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BUILDING THE BIOECONOMY

Examining National Biotechnology Industry Development Strategies

A Briefing Paper, April 2014

This report was commissioned by the Biotechnology Industry Organization (BIO). The views represented here are those of the authors only.

CONTENTS

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LIST OF ABBREVIATIONS

ANVISA	Brazilian National Health Surveillance Agency
API	Active Pharmaceutical Ingredient
A*STAR	Agency for Science, Technology and Research (Singapore)
BNDES	Brazilian Development Bank
CDSC	Central Drugs Standard Control (India)
CLs	Compulsory Licenses
CTNBio	Brazilian Biosafety Technical Commission
EMBRAPA	Brazilian Agricultural Research Corporation
EPA	US Environmental Protection Agency
FINEP	Funding Authority for Studies and Projects (Brazil)
FDA	US Food and Drug Administration
FDI	Foreign direct investment
GCP	Good Clinical Practices
GMP	Good Manufacturing Practices
GM	Genetically Modified
GMO	Genetically Modified Organism
ICT	Information and Communications Technologies
INPI	Brazilian Patent Office
IP	Intellectual Property
IPRs	Intellectual Property Rights
IRP	International Reference Pricing
NGO	Non-Governmental Organization
NIH	US National Institutes of Health
OECD	Organisation for Economic Co-operation and Development
PE	Private Equity
PCT	Patent Cooperation Treaty
PRO	Public Research Organization
RDP	Regulatory Data Protection
R&D	Research and Development
SFDA	State Food and Drug Administration (China)
SME	Small and Medium Enterprises
TRIPS	Trade-Related Aspects of Intellectual Property Rights
USDA	US Department of Agriculture
USTR	US Trade Representative
VC	Venture Capital
WHO	World Health Organization
WIPO	World Intellectual Property Organization
WTO	World Trade Organization

EXECUTIVE SUMMARY

This paper provides an overview of national innovation strategies, policies and best practices that relate to the building of a world-class biotechnology sector. It identifies key enabling policy input factors ranging from human capital, protection of intellectual property to infrastructure for research and development.

Through case study analysis the paper focuses on the biotechnology strategies of a sample of eight countries. The country sample is geographically and economically diverse with a mix of high-income mature OECD economies and middle income and emerging markets. The countries mapped are Brazil, China, India, Korea, Russia, Singapore, Switzerland and the United States. The point of reference for this overview is the development of a globally competitive biotech sector in which local biotech actors and stakeholders aim to and can compete globally.

Advances in biotechnology – which encompass health, food and agriculture, industrial and environmental segments – are at the heart of human society, both scientifically and economically. In 2009 the OECD predicted that by 2030 biotechnology could make up to 2.7% of member state GDP. The importance of biotechnology to future social and economic development is illustrated by almost every country today – both mature and emerging market – identifying and defining the field of biotechnology as a strategic priority to their national interest. And why wouldn't they? Breakthroughs and the increased use of agricultural biotechnology over the past few decades have allowed farmers to produce increasing amounts of crops and foods to feed a growing proportion of the world's population. In 2013 a record 175 million biotech hectares were grown globally. Significantly 54% of this production was concentrated in developing and emerging markets in Latin America, Asia and Africa. In Brazil, Argentina, India, China and South Africa biotech crops make up a growing (if not the biggest) form of crops. Similarly, in the health sector the importance of biotechnology cannot be overstated. Biologic medicines and technologies are increasingly being used in the treatment of patients with the most difficult conditions as well as in cutting-edge medical research.

This paper identifies seven enabling factors that together create an environment conducive to biotech innovation. The factors range from the institutional and eco-system level (such as levels of tertiary education and IP environment) to the more biotech specific (such as what type of biomedical and biotech R&D infrastructure does a country have in place and availability of technology transfer laws and mechanisms). The enabling factors are listed below together with a brief outline of the importance of each factor:

1. **Human capital** – A basic and fundamental building block for the biotech sector is the availability of high skilled and technically trained human capital.

2. **Infrastructure for R&D** – R&D infrastructure and capacity is critical to fostering innovation and activity in high tech sectors including biotechnology and is reflected by a number of country-level indicators including total R&D expenditure; patenting intensity; biotech R&D expenditure; life science investment levels; public-private partnerships; and academic and scientific citations.

3. **Intellectual property protection** – Intellectual property rights such as patents and regulatory data protection are historically of real importance to the biotech and biopharmaceutical innovation process as they incentivise and support the research and development of new biological technologies and products.

4. **The regulatory environment** – The regulatory and clinical environment in a given country or region plays a significant role in shaping incentives for innovation and establishing adequate levels of quality and safety for biotech products, particularly biopharmaceuticals.

5. **Technology transfer frameworks** – Technology transfer is an important mechanism for commercialising and transferring research from public and governmental bodies to private entities and private to private entities for the purpose of developing usable and commercially available technologies.

6. **Market and commercial incentives** – Market and commercial incentives can come through a number of different formats such as tax incentives, general support for basic research and R&D credits for investments in plant, equipment and other R&D infrastructure. For the biopharmaceutical sector market and commercial incentives are primarily determined by the existing pricing and reimbursement systems for medicines and health technologies. The manner and extent to which these policies are put in place can have a profound impact on the commercial and market incentives for innovation more broadly in the health sector as well as for biotechnology R&D and particularly in the biopharmaceutical sector.

7. **Legal certainty (including the rule of law)** – The general legal environment including as it relates to the rule of law and the rule of law within a business context is crucial to commercialization and business activities.

Based on the analysis identification of the enabling factors and country mapping the paper provides six recommendations and steps for countries to take. They are:

1. **Identify the biotechnology sector as an area of strategic importance** – Identifying the biotechnology sector as an area of strategic importance is the first step in successfully building a national biotechnology policy. By and large most countries included in this paper have directly or indirectly targeted biotechnology as a technology and industry of strategic importance to national economic development and growth.

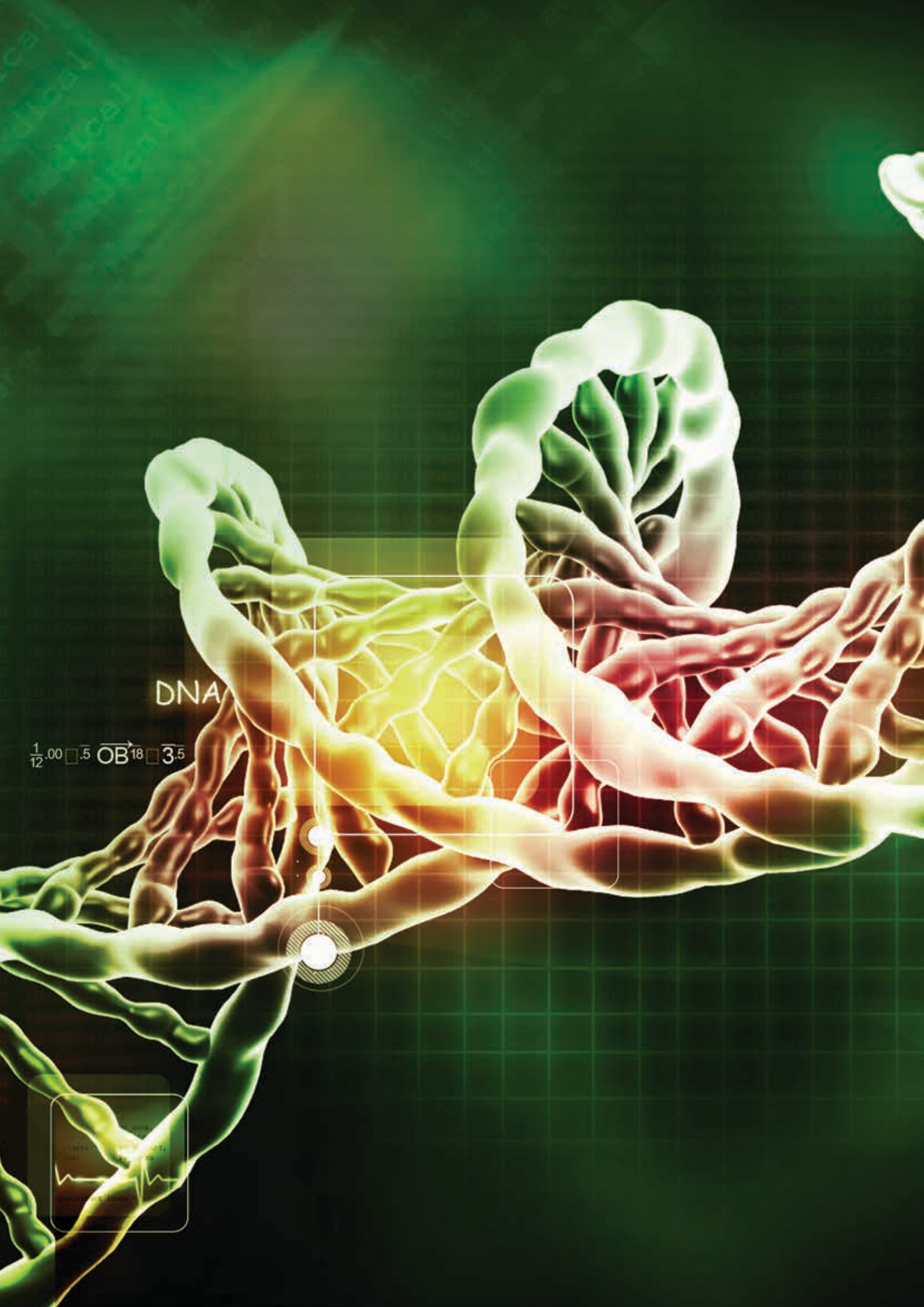
2. **Create a national blueprint** – The existence and creation of a blueprint of national biotechnology strategy can be a powerful tool in creating a vision and setting a goal for national aspirations. There are many ways in which governments can provide leadership and direction for the building of a biotechnology capacity. In some countries a more de-centralized, indirect approach has proven to be effective, such as in the US, whereas in others direct government leadership has been instrumental in creating the conditions for success. Examples include Korea and, certainly in the ag-biotech and biofuels sector, Brazil. Regardless of the type of governmental leadership strong governmental inter-agency and departmental coordination is required.

3. **Measure performance** – The measuring of performance of the biotechnology sector in a transparent and systematic fashion is of real importance to understanding progress made and challenges remaining in order to allow for mid-course corrections that may be necessary. This can be conducted either through recurring government review or independently through private, academic and non-governmental actors.

4. **Recognize and use existing best practices** – Although no two countries are the same and all face different circumstances, countries can learn from the experiences of each other. International best practices should be shared and repositories of information and resource sharing are all positive and worthwhile undertakings.

5. **Leverage national capabilities** – Understanding and focusing on one's comparative and competitive advantage can lead to the most effective allocation of resources. Country size, scientific and research strengths, geography and biodiversity are all important attributes. Some countries have natural strengths in some biotech sectors whereas others can compete and develop across the board.

6. **Enhance local and international cooperation** – Cooperation and partnerships between public and private, national and international stakeholders can be key in attracting investment and building up a world-class biotech industry. Singapore is a good example of a country which by leveraging its strengths and fully engaging in partnerships between government and the multi-national industry and between the public and private sectors has been able to in a relatively short time span build a cutting edge biomedical and biotech R&D capacity.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1 INTRODUCTION

That innovation is central to economic development is something few economists would dispute. Indeed, Joseph Schumpeter's 1939 declaration that "innovation is the outstanding fact in the economic history of capitalist society" is probably even truer today than it was when he first made it on the eve of World War II.[1]

In essence, innovation is the ability to create new uses, functions, processes and products from either existing products or processes or completely novel ones. Increasing economic productivity is fundamentally about innovating or displacing existing means and processes of economic production. From basic manufacturing to the provision of high-tech cutting edge services, innovation is central to growth and commercial success.

Firms, businesses and whole economies now face more than simply competitors from within their own national or regional markets; instead competition is both international and trans-national. Indeed, governments of all colors talk incessantly of the need to continue to innovate and build a 21st century knowledge economy. Examples include President Obama in his State of the Union message in 2011 when he emphasized the need for America to "out-innovate, out-educate, and out-build the rest of the world". Similarly, Britain's Conservative-Liberal government early on in their parliamentary term made increasing innovation a key part of their economic policy. In the BRIC economies innovation is also viewed as key to continued prosperity and economic development. Former Chinese Premier Wen Jianbao frequently spoke about the need for China to focus on science and innovation and become an innovation-driven economy and today innovation remains a key part of China's current economic policy and five year plan. In Brazil, the government has launched a number of policies aiming to stimulate innovation under both the "Competitive Development Policy" and the more recent *Brasil Maior* initiative. And while the Lisbon Agenda has quietly been dropped, in the EU the old innovation warhorse has been trotted out yet again. This time in the guise of the Europe 2020 strategy with an "Innovation Union" being one of the hallmark initiatives.[2]

But pursuing public innovation policies in more than name can be rather expensive. Given the devastating impact of the financial crisis of 2007-8, the subsequent global economic downturn and sovereign debt crises, public spending and investment in many economies are being squeezed. Yet while investment and funding remain fundamental to the success of innovation policies, apart from having the right amount of investment and funding, having the right kind of policies in place to promote innovation is absolutely crucial. Nowhere is this clearer than in the field of biotechnology.

