



From Test Tube to Patient:



National Innovation Strategies for the Biomedical Field

By Rachel Chu and Dr Meir Pugatch

 STOCKHOLM NETWORK

From Test Tube to Patient – National Innovation Strategies for the Biomedical Field

By Rachel Chu, Researcher, Stockholm Network and Dr Meir Pugatch, Director of Research, Stockholm Network

© Stockholm Network 2010. The views expressed in this publication are those of the authors and do not necessarily represent the corporate view of the Stockholm Network or those of its member think tanks.

Executive Summary

Biomedical innovation, including advances in biopharmaceuticals, medical devices and diagnostics, is at the heart of human society, not least because this type of innovation helps to save lives and to improve the quality of life. Furthermore, it is one of the major drivers of the modern market economy.

Nevertheless, while the importance of biomedical innovation continues to increase, in recent years it has become a much riskier, more complex and more costly endeavour.

Consequently, policymakers and stakeholders have an intensified interest in understanding and identifying the desired set of national policy tools needed to encourage biomedical innovation.

Accordingly, this paper sets the stage for discussing national innovation strategies in the biomedical field, with the aim of providing an overview of some of the best practices which support and enhance innovative activities in a given country.

The paper first outlines several theoretical elements concerning the issue of national innovation strategies. It points out that the formation of innovation strategies depends on understanding the need for a range of different tools to support biomedical innovation. Crucially, it also depends on the national context, meaning the set of strengths and weaknesses in the country vis-à-vis the factors of innovation in the biomedical field. The national context includes how the country or region performs in such factors as generating basic and translational research, in protecting intellectual property rights (IPRs) and in providing regulatory and market incentives for biomedical innovation. The national context also involves political and institutional dynamics, as well as societal and economic factors.

The paper argues that despite distinct national environments for innovation, in general, policymakers can benefit from understanding how other countries have sought to establish certain key components of biomedical innovation. With this in mind, the paper identifies and analyses five categories of key components of biomedical innovation: human capital and infrastructure, R&D, IP protection, the regulatory and clinical environment and market incentives for R&D. Embedded in this section are discussions of supportive measures taken by a range of countries and regions including Singapore, Scotland, Ireland, Israel, Québec, Germany, France, Sweden, the UK and the US.

The paper identifies several best practices and recommendations for countries seeking to increase biomedical innovation:

- (1) Build up a high-quality life science research infrastructure, including a focus on specific biomedical disciplines, in terms of personnel, technologies and facilities.

- (2) Encourage an active and comprehensive biomedical R&D environment by promoting a range of R&D activities, including basic, applied and translational R&D. This involves allocating a portion of R&D expenditure for basic research in the form of flexible and longer-term funding schemes, mostly aimed at universities and other research centres, and facilitating an environment that is conducive to technology transfer, collaboration and the flow of knowledge between scientists, clinicians and industry players, especially through biomedical clusters.
- (3) Offer IP protection which is relevant to the biomedical sector, including patents and other forms of IP such as data exclusivity and orphan drug protection.
- (4) Provide a positive regulatory and clinical environment by minimising administrative constraints associated with regulatory procedures and harmonising clinical requirements according to the ICH's standards of Good Clinical Practice and Good Manufacturing Practice.
- (5) Promote positive incentives for investment in R&D by:
 - (a) Limiting the use of pricing and reimbursement systems that disturb market signals;
 - (b) Supplementing public health expenditure with private expenditure; and
 - (c) Building up and strengthening a venture capital market for biomedical R&D.

This set of best practices should provide policymakers with a starting point for creating targeted and effective strategies to enhance biomedical innovation in their country or region, and for sharing their experiences.

Contents

1. Introduction	6
2. Key concepts relating to national innovation strategies	7
2.1 Defining national innovation strategies	7
2.2 The development of national innovation strategies	9
2.2.1 <i>The importance of innovation and the need for innovation strategy and policy</i>	9
2.2.2 <i>The national innovation context</i>	10
3. Key components for national innovation strategies in the biomedical field	12
3.1 Introduction to the biomedical field	12
3.2 Identifying key components	13
3.2.1 <i>Human capital and infrastructure</i>	13
<i>Human capital</i>	14
<i>Infrastructure</i>	15
3.2.2 <i>R&D</i>	16
<i>Basic R&D</i>	16
<i>Applied and translational R&D</i>	17
<u><i>Collaborative efforts</i></u>	18
<u><i>Technology transfer offices</i></u>	19
<i>Promoting translational R&D efforts</i>	20
<u><i>Macro Level</i></u>	21
<u><i>Micro Level</i></u>	22
3.2.3 <i>Intellectual Property protection</i>	25
3.2.4 <i>Regulatory and Clinical Environment</i>	27
<i>Legal and commercial procedures</i>	27
<i>Clinical procedures, standards and conditions</i>	27
3.2.5 <i>Market incentives for R&D</i>	28
<i>Pricing and reimbursement policies</i>	29
<i>Investment climate</i>	30
4. Concluding remarks and policy recommendations	32

I. Introduction

Biomedical innovation is at the heart of human society, not least because this type of innovation helps to save lives as well as to improve the quality of life. Biomedical innovation is one of the major drivers of the modern market economy, with pharmaceutical and biotechnology sectors being at the forefront of this activity. For example, according to 2007 EU figures, R&D investment rose exponentially in the knowledge-based industries, notably in the pharmaceutical sector where a 15.7% boost in investment elevated the industry to the top investor worldwide.¹

Nevertheless, while the importance of biomedical innovation continues to increase, in recent years it has become a much riskier, more complex and more costly endeavour. In particular, the cost, time and skills required to test the clinical safety and efficacy of biomedical products has skyrocketed as medicines and processes become more and more targeted to patient groups and even to individual patients. With only a small percentage of the products that undergo clinical testing ever entering the market, biomedical innovation involves an increasingly greater risk for investors.

Consequently, there is an intensifying interest among different countries in identifying the desired set of national policy tools needed to encourage biomedical innovation. This involves identifying the full range of frameworks, institutions and conditions that facilitate and promote innovation in general and in the biomedical field in particular, and also identifying the policies that support these factors. Of special interest at the moment is developing a positive environment for improving the translation of knowledge into a greater number of life-saving products benefitting the right patient groups, including through the creation of tools that refine and speed up the clinical trial process.

The issue of the best policy set for encouraging biomedical innovation is currently being debated and discussed in different forums. Yet, it would still seem that many stakeholders, including policymakers, lack sufficient knowledge (and at times even require a basic understanding) of the scientific, economic and legal fundamentals required to create positive national innovation strategies in the biomedical field.

Accordingly, this paper sets the stage for discussing national innovation strategies in the biomedical field, with the aim of providing an overview of some of the best practices which support and enhance innovative activities in a given country. The paper analyses several key components in both upstream and downstream processes: physical and human infrastructure; the R&D process, including basic, applied and translational R&D; protection of biomedical IPRs; the regulatory and clinical environment; and the market incentives for R&D, including the impact of pricing and reimbursement systems and the investment climate. The paper also takes several countries as case studies, discussing the ways in which the countries have sought to stimulate these components, ultimately crystallising from them a set of best practices.

¹ European Commission, Joint Research Centre, DG Research, *Monitoring Industrial Research: The 2007 EU Industrial Investment Scoreboard*, Office for Official publications of the European Union: Luxembourg, 2007, p. 15.

This paper takes the following structure. First, it outlines several theoretical elements concerning the issue of national innovation strategies, including the definition, basis and formation of innovation strategies. Second, it analyses five categories of key components of biomedical innovation: human capital and infrastructure, R&D, IP protection, the regulatory and clinical environment and market incentives for R&D. Embedded in this section are discussions of supportive measures taken by a range of countries and regions, including Singapore, Scotland, Ireland, Israel, Québec, Germany, France, Sweden, the UK and the US. Finally, the paper proposes a set of best practices countries should aim for in order to sufficiently support and promote biomedical innovation.

2. Key concepts relating to national innovation strategies

2.1 Defining national innovation strategies

For the purposes of this paper, a national innovation strategy or system refers to the measures that states or regions take in seeking to promote innovation in a particular sector. The nature of innovation itself is very broad, for example see the discussion on social and economic innovation in a previous Stockholm Network paper, *If it Ain't Broke, Don't Fix it*.² In this paper, however, we are focusing on technological or technical advances which are aimed at providing the market with new and improved products. Accordingly, we can use the definition given by the OECD Frascati Manual, which defines technological innovation as “the scientific, technological, organisational, financial and commercial steps, including investments in new knowledge, which actually or are intended to, lead to the implementation of technologically new or improved products or processes”.³

Innovation is a complex concept that entails different expressions. Most commonly, a distinction is made between “radical innovation”, or innovation based on completely new knowledge with outcomes that involve large technological advancements and often render existing products obsolete,⁴ and “incremental innovation”, or the improvement of already existing knowledge that is translated into improved products.⁵ Henderson and Clark add to these the idea of modular and architectural innovation, which distinguish between improvements to the different components of a product and improvements to the linkages between these components.⁶ Abernathy and Utterback link different models of innovation with the dynamic nature of the innovation process.⁷ In particular, they view the innovation “life cycle” as being characterised by a shift in focus from

² Pugatch, M. *If it Ain't Broke, Don't Fix it*, Stockholm Network, 2008, <http://www.stockholm-network.org/downloads/publications/Innovation.pdf> (Accessed 25 November 2009).

³ OECD, Proposed Standard Practice for Surveys of Research and Experimental Development, Frascati Manual (Paris: 2002), p.18

⁴ Abernathy, W. & Clark, K. “Mapping the Winds of Creative Destruction”, *Research Policy*, 1985, Vol. 14, pp. 3-22.

⁵ Kauffman S. *At Home in the Universe*, Oxford University Press: New York, 1995.

⁶ Henderson R. & Clark, K. “Architectural Innovation: The Reconfiguration of Existing Product Technologies and the Failure of Established Firms”, *Administrative Science Quarterly*, 1990, Vol. 35, pp. 9-30.

⁷ Abernathy, W. & Utterback, J. “Patterns of Innovation in Technology”, *Technology Review*, 1978, Vol. 80:7, pp. 40-47; See also

“product” innovation to “process” innovation (in terms of factors like production costs, volumes and market capacity), as market demand for the product increases and greater emphasis is placed on refining the design and finding the right production strategy.

Furthermore, innovation is influenced by various factors, including not only scientific and technological factors, but also societal and economic ones. For instance, Drucker identifies several external factors that affect innovation, such as the unexpected outside event, demographic change and the perceptions of societies about their own economic, political and social conditions.⁸ In addition, Rogers points to several cultural factors influencing the “diffusion” of innovation, such as the channels of communication, the relative time and rate of adoption and the social system through which innovation is adopted.⁹ At the same time, Utterback finds that new scientific or technological advances and opportunities also play a major role in innovation.¹⁰ Innovators are driven to look to all of these factors to gauge market demand for new products and to respond to the shifting needs and desires of the consumer that technological progress can bring about.

Across sectors, the process of innovation requires the existence of certain similar factors, such as active R&D efforts, funding and intellectual property rights (IPRs). However, other factors and stimuli will be different for each sector. This paper focuses on the life sciences sector, but for the moment also consider the fields of IT and green technology. It is the explosion of technologies in various fields (i.e. biomass, biofuels, solar, wind) that has caused the market for green technology to accelerate in the last several years. The need for standardisation and convergence of different platforms is the main stimulating factor for the rapid advances taking place in the software field. And, the complex and ongoing evolution of medicines and treatments toward personalised therapies continues to drive progress in the biomedical field.

