Table 4 - Impact on Emergent Business Models**

| **Institutional variable driving change** | **For the dominant two business models, what would we expect?** | **For future, this would encourage which types of experimental business models?** |
|---|---|---|
| Scientific and technological advances | Core asset of classical biotech | New firms started on classical biotech model<br>Stimulate models dependent upon specialized technology (platform, contract research, tool and component)<br>Stimulate models based upon coordination across technologies and products |
| Public research and the public-private interface | Core biotech dependent upon public research<br>Important for vertically integrated company | Stimulate models depend upon relational assets, such as network and access to talent (information; horizontal) |
| Regulation and institutions | Core asset for vertically integrated company | Stimulate models which focus upon information coordination (orchestrator; outsourcing; open source)<br>Increase value of IPR<br>Increase returns to having global linkages, and a position in the global network |
| Demand and consumers | Core asset of vertically integrated company<br>Relatively low importance to classical biotech firm | Stimulates all models which focus more upon demand and consumers (market makers, Services)<br>Speculative models may better link users and demand (systems integrator, open source) |

**Source:** Author.

In the future, all the health biotech firms will rely on a complex range of scientific and technological advances, from biomarkers and proteomics to cell therapy, as well as advances in medical understanding. These health biotech firms will shift away from the classic biotech business models, towards the more diverse set of models identified in this report. In the short run (five years), the business model of specialised supplier of knowledge, providing unique competencies and relying on external capital and network structures, will continue to exist and likely dominate. New business ventures within the "hot" areas of technological advance will be started, and find capital. In the longer run (20 years), many of the twelve additional

business models identified in this report will be developed, for reasons related to pressures from institutional drivers, such as societal trends, public policy and demand.

In summary, these future models are of two main meta-types, which will combine elements of several of the business models outlined above. One meta-type is to become essentially a new, smaller, and more agile company, using internal knowledge resources to specialise in R&D but with a greater focus on specific research tools, services and products. These are modifications of the classical biotech model, but the firms must focus more on economic returns to R&D investment and on market expansion and creation. More 'market pull' is needed than the traditional 'technology push', and so we can expect the development of other forms of experimental business models focusing upon markets and consumers.

The other meta-type is to focus on integrating and co-ordinating large-scale networks and information across actors and technologies, because they can exploit the inefficiencies of networks and distributed information. To do so, they must explicitly combine and integrate their internal knowledge assets with external network assets, in order to develop applications that can address human health care problems. Some of these are modifications of the vertically integrated model, but the firms must focus more upon intangible assets. Others of these are small and medium sized firms which specialize in these types of coordination mechanisms for knowledge, innovation, production, and marketing.

# 6. Implications for public policy

This report *Health Biotechnology: Emerging Business Models and Institutional Drivers* has addressed the future of firms and industry. In particular, the report focuses upon how and why firms involved in health biotechnology will evolve in the future. These firms will be diverse, ranging from the pharmaceutical firms and health service providers to specialised firms in biotechnology, bioengineering, biomedicine, and other intersections of biology, genomics and human health. Existing innovation policy goals associated with science and R&D should remain in place, along with a commitment to innovation-driven economic growth. Existing health policy goals will vary much more across different countries, but all health care provision systems must find compromises to balance immediate service delivery with long-term development of medical knowledge. This section draws upon previous sections of this report to discuss implications for public policy, starting from a broad perspective.

The first implication is that public policy must take decisive steps to act, to create the future. Practically, this involves modifying internal processes but also mobilizing public agencies so that more stakeholders are engaged in the debate. The reason is the answer to the first question which comes to mind is – are public policy initiatives needed at all, or can we leave everything to the firms? This question is important to pose, given the focus here upon firms .Moreover, public policy should stimulate, and deliver, different types of activities and societal results than private firms. In this case, public policy initiatives are clearly needed, both because they have been influential on firms in the past and because they can help form the institutional and market context within which firms operate. Clearly personalised medicine (P4 medicine) requires transformation within a broad range of actors, knowledge, institutions, networks, etc. Public policy can therefore help set the context for a radical shift in human health care, as specified in Section 4, and in such a way as to stimulate firms.

The second implication is that public policy needs to be concerned with the competencies and learning processes of public and private organizations, within their remit. This has to do with the efficient use of existing resources. Organizations which have, for example, worse routines for managing patients will have difficulties delivering high quality service at a reasonable price. Many of the public policy initiatives discussed in this report have to do with either

R&D and innovation, or regulation, or demand. Within public health, these are all areas which usually required detailed knowledge about technology ,markets and institutions, in order to do a good job. Many of these areas involve services. People are of crucial importance to delivering high quality services at the boundary of user-producer organizations. Hence, taking decisive steps to create the future requires great attention to developing and raising the competencies and learning processes, especially across organizations.

A related implication is that public policy should stimulate new knowledge about technology, medicine and markets and also stimulate experimentation with business models. Practically, this includes initiatives to stimulate private and public investment into R&D as well as new ways of appropriating the returns to R&D and of procuring goods and services for the public providers of health.

The emphasis upon experimentation runs counter to another common approach to public policy, namely deciding to prioritize one activity rather than another. Looking into the future of human health care, it is easy to see that huge transformations are possible. This also means that many uncertainties exist about, for example, how service providers will be organized, whether the fantastic ideas are translated into medical practise and new goods and services, which types of business models will prove sustainable and competitive, and so forth. Given this situation, the policy-maker should focus more about stimulating R&D, innovation and new knowledge and experimentation with business models. Over time, less viable options will be weeded out and more interesting options will become more common. Public policy will of course be involved in selection – such as through comparing and choosing amongst alternative treatments – but experimentation is also vital so that good ideas about the longer-term radical and incremental shifts in health care provision are tested and selected.