1.1 The future is Bio

Advances in biotechnology – which encompass health, food and agriculture, industrial and environmental segments – are at the heart of human society, both scientifically and economically. In 2009 the OECD projected that the importance of biotechnology would only grow over time and that in the areas of health care, agricultural production and industry, biotechnologies would have a massive socio-economic impact. Apart from the social benefits of being able to feed and treat the world's growing population, the economic contribution of biotechnology and biotechnology intensive sectors was only expected to increase. The OECD predicted that by 2030 biotechnology could make up to 2.7% of member state GDP.[3] And more recently in 2012, in the *National Bioeconomy Blueprint*, the Obama administration and US Government argued that the bioeconomy would "allow Americans to live longer, healthier lives, reduce our dependence on oil, address key environmental challenges, transform manufacturing processes, and

increase the productivity and scope of the agricultural sector while growing new jobs and industries."[4]

This importance of biotechnology to future social and economic development is illustrated by almost every country today – both mature and emerging market – identifying and defining the field of biotechnology as a strategic priority to their national interest. And why wouldn't they?

Breakthroughs and the increased use of agricultural biotechnology over the past few decades have allowed farmers to produce increasing amounts of crops and foods to feed a growing proportion of the world's population. In 2013 a record 175 million biotech hectares were grown globally.[5] Significantly 54% of this production was concentrated in developing and emerging markets in Latin America, Asia and Africa.[6] In Brazil, Argentina, India, China and South Africa biotech crops make up a growing (if not the biggest) form of crops.

Similarly, in the health sector the importance of biotechnology cannot be overstated. Biologic medicines and technologies are increasingly being used in the treatment of patients with the most difficult conditions as well as in cutting-edge medical research. For example, biotechnologies are increasingly part of the discovery, clinical and pre-marketing studies on traditional small molecule drugs. This includes biotech processes such as pharmacogenetics, gene sequencing and diagnostics through the identification of biomarkers. The path to new types of clinical and therapeutic environment – based on the personalization of medicines and medical treatments – is in large measure based on advances in biotechnology. Here pharmacogenetics and gene sequencing play a crucial role.

At the same time as the appreciation and recognition of the importance of biotechnology continues to increase, developing a sophisticated national biotechnology capacity has become a much riskier, more complex and costly endeavor.

Consequently, policymakers and stakeholders have an intensified interest in understanding and identifying the desired set of national policy tools needed to encourage the growth and development of the biotechnology industry from the most basic level of research to full-blown commercialized products.

1.2 Paper overview

The purpose of this briefing paper is to provide an overview of some of the best practices in place internationally that support and enhance biotechnology inputs and outputs.

The paper takes into account the specific requirements of the biotechnology sector and how biotech R&D takes place. It identifies key enabling policy input factors ranging from human capital, protection of IP to infrastructure for R&D.

The point of reference for this assessment is the development of a globally competitive sector; countries that wish only to develop a sector that is nationally competitive could in principle adopt a more protectionist set of policies. The consequence of such a strategy would however be to limit the ability of local players to succeed in world markets.

Through case study analysis the paper focuses on the biotechnology strategies of a sample of eight countries. The country sample is geographically and economically diverse with a mix of high-income mature OECD economies and middle income and emerging markets. The countries analyzed are Brazil, China, India, Korea, Russia, Singapore, Switzerland and the United States.

In addition to this Introduction the paper contains the following sections.

Section 2 looks at the importance of biotechnology innovation to future economic development and growth and provides a thorough discussion of the specific processes related to research, development and commercialization of biotechnologies and products. The section provides a spotlight on the biotechnology R&D process; how it has changed over the years; and what some of the challenges and opportunities associated with contemporary biotechnology research

are. The biotechnology R&D process is highly technical and specialized requiring advanced technological and human capital capabilities.

Section 3 describes the rationale and up-to-date thinking that underline national biotechnology strategies. It identifies seven enabling input and output factors that are of the most importance to making these strategies successful.

Section 4 discusses the national innovation and biotechnology strategies in eight countries: Brazil, China, India, Korea, Russia, Singapore, Switzerland and the United States.

For each country, this section provides:

- An introduction and general economic country overview;
- A description of the national innovation strategy and biotechnology strategy; and
- A table summarizing the key policies and initiatives in place for each of the seven enabling factors identified in section 3 organized around two themes:
  – Success stories; and
  – Stumbling blocks.

A deeper discussion and analysis of all seven of the enabling factors for each country included in the study are provided in Appendix I.

Based on this analysis section 5 provides recommendations.

2 BIOTECHNOLOGY INNOVATION

This section provides a discussion of the specific processes related to research, development and commercialization of biotechnologies and products. The section provides a spotlight on the biotechnology R&D process; how it has changed over the years; and what some of the challenges and opportunities associated with contemporary biotechnology research are.

2.1 Developing biotechnologies

Biotechnologies are today used in a wide variety of sectors and industries to produce everything from advanced biopharmaceutical medicines, genetically modified crops to household goods such as enzyme-based cleaning detergents. While these products and technologies share the characteristics of having been developed through or are the result of a biotech process, the R&D requirements to develop, commercialise, manufacture and maintain a product in the market can vary from one product or technology to another. For instance, manufacturers of biofuels face a different set of R&D challenges and set of regulations than do companies in the seed industry. Nevertheless, there are some important similarities that are shared across most biotech sectors. Most notable is the cost and complexity of the R&D required to develop a biological product or technology.

For instance, research, development and eventual commercialization of new biofuels require considerable time and capital.[7] The estimated cost of a biofuel processing facility is USD350 million per plant and the estimated period of time to move from a pilot phase to full commercialization is 12 years.[8] Similarly, within the crop protection sector (in which a number of companies increasingly integrate and make use of biotechnologies in their R&D activities) the cost of bringing a new product to market has increased significantly over the past two decades. According to research by the USDA, in 1995 the total cost from the research and discovery phase to registration and market approval was USD162 million.[9] By 2005 this had increased by close to two-thirds to USD254 million.

Looking at other biotech sectors one can see similar trends. For example, in the biopharmaceutical industry the cost of research and development has risen considerably over the last few decades. In 1979, the total cost of developing and approving a new drug stood at USD138 million. Almost 25 years later, in 2003, this figure was estimated to have rocketed to USD802 million.[10] A more recent estimate points to the total cost of drug development being approximately USD1.5 billion.[11] Significantly, different stages of R&D do not contribute equally to the composition of total cost. For biopharmaceuticals it is the clinical component which is the most costly and has increased the most. For example, clinical trials from Phase I to III account for approximately two thirds of the total cost of bringing a medicine to the market, even though they do not represent the longest period of drug development.[12] In addition to cost there is also the challenge of successfully developing new medicines and technologies and the length of time spent on developing a drug. On average, only one to two of every 10,000 synthesized, examined and screened compounds in basic research will successfully pass through all stages of R&D and go on to become a marketable drug. Furthermore, it takes between 10 and 15 years from the filing of a new patent to the day when a new medicine finally becomes available for patients to use.[13] Below Figure 1 provides a basic overview of the biopharmaceutical R&D process, with a particular focus on the stages of clinical research.

FIGURE 1: The biopharmaceutical R&D process

Research and discovery: Scientists attempt to isolate new chemical or biological entities using advanced screening and synthesising techniques.

Pre-clinical development: Initial safety tests and assessment studies, such as toxicology, are performed on animals.

Clinical development:

Phase 1: Initial phase tests a drug candidate in 20-100 healthy volunteers to assess how the body processes it and what side effects manifest themselves. A drug must show a minimum level of safety in order to move to the next phase of studies.

Phase 2: Examines a drug candidate's effectiveness in treating a targeted disease relative to other existing drugs or to a placebo. It explores whether the candidate acts against the disease and if it causes any adverse reactions in patients, and how this measures up to existing treatments. Studies involve 100 to 500 volunteers, all of whom experience the targeted disease or condition.

Phase 3: If the candidate is proven safe and effective in the first two phases, the study is shifted to a far larger scale, from 1,000 to 5,000 subjects. Studies test the safety and effectiveness of the drug candidate in different populations and conditions. This phase generates a large amount of data on the candidate in order to understand as clearly as possible the safety risks associated with the drug and to identify the right dosage and mode of use. Due to the scale of operations, Phase 3 studies are the most costly and time-consuming trials.

Registration: Results of pre-clinical and clinical studies and proof of meeting international standards are submitted to drug regulatory authorities for their review.

Phase 4: Biopharmaceutical companies must submit a plan for on-going monitoring and study of the drug as part of its approval for marketing. These studies are intended to safeguard larger scale use of the drug by monitoring any adverse effects that become evident as well as identifying what appears to be the most appropriate and effective manner of use.

2.2 R&D vs. manufacturing

Developing high technology processes and/or products such as bio-crops and biopharmaceuticals is not an easy task. As section 3 details below this involves highly specialised and expensive R&D infrastructure, trained and skilled human capital as well as a host of other physical and non-physical enabling factors. The R&D required to bring high-tech products to market is the most complex and demanding part of the development cycle. Manufacturing, on the other hand, can in some cases by comparison be less demanding. Often this basic fact and distinction between the demands of developing a national or regional R&D capability for high-tech products versus developing a manufacturing capability is overlooked in policy discussions. The manufacturing process can be confused with the R&D process. Yet it is important to note the distinction between the two.

For example, traditional "small molecule" pharmaceutical drugs (which are chemical and manufactured through a process known as chemical synthesis) are very difficult and costly to research and develop requiring high levels of technical infrastructure and skilled human capital. By comparison the manufacturing of such pharmaceutical drugs can be much less technically challenging depending on the specific composition of the pharmaceutical drug. Consequently, a small molecule pharmaceutical drug can be developed in one country yet it or its key constituent parts (such as the API) can be manufactured in a different location and by a different entity. Indeed, the outsourcing of pharmaceutical manufacturing and the manufacturing of APIs has been a common practice within the pharmaceutical industry for years.[14]

With regards to the development and manufacture of biological technologies and products there is, however, less of a distinction between the requirements of manufacturing and product development. While developing a biological product or technology also requires high levels of expertise

and advanced technical infrastructure, given the size, complexity and inherent instability of a biologic, the manufacturing process also requires a considerable level of stability and technical capacity.[15] Specifically, the manufacturing process must be consistent and not changed with new parts or processes introduced. Otherwise there is a risk that the quality and purity of the manufactured product is compromised.[16] These challenges – of maintaining stability, consistency to ensure a high quality product – are unique to the manufacturing of biologics and make the outsourcing of this manufacturing difficult and technically testing.[17]

In this respect developing a sophisticated biotechnology capacity can be considered as providing even more of a technical challenge than other high-tech products. Section 3 examines just how difficult this is and the challenges of making sure that all physical and non-physical enabling factors are in place to successfully build a world-class biotechnology capability.

3 NATIONAL STRATEGIES TO ENCOURAGE BIOTECHNOLOGY ACTIVITY

This section describes the rationale and up-to-date thinking that underline national biotechnology strategies. It identifies seven enabling input and output factors that are of the most importance to making these strategies successful.

3.1 What is a National Innovation Strategy?

In essence, a national innovation strategy or system refers to the measures that state actors or regions (such as the EU) take in seeking to promote innovation in general or in a particular sector. Former PC hardware producers and now management and information systems consultants IBM provide a succinct description:

National innovation policy centers on a broad agenda to fuel a nation's innovative capacity and it seeks action from government, industry, academia and workers. A national innovation strategy builds on a contemporary understanding of innovation and tries to create a consensus to act on the changes required to establish an effective national framework.[18]

Fundamentally, national innovation strategies are a set of policies and initiatives aimed at encouraging innovation on or at a macro or micro level. They can be coherent, synergistic plans for interconnected action or a laundry list of disparate initiatives that on their own promote innovation. Indeed, they can 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, say biotechnology). The type of policy pursued and the prospective effect (negative or positive) is largely a result of what type of innovation infrastructure and factors are already in place.[19] For example, it is difficult to produce an effective specific policy encouraging biotech innovation, if the basic educational infrastructure of educating and training scientists and researchers is not in place.

While a national innovation strategy is shaped by various elements and no two national strategies can be identical, there are a number of components or best practices which are necessary for putting in place and executing a national innovation strategy. Given the unique characteristics of biotech research and development outlined above in section 2, a number of key components can be identified that are essential in order to successfully promote biotech innovation in a given country.