It is important to note that among the various factors of innovation (in any sector), some factors are not explicitly manageable by policy, i.e. a social phenomenon, like the uptake of a cutting-edge technology, or external events, like the current financial and economic crisis. In contrast, other factors are able to be influenced by public and private policies or strategies. Such factors tend to be those that enhance technological advances and help shape the economic environment, including the base of scientists and engineers, the business environment and the level of IPR protection. Innovation strategies seek to enhance these types of factors in order to create an environment that incentivises and drives innovation.

It can also be noted that, in practice, national innovation strategies are not free-handed nor are they all identical. Rather, a national innovation strategy for a particular sector often must be tailored to fit within the country or region’s broader set of policies. For example, a policy that lowers taxes for SMEs may conflict with broader policies to manage the budget deficit. Or, public funding for R&D in one sector may not be available because of a commitment to target public spending towards another sector. Hence, national innovation

Utterback, J. “Mastering the Dynamics of Innovation,” *Harvard Business School Press*, 1994.

⁸ Drucker, P. *Innovation and Entrepreneurship*, Harper Business: New York, 1985, pp.52-53.

⁹ Rogers, E. *Diffusion of Innovations*, The Free Press: New York, 3rd edition, 1983, p. 5.

¹⁰ Utterback, M. “Innovation in Industry and the Diffusion of Technology”, *Science*, New Series, Vol. 183, No. 4125, 1974, pp. 620-626.

strategies reflect the particular political and economic context of the country or region. This will be discussed further in the next section.

2.2 The development of national innovation strategies

With this understanding of innovation in mind, we point out three concepts that broadly guide the development of a national innovation strategy in a given country.

2.2.1 *The importance of innovation and the need for innovation strategy and policy*

First, a national innovation strategy is founded on (what is understood to be) the importance of innovation, in general and in a particular field, to the country or region. At the most basic level, economic literature indicates a link between innovation and economic growth. (And, for the purpose of this paper, we can assume that economic growth translates into higher incomes and a better quality of life.) Both the Schumpeterian theory of “creative destruction” and newer theories on growth, particularly endogenous growth theory,¹¹ give innovation a central role in economic growth. The Schumpeterian perspective suggests that the constant process of replacing old ideas, goods, methods, etc. with new ones is the engine of economic progress.¹² In addition, in his famous parallel of the kitchen and the economy, Paul Romer, a key thinker in endogenous growth theory, argues that, “Human history teaches us ... that economic growth springs from better recipes, not just from more cooking”.¹³ Romer goes on to identify technological change as a key input of “better recipes”.

In addition to economic growth, technological innovation is necessary for facing many contemporary global challenges.¹⁴ For instance, new environmental and health-related technologies play a vital part in tackling climate change, ageing populations and diseases confronted by developing countries. Understanding the positive impact of innovation in a field to the country or region drives policymakers to encourage it.

It follows that policymakers also understand in what way economies can influence key factors of innovation. While we take the view that incentivising technological innovation is most successful via market-driven efforts, we nonetheless recognise the importance of policies and mechanisms supporting these efforts. Porter and Stern (2001) demonstrate that the national policy framework matters for success in innovative activity.¹⁵ For instance, policies can strongly influence the standards of the university system (such as via quality assurance assessments) or the level of venture capital invested in start-up companies (such as via robust IPR protection and an attractive tax environment for investment).

¹¹ Aghion, P and Howitt, P, *Endogenous Growth Theory* (MIT Press, 1998)

¹² Schumpeter, J, *Capitalism, Socialism, and Democracy* (Harper and Brothers, 1942), p.83

¹³ Romer, P, “Economic Growth”, *The Concise Encyclopedia of Economics*, 2nd edition, <http://www.econlib.org/library/Enc/EconomicGrowth.html>

¹⁴ “Making innovation strategy succeed in a globalised world”, Introductory remarks by Angel Gurría, OECD Secretary-General, delivered at the International Economic Forum of the Americas (Montreal, Canada, 8 June 2009) http://www.oecd.org/document/19/0,3343,en_2649_37417_42982163_1_1_1_1.00.html (Accessed 14 July 2009)

¹⁵ Porter, M and Stern, S, “National Innovative Capacity”, *The Global Competitiveness Report 2001-2002* (New York: Oxford University Press, 2001), p. 5 http://www.isc.hbs.edu/Innov_9211.pdf (Accessed 13 July 2009)

However, policymakers should be wary of policies that seek to dictate or anticipate the direction or form of innovation via a top-down process. After all, empirical evidence indicates that voluntary, market-driven forces have been and remain the strongest and most robust source of innovation.¹⁶

2.2.2 *The national innovation context*

The second concept that shapes a national innovation strategy is the national context for innovation in a particular field, meaning the set of strengths and weaknesses in the country vis-à-vis the factors of innovation in that field. Identifying the strengths and weaknesses in a given country depends on what are understood to be the scientific, economic, political and institutional factors influencing innovation in that field.

Most of the recent literature on national innovation strategies has moved beyond the traditional practice of focusing on narrow inputs, such as investment in R&D or the number of research personnel, as key factors of innovation.¹⁷ Instead, a broad range of factors (including various actors, institutions, etc) are considered, not only independently, but particularly in their linkages or interconnectedness.

For instance, the OECD emphasises that the various factors in the innovation process do not act in isolation, but through non-linear “flows of knowledge” between various actors and institutions.¹⁸ In general, these knowledge flows occur through 1) interactions among enterprises; 2) interactions among enterprises, universities and public research laboratories; 3) diffusion of knowledge and technology to firms (for instance, from customers, suppliers, competitors and public institutions); and 4) mobility of personnel (and the knowledge they carry with them), particularly between public and private sectors.¹⁹

Porter and Stern (2001)²⁰ simplify these knowledge flows, focusing on the reciprocal relationship between a nation or region’s common innovation infrastructure and its industrial clusters. The common innovation infrastructure refers to the set of cross-cutting investments and policies that set the basic conditions for innovation throughout an entire economy. This includes its pool of scientists and engineers, excellence in basic research, protection of intellectual property, tax-based incentives, anti-trust enforcement that encourages innovation-based competition and openness of the economy. The common innovation infrastructure supports the development of industrial clusters, or “geographic concentrations of interconnected companies and institutions in a particular field”.²¹ These are constituted of a supply of high-quality human resources, information infrastructure and risk capital; rivalry among local firms; sophisticated local demand; and the local presence of related and supporting industries. In turn, the cluster drives the common infrastructure. The key

¹⁶ To illustrate, US universities, which operate in a more decentralised and flexible research environment, seem to more successfully commercialise new knowledge than universities in Europe and Asia (i.e. Japan), which often have “centralised financing systems that lead to greater hierarchical control”. See Kowden, K and Yeo, B, “The Value of US Life Sciences: A White Paper Exploring Competitiveness, Delivery and Challenges”, Milken Institute, 2009, p.17, <http://www.milkeninstitute.org/pdf/USChamberLifeSciencesApril2009.pdf> (Accessed 24 September 2009).

¹⁷ “National Innovation Systems”, OECD (1997), p.9 <http://www.oecd.org/dataoecd/35/56/2101733.pdf> (Accessed 13 July 2009)

¹⁸ “National Innovation Systems”, pp. 11-12

¹⁹ Ibid, pp. 12, 18

²⁰ Porter and Stern, p.5

²¹ Ibid, p.6

to this mutual relationship is a variety of formal and informal institutions that bridge the two elements, such as the university system.

Models like these provide a sophisticated framework for the process of innovation and the role of key factors. It is important to add political and institutional dynamics to the framework, as these can often explain weaknesses or strengths in key factors of innovation.

Policymakers may be limited in what they are actually willing or able to undertake to address elements of innovation. For instance, they may be affected by societal demand for innovation in the field, the availability of finance to support the policies, the political capital of the government allowing it to create policies involving structural adjustments and the attitude of the government towards sourcing its own innovation (as opposed to importing it²²).

Even if the political context is favourable to innovation policies, the way in which they are implemented via various institutions and spheres can lead to inefficiencies and conflicts of interest that impede the success of the policies in boosting factors of innovation. Therefore, the political and economic environment, as well as the degree of coordination and rationalisation by various actors and innovation policies, are also included in the innovation framework.

Based on a broad framework like the one described in this section, the national innovation context can be evaluated. From this, strategies can be targeted to support, as much as possible, the factors that are strong and facilitate changes to the factors that are weak.

In doing so, national innovation strategies may consist of both generic policies (those that generally address factors of innovation) and specific policies (those that address components specific to innovation in the targeted field). For instance, in some countries, enhancing the entire science base is necessary, while in others general scientific human resources are sound, but particular disciplines (i.e. molecular biology, genetics) need improvement. On the one hand, policymakers want to address the specific features and needs of the field under consideration (with the exception of certain framework conditions, like IPRs and regulatory conditions). On the other hand, if general factors are weak, specific measures may not be successful. Therefore, it is important to evaluate the ideal scope of innovation policies and tailor them to be generic or specific, based on the condition and characteristics of the national innovation system in general and in the particular field.

In summary, a national innovation strategy is shaped by various elements, including how important innovation is understood to be, the strengths and weaknesses in the country with regards to innovation in a particular field, and the general political, economic and societal environment. These elements often limit a national innovation strategy as well as guide the direction of the strategy for the particular country.

²² Singh, L, "Globalization, national innovation systems and response of public policy", Munich Personal RePec Archive Paper No. 641 (November 2006) p12, http://mpira.ub.uni-muenchen.de/641/1/MPRA_paper_641.pdf (Accessed 14 July 2009)

However, notwithstanding the aspects of a strategy that are country-specific, it is possible to identify several broad components or best practices that need to be in place as part of a national innovation strategy. As we mentioned before, these components differ depending on the sector targeted by the strategy; in this paper, we are focusing on the biomedical field.

3. Key components for national innovation strategies in the biomedical field

3.1 Introduction to the biomedical field

The biomedical field is a huge and rapidly growing field involving a wide range of revolutionary health technologies, including pharmaceuticals, medical devices and diagnostics, which identify, treat and prevent illness. Among the many advances over the last few decades are highly-selective therapies with fewer side effects and quicker and more accurate diagnostic tests, as well as devices that aid in the biomedical R&D and manufacturing process itself.

Nevertheless, innovation in the biomedical field is unique compared to innovation in other sectors in that it is very complex, principally because of the time and resources required and the rate of success of R&D efforts. This is particularly so for innovation using biotechnology, such as biopharmaceuticals and bio-diagnostics. For example, the cost of developing medical devices, such as implants, seems to be much lower than the cost of developing biopharmaceuticals (which will be discussed below). Therefore, because biotech inventions are the most complex and novel at this time, this paper will focus on biological products, with a special concentration on biopharmaceuticals when it comes to issues like intellectual property protection and pricing and reimbursement policies. Policies particular to medical devices and diagnostics with regards to these issues will not be covered here.