It is equally clear that different regions and countries are likely to follow somewhat different trajectories, and so varying outcomes are possible. The choice between new ways of addressing the public-policy interface will likely depend on many historical political and economic compromises. One country and its political-economic system may become (or remain) conservative, and focused on existing treatments. Another system may promote innovation, and develop forward-looking, exploratory regulation in consultation with firms and stakeholders.. Therefore, the main issue is not which trajectory and compromise; rather, the main issue is that public policy identifies and addresses new challenges and thereby allows experimentation with business models and sectoral system of innovation.

A fourth implication relates to developing the private-public interface. The complexity of the innovation system in health biotech already suggests that public policy has already started to adopt new ways to address the public-private interface, such as commercialization of academic research. The bioeconomy of the future will continue to rely on a mixture of public and private organizations in order to apply the advances of biotechnology to solve human health care issues. It is expected that the current core public and private actors will remain essential, because they have heterogeneous competencies and ways of organising the development and diffusion of knowledge. The interface between investments into private R&D and public R&D must be further analyzed, to design better future public policy. This matters for society, in order to stimulate growth and industrial competitiveness and in order to apply the advances of biotechnology to solve human health care issues.

A major issue is how health care provision will develop, including the variety of public and private interlinkages and co-ordination mechanisms. Different forms of health care provision will be used within different regions and countries, and this will affect whether, and how quickly, society will be able to apply the advances of biotechnology to solve human health care issues. Practically, this implies the need to understand the strengths and weaknesses of a specific health care system, in order to determine where new businesses can be started.

In finishing, these public policy implications will have need research. Especially, new ways of thinking about public policy must be developed, at the public-private interface, in order to stimulate emerging business models and institutional drivers in health biotech. Public policy must address aspects related to innovation, especially co-ordinating network mechanisms, stimulating R&D activities to solve sequences of problems, negotiating long-term goals, and developing responsive institutional and regulatory frameworks. New thinking is also needed about how to share costs and benefits, about why firms rely on public initiatives for resources and incentives, and how to engage individuals and stakeholders in the development process.

So, public policy has already had to face the challenge of working within these decentralised, distributed systems – with unclear public-private boundaries. Additional research on business models is also advisable. For example, one way to stimulate new public policy thinking is to further develop concepts and management tools similar to those used by firms when managing value chains, alliances and supply networks. A second way to reconsider public policy is to identify expected changes to the variables that previously drove innovation in health biotech. For example, collaboration with the public sector will become more difficult, and allow fewer externalities from which biotech firms have benefited in the past. Will only some regions then succeed in attracting those firms, or will firms turn to an open model? Yet another way is to apply concepts of modularity, components, and systems thinking to facilitate better medical research and practice. Public policy, firms and many other actors in the innovation system will need to integrate and combine not only scientific, medical and technological competencies, but also co-ordination mechanisms and network linkages between organisations and individuals.

The overall recommendation is clearly that a main role for public policy to reach the Bioeconomy of the future is to stimulate product, process and organizational innovations. Innovations within health biotech usually take place across boundaries of user-producers and of public-private actors. Private firms play a role, but so do public health providers. Because the institutional and market context is expected to have dramatically changed within thirty years, implications for public policy can be discussed by analyzing and finding new ways to stimulate firms within this institutional and market context.

Still, the reason that this report has placed the emerging business models in relation to four institutional drivers of change is that these firms will play major roles in future scenarios about the Bioeconomy. The firms will be highly influenced by their context, including institutional drivers, or what we can call the broader sectoral system of innovation. The reason comes back to the core of our analysis, namely the “economic model” or “business model”. Many practitioners use the concept, as does the literature, to analyse how firms do business. These models specify the firm’s core competencies and how they are turned into offerings for customers, so that the firms can generate sales and possibly profits. Hence, firms must be placed in relation to both internal assets and the external context.

Public policy can help stimulate innovation to meet the future health needs by stimulating development across boundaries. Examples include co-ordinating network mechanisms; stimulating R&D activities to solve sequences of problems; negotiating long-term goals; and developing responsive institutional and regulatory frameworks. While these types of recommendations may sound diffuse, they can be translated into specific actions, to help improve public policy to reach the longer-term objectives. To take the first example of public policy co-ordinating network mechanisms, assume that the objective is treatment around a major disease category, like diabetes or avian flu. Co-ordinating network mechanisms would thereby imply that public policy-makers assemble stakeholders, in order to ensure that researchers, users, patient groups and those producing goods and delivering services exchange relevant information about emergent problems, new solutions, and ways of combining goods and services to best address the underlying medical-social-economic problems. Indeed, many research and innovation policies have moved in this direction of stressing public-private

partnerships and network effects during the past decade. Still, health biotech poses particular challenges in terms of defining stakeholders, whom is involved in innovation, and how to stimulate the greatest returns to combined public and private efforts to transform human health.

In identifying the main actors it becomes clear that biotech firms develop within a fairly unique organisational framework. Health biotech differs from many mature sectors in the amount of private and public investments into R&D and the dependency on innovation resulting from long-term, uncertain R&D investments. In particular, the diversity of actors, organisational set-ups and levels of complexity quickly become evident. The firms are of many different types, running from very small (<10 persons) start-up firms to very large (>100 000 person) incumbent firms. The networks and co-ordination mechanisms for research and health care provision often include different types of public, private and public-private organisations. Regional and national variations in these variables have been observed as well. Firms thus face the complexity of needing to position themselves within the global health biotech system of innovation.

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