3.2 Promoting biotech innovation: Seven enabling factors

Designing an environment that is conducive to the innovation, research, commercialisation and marketing of biological products and technologies is not an exact science. There are a myriad of factors that potentially can affect, encourage or discourage rates of biotech innovation. Relevant policies and factors range from those specific to the biotechnology sector and the life sciences to more general ones affecting broader levels of innovation and economic activity. Moreover, every situation, country or region is different. Depending on the structure of a particular economy and levels of overall socio-economic development, different countries have greater or lesser needs in specific policy areas.

Still, putting these considerations aside, it is possible to piece together a framework and identify a number of enabling factors that together create an environment conducive to biotech innovation. Table 1 summarizes these factors:

TABLE 1: Enabling factors
• Human capital
• Infrastructure for R&D
• Intellectual property protection
• The regulatory environment
• Technology transfer frameworks
• Market and commercial incentives
• Legal certainty (including the rule of law)

The following pages provide a description of each enabling factor and its importance in contributing to an environment that encourages and promotes biotech innovation and research.

Human capital

High skilled and technically trained human capital is one of the most fundamental features that successful biotech innovation is reliant upon. A number of general and biotech specific studies have found that without the right human capital it is virtually impossible to create the conditions in which biotech innovation can take place. For example, a 2006 OECD study of biopharmaceutical innovation emphasized the importance of human capital and availability of skilled and trained scientists, researchers and technicians.[20] Similarly, the National Science Foundation's *Science and Engineering Indicators* place a strong emphasis on levels of education, strength of higher education and number and quality of researchers when compiling its indicators.[21]

Human capital refers to and can be measured by: higher education rankings, life science and medical college rankings, life science graduates, number of life science, biotech/or biomedical professionals and researchers, education levels, and researchers and scientists.

Infrastructure for R&D

Combined with having adequate, educated and technically proficient levels of human capital, R&D infrastructure and capacity is critical to successfully fostering innovation and activity in high tech sectors including biotechnology.[22]

A country's R&D capacity and available infrastructure for R&D is reflected by a number of different indicators including total R&D expenditure; patenting intensity; biotech R&D expenditure; life science investment levels; public-private partnerships; and academic and scientific citations.

In the biopharmaceutical sectors clinical regulation is of particular importance in attracting investment and clinical trials. A 2012 study by Charles River Associates found that clinical regulations and the regulation of clinical research activities played an important role in determining clinical trial location.[23]

What types of policies are in place to encourage the building and introduction of these types of facilities and initiatives? Governments and countries can on the one hand support the building of R&D infrastructure through direct support and government funded and operated facilities and also through public-private partnership.

Intellectual property protection

IPRs are historically of real importance to the biotech and biopharmaceutical innovation process. For biopharmaceutical as well as non-pharmaceutical biological products and technologies the evidence suggests that IPRs incentivise and support the research and development of new biological technologies and products.[24] In particular patents and other forms of exclusivity for biopharmaceuticals such as regulatory data protection and special exclusivity incentives for the protection and production of orphan drugs provide research-based companies with an incentive to invest vast sums in R&D and the discovery of new biotech drugs, products and therapies. As noted above, the research process for biopharmaceuticals (and many other biotech products) is unique in its time, cost and high rate of failure. The market exclusivity period provided by IPRs give firms the protection and incentive needed to recoup

R&D investments made. Evidence suggests that many drugs and therapies would not have been discovered had it not been for the incentive and protection provided by these IPRs. For instance, analysis of market exclusivity periods and legislation finds that the combination of market exclusivity and income from patent protection drives private investment in innovation, which contributes to new drug development.[25] Older studies have estimated that between 60-65% of pharmaceutical products would not have been introduced or developed in the absence of patent protection.[26] For biologics exclusivity periods under RDP are of particular importance as there may be a so-called 'gap' in patent protection between a biosimilar and the innovator, reference product. Because of the inherent characteristics of large molecule biologics a biosimilar can be approved for marketing – based on a comparison to a reference product – yet not directly infringe any existing, in force patents for the reference product due to differences in structure, administration, or mechanism of action. Under this scenario the exclusivity provided by a RDP term is critical to a biotech innovator.

The regulatory environment

The regulatory and clinical environment in a given country or region plays an important role in shaping incentives for innovation and establishing adequate levels of quality and safety for biotech products, particularly biopharmaceuticals. A strong regulatory environment creates the conditions for the production and sale of high quality products and technologies.[27]

Procedures, standards and conditions are to a large extent dependent on the regulatory framework and regulations in place. Different biotech sectors have different needs and regulatory structures in place. The regulation of GM crops, for example, may be carried out by a separate entity from that which regulates biopharmaceuticals. This is often the case with other biotech products as well such as biofuels. Depending on the product there may be some regulatory overlap and more than one agency or body may be involved. For example, in the US divisions within the USDA, FDA and other federal agencies, including the EPA, regulate different biological products and technologies.[28]

Overall the most advanced and innovative biotech markets in the world are also those which have the highest levels of clinical and regulatory standards. Looking at biopharmaceuticals this is achieved through setting and imposing high clinical and manufacturing standards through GCPs and GMPs as well as post-marketing surveillance through pharmacovigilance programs. A country which wishes to develop an industry that is competitive in international markets (as opposed to simply dominant in its home market) needs to develop a regulatory system that is aligned with international best practice. This is illustrated by, for example, the growing focus of major drug authorities, such as the FDA, on ensuring that international manufacturers and non-US manufacturing adheres to FDA standards and the establishment of foreign offices and increased inspections of foreign manufacturers and suppliers.[29]

While it may impose substantial costs on manufacturers to comply with these standards they also give patients confidence in new biomedical products being safe and effective. There are a number of efforts both at the national and international level to minimise the cost of these high standards through the coordination and harmonisation of clinical and regulatory standards. In the biopharmaceutical sector, for instance, this includes the International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use.

Technology transfer frameworks

Technology transfer is a critical mechanism for commercialising and transferring research from public and governmental bodies to private entities and private to private entities for the purpose of developing usable and commercially available technologies. Technology transfer activities that are based on academic-industry and public-private sector collaborations provide a significant and distinct contribution to the economic strength and well-being of countries in which such activities take place. The process enables public research institutions to obtain access to commercial research funds, state-of-the-art equipment and leading-edge technologies, while allowing industry to benefit from the extensive knowledge and ingenuity of

academic researchers. To better understand the potential impact of technology transfer on innovation and economic development it is worth considering the US which has become regarded as a pioneer and leader in this field.

In the 1980s the US passed two path-breaking pieces of legislation: the Patent and Trademark Law Amendments Act of 1984 and 1986 (the Bayh-Dole Act) and the Stevenson-Wydler Technology Innovation Act, which was later amended by the Federal Technology Transfer Act of 1986 and the Technology Transfer Commercialisation Act in 20003. This legislation attempted to supply federal laboratories (e.g. the NIH) and universities using federal funds with the incentives needed to work with industry for the purpose of translating early stage research into usable products in the market place for the benefit of the wider public. The legislation sought to secure the above goals through three major changes to the IP system. First, they allowed universities and federally funded bodies to retain ownership of the proprietary knowledge stemming out of the research and daily activities of these institutions, including the ability to own patents on their inventions. Second, they encouraged these institutions to become much more proactive and professional in the management and exploitation of their IPRs by creating professional technology transfer offices. Finally, the legislation sought to stimulate the commercial and financial aspects of public-private collaboration, with the intention of creating new businesses (such as spin-off companies) and generating income for the institutions, as well as for the researchers.

The new laws led to a flood of technology transfer activities based on the exploitation and commercialization of IPRs. A decade after the legislation was passed the combined campuses of the University of California became the top recipient in the US of biotechnology patents; a position formally held by the pharmaceutical company Merck.[30] Indeed, *The Economist* called Bayh-Dole "Possibly the most inspired piece of legislation to be enacted in America in the last half-century".[31] More recent analysis shows the significant economic contributions that the non-profit and university sector has made. For example, using fifteen years of data from the annual Association of University Technology Managers survey a 2012 study estimating the economic contribution of licensing activity by academic institutions found that in the US the contribution of academic licensing to gross industry output ranged from USD199-836 billion (2005 USD).[32] Contributions to GDP were equally significant estimated at between USD86-388 billion (2005 USD).[33]

University technology transfer activity has increasingly become recognized by policy-makers in a growing number of countries as a powerful driver of economic growth and innovation. Since the US technology transfer system of public-private partnerships was put in place many countries have sought to emulate it. Canada (1985), Japan (1998), UK (1998), Germany (1998, 2001), France (1999), Austria (2002), Italy (2001), Belgium (1999), Spain (1986), Denmark (2000), Switzerland (2002), Netherlands (1998) and Korea (1998, 2000 and 2001) have all adopted frameworks aimed at promoting technology transfer between public private partnerships through the exploitation of IPRs.[34] As will be discussed in below for the case study countries the evidence suggests that in countries that have adopted these frameworks, technology transfer activity has steadily increased.

Although primarily considered within a public-private, academic-industry context, it is also worth mentioning that in many countries it is not

only the regulatory and legislative framework for technology transfer from public to private entities that can be challenging, but also for transfer activities between private entities.

But developing successful technology transfer platforms is not a simple task, even in mature markets where such activities have long been established. An effective technology transfer platform depends on a wide range of factors, such as the establishment of a technology transfer offices which employs IP experts and marketing professionals; industry oriented scientists; entrepreneurs and companies seeking seed technologies to license from the university and then develop; governmental grants to support the process and a strong national IP system that allows a university/ academic institution to protect and license its inventions.

The availability of technology transfer frameworks can be measured by examining the existence of relevant policies, laws and/ or frameworks as well as their actual use through university patenting rates, licensing agreements and commercialisation activities in all sectors and between all relevant entities.

Market and commercial incentives

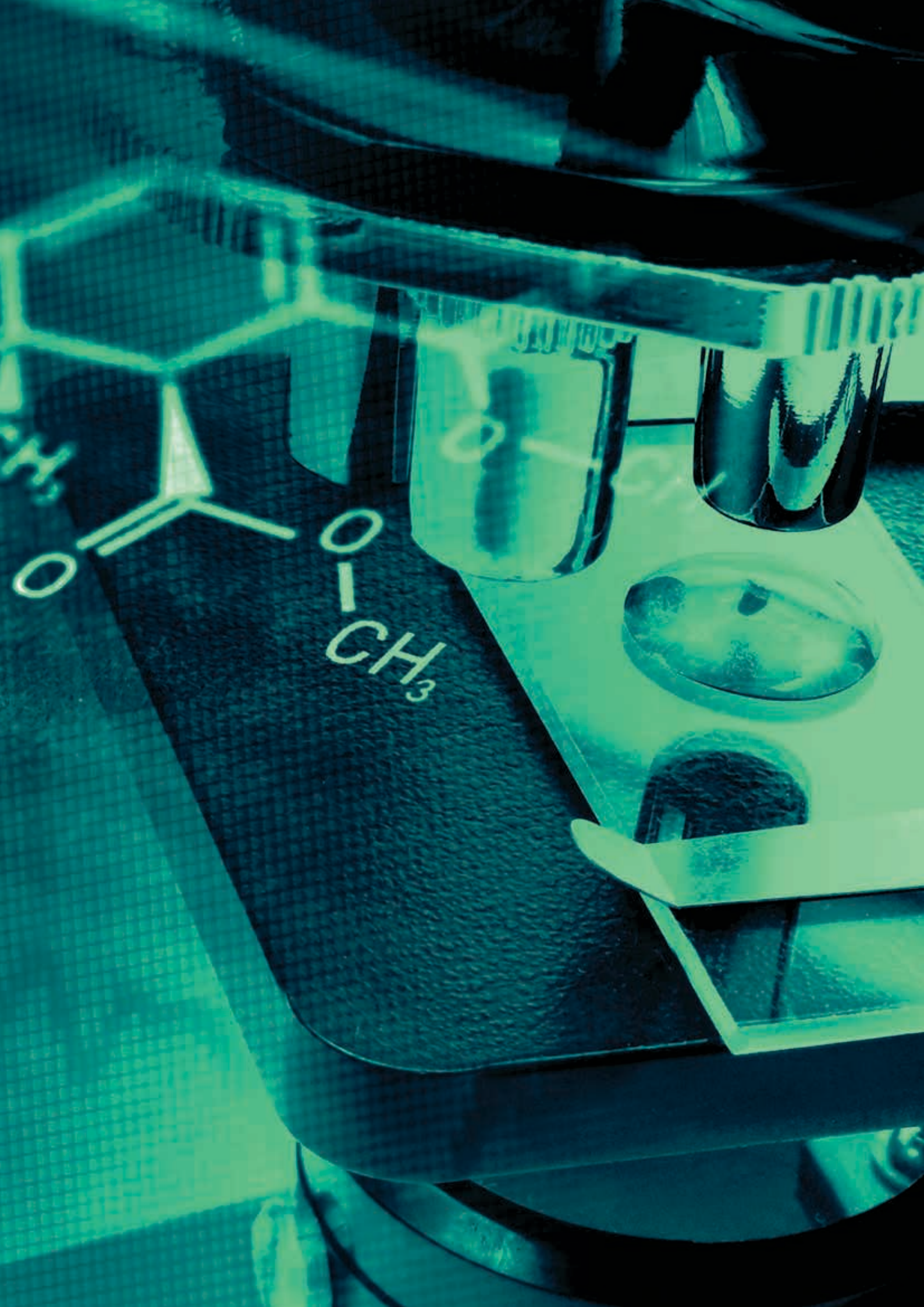
Market and commercial incentives can come through a number of different formats. These include tax incentives, general support for basic research and R&D credits for investments in plant, equipment and other R&D infrastructure.