The R&D process for biotech products has become very complicated and lengthy. This is first due to the process of testing new products in patients via clinical trials. Between 1999 and 2005 the number of procedures per trial increased from 96 to 158 and the length of a trial rose from 460 to 780 days.²³ It is also increasingly difficult to recruit and retain volunteers. Second, the number and range of players involved in the R&D pipeline is extensive. For instance, a research institution or biotech start-up may out-license its new knowledge to a larger biotech or pharmaceutical firm, which will develop and commercialise the product, perhaps contracting part of the clinical research to local pharmaceutical or clinical research companies. Furthermore, to mass produce new products at high quality, meeting strict health regulations, requires a significant investment. In all, the whole biomedical R&D process requires enormous skill and for

²³ Tufts Center for the Study of Drug Development, "Growing Protocol Design Complexity Stresses Investigators, Volunteers," Impact Report 10, no. 1 (January/February 2008).

biopharmaceuticals, is estimated to take 10 to 15 years.²⁴ Moreover, the total cost to develop one new biological drug has jumped from \$800 million in 2000 to \$1.3 billion in 2005.

On top of this, biomedical innovation involves a huge amount of risk, with a low rate of commercial success for most products that make it to the market. For instance, in the biopharmaceutical sector, it is estimated that of the 5,000 and 10,000 molecules that are identified during the drug discovery process,²⁵ only five of those enter clinical testing, and of these five compounds, only one will eventually be approved for marketing.²⁶ Yet, it is calculated that on average, \$615 million of the investment in a new compound takes place before clinical testing begins.²⁷ And, of those products that are successfully approved and enter the market, just two in 10 ever produce revenues that match or exceed average R&D costs.²⁸ This reflects factors like competing drugs entering the market around the same time and safety risks or side effects that become apparent once the product is in the market.

3.2 Identifying key components

With the particular challenges associated with the biomedical field in mind, several key components can be identified that are considered essential in order to successfully promote biomedical innovation in a given country.

There are many ways of dividing different components of biomedical innovation in the literature. In this paper we look at the following five categories – human capital and infrastructure, R&D, IP protection, the regulatory and clinical environment, and market incentives for R&D. These categories try to highlight the components we understand to be most relevant currently and to capture both the downstream and upstream aspects of innovation. In other words, they look at factors which not only directly enable innovation to take place, but also indirectly affect it.

3.2.1 *Human capital and infrastructure*

The biomedical innovation system is driven by several science and technology push factors,²⁹ including a steady source of cutting edge advances in the life sciences, bioengineering and bioinformatics. This, in turn, depends on a sustained supply of infrastructure – highly qualified personnel, technologies and facilities – in research forums.

²⁴ PhRMA, "Pharmaceutical Industry Profile 2009", 2009, Inside cover.
<http://www.phrma.org/files/PhRMA%202009%20Profile%20FINAL.pdf> (Accessed 12 June 2009).

²⁵ PhRMA, "Pharmaceutical Industry Profile 2009", Inside cover.

²⁶ Tufts Center for the Study of Drug Development, "New Drugs Entering Clinical Testing in Top 10 Firms Jumped 52% in 2003-2005," Impact Report 8, no. 3 (May/June 2006).

²⁷ Tufts Center for the Study of Drug Development, "Cost to Develop New Biotech Products is Estimated to Average \$1.2 Billion," Impact Report 8, no. 6 (November/December 2006).

²⁸ J. Vernon, J. Golec, and J. A. DiMasi, "Drug Development Costs When Financial Risk Is Measured Using the Fama-French Three Factor Model," unpublished working paper, January 2008.

²⁹ OECD, *Innovation in Pharmaceutical Biotechnology: Comparing National Innovation Systems at the Sectoral Level*, Paris: OECD, 2006, p.171.

Human capital

The human capital component mainly refers to the ability of academic institutions, national laboratories, biomedical research centres, hospitals, etc. to train high-quality scientists, engineers and technicians.

This begins with addressing the quality of the entire life science research system. It should cover both a range of disciplines, including natural sciences, engineering and technical studies, and education levels (i.e. from primary education to master and doctoral levels). Public investment in life science research, especially during basic research and very early stages of applied research, is also found to be an important aspect of the ability to bridge the gap between more academic types of research and the translation of this research into concrete products and technologies in the market.³⁰ In addition, attractive career opportunities and terms of employment in research facilities help to build up the system.

The US has helped support its life science research base via grants from the National Institutes of Health to universities and independent labs since 1946.³¹ California and Massachusetts, which both have vibrant biomedical sectors, are the top recipients of NIH funding. For instance, in 2007 researchers in California received 7,357 grants worth \$3.2 billion.³² Israel, which is ranked first in the world for total public expenditure on education as a percentage of GDP,³³ spends around 40% (or \$400 million) on life sciences and 50% (or \$200 million) of that is allocated to R&D. Part of this spending is made possible through attaching a royalty-bearing scheme to research grants, in which grants are repaid in the form of royalties on sales of the resulting products.³⁴ Sweden has doubled its spending on basic research for the period 2009-2012; it is allocating SEK 5 billion (\$726 million) over four years, around 1% of GDP.³⁵ France's National Research Agency is allocating a higher level, 50%, of its budget in 2010 to basic research, up from 27% in 2007.³⁶

It is also important that the scope of research covers scientific disciplines relevant to biotechnology research, such as stem cell biology, genomics and proteomics, genetic engineering, clinical pharmacology, biomedical imaging and bioinformatics. These disciplines are crucial for discovering and evaluating future biomedical advances, which should become more and more selective and personalised.³⁷ In addition, interdisciplinary collaboration among different fields, such as via joint publications, acts as a kind of cross-pollination of ideas. Encouraging programmes in a number of pertinent biomedical sciences as well as linkages between the

³⁰ OECD, *Innovation in Pharmaceutical Biotechnology* (2006), pp. 167-8.

³¹ California Healthcare Institute and Price Waterhouse Coopers, *California's Biomedical Industry*, 2009, PWC, p.60, http://www.pwc.com/en_GX/gx/pharma-life-sciences/pdf/chi-ca-biomed-report.pdf (Accessed 2 November 2009).

³² Ibid.

³³ See IMD, *Global Competitiveness Yearbook*, 2009.

³⁴ Israel Life Science Industry, "Financing History", 2009, http://www.ilsa.org.il/industry_financing_history.asp (Accessed 2 November 2009).

³⁵ Swedish Ministry of Education and Research, "A boost to research and innovation", October 2008, <http://www.sweden.gov.se/content/1/c6/1/1/49/96/f9fd5d.pdf> (Accessed 25 November 2009). See also, Krantz, T. "New Worlds - New Solutions - Research and Innovation as a Basis for Developing Europe in a Global Context - The Swedish Presidency of the European Union", Minister for Higher Education and Research, 2009, <http://www.sweden.gov.se/sb/d/12040/nocache/true/a/130142/dictionary/true> (Accessed 25 November 2009).

³⁶ Casassus, B. "Bright Spots for French Science Budget", *Science Insider*, 1 October 2009, <http://blogs.sciencemag.org/scienceinsider/2009/10/bright-spots-fo.html> (Accessed 25 November 2009).

³⁷ The Royal Society, "Personalised Medicines: Hopes and Realities", 2005, p.34 <http://royalsociety.org/displaypagedoc.asp?id=23244> (Accessed 25 September 2009).

programmes improves the prospects for novel and needed discoveries. It generates human resources that can create and apply new knowledge or operate new technical components.

Singapore is a striking example of a country that in the last decade has built up an active biomedical science system from almost no base prior to 2000.³⁸ As part of the Biomedical Science Initiative, it has developed programmes in a range of disciplines, including bioprocessing, chemical synthesis, genomics and proteomics, cell biology, bioengineering, nanotechnology, computational biology, clinical pharmacy, medical imaging and bioinformatics. Efforts to amass national talent and attract foreign scientists and researchers involved scholarship and fellowship programmes, as well as boosting salaries and funding support,³⁹ and diversifying the structure of grant schemes to permit exploratory research. Grants have also been used to promote interdisciplinary and cross-agency collaboration.

In addition, it is suggested that there is the need to promote managerial and entrepreneurial skills, perhaps integrating courses in management, communication and economics into biomedical disciplines.⁴⁰ Business components would aim to encourage and train “entrepreneurial scientists”, those that want to take new ideas to the market especially by starting a company. It is proposed that business training would help entrepreneurial scientists identify commercial opportunities and would improve the survival of biomedical start-ups.⁴¹ Scotland has taken such an approach – the University of Aberdeen is pioneering the BioBusiness programme for its biomedical science students⁴² and the Scottish Institute for Enterprise is working to network entrepreneurial scientists with business and financial contacts.⁴³ Singapore has also incorporated programmes on “technopreneurship” and consultancy for high-tech start-ups into its biomedical research system.⁴⁴

Infrastructure

In order to train scientists, engineers and technicians and to facilitate their research, it is crucial that they have access to the necessary physical infrastructure – to laboratories and other facilities equipped with cutting-edge biotechnologies. Therefore, expenditure on science education and R&D should include investment in physical infrastructure and in the latest devices and tools.

Building state-of-the-art infrastructure (including several pharmaceutical and molecular biology research institutions) as well as accessing a growing base of industry R&D facilities has been a key part of Singapore’s

³⁸ Holmes, E and Low, E, “BMS Phase 2 Initiative Funding Framework”, Ministry of Health/National Medical Research Council, 2007, https://www.nmrc.gov.sg/corp/uploadedFiles/NMRC/News_VIEWS_And_Events/Speeches/BMS%20Phase%20%20Funding%20Framework.pdf (Accessed 2 November 2009).

³⁹ One example of attracting world-class scientists is the StaR award, which includes funding for salary and an annual budget for research support for five years as well as a one-time start-up grant. (See Barnes, K, “Singapore pushing to dominate translational research in Asia”, 5 June 2008, <http://www.outsourcing-pharma.com/Preclinical-Research/Singapore-pushing-to-dominate-translational-research-in-Asia> [Accessed 2 November 2009].)

⁴⁰ OECD, *Innovation in Pharmaceutical Biotechnology* (2006), p. 172.

⁴¹ Toole, A and Czarnitzki, D, “Exploring the Relationship Between Scientist Human Capital and Firm Performance: The Case of Biomedical Academic Entrepreneurs in the SBIR Program”, ZEW - Centre for European Economic Research Discussion Paper No. 07-01, 2008, pp.21-2, http://papers.ssrn.com/sol3/papers.cfm?abstract_id=966125 (Accessed 25 September 2009).

⁴² Life Sciences Scotland, *Scottish Life Sciences 2008 Review*, p.6, http://www.scottish-enterprise.com/publications/scottish_life_sciences_review.pdf (Accessed 2 November 2009).

⁴³ Scottish Enterprise, “How we can help”, 2009, <http://www.scottish-enterprise.com/lifesciences-initiatives> (Accessed 2 November 2009).

⁴⁴ Holmes and Low (2007).

strategy to create a competitive biomedical sector. Scotland has also invested heavily in research infrastructure in the last few years. For instance, a £23 million Centre for Health Science in Inverness has recently opened, the £60 million Scottish Centre for Regenerative Medicine at the University of Edinburgh is currently under construction, and most recently, a £36 million drug research facility will be built at the Institute of Pharmacy Biomedical Sciences (University of Strathclyde).⁴⁵ Cost-sharing arrangements may also help improve access to high quality facilities. For instance, the Irish Clinical Research Infrastructure Network shares infrastructure and information systems among several universities and hospitals for clinical trials.⁴⁶

3.2.2 R&D

Countries need the capacity to engage in different stages of R&D, including basic, applied and translational R&D. In addition to physical and human infrastructure, this capacity is generated by frameworks that seek to bring new discoveries into the clinical setting and the market. Such frameworks include technology transfer programmes and collaborative initiatives, as well as structural conditions that facilitate the creation and growth of biomedical firms.