For the biopharmaceutical sector market and commercial incentives are primarily determined by the existing pricing and reimbursement systems for medicines and health technologies. Most health care systems have in place either direct or indirect mechanisms for regulating and adjusting the pricing and reimbursement of medicines. In Europe this is frequently done directly through pricing and reimbursement negotiations between health ministries or government agencies and biopharmaceutical manufacturers. Prices are often determined through complicated formulas of internal and external reference pricing that compare the cost of medicines in a number of countries. Many countries have also adopted advanced systems of pharmaco-economic and cost-effectiveness analysis and comparisons. In other more diversified systems such as in the US, the price and cost of medicines is to a greater extent influenced by pure market factors. However, payers – be they public bodies such as Medicare and Medicaid or private health insurers – still set formularies and reimbursement guidelines.

The continued rise of health care costs in mature and emerging markets has put more pressure on health authorities and payers to limit future increases in health spending. The manner and extent to which these policies are put in place can have a profound impact on the commercial and market incentives for innovation more broadly in the health sector as well as for biotechnology R&D and particularly in the biopharmaceutical sector.[35] Academic research and modelling suggests that for biopharmaceutical products restrictive pricing and reimbursement policies limit and delay new product launches. For example, a 2007 study investigating the impact of price controls on product launches in several OECD and middle-income economies found that price controls (and other supply side controls) have a significant impact on potential product entry, reducing the likelihood of entry by roughly 75% compared with a market having no price controls.[36]

Legal certainty (including the rule of law)

The general legal environment including as it relates to the rule of law and the rule of law within a business context is crucial to commercialization and business activities.[37] A sound and predictable legal and administrative framework contributes to an environment in which research and ideas can be more successfully commercialized, licensed and marketed. Countries in which administrative and legal justice is harder to attain and in which dispute resolution and enforcement of contracts and rights is a challenge are less likely to encourage general entrepreneurial activity including in the biotech sector. The legal and business environment of a given country can be mapped through existing international indices such as the World Justice Project's *Rule of Law Index*.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4 MAPPING NATIONAL INNOVATION STRATEGIES

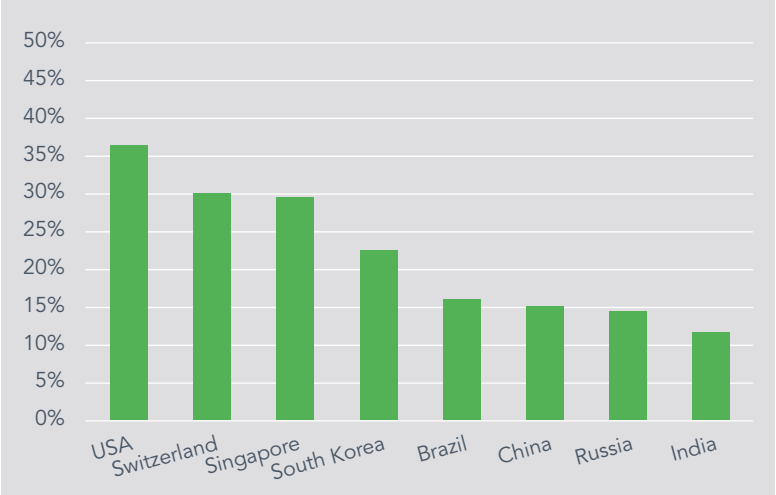
The following section will map the national innovation strategies and policies in place for biotech innovation for eight mature and emerging market economies: Brazil, China, India, Korea, Russia, Singapore, Switzerland and the US.

Using the seven enabling factors outlined above in section 3 as reference points this section will map the policies, factors and best practices that are in place in each of the studied countries. For each country an overview of the NIS and biotechnology policies will be provided together with a table summarizing the key policies and initiatives in place for each of the seven enabling factors including the type of best practices that are in place as well as areas in which there is room for improvement. For the sake of conciseness this section does not include a detailed discussion of each enabling factor for each country. Instead, a deeper discussion and analysis of all seven of the enabling factors for each country included in the study is provided below in Appendix I.

As mentioned above these countries provide a good sample for a number for reasons. First, together they make up a substantial share of world economic output with all, bar Singapore and Switzerland, in the top-15 of the world's largest economies measured by purchasing power parity per the latest figures from the World Bank.[38] Second, in terms of level of development, they are a good mix of, on the one hand, mature economies that rely on innovation to drive economic growth with a number of emerging markets that increasingly are looking for innovation and knowledge-based activities to drive their own economic development. Third, all countries have policies in place and have expressed a desire to develop their respective biotechnology sectors. Finally, there are some notable differences between the countries in terms of their capabilities and specifically their rate of innovativeness. To begin with on a macro basis some countries are considered as being more proficient in promoting and generating both general rates of innovation as well as biotech innovation. At a more granular level some countries also have strengths in particular areas of biotechnology. For example, Brazil has for many years been a pioneer in using and developing GM crops and developing agricultural biotechnology. In 2013 Brazil had 40.3 million hectares of biotech crops under cultivation growing maize, soybeans and cotton; second in the world only to the US.[39] And as will be discussed in more detail below the Brazilian Government through EMBRAPA has for decades been closely involved in the R&D and commercialisation of agricultural biotechnologies.

A good place to start and get a sense of the general level of the biotechnology sector in each country is the *Scientific American Worldview* Scorecard. Published annually since the late 2000s the Scorecard provides an assessment of countries' relative innovative capabilities and successes as they relate to biotechnology.[40] Opposite Figure 2 provides the 2013 Scorecard country scores for the eight countries examined in this briefing paper. The

FIGURE 2: *Scientific American Worldview* Scorecard 2013, countries sampled[41]



Source: Scientific American (2013)

maximum available score in the Scorecard is 50 and is calculated on the basis of performance in a range of biotech related categories and factors.

As would be expected the countries with the highest overall scores are relatively mature markets with well-established life sciences and biotech sectors. Indeed, the US, Switzerland and Singapore were all in the top five for the entire Scorecard and not just in this comparison.

The below discussion echoes one of the broader findings and points made in *Scientific American*'s research and Scorecard: that is, while the overall level of biotech innovation can grow in all the BRICS, interestingly each country already has strengths in specific policy areas and specific enabling factors.

4.1 Brazil

Together with China and India, the emergence of Brazil has been one of the major economic stories of the first decade of the 21st century. The Brazilian economy is now considered one of the most important in the world. Since the late 1990s it has recorded steady GDP growth at just under 3% per year, with a slight dip in 2012 when growth was 0.9%.[42] The latest World Bank national accounts figures from 2012 show total Brazilian GDP at PPP just over USD 2.3trillion.[43] Brazil is a middle income country with an estimated 2012 GDP per capita of USD11,340 per the World Bank.[44] Increased Brazilian economic competitiveness is also reflected in its global economic competitiveness ranking. The World Economic Forum's 2013-14 Global Competitiveness rankings ranked the Brazil as the 56th most competitive economy in the world.[45]

Brazil has a number of innovation policies in place both at the federal and state level with some form of national innovation policies and frameworks having been in place for decades. A number of important government institutions and agencies such as BNDES, FINEP and others have been supporting innovation and investment in Brazil since the 1970s.[46] (The work and role of both FINEP and BNDES are discussed in more detail in Appendix I.) In recent years there have been a number of specific innovation national policies and initiatives introduced. In 2004 the National Innovation Law was passed. This legislation sought to incentivise innovation within the public sector (particularly at universities) and innovation partnerships between academic institutions and the private sector.[47] In 2011 the Brazilian Government launched the *Brasil Maior* plan a, socio-economic development initiative in response to the financial crisis and global economic downturn. This plan places an emphasis on promoting innovation and focuses on developing a number of high tech sectors including ICT, aerospace, biofuels and health care.[48] The Brazilian Ministry of Science, Technology and Innovation has a long standing and active involvement in guiding national innovation policy as does the Ministry of Development, Industry, and Foreign Trade.

With regards to the use and development of biotechnology this has been a part of Brazilian public policy for many years. As mentioned in the Introduction EMBRAPA has long supported the use of biotechnology in agricultural production. Brazil has also relied on biofuels (sugar-cane ethanol) as a primary source of transportation energy since 1975 and the introduction of the Brazilian National Alcohol Program (Proalcool).[49]

Most recently biotechnology was identified as a national strategic priority in 2003 culminating in the 2007 decree No. 6,041 (*Política de Desenvolvimento da Biotecnologia*). This decree focused on building the international competitiveness of Brazilian biotechnology and contains policies relating to direct support for R&D, the building of R&D infrastructure, human capital training and development as well as improvements to the existing regulatory framework and other policies.[50] The decree also established the National Biotechnology Committee (*Comitê Nacional de Biotecnologia*) to coordinate the implementation of the Government's biotechnology policies. The Committee is comprised of 23 Federal-level agencies and ministries all devoted to growing Brazil's biotech sectors. Although the Committee is still in its formative stages in terms of practical application and so far results have been limited, in many ways the Committee can be viewed as a model for other countries trying

to coordinate biotechnology policy right across the government. It provides stakeholders and government officials with a potential central meeting point and body to discuss and coordinate biotechnology policy right across government.

Below Table 2 provides an overview of the best practices in place for the seven enabling factors. It lists policy areas of best practice and areas where there is still room for improvement. The purpose of this table is to give readers a sense for what policies are in place and some of the outputs they have produced. A more detailed discussion of the enabling factors is provided in Appendix I.

TABLE 2: Enabling factors in Brazil

Enabling factors	Success stories	Stumbling blocks
Human capital	• Growing research workforce; doubling in size since 2000 • Ciência sem Fronteiras (Science Without Borders) – promising program to build human capital	• Lack of a skilled work force • Low % of population in tertiary education
Infrastructure for R&D	• Relatively high level of R&D spending • Successful ag-biotech and biofuels partnership programs e.g. BNDES/FINAP PAISS and EMBRAPA-BASF Cultivance	• Health biotech sector capacity less mature than ag-biotech and biofuels • Funding conditions from government agencies • Challenging regulatory environment for clinical trials
Intellectual property protection	• WTO member and TRIPS signatory • 20 year patent term protection provided • 10 year minimum patent term period • RDP in place for agrochemicals	• ANVISA involvement in pharmaceutical patent examination process • RDP not available for biopharmaceuticals for human use • No patentability for isolated microorganisms, (e.g. bacteria and yeast) in industrial and environmental biotech
Regulatory environment	• Biosimilar pathway introduced • Relatively clear regulatory regime in place: ANVISA responsible for regulation of biologics and biosimilars and CTNBio responsible for biotech and GM products	• INPI long processing times and large backlog (estimated at 8-10 years)
Technology transfer frameworks	• Framework in place through 2004 Innovation Law • Patenting and licensing activities at universities and PROs increased sine 2004	• Tech transfer and commercialization still by international comparisons low • Universities have limited tech-transfer capacity • Publication requirements and registration of licensing fees
Market and commercial incentives	• R&D tax credits are in place through Law No. 11.196	• Some R&D tax credits limited through being contingent on issuing of patent – long backlogs at INPI reduce attractiveness • Strict biopharmaceutical pricing environment • Extensive use of IRP
Legal certainty (including the rule of law)	• Government anti-corruption push; new anti-corruption law introduced 2014 • Independent judiciary	• Patent disputes are resolved relatively quickly and preliminary injunctions are also granted, but overall the judiciary and many administrative bodies are over-burdened

4.2 China

China is the 2nd largest economy in the world with an estimated 2012 total national output of USD12.3 trillion measured on a PPP basis.[51] However, measured on a GDP per head basis China is a middle income country with a per capita income of USD6,091 for 2012 at current USD.[52] China is the world's 29th most competitive economy according to the World Economic Forum 2013-14 Global Competitiveness rankings.[53]

Chinese policymakers have for a number of years made innovation a central part of economic and industrial policymaking. The main policy instruments and planning tools include the "Medium- and Long-term Plan for Science and Technology Development 2006-20" launched in 2006 and the more recent Twelfth Five-Year Plan, 2011-2015".[54] Both plans emphasize the need for China to grow its innovation capacity and have set ambitious general targets and sector specific ones, including for biotechnology. For example, the former set as a target the increase of R&D spending as a percentage of GDP to 2% by 2010 and 2.5% at a minimum by 2020.[55] The plan also included economic growth targets linked to technological advances as well as emphasizing the need for the development of an indigenous high-tech capability through a policy of "indigenous innovation".