Today, R&D takes place in a range of research forums, including universities, hospitals, and public research institutions as well as biotechnology, pharmaceutical and clinical research firms. The stages of R&D taking place in different forums may vary, for instance basic R&D tends to occur in the university or public research arena, while applied research may take place in universities or in firms. However, as this section emphasises, it is important that efforts at various stages of R&D are taking place and that the results of these different efforts are shared among R&D forums.

Basic R&D

Promoting basic research – which may be defined as exploratory work aimed at expanding knowledge of phenomena, without an obvious application⁴⁷ – is crucial for maintaining a national knowledge pool to supply future biomedical innovations. Basic R&D efforts require investment but do not offer a guaranteed return and therefore, as mentioned above, tend to take place in publically funded forums.

It is often the case that applied research is focused on in lieu of basic research. Some countries traditionally concentrate more on advanced R&D work (for instance, the Netherlands and Norway).⁴⁸ In addition, the increasing complexity of biomedical research has tended to incentivise countries to fund short-term,

⁴⁵ Life Sciences Scotland, *Scottish Life Sciences 2008 Review*, p. 10.

⁴⁶ Molecular Medicine Ireland, “About ICRIN”, 2009, <http://www.molecularmedicineireland.ie/page/g/t/24> (Accessed 2 November 2009).

⁴⁷ OECD, Glossary of Statistical Terms, 2003, <http://stats.oecd.org/glossary/detail.asp?ID=192> (Accessed 22 October 2009). See also Lawrence Berkeley National Laboratory, “Basic and Applied Research”, LBL’s Ethical, Legal and Social Issues in Science program, <http://www.lbl.gov/Education/ELSI/research-main.html> (Accessed 22 October 2009).

⁴⁸ OECD, *Innovation in Pharmaceutical Biotechnology* (2006), pp. 168-9.

(relatively) quickly commercialised research.⁴⁹ However, it can be argued that to neglect basic R&D is myopic – it is to remove the foundation for future innovation.

The structure of funding contracts appears to play one of the most important roles in promoting basic research activity. There seems to be a consensus that flexible, long term grants best assure scientists that they have the room to experiment and take risks in their research. For instance, the UK's Royal Society reports that many of the successful spin-out companies and research collaborations with industry have emerged from “well-funded” scientists.⁵⁰

Applied and translational R&D

However, it is of strategic importance that scientists also build on new discoveries emerging from their research with concrete medical and commercial objectives in view (traditionally known as applied research). The OECD has demonstrated that the worst performers in biomedical innovation have not implemented measures to stimulate the commercialisation of knowledge.⁵¹ New discoveries must ultimately be brought into the clinical arena and eventually into the market.

In the healthcare sector, the current thought is to extend this idea beyond just bringing new biomedical discoveries to clinicians, to ensuring that new therapies reach and benefit actual patients (thereby maximising investment in R&D). Known as translational R&D, it involves measuring the impact of new therapies on patients (i.e. taking into account the effect of multiple medical conditions as well as demographic and economic factors), with the goal of improving treatments and targeting therapies to the right patient groups as much as possible.⁵²

Translational research can be understood in different ways and includes a range of R&D phases and forums (“from the bench to the bedside”). In this section, we will focus on the process of shaping new biomedical discoveries into tangible ideas that then can be further developed into needed and marketable products and tested in the clinical setting (both on a large scale and on specific patient groups).⁵³ Here, translational research involves both laboratory and clinical R&D taking place in various research forums. It also involves frameworks that channel new discoveries to clinicians and industry players, such as joint initiatives and technology transfer

⁴⁹ Ibid. See also: Allen, K. “Commercial focus ‘is harming scientific research’”, *The Guardian*, 12 October 2009, <http://www.guardian.co.uk/business/2009/oct/12/scientists-for-global-responsibility> (Accessed 13 October 2009).

⁵⁰ The Royal Society, “Response to the ‘Next steps’ consultation on ‘Maximising the impact of science on innovation’”, 2006, p.2, <http://royalsociety.org/displaypagedoc.asp?id=22675> (Accessed 25 September 2009). See also Allen, K. “Cambridge role in ‘innovation nation’ at risk as private sector cash dries up”, *The Guardian*, 20 September 2009, <http://www.guardian.co.uk/business/2009/sep/30/cambridge-innovation-nation-funding> (Accessed 5 October 2009).

⁵¹ See OECD, *Innovation in Pharmaceutical Biotechnology* (2006), p.163.

⁵² See Lean, M., Mann, J., Hoek, J., Elliot, R., & Schofield. “Translational research: from evidence-based medicine to sustainable solutions for public health problems”, *British Medical Journal*, 2008, 337:a863.

⁵³ Cancer Research UK, *Translational Research*, 2004, <http://info.cancerresearchuk.org/cancerandresearch/aboutcancerresearch/differentareasofresearch/translational/> (Accessed 23 October 2009). See also Wellcome Trust, *What is translational research?*, <http://www.wellcome.ac.uk/Funding/Technology-transfer/WTD027704.htm> (Accessed 23 October 2009).

offices. Most importantly, it involves a great deal of collaboration and flow of ideas and experiences between different researchers, clinicians and biomedical firms.⁵⁴

Here, we can develop the importance of joint R&D activities, both among academic and clinical researchers and among researchers and industry, and technology transfer offices.

Collaborative efforts

Cooperative initiatives among laboratory scientists and clinicians are crucial to targeting new discoveries toward novel and needed products or methods. This kind of collaboration will become even more central with the rise of personalised medicine.⁵⁵ The flow of ideas and evidence is a two-way street – scientists present clinicians with what they have discovered in the lab and clinicians give feedback on potential applications of their discoveries based on clinical evidence and demand, helping to pinpoint the applications with the most health and economic value. Clinician feedback may then spawn new research to enhance existing technologies or develop new lines of R&D.⁵⁶ It is also possible for clinicians to engage in research activities by, for instance, having research facilities located in hospitals.

In Ireland, the R&D activities of scientists at several universities (i.e. Trinity College Dublin, Royal College of Surgeons, National University of Ireland Galway) and clinicians at their associated hospitals are coordinated under a single not-for-profit company, Molecular Medicine Ireland (MMI). The aim of MMI includes increasing dialogue and collaboration among academic researchers and clinicians.⁵⁷ Another case in point is the Scottish Stem Cell Network, which links the stem cell research community, including academic, clinical and industry-based research groups, in a discussion and learning forum.⁵⁸ Furthermore, Singapore's network of multidisciplinary biomedical research institutes has facilitated the growth of the International Molecular Biology Network for Asia and the Pacific Rim, which involves a wide range of nearby foreign research institutes and has been a key contributor to the Human Genome Project (by sequencing the genome of the puffer fish).⁵⁹

Collaborative vehicles among researchers and industry players are also crucial for encouraging the movement of new knowledge to a marketable product. This may include joint research projects between research institutes and biomedical firms or scientists engaging in commercial activities, i.e. part ownership, consulting contracts or membership on company advisory boards. Such efforts help ensure that new discoveries come to the attention of firms that can then develop products and market them. In addition, clinicians' experience with therapies in different patients can be fed back to firms and scientists to help tailor therapies appropriately and to develop and incorporate technologies that help collect the evidence health authorities will likely need to

⁵⁴ Collaboration between all of these actors is also paramount in later stages of translational research, including clinical trials and post-marketing pharmacovigilance, in order to encourage real and practicable innovation. (For instance, see the second and third phases of translational research in Lean, et al, 2008.)

⁵⁵ The Royal Society, "Personalised Medicines: Hopes and Realities" (2005), p.34.

⁵⁶ OECD, *Innovation in Pharmaceutical Biotechnology* (2006), p.171.

⁵⁷ Molecular Medicine Ireland, "About MMI", 2009, <http://www.molecularmedicineireland.ie/page/g/s/2> (Accessed 2 November 2009).

⁵⁸ See Scottish Stem Cell Network, <http://www.sscn.co.uk/> (Accessed 2 November 2009).

⁵⁹ Chaturvedi, S, "Evolving a National System of Biotechnology Innovation: Some Evidence from Singapore", Research and Information System for the Non-Aligned and Other Developing Countries, p.17, http://fbae.org/2009/FBAE/website/images/pdf/important-publication/Singapore_Paper.pdf (Accessed 2 November 2009).

approve and reimburse new products (which is increasingly specific). Furthermore, scientists initiating or participating in spin-offs based on their research helps to expand the sector and develop a local market.⁶⁰ Indeed, collaborative linkages can benefit the firm. For instance, one study found that in firms with affiliations with scientists, employment and production grew faster than in firms without such an affiliation.⁶¹ Furthermore, start-ups can gain access to research facilities and equipment.⁶²

The Kent Ridge Digital Lab (formed of the Information Technology Institute and Institute of System Science) in Singapore is an example of knowledge flowing from academic into industry via scientists themselves moving into industry – in two years its staff formed ten spin-off companies utilising its technologies, including IT infrastructures for life sciences.⁶³ In Ireland, seven joint research Centres for Science, Engineering and Technology have been established, including the Alimentary Pharmabiotic Centre which partners multiple departments at the University College Cork with leading multinational companies⁶⁴ A similar partnership was created between a leading pharmaceutical company and four of Scotland's leading universities and four regional NHS boards to carry out research focused on the development of "biomarkers" (new proteins that can act as simple tests for diagnosing and monitoring disease, as well as the progress and response to treatment). Biomarkers are intended to be used in clinical testing in Scottish research centres, with the aim of speeding up the translation of new treatments from testing to use by the right groups of patients.⁶⁵

Technology transfer offices

The active transfer of knowledge and know-how from public and governmental bodies to private entities for the purpose of developing usable technologies also plays a major role in biomedical innovation. Technology transfer activities can be based on non-proprietary knowledge, such as occur in patent pools, or on proprietary knowledge. The latter generally use contractual arrangements (such as license agreements) based on patents or other IPRs as a platform for actively transferring knowledge. Technology transfer programmes and offices manage and facilitate patenting and licensing activities for scientists and research institutions. Technology transfer offices also link scientists and institutions with funding (commercial or public) and with companies or entrepreneurs wishing to access new technologies.

There is ongoing debate about the extent to which IPRs assist or hinder technology transfer activities, particularly when it comes to developing countries. The transfer of knowledge intended for biomedical medicines and treatments is an especially heated issue. However, evidence suggests that IP-based technology transfer, especially via licensing patents, is important for biomedical innovation in developing as well as

⁶⁰ Casper, S. and Karamanos, A. "Commercialising Science in Europe: The Cambridge Biotechnology Cluster", *European Planning Studies*, Vol.11, No. 7.

⁶¹ Zucker, L., Darby, M., and Armstrong, J. "Geographically localized knowledge: spillovers or markets", *Economic Inquiry*, Vol.36, No.1, p.65.

⁶² Gardner, P. "NIH: Moving Research from the Bench to the Bedside", Testimony of Phyllis Gardner on behalf of BIO to Energy and Commerce Committee, BIO, 2003, <http://www.bio.org/ip/action/tt20030710.asp> (Accessed 25 September 2009).

⁶³ Chaturvedi, p. 16.

⁶⁴ Ahern, M, "Address by Minister for Innovation Policy at the Ernst and Young Pharmaceutical Forum", Department of Enterprise, Trade and Employment, 2007, <http://www.entemp.ie/press/2007/20070919.htm> (Accessed 2 November 2009).

⁶⁵ Wyeth, "Research and Development", 2009, <http://www.wyeth.co.uk/Home/AboutWyeth/ResearchDevelopment/TranslationalMedicineResearch/tabid/125/Default.aspx> (Accessed 2 November 2009).

developed countries.⁶⁶ Indeed, in countries like Singapore, Kenya, Nigeria and Brazil, technology transfer activities based on the exploitation of IPRs are bringing significant benefits to their economies as well as allowing them to better address domestic health concerns.

Importantly, governments have facilitated the creation of technology transfer offices by first supporting an overall level of IP protection and also by enacting legislation that permits the commercialisation of knowledge using IPRs⁶⁷. Most countries model their technology transfer framework on the US's 1980 Bayh-Dole Act and 1986 Federal Technology Transfer Act, which essentially provide public research bodies with the ability to own and commercialise their IPRs.⁶⁸ Technology transfer offices now exist across many countries (including Canada, Korea and several European countries) and are becoming increasingly popular in countries that have traditionally focused more on in-house R&D (i.e. Japan).⁶⁹ Perhaps one indication of this is the significant rise in patenting activity among universities⁷⁰ and research institutes (patenting by biotech firms has also risen) in the last 15 years, compared with a decrease in patenting by pharmaceutical firms.⁷¹

Promoting translational R&D efforts

A range of factors appear to contribute to building up the frameworks and conditions that encourage translational R&D activities. These include factors promoting successful collaborative initiatives and technology transfer programmes, as well as supporting the creation and growth of biomedical firms (which, in most cases, are the players who carry on the development of a product, test it in the clinical setting and bring it into the market). We can separate these factors into “macro”, or regional-level elements – including the existence of biomedical clusters, the size and scope of the biomedical market and the society’s attitude toward risk – and “micro”, or firm and institution-level elements – including those promoting technology transfer offices, institutional collaboration, and firms’ in-house capacity. There are also several other factors affecting incentives for R&D, including the IP, regulatory and investment climate, which will be discussed in later sections.

⁶⁶ See Diamant, R., Davidson, H., & Dr Pugatch, M. “Promoting Technology Transfer in Developing Countries: Lessons from Public-Private Partnerships in the Field of Pharmaceuticals”, Stockholm Network, 2007, http://www.stockholm-network.org/downloads/publications/Promoting_Technology_Transfer_1.pdf (Accessed 25 November 2009). See also, Bremer, H. “University Technology Transfer: Where Have We Been? Where Are We Going?”, *Journal of the Association of University Technology Managers*, Vol.1, March 1989.

⁶⁷ Diamant, Davidson and Pugatch (2007), p.7.

⁶⁸ The Bayh Dole Act gives universities and businesses operating under federal contracts ownership of their intellectual property (instead of the government). The Federal Technology Transfer Act (which replaced the 1980 Stevenson-Wydler Technology Innovation Act) requires federal laboratories to actively seek opportunities to transfer new technologies to the marketplace, as well as allows federal laboratories to enter into Cooperative R&D Agreements (CRADAs) with the private sector. (“NIH: Moving Research from the Bench to the Bedside”, Testimony of Phyllis Gardner on behalf of BIO to Energy and Commerce Committee (10 July 2003) <http://www.bio.org/ip/action/tt20030710.asp> (Accessed 25 September 2009))

⁶⁹ However, the IPR framework in Japan still presents difficulties for motivating tech transfer, since often universities own the invention, rather than inventor. (DeVol, R and Bedroussian, A, “Mind to Market: A Global Analysis of Universities Biotechnology Transfer and Commercialization”, Milken Institute (September 2006), p.263 http://www.milkeninstitute.org/pdf/mind2mrkt_2006.pdf (Accessed 25 September 2009))

⁷⁰ For instance, between 2001 and 2006, patent filings in biotechnology by US universities rose by 46 percent. (Kowden, K and Yeo, B, “The Value of US Life Sciences: A White Paper Exploring Competitiveness, Delivery and Challenges”, Milken Institute (April 2009), p.16 <http://www.milkeninstitute.org/pdf/USChamberLifeSciencesApril2009.pdf> (Accessed 24 September 2009))

⁷¹ See OECD, *Innovation in Pharmaceutical Biotechnology* (2006), pp.150-1.

Macro Level

Evidence is increasingly demonstrating that the presence of biomedical clusters – which are “geographic concentrations of interconnected companies and institutions” – causes the biomedical sector to flourish.⁷² Clusters may involve universities, hospitals, public research institutions and biotech and pharmaceutical firms, as well as risk capital firms and “related and supporting industries”, like clinical research firms.⁷³ Clusters are able to incite and facilitate collaborative R&D as well as commercialisation efforts by, for instance, providing proximate suppliers, partners, finance and expertise and stimulating pressure (from competitors, customers, etc.) to bring new technologies to the market. Porter and Stern (2001) suggest that the growth of clusters can be supported by targeting many of the regulatory and market conditions discussed in later sections, as well as the human capital elements discussed above (especially if these elements produce a critical mass of high quality research institutes in close proximity).

Here we can mention the importance of having a well built-up pharmaceutical (or other major biomedical player) market and it being linked it with a cluster or clusters. Although a country or region can develop the capacity to perform clinical trials and to commercialise products (especially in a cluster environment), having existing large downstream players gives momentum to these efforts. Beyond acting as customers for developed products (to take new products through the third and largest phase of clinical trials), big companies help grow the market, increase competition and attract skilled resources.⁷⁴ In small countries or others where a large market does not exist, countries can attract multinational companies by, for instance, providing clinical research or manufacturing sites, as well as partners for research.⁷⁵ Israel is an example of a country that has adapted to its small size by capitalising on its capacity to provide clinical research and entering into national R&D cooperation agreements with areas like the EU, China and Hong Kong, in which Israeli companies provide technology with partner companies providing manufacturing and marketing expertise.⁷⁶

Singapore’s main biocluster, Biopolis, comprises 25 domestic and international firms and five biomedical research institutes and is in close proximity to the National University of Singapore and the Singapore Science Parks.⁷⁷ These factors allow Biopolis to provide shared state-of-the-art infrastructure, resources and services catering to the full spectrum of R&D activities and to create economies of scale.⁷⁸ The biocluster is set to expand into a new laboratory space next year. Building up a high quality biomedical research base, as well as attractive framework conditions, has allowed Singapore to attract a number of multinational pharmaceutical companies, which are now supporting the development of a domestic biomedical industry, particularly in fields of biologics and translational and clinical research.⁷⁹

⁷² Porter and Stern (2001), p. 12; Bagchi-Sen, S. “The US biotechnology industry: industry dynamics and policy”, *Environment and Planning C: Government and Policy*, Vol. 22, p.6.

⁷³ Ibid.

⁷⁴ OECD, *Innovation in Pharmaceutical Biotechnology* (2006), p.171. See also, Dahlander, L. and McKelvey, M. “Revisiting Frequency and Spatial Distribution: Innovation Collaboration for Biotech Firms”, Paper presented at DRUID’s Summer 2003 Conference, Helsingore, June 12-14.

⁷⁵ Ibid., p.83.

⁷⁶ Israel Life Science Industry, “Financing History”, 2009, http://www.ilsa.org.il/industry_financing_history.asp (Accessed 4 November 2009).

⁷⁷ Barnes (2008).

⁷⁸ See Biopolis, http://www.one-north.sg/hubs_biopolis.aspx (Accessed 2 November 2009).

⁷⁹ Barnes (2008).

The Massachusetts biotech “supercluster”, located primarily on the eastern seaboard of the state of Massachusetts, is one of the oldest biomedical clusters in the US. An environment of 122 colleges and universities and the top five research hospitals funded by the US National Institute of Health, as well as a healthy inflow of public seed money (via federal Small Business Innovation Research (SBIR) grants) and venture capital (it captures just over 18% of all US biotech VC investment) in the region, has provided a rich breeding ground for biotech companies.⁸⁰ As a result, the region has built up some of the world’s largest biotech firms, attracted large pharmaceutical companies to establish major R&D facilities in the area and amassed supportive industries, including bioprocess companies.⁸¹ Consequently, the cluster has grown to contain over 430 biotech companies.

Finally, the social and economic implications associated with a society’s attitude toward risk and failure affect incentives for R&D efforts by the biomedical industry. In particular, the level of risk averseness in a given culture and its impact on business conditions can discourage the creation of spin-offs or deter SMEs from exploring new opportunities via R&D. This attitude may be visible in the lack of sophisticated private equity markets, in the reluctance of scientists to engage in start-ups, in the emphasis on publishing new discoveries over patenting them or in punitive bankruptcy laws. However, countries can take measures that may help counter this effect and encourage R&D efforts by firms, albeit over the long-term. These efforts include structural reforms (i.e. reforming bankruptcy law, removing red tape or offering tax incentives for start-ups) and initiatives that seek to share risks and costs via collaboration between biotech and pharmaceutical firms.⁸² Efforts to train entrepreneurial scientists, like those in Scotland discussed earlier, may also help to broaden cultural perspectives regarding risk.

Micro Level

Here we look more directly at what institutions and firms can do to improve and maximise frameworks and conditions that facilitate translational efforts.

Institutions can take steps to promote the existence as well as the effectiveness of technology transfer offices. Of course, technology transfer services rely first on the presence of national or regional legislation that permits and assists technology transfer. Individual institutions then have to incorporate this into their research structures, perhaps setting up offices that manage IP and other opportunities for the staff. However, the OECD has found that for technology transfer programmes to fully capitalise on university research (i.e. to increase patenting, licensing and spin-off efforts) attention must also be paid to issues like the quality of personnel, the appropriateness of the IPR model and the coordination of programmes across a region.⁸³ In

⁸⁰ Massachusetts Biotechnology Council, “Massachusetts by the numbers”, 2009, http://www.massbio.org/economic_development/the_massachusetts_supercluster/massachusetts_by_the_numbers (Accessed 4 November 2009).

⁸¹ Massachusetts Biotechnology Council, “Massachusetts BioReady Community Seminar”, http://www.massbio.org/writable/editor_files/sample_bioready_seminar.pdf (Accessed 4 November 2009).

⁸² OECD, *Innovation in Pharmaceutical Biotechnology* (2006), pp.53, 100.