Within both the Medium- and Long-term Plan for Science and Technology Development and the Twelfth Five-Year Plan biotechnology figures prominently. For example, in the latter the "biological industry" is identified as one of seven strategic industries to be developed and invested in.[56] Specifically, developing an advanced R&D, manufacturing and industrialization capability is outlined as priorities. In terms of concrete investment and size of funds the development of a biotech capacity is set to receive a share of the USD1.7 trillion Chinese policymakers have allocated to the implementation of the plan.[57] The Chinese Government has also made additional pledges of close to USD12 billion for the next five-year plan to the biotechnology sector.[58]

Opposite Table 3 provides an overview of the best practices in place for the seven enabling factors. It lists policy areas of best practice and areas where there is still room for improvement. The purpose of this table is to give readers a sense for what policies are in place and some of the outputs they have produced. A more detailed discussion of the enabling factors is provided in Appendix I.

TABLE 3: Enabling factors in China

Enabling factors	Success stories	Stumbling blocks
Human capital	• Chinese universities becoming more competitive internationally e.g. Peking and Tsinghua • Highest number of university science and technology graduates in the world	• Relatively low level of researchers as a proportion of total workforce • Low level of tertiary education as % of population
Infrastructure for R&D	• High level of R&D spending – absolute and % of GDP • World leader in patenting activity	• Limited R&D clinical capacity: low levels of clinical trials • Low levels of basic and translational research investment
Intellectual property protection	• WTO member and TRIPS signatory • 20 year patent term protection provided • RDP in place NCEs	• Challenging enforcement environment: High rates of counterfeit medicines • No availability of RDP for biologics • Narrow patent protection for biologics
Regulatory environment	• SFDA has by comparison to other emerging markets extensive regulatory framework	• No biosimilar pathway • Regulation of non-innovative biologics outside international best practices • Regulatory requirements and procedures for clinical trials are onerous and delay product registration • Barriers for ag-biotech: i) product must be registered and approved in country of export prior to application for approval in China; and ii) import applications must include viable seeds • Indigenous innovation policies
Technology transfer frameworks	• Legal framework in place since early 2000s • University patenting increases by almost 50% per year • Increased tech transfer, licensing and spin-offs	• Quality of patent applications • Universities have limited capacity to fully commercialize innovations
Market and commercial incentives	• R&D tax credit available and reduced rates of corporation tax and VAT for qualifying high-technology enterprises	• Strict reimbursement policies have limited the number of biological drugs available
Legal certainty (including the rule of law)	• New government led anti-corruption push	• Legal redress, enforcement of contracts and administrative justice inconsistently available or applied

4.3 India

India is the third largest economy in the world with an estimated 2012 total national output of USD4.8 trillion measured on a PPP basis.[59] However, measured on a GDP per head basis India is a lower middle income country with a per capita income of USD1,489 for 2012 at current USD.[60] India is the 60th most competitive economy in the world according to the World Economic Forum 2013-14 Global Competitiveness rankings.[61]

India is in the midst of an ambitious ten-year plan launched in 2010 as the "Decade of Innovation". The plan is characterised by what Indian policymakers have stressed as the need for Indian innovation and growth to be socially inclusive.[62] In particular a point of emphasis has been on defining and aiming policies at frugal innovation targeting services, products and developments for low income individuals. The over-riding theme of India's innovation framework has been the need for innovation to be conducted within a specific Indian/ developing world socio-economic context.[63]

A number of specific policy documents and institutions have been set up to monitor the progress of the plan and outline areas and sectors of strategic interest and priority. They include the National Innovation Council whose role it is to guide Indian innovation and help shape government policies. This Council also has a role as a general voice for and promoter of innovation activities in India and by Indian institutions including higher education and research institutions.

In terms of concrete goals the plan set as a target raising total spending on R&D as a percentage of GDP to 2% with the contribution of industry and private sector spending to double.[64] More recently a government supported venture capital fund, the India Inclusive Innovation Fund, was established.[65] The purpose of the fund is to provide seed capital and investments in small, medium and micro size businesses that specialise in socially needed innovation. The announced budget for the fund is INR5 billion (500 crores).[66]

Looking at biotechnology the Indian biotechnology sector is by international standards and compared to other countries well-developed. The sector has grown considerably over the past decade from a total estimated market size of USD1.1 billion in 2005 to USD4.3 billion in 2013.[67] Biopharmaceuticals constituted the largest value share of the Indian biotechnology industry making up just under two-thirds of total 2013 value. But India is also a large producer of GM crops: the country is the fourth largest grower of ag-biotech crops in the world with 11million hectares of cotton under cultivation in 2013.[68]

In terms of biotechnology specific policies India has had a national biotechnology plan in place for a number of years. As mentioned, biotechnology was included as a strategic priority in the "Decade of Innovation" plan together with other sectors such as the nuclear and defence industries, ICT software and space technology.[69] India has had a separate Department of Biotechnology since the mid-1980s and biotechnology retains a prominent place in national policymaking. For example, in 2007 a "National Biotechnology Development Strategy" was released. This Strategy identified a number of areas for targeted investment and expansion. They included launching public private partnerships with 30% of the total departmental budget allocated to this goal; the expansion of existing university programs; expansion of doctoral and post-doctoral programs; international training programs; the creation of 50 biotech centers for excellence; building of biotech incubators and parks; and a host of other initiatives.[70]

In 2014 a new draft National Biotechnology Strategy was issued building on the 2007 draft. This Draft Strategy hopes to further develop India's biotech capacity by continuing the work commissioned and begun in the 2007 plan as well as targeting specific sub-sectors such as agricultural biotechnology which are now recognised as a priority.[71] Overall the 2014 Strategy shifts the focus to the translational and developmental elements of biotech R&D. Out of the 10 guiding principles identified in the Strategy, four relate to translating R&D into tangible products and services and the targeting of areas of need in the Indian bioeconomy.[72]

The Indian Government also has in place a "National Biofuels Policy". The aim of this policy is to reduce dependence on fossil fuels and shift Indian transportation fuels towards renewable sources.[73]

Below Table 4 provides an overview of the best practices in place for the seven enabling factors. It lists policy areas of best practice and areas where there is still room for improvement. The purpose of this table is to give readers a sense for what policies are in place and some of the outputs they have produced. A more detailed discussion of the enabling factors is provided in Appendix I.

TABLE 4: Enabling factors in India

Enabling factors	Success stories	Stumbling blocks
Human capital	• High total number of academic papers published	• Low university rankings; outside top 200 generally and 100 for life sciences • Low rate of researchers as a percentage of population; lowest among the BRICs
Infrastructure for R&D	• Targeted biotech initiatives in place: Biotechnology Industry Partnership Programme and Small Business Innovation Research Initiative	• Low levels of R&D spending - 0.76% of GDP • Limited R&D clinical capacity: low levels of clinical trials • Low levels of basic and translational research investment • Limited R&D biopharma investment
Intellectual property protection	• WTO member and TRIPS signatory	• Section 3(d) and patentability requirements outside international best practice • No RDP • Use of compulsory licenses and patent revocations • Limited protection of plant varieties
Regulatory environment	• Biosimilar guidelines introduced in 2012	• High rates of counterfeit and substandard drugs • Regulatory authority for biopharmaceuticals and ag-bio is spread out over various layers of the Indian central and state government • Since 2011 no applications for field trials or commercialization of GM seeds approved
Technology transfer frameworks	• Incubators and tech transfer offices in place in some institutions	• Low rates of university patenting • Low rates of tech transfer • Not passed a Bayh-Dole type bill
Market and commercial incentives	• R&D tax credits and credits for special economic zones in place	• New 2013 Drug (Prices Control) Order place strict price controls on large number of biopharmaceuticals
Legal certainty (including the rule of law)	• New 2013 anti-corruption law, Lokpal Act	• Legal redress, enforcement of contracts and administrative justice inconsistently available or applied

4.4 The Republic of Korea

The Republic of Korea (henceforth Korea) is the 12th largest economy in the world with an estimated 2012 total national output of USD1,540 billion measured on a PPP basis.[74] However, measured on a GDP per head basis Korea drops to 31st place with a per capita income of USD22,590 for 2012 at current USD.[75] Korea is the world's 25th most open and competitive economy according to the World Economic Forum 2013-14 Global Competitiveness rankings.[76]

Korea has a number of government bodies that oversee and direct national research and innovation policies. The most important are the Presidential Advisory Council on Science & Technology and the National Science and Technology Council. The latter has been the highest decision-making body on innovation and technology issues since the late 1990s.[77] This National Science and Technology Council is made up of five different committees, each responsible for a specific aspect of national innovation. Additionally, ministries with a science and technology mandate have their own advisory committees to help them formulate policy.[78]

Government research institutes have been critical in the development of the Korean biotech sector as well as science and technology industries in general in research in the public sector. These are semi-autonomous research centres established and funded by the Government, yet independent, non-governmental organisations. Even though their position has been progressively challenged by universities, these institutes were crucial in the technological development of Korean industries over the last four decades.[79]

The Korean Government began promoting biotechnology in the 1980s. After establishing a basic plan for the promotion of biotechnology (Biotech 2000 in 1994) the Government started to coordinate policies and expand its investment in R&D.[80]

Korea has a number of specific biotech policies in place. These range from direct support for R&D activities, to biotech networks, technology transfer and commercialisation bodies. Indeed, the building of the Korean biotechnology industry has benefited immensely from government-backed initiatives through the Law for the Creation and Promotion of the Government Research Institutes enacted in 1999. This program sought to promote technology transfer and the commercialisation of biotechnology through start-ups, venture capital partnerships and spin-offs. As of August 2007, 1,386 ventures had been spun off from these institutes and 482 from universities.[81] The success of this initiative and of the Korean biotechnology sector in general is reflected by the 612 publications and 277 patents issued in 2012 alone.[82]

Korea is targeting the top biotech economies through its *Bio-Vision 2016* plan. By 2016, Korea expects to move from 12th place to 7th worldwide in terms of science-technology published papers, and from 15th to 7th with regards to competiveness in patented technology.[83] Further, it seeks to increase its biotech number of R&D manpower from 9,500 to 17,300, and the industrialized market value of the biotechnology market from KRW2.7 trillion to KRW60 trillion.[84] The *Bio-Vision 2016* is based on four main pillars: (1) achieving multi-ministerial coordination and an efficient budget allocation system, (2) facilitating overall R&D activities, (3) realigning industrial systems and securing commercialization infrastructures, and (4) acquiring social consent for safety ethics. [85]

Below Table 5 provides an overview of the best practices in place for the seven enabling factors. It lists policy areas of best practice and areas where there is still room for improvement. The purpose of this table is to give readers a sense for what policies are in place and some of the outputs they have produced. A more detailed discussion of the enabling factors is provided in Appendix I.