⁸³ OECD, *Innovation in Pharmaceutical Biotechnology* (2006), pp.169, 175-6.

particular, personnel should have biomedical and legal expertise (regarding the technology itself and its commercial use and value, as well as contract design and licensing negotiations). The IPR model should try to balance rewards to the inventor and the institution (i.e. encouraging individuals to protect their discoveries and, at the same time, incentivising institutions to support this).⁸⁴ Furthermore, technology transfer programmes should be sufficiently consistent across institutions in a region, in order to facilitate collaborative efforts as well as simplify the process for firms in the area seeking to acquire protected knowledge. Therefore, institutions may see more success in technology transfer programmes by allocating sufficient funding and competent human resources, by shaping an IPR model that is appropriate for the institution and by seeking to build, as much as possible, a coherent technology transfer structure among institutions in the area.⁸⁵

For instance, Germany introduced a new IPR model in 2002 that transfers a degree of IP ownership away from the head of the research group to the university, in order to take into account the interests of both the university and the inventor.⁸⁶ Furthermore, to support the biomedical industry in Israel, most of the university technology transfer companies there ensure that they employ experts in the biotechnology and pharmaceutical sectors (among experts in other fields).⁸⁷

Funding schemes covering early stage R&D (for which a gap in venture capital funding seems to exist), such as the US SBIR program and the Advanced Technology Program, have also helped facilitate commercialisation efforts via technology transfer offices.⁸⁸ The SBIR program offers contracts or grants to small businesses. The Advanced Technology Program helps with early stage investment in “enabling” technologies that are essential to the development of new products, i.e. a stem cell culturing device, by sharing the cost with companies.⁸⁹

For collaborative efforts, the fluid movement of scientists across establishments is important.⁹⁰ Many factors contribute to driving this kind of movement, including proximity to hospitals and firms (i.e. in a cluster environment) and an IPR scheme that allows ownership by private actors. Institutional flexibility is also crucial. For instance, in the early part of this decade, France ended a regulation which prohibited scientists from initiating or taking part in start-up activities if they concurrently worked for a public research institute. Freeing barriers like this facilitates the flow of scientists and knowledge among the lab, clinical and commercial spheres. Other strategies to promote this flow may be to create a “professional” track within scientific disciplines, in which commercial rewards are offered to scientists as opposed to more traditional academic rewards,⁹¹ and student internship placements within biomedical firms.

⁸⁴ Ibid.

⁸⁵ OECD, *Innovation in Pharmaceutical Biotechnology* (2006), p.186. See also DeVol and Bedroussian (2006), p.22.

⁸⁶ Kresse, H. “The German Biotechnology Sector 2006: Analysis and Opportunities for UK Enlargement”, ERBI/University of Cambridge, 2006, p.50, http://www.erbi.co.uk/SITE/UPLOAD/DOCUMENT/ukti%20reports/Germany_2006.pdf (Accessed 4 November 2009).

⁸⁷ See Israel Tech Transfer Organization, “Partners”, 2009, <http://www.ittn.org.il/partners.php> (Accessed 4 November 2009).

⁸⁸ Toole and Czarnitzki, p.21.

⁸⁹ In 2009, the Advanced Technology Program was replaced by the Technology Innovation Program. (“NIH: Moving Research from the Bench to the Bedside”, Testimony of Phyllis Gardner on behalf of BIO to Energy and Commerce Committee (10 July 2003) <http://www.bio.org/ip/action/tt20030710.asp>; Technology Innovation Program <http://www.nist.gov/tip/>) (Accessed 25 September 2009))

⁹⁰ See Owen-Smith, J., Riccaboni, M., Pammolli, F., & Powell, W. “A Comparison of U.S. and European University-Industry Relations in the Life Sciences”, *Management Science*, Vol.48, No.1, January 2002, pp.24-43.

⁹¹ Milken Institute, “People First: Developing Human Capital for Accelerating Medical Treatments and Research” (Summary of Panel Discussion at the Milken Institute Global Conference, *Prospering in a Changing World*, Los Angeles, 26 April 2004), <http://www.milkeninstitute.org/events/events.taf?function=show&cat=allconf&EventID=GC04&level1=program&level2=agenda&Evid=393> (Accessed 23 September 2009)

To push universities towards businesses, Massachusetts provides cooperative research grants through the Life Science Initiative in which public funding must be matched by an industry partner. Furthermore, to incentivise businesses to link with universities, biomedical manufacturers are eligible for a 15% state R&D tax credit for costs related to university-based research.⁹² The SEEKIT programme in Scotland funds joint research projects between biomedical start-ups and public research institutes (in which the start-up provides R&D suggestions based on market demand).⁹³

For collaboration with clinicians, the relationship between clinicians and some industry actors may already be established via doctors' involvement in the clinical evaluation process. Nonetheless, clinicians can be brought further into the research sphere alongside their clinical responsibilities, and earlier in the innovation process, especially with the help of funding and flexible institutional environments (i.e. allowing dedicated time for research).⁹⁴ Efforts at improving translational research are particularly focused on facilitating this kind of collaboration between clinicians, laboratory scientists and business actors, such as those occurring in Singapore and Scotland discussed earlier.

Finally, the in-house capacity of firms to manage translational R&D is important. This includes the quality of human capital and technology within or available to firms. In addition, good business sense and the ability to recognise innovative applications of new technologies are crucial. The amount that firms re-invest in R&D plays a role in facilitating their own capacity, as do the surrounding framework conditions that are discussed here and in later sections, especially the availability of venture capital.

Regions with an active biomedical sector tend to be those that have seen a high degree of re-investment in R&D by existing firms. For instance, in the last decade, business R&D expenditure in Ireland has tripled to over €1.5 billion annually.⁹⁵ In Scotland, several biotech and pharmaceutical companies are currently re-investing in equipping their facilities with cutting edge technologies or upgrading their manufacturing capabilities.⁹⁶ The Québec biomedical industry, particularly the biomanufacturing sector, invests over \$500 million annually to update and expand existing facilities, which is more than double the level of investment that occurred a decade ago.⁹⁷ To encourage re-investment in R&D, Massachusetts offers tax exemptions for sales tax on the construction of life science facilities.⁹⁸ In Israel, high tech companies can qualify for grants covering the cost of fixed assets used in production facilities in designated areas.⁹⁹

⁹² Massachusetts Biotechnology Council, "Incentives", 2009, http://www.massbio.org/economic_development/massachusetts_incentives (Accessed 4 November 2009).

⁹³ Scottish Government, "SEEKIT", 2009, <http://www.scotland.gov.uk/Topics/Business-Industry/support/16879/14127> (Accessed 4 November 2009).

⁹⁴ Clark, S, "Review of the National Innovation System: Response from the Bio21 Cluster", Australian Government Department of Innovation, Industry, Science and Research, p.2, [http://www.innovation.gov.au/innovationreview/Documents/239-Bio21_Cluster\(2\).pdf](http://www.innovation.gov.au/innovationreview/Documents/239-Bio21_Cluster(2).pdf) (Accessed 25 September 2009).

⁹⁵ Ahern (2007).

⁹⁶ Life Sciences Scotland, *Scottish Life Sciences 2008 Review*, p. 11.

⁹⁷ Québec Ministry of Economic Development, Innovation and Export Trade, *Québec Biopharmaceutical Strategy*, 2009, p.10, http://www.mdeje.gouv.qc.ca/fileadmin/sites/internet/documents/publications/pdf/ministere/strategie_biopharma_en.pdf (Accessed 4 November 2009).

⁹⁸ Massachusetts Biotechnology Council, "Incentives".

⁹⁹ Israel Life Science Industry, "Financing History" (2009).

In sum, a range of structures and conditions help ensure that a steady stream of new biomedical knowledge is translated into needed products. Countries can establish effective structures and positive conditions by strengthening the factors discussed here.

3.2.3 Intellectual property protection

IPRs are crucially important to the biopharmaceutical innovation process. Generally speaking, IPRs have two major functions. First, they are used as “insurance” during the different stages of research and development. As explained before, the development of innovative biopharmaceutical products is a time-consuming, expensive and risky business. Combined with fierce competition surrounding the introduction of new drugs, this drives research-based pharmaceutical companies to seek the protection of IPRs, as a means of protecting their massive R&D investment. Indeed, it is estimated that between 60 to 65% of pharmaceutical products would not have been introduced or developed in the absence of patent protection.¹⁰⁰ Secondly, IPRs function as the main business platform upon which research-based companies are able to recoup investments and generate the commercial returns from the introduction of a new successful drug to the market.

Specifically, the ability to patent biotechnology inventions is essential for the development of biopharmaceutical products. This includes patents that cover isolated genes or proteins as well as methods of treatment using genes or proteins (known as “process” innovations¹⁰¹). In addition, patent term extensions, which are available in different countries (for example, in the US¹⁰² and in the EU, where they are known as Supplementary Protection Certificates¹⁰³), and usually afford up to five additional years on the patent term, especially support complex biotech innovations that involve lengthy R&D periods.

Other forms of IP protection, such as data exclusivity and protection of orphan drugs are also very important to the process of introducing new bio-pharmaceutical treatments and technologies.

For example, data exclusivity refers to the protection of the data submitted by pharmaceutical companies to regulatory authorities for the purpose of obtaining marketing approval for new drugs. Gathering and generating the data from pre-clinical and clinical trials represents the bulk of the R&D process and requires a huge investment by pharmaceutical companies. Altogether, this involves a preclinical phase and four clinical phases (including post-approval research) and represents at least two-thirds of the process. The Tufts Center for the Study of Drug Development estimates that for biopharmaceuticals, on average, \$615 million is invested

¹⁰⁰ Mansfield, E. 'Patents and Innovation: An Empirical Study', *Management Science* (February, 1986), pp. 173-181

¹⁰¹ Introducing a narrower position on “process” innovations is under debate in the US at the moment. A rule known as the “machine or transformation” test (under which a “process” innovation is only eligible for a patent “if it is tied to a specific machine or if it transforms a particular article or substance to a different state of thing”) was introduced last year as part of *Bilski v. Doll* (2008). It is reportedly intended to target business methods and abstract processes, but stands to affect the patent eligibility of important process-based biomedical innovations. The appeal is currently pending before the US Supreme Court. (See BIO, “BIO Urges Supreme Court to Reject Rigid Bilski Rule”, 2009, http://www.bio.org/news/pressreleases/newsitem.asp?id=2009_0806_01 [Accessed 25 August 2009].)

¹⁰² Public Law No.98-417, 24/9/1984. See The Library of Congress, “S.1538”, <http://thomas.loc.gov/cgi-bin/bdquery/z?d098:SN01538:@@@D&summ2=m&|TOM:/bss/d098query.html> (Accessed 5 October 2009).

¹⁰³ In the EU, these are known as supplementary protection certificates (SPCs). See EurLex, “Council Regulation (EEC) No 1768/92 of 18 June 1992 concerning the creation of a supplementary protection certificate for medicinal products”, <http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=CELEX:31992R1768:EN:HTML> (Accessed 5 October 2009).

during the preclinical testing phases and another \$626 million during clinical testing.¹⁰⁴ Considering the vast financial resources and extensive time required to acquire and prepare registration data, this data can be viewed as proprietary know-how belonging to pharmaceutical companies.

The very idea of data exclusivity is linked to the responsibility and willingness of governments to protect this data. Essentially, data exclusivity defines the number of years that will elapse before regulatory authorities may review and approve the use of a generic substitute on the basis of the data that was submitted to these authorities by the owner of the original drug. For example, data exclusivity in the United States is provided for by Section 355 of the Federal Food, Drug, and Cosmetic Act of 1997.¹⁰⁵ The US model provides a five-year period of data exclusivity to new drugs and three years of data exclusivity to new indications of existing drugs. In March 2004 the European Parliament harmonised national laws and upgraded Directive 2001/83/EC in order to provide a data exclusivity period known as the “8-plus-2-plus-1” formula. Pharmaceutical companies are provided with eight years of data exclusivity, two years of marketing exclusivity (in which the generic drug may be approved for use by the authorities but cannot be marketed) and an additional year of protection for new indications of existing products.¹⁰⁶

Data exclusivity improves incentives for pharmaceutical companies not only prior to the product’s approval but also during the post-marketing stage (in which further clinical investigations in different countries and different populations try to fill in the gaps in knowledge of the product).