TABLE 5: Enabling factors in Korea

Enabling factors	Success stories	Stumbling blocks
Human capital	• High level of tertiary education in population • Strong growth in life science graduates since 2000 • High level of researchers as % of workforce	• Only two universities in top 100 for life sciences
Infrastructure for R&D	• Highest level of R&D spending % of GDP in OECD • High level of biotech R&D spending • High level of clinical trials	• Outside top-10 in ranking of venture capital attractiveness
Intellectual property protection	• Strong IP environment • RDP available • PTE available	• Patent enforcement at borders can be challenging • Data requirements for pharmaceutical patent applications exceeds international best practices • Uncertainty over implementation of patent linkage regulations
Regulatory environment	• Biosimilar guidelines introduced in 2009 • Biopharmaceutical and biotech regulators generally highly regarded	• Negative public attitudes towards GM foods
Technology transfer frameworks	• High rates of tech transfer – Strong growth in licensing income, patenting since 2000 • Comprehensive legal framework in place • Number of government initiatives and institutes in place to provide help and support	• Licensing and royalty income still behind the US and other high performing countries
Market and commercial incentives	• High tech investment tax credits available	• Strict pricing and reimbursement policies in place with annual price cuts
Legal certainty (including the rule of law)	• Legal environment is generally considered stable and certain	

4.5 Russia

Russia is the 6th largest economy in the world with an estimated 2012 total national output of USD3.373 trillion measured on a PPP basis.[86] However, measured on a GDP per head basis Russia ranks near the bottom quarter of countries worldwide with a per capita income of USD14,037 for 2012 at current USD. [87]

Looking at the competitiveness of the economy, Russia trails many industrialized and emerging economies at 64th place according to the World Economic Forum 2013-14 Global Competitiveness rankings.[88] Recent figures on GDP growth indicate a significant slow-down, dropping from 3.4% in 2012 to 1.8% in 2013.[89] Current international circumstances may have a negative short- to mid-term impact on the Russian economy.[90]

Since the financial crisis in 2008-9, the Russian government has targeted innovation and the development of its science and technology capabilities as a main impetus behind diversifying and modernizing the economy. The government's innovation strategy is focused mainly on enhancing and transforming its basic research capabilities into commercial activities, both in traditionally strong fields such as aerospace and nuclear energy as well as new fields such as nanotechnology, medical technologies and alternative fuels.[91]

The Ministry of Education and Science and the Ministry of Economic Development are the primary bodies charged with overseeing new initiatives on innovation, supported in specific areas and with distinct budgets by several other entities. For example, the President's Commission for Modernization and Technological Development and the Parliamentary High Technology and Innovation Commission are responsible for directing and coordinating R&D policies, with several different agencies controlling the actual allocation of funding.[92] Currently R&D mainly takes place in public research institutions and state-owned enterprises and the large majority of funding has traditionally targeted these bodies, but in the most recent initiatives enhancing academic and private sector R&D has become a major priority.[93]

The Strategy for Innovative Development of the Russian Federation 2020 (2020 Strategy), introduced in 2011, is the main document guiding innovation policy in Russia today.[94] The 2020 Strategy sets out several benchmarks and targets in relation to science and technology indicators including the development of human capital and private sector innovation, promoting of a favorable environment in the public sector and building of international science and technology cooperation.[95] Under the 2020 Strategy umbrella, the Development of Science and Technology Program 2013-2020 is aimed at bolstering basic research capacities and infrastructure needed across key sectors and promoting applied research in cooperation with industry through a combination of public and private funding and fiscal incentives.[96] The measure was developed in cooperation with academia and business representatives.

Biotechnology is one of the Russian government's strategic innovation priorities under the 2020 Strategy. The State Coordination Program for the Development of Biotechnology (BIO 2020) and the Strategy of Development of the Pharmaceutical and Medical Industries (Pharma 2020) are among several policy instruments aimed at building a bio-industry in Russia, starting with creating the necessary human and physical capital.[97] The bulk of the funding is aimed at the bioenergy, biopharmaceuticals, agriculture and food biotechnology and industrial biotechnology fields, relying on a mix of government funding and FDI.[98] The field of biotechnology is also a key focus in research programs of the Russian Academy for Sciences, the Russian Academy of Medical Sciences and the Russian Agriculture Academy. In addition, state-owned enterprise, Rusnano, focused on developing the nanotechnology industry in Russia, co-finances R&D projects and infrastructure building including in the field of biotechnology.[99]

The Russian Foundation for Basic Research provides direct grants to researchers and scientists in basic research.[100] The Foundation for Assistance to Small Innovative Enterprises provides grants and loans to innovative SMEs seeking to commercialize basic research, including in the seed and start-up phases.[101] The Russian Foundation for Technological

Development also offers loans to public-private ventures aimed at bringing to market new technologies.[102]

Below Table 6 provides an overview of the best practices in place for the seven enabling factors. It lists policy areas of best practice and areas where there is still room for improvement. The purpose of this table is to give readers a sense for what policies are in place and some of the outputs they have produced. A more detailed discussion of the enabling factors is provided in Appendix I.

TABLE 6: Enabling factors in Russia

Enabling factors	Success stories	Stumbling blocks
Human capital	• Strong tertiary education enrolment • Relatively large research workforce	• University publications • Life sciences graduates and publications
Infrastructure for R&D	• Development of 'bio-clusters' e.g. Skolkovo Innovation Center • Wide range of tax incentives for R&D companies	• Academic and private sector (not state-owned) R&D • Expenditure on biotech R&D across all sectors • Patenting activity by R&D entities • FDI by research-based companies
Intellectual property protection	• WTO member and TRIPS signatory • Patents available for biologic compounds • RDP regime in place	• Enforcement of biopharmaceutical patents • Implementation of RDP in relation to biologics
Regulatory environment	• Ongoing process of GMP implementation • Planned introduction of pathway for domestic cultivation of GM crops	• Biopharmaceutical and biosimilars approval pathways • Regulatory burden, i.e. local clinical trials, and registration delays • Proposed ban on all GM crops (locally produced and imported)
Technology transfer frameworks	• Framework and funding for university-private sector spin-offs • Funding for high-tech companies-universities' shared R&D facilities • Significant private sector efforts to link research institutions with firms, e.g. Russian Technology Transfer Network	• Patenting by individual universities and public research organizations
Market and commercial incentives	• Fiscal incentives for establishing local presence • Listing of biopharmaceutical products on reimbursement list by brand name in addition to generic name	• Preferential treatment for locally manufactured products in biopharmaceutical pricing and procurement policies • Unaccompanied by other framework conditions sufficient to stimulate investment in production and R&D facilities
Legal certainty (including the rule of law)		• Challenging environment • Problem areas include corruption and availability of legal redress

4.6 Singapore

Singapore is the 42nd largest economy in the world with an estimated 2012 total national output of USD323 billion measured on a PPP basis.[103] However, measured on a GDP per head basis Singapore is one of the richest countries in the world with a per capita income of USD51,709 for 2012 at current USD.[104] Singapore is the world's second most open and competitive economy according to the World Economic Forum 2013-14 Global Competitiveness rankings and has held this position for years.[105]

Singapore recognized the economic significance of expanding and developing a high tech R&D capacity in the late 1980s and early 1990s. Through a number of initiatives the Government targeted the development of an R&D capability specific to high-technology niches in order to promote the advancement of Singapore to a level similar to more mature economies.

Today the Ministry of Trade and Industry is responsible for the coordination of science and technology policies and for the formulation of key economic policies. The Ministry has three main statutory bodies focusing on the implementation of science, technology and innovation policies. The Economic Development Board is the lead government agency that promotes inward FDI and the promotion of the knowledge-based industries. The board focuses on raising the level of private-sector R&D in Singapore by attracting multinational companies to base their corporate R&D activities there.[106] A*STAR focuses on the development of domestic R&D capabilities, which includes the overseeing of public research institutes. Under the A*STAR, the Bio-Medical Research Council promotes R&D and develops human capital in the life sciences, the Science and Engineering Research Council promotes similar outcomes but targets science and engineering. A*STAR at present oversees 21 research institutes, centers and consortia.[107] The Standard Productivity and Innovation Board focuses on promoting entrepreneurship and growth of SMEs through financing.

In terms of biotechnology and the biomedical field the Biopolis initiative started in the early 2000s has fostered regular and engaging public-private partnerships leading to advanced R&D. Singapore is widely viewed as having successfully developed a competitive advantage in the sector of biomedical sciences and accordingly has focused on this sector to promote future growth. The Biomedical Sciences Industry Partnership Office serves as a contact point and acts to match companies' R&D needs to expertise that can be found in research hospitals, academic research institutions and public research institutions in Singapore.[108] Singapore has developed world-class R&D and manufacturing capabilities and has seen tremendous growth in the presence and investment by multinational, research-based companies. Today a number of products are manufactured for global markets in Singapore with government estimates of this manufacturing at circa SGD23 billion.[109] Examples of biological products being manufactured in Singapore include Roche's Lucentis, Avastin and Herceptin.[110]

Opposite Table 7 provides an overview of the best practices in place for the seven enabling factors. It lists policy areas of best practice and areas where there is still room for improvement. The purpose of this table is to give readers a sense for what policies are in place and some of the outputs they have produced. A more detailed discussion of the enabling factors is provided in Appendix I.

TABLE 7: Enabling factors in Singapore

Enabling factors	Success stories	Stumbling blocks
Human capital	• High ranking for National University of Singapore • High level of researchers as % of workforce	• Relatively low level of biotech patenting by National University of Singapore compared to overall rankings
Infrastructure for R&D	• Well-developed biomedical R&D infrastructure e.g. Biopolis • High level of biomedical R&D spending • High level of clinical trials	• Below OECD average on R&D spending as % of GDP
Intellectual property protection	• Strong IP environment • RDP available • PTE available	
Regulatory environment	• Biosimilar guidelines introduced in 2009 • Biopharmaceutical and biotech regulators generally highly regarded	• Innovative biopharma products are generally not approved without prior approval in other jurisdictions
Technology transfer frameworks	• High rates of tech transfer • Government initiatives in place e.g. Biomedical Sciences Industry Partnership Office	• Licensing income still behind top US institutions
Market and commercial incentives	• Generous tax credits available for qualifying R&D	
Legal certainty (including the rule of law)	• Legal environment is generally considered stable and certain	

4.7 Switzerland

Switzerland is the 29th largest economy in the world with an estimated 2012 total national output of USD426 billion measured on a PPP basis.[111] However, measured on a GDP per head basis Switzerland is one of the richest countries in the world with a per capita income of USD78,295 for 2012 at current USD.[112] Switzerland is the world's most open and competitive economy according to the World Economic Forum 2013-14 Global Competitiveness rankings and has dominated these rankings for years.[113]

Switzerland has a number of government bodies that oversee and direct national research and innovation policies. The Federal Department of Home Affairs is responsible for the support of basic research and higher education.[114] It has several agencies responsible for various aspects of national innovation. For example, the State Secretariat for Education and Research is responsible for drafting policy in the areas of science, research and universities.[115] In addition, there is the Swiss National Science Foundation, the country's biggest supporter of basic research; the Board of the Federal Institutes of Technology which oversees and sets policy for federal institutes of technology; and the national innovation promotion agency KTI which is the main public funding source for applied R&D. The KTI is of particular importance as it backs and promotes joint R&D projects between private and public sector institutes.

The quadrennial Education, Research and Technology parliamentary bill outlines the Swiss Governments' blueprint and views for innovation policy.[116] This bill is produced through a lengthy consultation and review process involving all private industry and public stakeholders.[117] Indeed, Switzerland has a tradition of close cooperation between industry and private sector institutions with all of the above public bodies in shaping and developing national innovation policy.

In the biotechnology field Switzerland has a number of specific policies in place. These range from direct support for R&D activities, to biotech networks, technology transfer and commercialisation bodies as well as direct help for start-ups from the federal government. Indeed, the building of the Swiss biotechnology industry has benefited immensely from government-backed initiatives through the National Sciences Foundation and its SPP BioTech program launched in 1992. This program sought to promote technology transfer and the commercialisation of biotechnology through start-ups, venture capital partnerships and spin-offs.[118] The success of this initiative and of the Swiss biotechnology sector in general is reflected in the increased number of patents per capita. Since 2001 Switzerland has seen its patents per capita increase by over 300%; far higher than other top biotech countries.[119]

The Swiss National Science Foundation provides direct grants to researchers and scientists in basic research. The Commission for Technology and Innovation – the federal body responsible for innovation – provides direct assistance to start-ups and small businesses. The Commission assists with technology transfer and linking universities and Swiss start-ups to promote and commercialise new products and technologies.

Below Table 8 provides an overview of the best practices in place for the seven enabling factors. It lists policy areas of best practice and areas where there is still room for improvement. The purpose of this table is to give readers a sense for what policies are in place and some of the outputs they have produced. A more detailed discussion of the enabling factors is provided in Appendix I.

TABLE 8: Enabling factors in Switzerland

Enabling factors	Success stories	Stumbling blocks
Human capital	• High ranking for universities in life sciences – 2 in top 15 • Doubling in no. of life science graduates since 2000	• Below OECD average on number of researchers in relation to the total work force
Infrastructure for R&D	• High level of R&D spending as % of GDP • Well-developed biomedical R&D infrastructure • High level of biotech R&D – 13% of total • High level of clinical trials	• Biomedical R&D spending concentrated in national giants e.g. Novartis, Roche
Intellectual property protection	• Strong IP environment • RDP available • PTE available	
Regulatory environment	• Biopharmaceutical regulators highly regarded	• Since 2005 moratorium on the use of GM crops
Technology transfer frameworks	• High rates of tech transfer • Number of government initiatives and institutes in place to provide help and support e.g. KTI	• Successful commercialization rates still behind US
Market and commercial incentives	• Relatively relaxed P&R policies for non-basic list pharmaceuticals • Tax relief available for biofuels	• Strict P&R policies for biopharmaceuticals on basic insurance list • Limited amount of general R&D tax credits
Legal certainty (including the rule of law)	• Legal environment considered highly stable and certain	

4.8 United States

The United States is the world's largest and most dynamic economy. Even in light of the recent financial crisis and recession, in which GDP fell by close to 6%, the US is the biggest economy in the world measured by total output. The latest World Bank national accounts figures from 2012 show total US GDP at PPP just over USD16 trillion.[120] The US is also one of the world's richest economies in terms of per capita income with an estimated 2012 GDP per capita of USD51,749 per the World Bank.[121] The US economy is also one of the world's most open and innovative. The World Economic Forum's 2013-14 Global Competitiveness rankings ranked the US economy as the fifth most competitive economy in the world.[122]

The Federal Government under President Obama has published a number of strategy documents to promote long-term innovation and strengthen the economy. They include the 2009 document, *A Strategy for American Innovation: Driving Towards Sustainable Growth and Quality Jobs*, and the 2011 follow-up, *A Strategy for American Innovation: Securing our Economic Growth and Prosperity*. Both of these include specific policies on encouraging innovation in the fields of alternative energy, basic research, ICT, health and education.

The first strategy document was released within the first year of the Obama administration and drew heavily on the American Recovery and Reinvestment Act of 2009 and the President's first budget. Both the 2009 stimulus package and budget contained substantial increases in funding for health IT and biomedical research.[123]

Specifically, the stimulus, according to one estimate, provided over USD150 billion in new funds for health care.[124] In terms of life sciences innovation and research, USD19.2 billion of this money was devoted to promote the use of health information technology through direct grants and financial incentives through Medicare and Medicaid.[125] In addition, the legislation provided an additional USD10 billion (of which USD8.2 billion was for direct research grants) to the NIH.

The second document, released in February 2011, builds on the first strategy paper by proposing both new policies as well as expanding existing ones. For example, the 2011 patent reform (America Invents Act) was part of the "New Initiatives" section.[126] Aside from these two quite recent documents, the US Government has a long tradition of supporting basic as well as applied research in the life sciences and biotech field.

There are also state level initiatives that, while not formally part of a national innovation strategy, nevertheless contribute to the strengths of the enabling categories and to the overall capability to perform biotech innovation. In some states, such as California and Massachusetts, these efforts have been real drivers in encouraging biotechnology innovation (discussed in Appendix I).

With regards to biotechnology specific innovation policies the most recent initiative is the President's *National Bioeconomy Blueprint*. This document outlined a range of Federal policy initiatives aimed at furthering the building and development of the biotech sector in the US. The document was organized around five strategic objectives each of which included a range of policies. Opposite Table 9 provides an overview of the five objectives and the major policy areas and/or policy changes each addressed.

Opposite Table 10 provides an overview of the best practices in place for the seven enabling factors. It lists policy areas of best practice and areas where there is still room for improvement. The purpose of this table is to give readers a sense for what policies are in place and some of the outputs they have produced. A more detailed discussion of the enabling factors is provided in Appendix I.

TABLE 9: Summary, *National Bioeconomy Blueprint*[127]

Strategic Objective	Policy Examples
Support R&D investments that will provide the foundation for the future bioeconomy	• Increased coordination and focus by federal agencies on strategic biotech R&D support • Greater emphasis on developing foundational technologies • Increased focus on promoting and supporting interdisciplinary research through NSF and other federal bodies • Use of creative research funding mechanisms such as prizes
Facilitate the transition of bioinventions from research lab to market, including an increased focus on translational and regulatory sciences	• Strategic focus on translating basic research into commercialized products and services • NIH work through National Center for Advancing Translational Sciences and FDA-NIH partnership in research into regulatory sciences • Greater focus by federal agencies in procuring bio-based products • Improved technology transfer frameworks through the NIH, improvements to the Small Business Innovation Research programs and tech transfer from Federal laboratories
Develop and reform regulations to reduce barriers, increase the speed and predictability of regulatory processes, and reduce costs while protecting human and environmental health	• FDA will reform drug and medical device regulatory framework • Parallel review of new products and technologies by FDA and Centers for Medicare & Medicaid Services • USDA reform of regulatory review process
Update training programs and align academic institution incentives with student training for national workforce needs	• Increased focus by Federal Government through academic and jobs training programs on specialized skills including life sciences, bioengineering and biotechnology • Emphasis on job and careers preparation for life science graduates outside academia
Identify and support opportunities for the development of public-private partnerships and precompetitive collaborations – where competitors pool resources, knowledge, and expertise to learn from successes and failures	• Increased emphasis on collaboration between public and private entities • NIH will work with manufacturers and innovators to develop pharmaceutical compounds not in use and using approved and existing therapies for new indications • Public-private partnerships on variety of issues from standardization of protein measurements to food security to development of a genetically modified sugar cane crop

TABLE 10: Enabling factors in the US

Enabling factors	Success stories	Stumbling blocks
Human capital	• Highest performing higher education system in the world • Strongest human capital in life sciences in the world e.g. no. of graduates, institutional rankings etc.	• Below highest performing countries on number of researchers in relation to the total work force
Infrastructure for R&D	• Largest absolute spender on R&D in the world • State of the art biomedical R&D infrastructure • Highest level of patenting in the world – general and biotech • Highest level of clinical trials in the world	• Level of R&D spending as % of GDP below highest performing countries in OECD
Intellectual property protection	• Strong IP environment • RDP available • PTE available	• Uncertainties over patentability of basic biotech inventions e.g. 2013 Molecular Pathology v Myriad Genetics and 2012 Prometheus Laboratories, Inc v Mayo Collaborative Services
Regulatory environment	• Biopharmaceutical regulators highly regarded • Coordinated Framework for Regulation of Biotechnology viewed as successful in promoting biotech sector	• Long processing times at FDA and USDA
Technology transfer frameworks	• Bayh-Dole framework widely viewed as successful in promoting tech transfer • Highest rates of licensing, patenting by universities in world	
Market and commercial incentives	• Relatively free market for pricing of pharmaceuticals	• R&D tax credits not permanent; currently expired
Legal certainty (including the rule of law)	• Legal environment considered stable and certain	• Ranked 19th on Rule of Law Index 2014

5 RECOMMENDATIONS

Creating an environment that promotes creativity, innovation and actual real-life economic gains is not an easy task regardless which sector or industry it is. It requires putting in place a host of enabling factors at the general, more macro level, as well as those that are more specific and targeted at the micro level. This is no different for the biotechnology sector.

The purpose of this paper has been to give an overview of some of the best practices in place internationally that support and enhance biotechnology inputs and outputs. The paper has identified seven enabling factors ranging from the institutional and eco-system level, such as levels of tertiary education and IP environment, to the more biotech specific, such as what type of biomedical and biotech R&D infrastructure does a country have in place and availability of technology transfer laws and mechanisms. Through mapping the policies, factors and best practices that are in place in each of the studied countries the paper has provided an overview of which factors are in place, examples of success stories and where there have been stumbling blocks in each country. It is important to reiterate that the point of reference for this assessment is the development of a globally competitive sector; countries that wish only to develop a sector that is nationally competitive could in principle adopt a more protectionist set of policies. The consequence of such a strategy would however be to limit the ability of local players to succeed in world markets.

For the sake of conciseness the preceding sections have not included a detailed discussion of each enabling factor. Instead, a deeper discussion and analysis of all seven of the enabling factors for each country included in the study is provided below in Appendix I.

Based on the analysis and mapping of the national innovation systems and biotechnology policies and enabling factors in place in the eight case study countries it is possible to piece together six recommendations. They are:

1. **Identify the biotechnology sector as an area of strategic importance** – Identifying the biotechnology sector as an area of strategic importance is the first step in successfully building a national biotechnology policy. By and large most countries studied in this paper have directly or indirectly targeted biotechnology as a technology and industry of strategic importance to national economic development and growth.

2. **Create a national blueprint** – The existence and creation of a blueprint of national biotechnology strategy can be a powerful tool in creating a vision and setting a goal for national aspirations. There are many ways in which governments can provide leadership and direction for the building of a biotechnology capacity. In some countries a more de-centralized, indirect approach has proven to be effective, such as in the US, whereas in others direct government leadership has been instrumental in creating the conditions for success. Examples include Korea and, certainly in the ag-biotech and biofuels sector, Brazil. Regardless of the type of governmental leadership strong governmental inter-agency and departmental coordination is required.

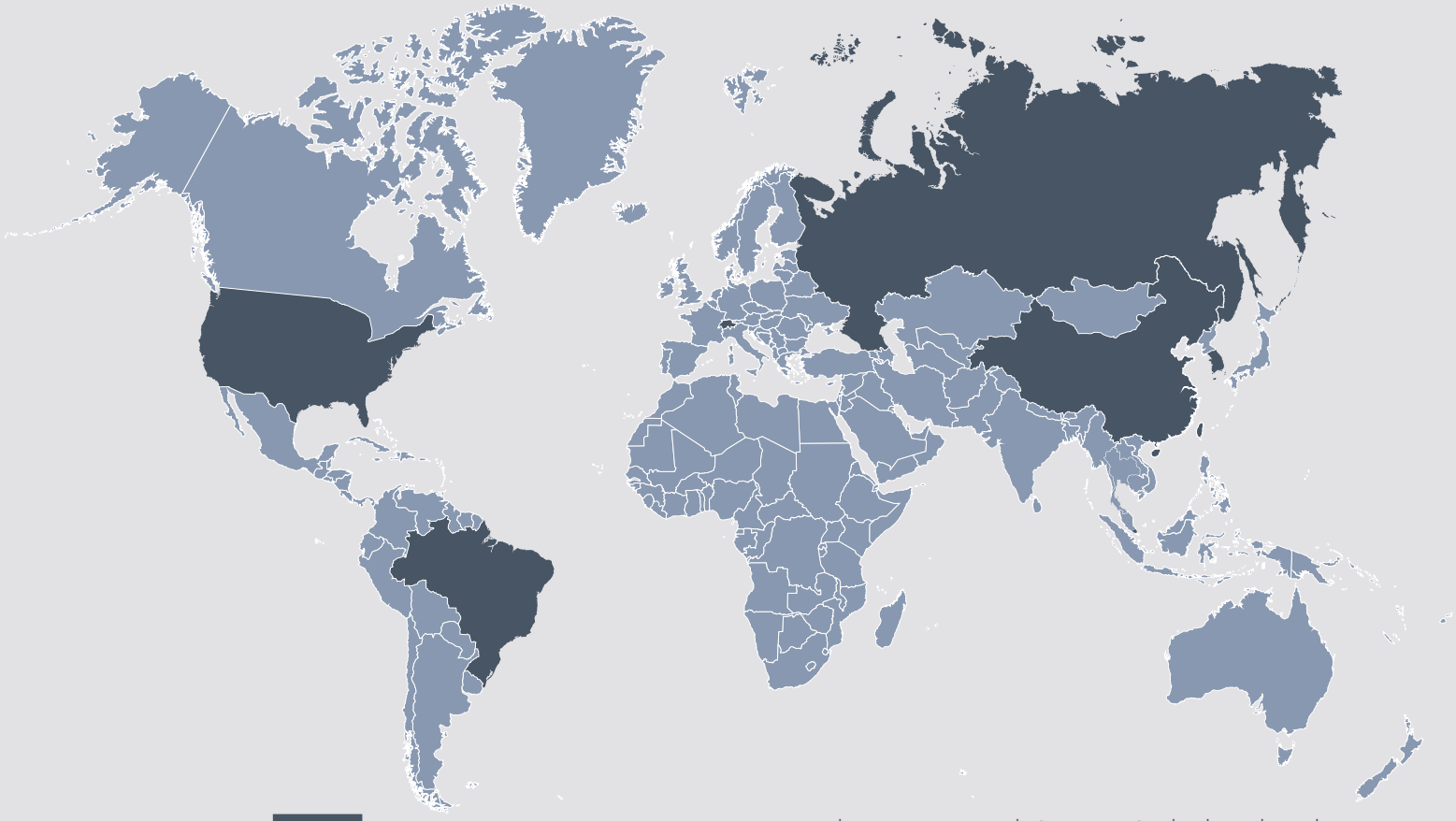
3. **Measure performance** – The measuring of performance of the biotechnology sector in a transparent and systematic fashion is of real importance to understanding progress made challenges remaining in order to allow for mid-course corrections that may be necessary. This can be conducted either through recurring government review or independently through private, academic and non-governmental actors.

4. **Recognize and use existing best practices** – Although no two countries are the same and all face different circumstances, countries can learn from the experiences of each other. International best practices should be shared and repositories of information and resource sharing are all positive and worthwhile undertakings.

5. **Leverage national capabilities** – Understanding and focusing on one's comparative and competitive advantage can lead to the most effective allocation of resources. Country size, scientific and research strengths, geography and biodiversity are all important attributes. Some countries have natural strengths in some biotech sectors whereas others can compete and develop across the board.