In the age of biologics and biosimilars (so-called “generic” substitutes to biologics), clinical data and data exclusivity become increasingly important. As medicine becomes more personalised and patient-centred, it requires more extensive clinical testing and potentially, a longer period of data exclusivity. There is even the possibility that the clinical data generated by biosimilar manufacturers (which is required for approval in many countries, although it is generally not as extensive as the data submitted by biologic manufacturers) should also receive protection. There are currently several different proposals for addressing the dilemmas associated with data exclusivity for biologics and biosimilars, particularly in the US, where legislation on the approval of biosimilars is currently under debate.

In addition, the protection of orphan drugs is important. This includes the existence of a comprehensive regulatory framework for companies who pursue R&D in rare diseases, which also includes an extended period of exclusivity. It can help reduce the risk surrounding R&D in life-threatening or debilitating diseases that only affect a small set of the population.

¹⁰⁴ PhRMA, “Pharmaceutical Industry Profile 2009”, pp.36-39.

¹⁰⁵ USFDA, United States Federal Food, Drug, and Cosmetic Act of 1997, Chapter 5, “Drugs and Devices”, Section 355, 25 United StatesC. 305(c)(D)(ii) and (iii), www.fda.gov/opacom/laws/fdcact/fdcact5a.htm.

¹⁰⁶ See Legislative Resolution on the Common Position Adopted by the Council with a View to Adopting a European Parliament and Council Regulation Laying Down Community Procedures for the Authorization and Supervision of Medicinal Products for Human and Veterinary Use and Establishing a European Medicines Agency, 10949/2/2003–C5-0463/2003–2001/0252(COD), Strasbourg, 17 December 2003, P5_TA-PROV(2003)0577; See also, Directive 2001/83/EC of the European Parliament and of the Council of 6 November 2001 on the Community Code Relating to Medicinal Products for Human Use, *Official Journal of the European Communities*, 28 November 2001, L 311/67.

The US and the EU both have frameworks in place to incentivise R&D in rare diseases. The US Orphan Drug Act (1983) provides seven years of marketing exclusivity to pharmaceutical companies engaging in orphan drug efforts, as well as federal tax credits (up to 50% of costs) for R&D, waivers of approval and maintenance fees and protocol assistance (scientific advice during the development phase).¹⁰⁷ The EU's framework, established in 1999-2000 via Regulations No 141/2000 and No 847/2000, offers 10-year marketing exclusivity, together with fee reductions or exemptions and protocol assistance.¹⁰⁸

3.2.4 Regulatory and Clinical Environment

The regulatory and clinical environment in a given country or region plays an important role in affecting incentives for biomedical innovation, including ensuring that new products are safe and effective. In this section, the regulatory and clinical environment is comprised of standards and procedures affecting both commercial activities (including company start-up and patenting and licensing efforts) and clinical activities (including clinical trials and product approval).

Legal and commercial procedures

In many cases, legal and commercial requirements (i.e. procedures and fees for business start-up, patenting and licensing activities) facing biomedical companies can have a negative effect on incentives, particularly in the form of administrative constraints. Such requirements may be streamlined in order to minimise the burden on researchers, research institutions and small businesses. For instance, the World Bank's *Doing Business* survey indicates that a wide range exists in countries' procedures for starting a business, including three procedures and three days in Singapore compared with 10 procedures and 47 days in Spain. In addition, the Biotechnology Industry Organisation (BIO) supporting US biotech companies recommends charging patent and related fees according to the cost of service.¹⁰⁹ If, for example, services are conducted electronically, fees could be reduced, as has been implemented recently by the UK's Intellectual Property Office.¹¹⁰

Clinical procedures, standards and conditions

While certain procedures related to clinical trials could be considered in some cases to be excessive, the use of high standards can also be seen as helping to create a market for biopharmaceutical and other biomedical products – they assure consumers of a product's viability and thereby facilitate demand for it.

¹⁰⁷ FDA, "Overview: Developing Products for Rare Diseases and Conditions", 2009,

<http://www.fda.gov/ForIndustry/DevelopingProductsforRareDiseasesConditions/Overview/default.htm> (Accessed 26 November 2009).

¹⁰⁸ EMEA, "Orphan drugs and rare diseases at a glance", 2007, <http://www.emea.europa.eu/pdfs/human/comp/29007207en.pdf> (Accessed 26 November 2009). See also, EMEA, "Human medicines – Orphan medicinal products", 2008, <http://www.emea.europa.eu/htms/human/orphans/intro.htm> (Accessed 26 November 2009).

¹⁰⁹ BIO, "Statement of BIO for the Oversight hearing on 'The US Patent and Trademark Office: Fee Schedule Adjustment and Agency Reform' before the Subcommittee on Courts, the Internet and Intellectual Property House Judiciary Committee, US House of Representatives", 2002, p.2, <http://www.bio.org/ip/action/20020725.pdf> (Accessed 6 October 2009).

¹¹⁰ Out-law.com, "UK trademark and patent fees to drop", *The Register*, 11/3/09, http://www.theregister.co.uk/2009/03/11/cheaper_trade_marks/ (Accessed 6 October 2009).

However, this is only true if the approval standards assess the quality, safety and efficacy of products to a high level, according to the International Conference on Harmonisation's (ICH) standards of Good Clinical Practices (GCP) and Good Manufacturing Practices (GMP), and require a system for monitoring products once they are in the market (known as pharmacovigilance). Inadequate approval standards may promote the presence of substandard drugs in the market, which could affect demand for high quality drugs and discourage investment in new products. Conversely, high standards will encourage the widespread use of GCP and GMP and support new biomedical advances.

Although high clinical standards are necessary for ensuring the effectiveness and safety of new products, as a result the clinical trial process is complex and costly, and increasingly so as products become more sophisticated (i.e. with personalised medicines).¹¹¹ For countries utilising the ICH standards, it is argued that meeting clinical requirements for each jurisdiction involves duplicate efforts and is unnecessary and costly. Harmonising requirements as much as possible may facilitate more efficient use of investment.

In addition, companies need the capacity, including the expertise, finance, infrastructure and patient candidates, to carry out high quality clinical tests. Pharmaceutical and other biomedical companies often seek to access these resources via a partnership or contract with a clinical research organisation (CRO) operating domestically or in other countries, where testing is cheaper and volunteers are more plentiful. CROs also provide expertise on the local population and regulatory framework as well as networks with healthcare institutions and practitioners, which are all crucial for conducting complex population and patient-specific clinical trials (i.e. for rare diseases or personalised medicines).

Fostering collaborative initiatives with practitioners and scientists of different disciplines may also provide opportunities for cost-sharing and quality assurance in clinical trials.¹¹² Germany's coordination centres for clinical trials (KKS) in university hospitals, funded by the Federal Ministry of Education and Research (BMBF), and disease-specific "competence networks" of scientists and doctors are an example of initiatives that may help facilitate complex clinical investigations.¹¹³ In addition, advances occurring in the field of bioinformatics should help streamline clinical trials.¹¹⁴

3.2.5 Market incentives for R&D

Market incentives for biomedical R&D, particularly biopharmaceutical R&D, include the market environment, in terms of pricing and reimbursement policies, and the investment climate (including the venture capital market and the tax environment).

¹¹¹ FDA, "Clinical Trials Transformation Initiative", 2009,

<http://www.fda.gov/ScienceResearch/SpecialTopics/CriticalPathInitiative/SpotlightonCPIProjects/ucm083241.htm> (Accessed 5 October 2009).

¹¹² Faster Cures, "Patients Helping Doctors (PHD) Program: How Can We Improve Recruitment and Retention in Clinical Trials?", http://www.fastercures.org/objects/pdfs/factsheet/Fastcures_ClinicalTrialsv3.pdf (Accessed 5 October 2009).

¹¹³ Federal Ministry of Education and Research, "Patient-oriented clinical research", <http://www.gesundheitsforschung-bmbf.de/en/161.php>. See also, Federal Ministry of Education and Research, "Competence Networks in Medicine", <http://www.gesundheitsforschung-bmbf.de/en/159.php> (Accessed 5 October 2009).

¹¹⁴ Clark, pp.2-3.

Pricing and reimbursement policies

Rising demand for healthcare in response to new biomedical innovations, and subsequent increases in healthcare costs, have left many governments struggling to maintain equitable healthcare provision whilst allowing patients to access new health technologies.

With most governments trying to stabilise, if not decrease, their health spending, over the years many have resorted to measures that interfere with the healthcare market in order to prevent the pharmaceutical and medical expenditures of their healthcare systems from skyrocketing. These measures include regulation of the price of different products, as well as of how much the healthcare system will pay (and in turn, how much the patient will need to pay) for these products. Some countries seek to rationalise pricing and reimbursement decisions via health technology assessment (HTA) bodies, which assess products' utility, efficiency and cost-effectiveness for the targeted population.¹¹⁵

While it is understandable that governments need to control healthcare costs and make informed decisions about healthcare spending, efficiency measures such as the ones described above are not likely to be sustainable over the long-term, in terms of patients' ability to access new health technologies. As a wider range of new health technologies become available, public demand for them will only increase and in turn, public healthcare expenditure will have to tighten further.

To optimise patients' access to new innovations, health systems will likely need to rely more on different funding mechanisms, including a mix of private and public spending on healthcare. For instance, for treatments costing more than what is covered by public health funding, patients may in future be able to cover the balance of the costs by taking out supplementary insurance or paying out of pocket. Or, health systems may partner with biomedical companies, for instance via cost-sharing schemes, in which the company covers part of the cost of treatment for a determined period of time or set of patients.

From the perspective of a public health system, enlarging the market for health technologies runs against its objectives to provide equitable care within a limited public budget. However, instead of restricting the availability of new therapies in line with what the public purse can offer, access to these therapies can be made possible by sharing health expenditure among public and private actors. Allowing for additional funding sources increases the size of the market for biomedical technologies; governments may maintain the public healthcare system, and patients can choose to access technologies not available under the system as they desire.

¹¹⁵ Countries using HTAs include the UK, Australia, Canada, Sweden and the US (used by private insurers and Medicare). Some HTAs are binding on the pricing and/or reimbursement decision, while others are used for reference.

Investment climate

The OECD has found a robust link between strong performance in innovation and well-developed markets for private equity and (early stage) venture capital (VC).¹¹⁶

Therefore, to support biomedical innovation at a basic level, private equity (and in particular, VC) markets need to be sufficiently developed, in terms of the amount of available VC and the number of venture capitalists in the market, as well as the culture of financing risky projects.¹¹⁷

Israel's Hezkek Fund (funded by the Israeli Ministry for Trade and Industry), which provides an incentive for private equity funds to invest in seed stage companies, has contributed to building up a VC market there. The Hezkek Fund invests together with private equity funds, in return for an equity stake in the seed stage company. The private equity fund then has the potential to increase its upside from the investment by having the option, in the future, to buy out the Hezkek Fund's equity stake. The incentive to the private equity fund to invest initially is equal to the exercise of the future option.¹¹⁸

Even in well-developed markets, accessing VC is often still extremely challenging. In particular, this last decade has seen an increasing reluctance of venture capitalists to invest in biomedical R&D, owing to the high risk profile of many biomedical projects and the protracted time horizon for expected returns.¹¹⁹

Waning or non-existent VC has probably hit "follow-up" financing the hardest. Biotech start-ups have actually fared relatively well due partly to an increase in government initiatives to provide public seed and start-up capital (see the earlier discussion on SBIR grants and the Advanced Technology Programme). However, a gap has emerged in follow-up capital for clinical development of biomedical inventions, leading to stagnant growth in the medium-term and quick exits (i.e. licensing new technologies instead of developing them for commercialisation). This has been observed in many different countries, including Belgium, Germany, Finland, France and Israel.¹²⁰

It is suggested that in some cases biotech firms have helped contribute to this gap by not aiming to fully develop their proprietary knowledge, focusing more on contracting their research. In turn, this has possibly decreased their attractiveness to already shaky investors. Improving mutual understanding of the needs of biomedical firms and investors and perhaps additional funding measures (i.e. reducing the corporate tax rate for VC firms or allocating funding to support VC funds) may help incentivise greater focus of VC on follow-up funding.¹²¹

¹¹⁶ OECD, *Innovation in Pharmaceutical Biotechnology* (2006), p.163.

¹¹⁷ *Ibid.*, p.156.

¹¹⁸ Israel Life Science Industry, "Financing History" (2009).

¹¹⁹ *Ibid.*, p.171

¹²⁰ *Ibid.*, pp.173, 177. Although, it can be noted that one US study has shown that SBIR-funded start-ups tend to receive significantly more follow-up venture capital funding than other start-ups (Kowden and Yeo [2009], p.17).

¹²¹ OECD, *Innovation in Pharmaceutical Biotechnology* (2006), pp.184-5.

For instance, as part of the Life Sciences Initiative, the Massachusetts state government will match investment funds of \$100,000 to \$500,000 in early stage life science companies, in an effort to help them leverage additional sources of capital.¹²² The Israeli government is also proposing a similar measure specifically for the biotech field, in which two funds (a total of NIS 200-350 million) will match private investments in biopharma and medical device companies.¹²³ The funds are to be invested only in companies that are already engaged in clinical development stages and the government is exploring ways to incentivise private partners to remain investing in companies until they reach maturity, via a government benefit programme or other mechanisms.¹²⁴

In addition, the tax burden can discourage investment in R&D activities, especially for start-ups (indeed, it may impede their survival). Hence, having a low corporate tax level as well as tax credits for small and medium-size businesses (SMEs) and for R&D (applicable to innovative firms of all sizes) has been shown to spur investment by both biotech and large pharmaceutical firms.¹²⁵ Besides the examples of tax incentives targeting specific aspects of biomedical R&D discussed in earlier sections, many countries have taken general measures to create a positive tax environment. For instance, Ireland lowered its corporate tax rate in the 1980s, giving it a competitive rate relative to the rest of Europe.¹²⁶ Quebec offers one of the lowest corporate tax rates in North America (30.9%)¹²⁷ and in 2006 made sizeable improvements to its R&D tax credit. The ceiling for the amount of assets that entitle companies to an enhanced tax credit rate (calculated at 37.5%) was raised from \$25 million to \$50 million.¹²⁸

In addition, a light regulatory burden (discussed earlier) and the openness of the economy (i.e. lack of export tariffs) can also support the targeting of funds towards R&D.¹²⁹

While there are numerous factors that can be targeted in efforts to boost innovation in a given country or region, this section has tried to capture the most important factors for biomedical innovation at this point in time. Furthermore, it has identified the ways different countries have chosen to build up these factors for themselves.

¹²² Massachusetts Biotechnology Council, "Incentives".

¹²³ Israeli Ministry of Finance and Ministry of Industry, Trade and Labor, "Appendix I – Request for Information: Government-backed biotechnology funds", p.1, 2009, <http://www.moit.gov.il/NR/rdonlyres/7356AAB8-1CC9-431D-8219-D5120210BA55/0/RFIBiotechFundsSummaryofTermsAppendixEnglishversion.pdf> (Accessed 27 November 2009).

¹²⁴ Ibid., p.7.

¹²⁵ Greenwood, J. "BIO's Letter to House and Senate Leaders", BIO, 12 June 2008, http://bio.org/letters/20080612_BIO_RD_letter.pdf (Accessed 29 September 2009).

¹²⁶ Hansen, A. "Ireland's Low Corporate Tax Rate Leads to Prosperity", Tax Foundation, 6 July 2005, <http://www.taxfoundation.org/blog/show/626.html> (Accessed 6 November 2009).

¹²⁷ Invest Québec, "Financial Solutions and Taxation – Corporate Tax Rates", 2009, <http://www.investquebec.com/en/index.aspx?page=1789> (Accessed 6 November 2009).

¹²⁸ Québec Ministry of Economic Development, Innovation and Export Trade, "An Innovative, Prosperous Québec", 2006, p.35, http://www.mdeie.gouv.qc.ca/fileadmin/sites/internet/documents/publications/pdf/ministere/strategie_innovationEN.pdf (Accessed 6 November 2009).

¹²⁹ Porter and Stern (2001), p.5.

4. Concluding remarks and policy recommendations

Biomedical innovation has always been crucial for saving lives and improving the quality of life, and this trend is only increasing. As the scope and number of biomedical innovations rise, we are enjoying longer and more comfortable lives. In particular, biotechnology inventions are revolutionising our ability to predict, track and combat disease. Biomedical R&D has become a major driver of economic growth, with the pharmaceutical and biotechnology industries in particular drawing record amounts of investment each year.

Yet biomedical innovation is also increasingly challenging, in relation to other forms of innovation, in terms of the costs, length and risks involved. This is especially true for innovations involving biotechnology. As biotech innovations become more and more patient-centred, so the resources and the gamble involved rise.

Therefore, countries and regions have an interest in supporting an environment that promotes biomedical innovation as much as possible. This paper has identified five major components of such an environment: physical and human infrastructure; the R&D process, including basic, applied and translational R&D; protection of biomedical IPRs; the regulatory and clinical environment; and the market incentives for R&D, including the impact of pricing and reimbursement systems, and the investment climate.

The ways in which different countries and regions choose to support these components of biomedical innovation depend on the national innovation context, the strengths and weaknesses in a given area with regards to innovation. Innovation strategies are shaped according to the condition of different scientific, economic, political and institutional factors, making specific strategies different from country to country.

However, in general, policymakers can benefit from understanding how other countries and regions have sought to establish these components. In examining different approaches in a number of areas, this paper identifies several best practices that countries and regions seeking to build up biomedical innovation should aim to achieve:

- (1) They should seek to build up a high-quality life science research infrastructure, including a focus on specific biomedical disciplines, in terms of personnel, technologies and facilities. Competitive investment frameworks can also incorporate incentives for interdisciplinary collaboration and improving familiarity with the business world.
- (2) They should seek to encourage an active and comprehensive biomedical R&D environment by promoting a range of R&D activities, including basic, applied and translational R&D. They should allocate a portion of R&D expenditure for basic research in the form of flexible and longer-term

schemes, mostly aimed at universities and other research centres. To encourage applied and translational R&D, they should facilitate an environment that is conducive to collaboration and the flow of knowledge between scientists, clinicians and industry players (including biomedical SMEs and large pharmaceutical companies).

Creating a collaborative environment includes promoting the factors of successful collaborative initiatives and technology transfer programmes, as well as supporting the creation and growth of biomedical firms. Broadly speaking, this involves supporting the development of regional clusters composed of various R&D forums, from universities and hospitals to SMEs and pharmaceutical companies. It involves established biomedical companies reinvesting in their own R&D operations. It also entails forming an IPR model that optimises the incentives of the researcher and the research institution, amassing biomedical and legal experts in technology transfer offices and increasing collaboration among the offices in a region. Finally, it may also require investment schemes that incentivise collaborative work, measures allowing public-private ownership of IPRs and flexible institutional environments.

- (3) They should seek to afford IP protection which is relevant to the biomedical field, including patents and other forms of IP such as data exclusivity and orphan drug protection.
- (4) They should seek to provide a positive regulatory and clinical environment, in terms of public safety and administrative burden. They should do so by minimising administrative constraints associated with regulatory procedures, such as those required to start a business, to patent or license a product and, in some cases, to operate clinical trials. Countries should also harmonise clinical requirements according to the ICH's standards of Good Clinical Practice and Good Manufacturing Practice. Finally, they may want to facilitate cost-sharing and outsourcing schemes for clinical trials, as long as these maintain high clinical standards.
- (5) They should seek to promote positive market incentives for investment in R&D:
 - a. They should limit the use of pricing and reimbursement systems that disturb market signals for innovative pharmaceuticals.
 - b. They should also balance the promotion of generic products with innovative products. In doing so, countries may want to implement public-private arrangements like cost-sharing schemes or allow patients to take out supplementary insurance.
 - c. Furthermore, they should create a positive investment climate by building up and strengthening a venture capital market for biomedical R&D, through lowering the tax burden for venture capital firms and for biomedical businesses. They may also want to utilise public measures to support private equity markets, such as matching private investment with public investment.

Table I below sums up these recommendations and offers a complete picture of the efforts needed to best promote biomedical innovation in a country or region.

The best practices discussed here are by no means comprehensive and countries will need to adapt them to their particular economic, social, political and institutional context. However, they give policymakers a starting point for creating a targeted and effective strategy to enhance biomedical innovation in their country or region, and for sharing their experiences. Knowledge of the different factors of innovation and of which policies work and which do not work provides a foundation for establishing a robust framework in which biomedical innovation can flourish in a given country or region.

Table I: Best Practices for Incentivising Biomedical Innovation

CATEGORY	BEST PRACTICES
Human capital and infrastructure	<ul style="list-style-type: none"> • Invest in life science research system, including in specific biomedical disciplines, in terms of personnel, technologies and facilities • Incentivise interdisciplinary collaboration • Improve scientists' familiarity with the business world
R&D	<p>Basic R&D</p> <ul style="list-style-type: none"> • Create flexible and long-term funding schemes for basic research <p>Applied and translational R&D</p> <ul style="list-style-type: none"> • Support the development of regional biomedical clusters • Incentivise collaboration and risk-sharing between biomedical firms • Encourage re-investment in R&D by established companies • Create flexible institutional environments • Incentivise collaboration between laboratory scientists, clinical and industry actors • Allow public-private ownership of IPRs • Form IPR model that optimises incentives of inventor and institution • Ensure tech transfer offices have biomedical and legal experts
IP protection	<ul style="list-style-type: none"> • Afford protection in the field of patents, including patents for biotechnology inventions • Afford other relevant forms of IP, such as data exclusivity and protection of orphan drugs
Regulatory and clinical environment	<ul style="list-style-type: none"> • Minimise administrative constraints associated with starting a business and patenting and licensing activities • Harmonise clinical requirements according to ICH standards • Facilitate cost-sharing and outsourcing schemes for clinical trials
Market incentives for R&D	<ul style="list-style-type: none"> • Limit the use of pricing and reimbursement systems that disturb market signals • Balance the promotion of generic products with innovative products • Implement cost-sharing schemes between health systems and private actors, such as pharmaceutical companies and insurers • Lower tax burden for venture capital and biomedical firms • Create schemes in which public investment matches private investment, especially for follow-up financing