6. **Local and international cooperation** – Cooperation and partnerships between public and private, national and international stakeholders can be key in attracting investment and building up a world-class biotech industry. Singapore is a good example of a country which by leveraging its strengths and fully engaging in partnerships between government and the multi-national industry and between the public and private sectors has been able to in a relatively short time span build a cutting edge biomedical and biotech R&D capacity.

APPENDIX I – DETAILED DISCUSSION: THE ENABLING FACTORS AND COUNTRY CASE STUDIES



Brazil

Human capital

Brazilian universities are not widely recognized in general international rankings. No Brazilian university is included on the 2013-14 *Times Higher Education* rankings. However, looking at the life sciences the University of São Paulo is included in the top 100 at 93rd place.[128] In terms of academic and research publications, Brazil has a relatively high number of scientific and technical journal articles published. Data from the World Bank shows that for the latest available year (2009) 12,306 such articles were published.[129] This is an increase of almost 100% since 2000 when 6,407 articles were published.

Examining the number of graduates in higher education and number of researchers Brazil has seen a steady increase in the last decade. In the latest year for which comparable data is available (2011) Brazil had a total of 11 million people in the age group 25-64 attaining some level of tertiary education.[130] As a percentage of the total population in the age group 25-64 that has attained some level of tertiary education, this was a rate of 12%.[131] This is higher than that of China at 4% but behind that of Russia at 53%. Looking at number of researchers in the population the latest (2010) data from the World Bank shows that Brazil had 703 researchers per million people.[132] This is almost a doubling of researchers since 2000 when the equivalent figure per million population was 423. Other economies, such as Russia, during the same time period actually saw their number of researchers shrink.

In terms of promising policy initiatives relating to the building of human capital Brazil in 2011

introduced an international student exchange program *Ciência sem Fronteiras* (Science Without Borders). This program seeks to:

- place Brazilian science and technology students at international universities and research institutions;
- attract foreign science and technology students to study in Brazil;
- internationalize Brazilian higher education institutions by promoting partnerships and collaboration with institutions in other countries; and
- promote the return of Brazilian scientists and graduates to Brazil.[133]

Infrastructure for R&D

Brazil is a major investor in research and development in Latin America. In 2011, Brazilian gross domestic R&D spending totalled USD25.3 billion at PPP.[134] Brazil also has a relatively competitive level of R&D spending as a percentage of GDP in comparison to other BRICS and middle income countries. 2011 figures show R&D spending as a percentage of GDP at 1.16%.[135] This is lower than the OECD average of 2.40%, but higher than Russia, India and Poland and roughly on par with Italy and Spain.[136]

Looking at rates of patenting Brazil is on absolute and per capita terms not a prolific patenting country. In 2010 residents of Brazil were part of the filing of 0.56 patents under the triadic patents family.[137] Similarly, looking at biotechnology patenting rates filed under PCT Brazilian residents were part of 25.9 filings in 2011.[138]

R&D infrastructure and capacity varies from biotech to biotech sector. As explained, while Brazil has traditional strengths in biofuels and agricultural biotech it has a less developed capacity in health biotech. For example, EMBRAPA has through a number of private-public partnerships developed and brought to market new ag-biotech products and technologies. In 2010, for instance, the Cultivance-e soybean was approved for market by CTNBio. This herbicide-tolerant soybean was developed jointly by BASF and EMBRAPA in Brazil all the way from the R&D and laboratory stages to a commercial phase.[139] Similarly for biofuels BNDES and FINEP are supporting the growth and development of the biofuels and sugar-cane ethanol industry through the PAISS plan, an initiative to develop second generation bio-ethanol and new uses of sugarcane biomass.[140]

These partnerships are also growing in importance in the health biotech sector. For example, BNDES has provided direct support and grants for the building and development of R&D and biotechnology manufacturing sites with domestic as well as international private sector partners. In 2013 BNDES in partnership with Novartis began to build a biotechnology plant in the Northeast of Brazil (Pernambuco).[141] Although there are still challenges in translating this support into concrete biopharmaceutical products and fully commercialized technologies (discussed below), nevertheless this is an area of increasing prioritization for the Brazilian Government. BNDES provides a significant amount of funding for biomedical and biopharmaceutical research, manufacturing and innovation. The agency provides direct funding, loans and seed capital. For example, under its *Profarma* program (in 2013 the third phase of the program was renewed) a BRL5 billion budget has been allocated to the pharmaceutical health sector till 2017.[142] In 2013 the agency announced the funding of a separate stream specifically for biotechnology, Profarma-Biotechnology, which will target health biotechnology and the furthering of a domestic R&D capacity.[143] FINEP is also a major provider of research grants to biotech companies and has been providing support for the biotech sector since 2001.[144] Through the INOVAR program it also acts as a source of venture capital, seed and private equity capital.[145]

Brazilian biotech companies appear to be welcoming this support but are also asking for important changes in program rules. For example, in a 2008 survey by *Nature Biotechnology* support from government agencies and development banks such as BNDES and FINEP was significant with over half of the firms surveyed citing them as

major funding sources.[146] Although reliant on these sources of funding a number of the firms surveyed pointed to some challenges in accepting this funding. In particular, they cited requirements to seek approval for the licensing of a technology developed through partial funding from the funding agency and the conditioning of funding on the work being carried out in Brazil even though the technical capacity may not always be present.[147]

With regards to clinical trials although the total number of trials in Brazil is relatively high with currently 3,804 trials being conducted in Brazil out of a regional total of 5,606 in Latin America, Brazil is still behind other markets on an absolute and per capita basis.[148] Overall the clinical trials environment is challenging and clinical research in Brazil is below levels expected. Brazil has less than 2% of the clinical centers in the world performing research and according to local scientists and clinicians it is losing potential trials to other countries due to its regulatory requirements.[149] Approval for clinical research needs to go through two separate bodies (CONEP, the National Commission for Ethics in Research, and ANVISA) and can stretch to over one year compared to three months in the US and EU.[150]

Intellectual property protection

The protection and enforcement of intellectual property rights in Brazil is challenging, particularly in the biopharmaceutical space. Brazil is a signatory of the TRIPS agreement and provides standard 20 year patent protection. Brazil also has a 10 year minimum patent term. However, ANVISA has the right to provide prior consent to pharmaceutical patents that are being examined by the INPI. Consequently, decisions on whether to grant a pharmaceutical patent are not solely based on the examination by patent specialists and officials at INPI, but also by ANVISA. Brazil also does not allow patents for secondary claims for novel uses. With regards to biotechnology patentability rules for biotech are narrow by international comparisons. For example, fundamental research areas in industrial and environmental biotech such as isolated microorganisms (including bacteria and yeast) are not patentable.[151] Existing patent law only allows patents for transgenic microorganisms even though the use of all microorganisms in biotech R&D is increasing and leading to new innovations.[152]

Unlike many OECD economies and a growing number of middle income countries Brazil only provides regulatory data protection of submitted clinical test data for fertilizers, agrochemical products, and pharmaceuticals for veterinary use. Pharmaceuticals for human use are not covered by existing regulations.

The regulatory environment

Biotechnology in Brazil is regulated primarily by ANVISA and CTNBio. ANVISA is responsible for the regulation of biologics as well as biosimilars (a pathway was introduced in 2010/11).[153] CTNBio is responsible for the regulation of all activities (including research and commercialization) of biotech and GM products or technologies.[154]

With regards to the processing of patent applications the INPI continues to have a large backlog of patents (estimated at 8-10 years) and processing times are quite long.[155]

Technology transfer

Brazil has a number of policies and regulations in place to promote the transfer of technology. For instance, a key tenet of the 2004 Innovation Law was to encourage the transfer and commercialization of technologies through incubation services for public researchers and greater encouragement of start-up activities.[156] The law provides incentives including royalty guarantees to inventors. Since 2004 and passage of the law Brazilian universities have increased both their patenting and licensing activities. Although by international comparison still quite limited, there has been growth in the use of IPRs by Brazilian universities and public research bodies. For example, between 2000 and 2007 patenting by universities more than quintupled, from 60 patents to 325.[157] During the same time period, patenting by public research organizations increased from 20 to 39. Similarly, a 2011 survey of 7 universities in Brazil found that patenting, licensing and collaboration was taking place between universities and industry but that this was still at an incipient stage.[158]

Still, there are regulatory and formal requirements in place that limit the attractiveness of licensing. For example, to become effective and binding on third parties licensing agreements must be published in the INPI's *Official Gazette*.[159] Agreements must also be approved by INPI. In addition, there are limitations on feeds and payments between the contracting parties.[160] Exclusive licensing agreements are also subject to more onerous publication requirements than non-exclusive licenses making this process more time-consuming.[161]

Market and commercial incentives

With regards to the biopharmaceutical market relatively strict price controls are in place. IRP is used extensively and is calculated on the lowest average ex-manufacturing price of the biopharmaceutical product in a basket of countries. Countries included in the basket are Australia, Canada, Spain, US, France, Greece, Italy, New Zealand and Portugal as well as the country of origin of the drug. In addition, there is a separate price calculation for "exceptional medicines" to which a "Coefficient Adequacy Price" (*Coeficiente de Adequação de Preço*) or CAP is applied.[162] The CAP is calculated comparing Brazil's GDP with the GDP of the selected reference country. CAP calculation can be applied when the product being priced is not on the market in at least 3 countries in the IRP basket.

Brazil has R&D tax credits in place under Law No. 11.196. These include a potential 60% deduction on corporation tax liability and social contributions.[163] This deduction can also escalate if there is a year-on-year cumulative increase in R&D spending. There is an additional 20% deduction provided once an invention has been patented. However, this is available only once a patent has been issued.

Brazil also has in place policies and laws encouraging local manufacturing in a number of industries including biopharmaceuticals. The 2010 law 12,349 established preferences for businesses producing goods in Brazil with a local preference margin of up to 25% over an equivalent bid from an importing company.[164] As part of the *Brasil Maior* initiative these preference margins were extended to the pharmaceutical industry in 2012 under decrees 7709 and 7713 with margins ranging from 8 or 20 percent.[165]

Legal certainty (including the rule of law)

The Brazilian judiciary is independent although the courts are overburdened and the resolution of contract disputes can be a lengthy process.[166] These challenges are reflected in Brazil's ranking on international indices measuring the rule of law. For example, in the 2014 *Rule of Law* Index Brazil ranked 42nd out of 99 countries mapped.[167] A major anti-corruption law came into effect in 2014 and although the effects remain uncertain it is regarded as having the potential to improve the legal and business environment in Brazil.[168]

China

Human capital

Chinese universities are becoming more competitive internationally. In the 2013-14 *Times Higher Education* rankings Peking University is ranked 45th overall and Tsinghua University is ranked 50th.[169] Looking at academic and research publications, China has a high number of scientific and technical journal articles published. Data from the World Bank shows that for the latest available year (2009) over 74,000 articles were published.[170] This is almost a four-fold increase since 2000 when 18,478 articles were published.

The past decade China has seen tremendous growth in the number of university graduates particularly in science and engineering. The total number of natural science and engineering graduates has jumped from just under 240,000 in 1998 to over 1.1million in 2010 and China produces by far the greatest absolute number of these graduates in the world.[171] China also produces a very high number of doctoral degrees in science and engineering. In 2010 this was close to 31,000 degrees with only the US, at just over 33,000, having a higher rate.[172]

Similarly, a growing share of China's workforce consists of researchers. Looking at the number

of researchers in the population the latest (2010) data from the World Bank shows that China had 863 researchers per million people.[173] This is an increase of close to 60% since 2000 when the equivalent figure per million population was 547.

Infrastructure for R&D

China is a leading investor in research and development. In 2008, gross domestic R&D spending totalled USD208 billion at PPP.[174] In absolute terms this is the second highest level in the world behind only the US. As a percentage of GDP R&D spending in China is quite high compared to other countries. 2012 figures show R&D spending as a percentage of GDP at 1.98%, which is greater than many higher income countries such as Spain (1.30%) and the UK (1.72%) as well as the estimated EU28 average (1.97%).[175] Chinese R&D spending is largely made up of industry spending. The latest data from 2012 show industry expenditure on R&D at 74% of the national total.[176]

Chinese patenting activity has grown tremendously in the past decades. Looking at high-quality patents filed under triadic patenting, the Chinese share of the global total is 2.13% at 2011 figures.[177] This is a significant increase from levels in 2000 when China had a global share of 0.16%. Looking at biotechnology patents China is now one of the top patenting countries in the world. In 2011 the number of patents filed by Chinese residents under the PCT was 443.[178]

China's biomedical and biotech R&D capabilities have expanded and are increasing by the year. For example, in the biopharmaceutical space a growing number of multinational innovators are conducting R&D and investing in R&D facilities in China.[179] Still, despite this growing investment and the obvious appeal of the Chinese biopharmaceutical and biotech market significant challenges remain in the available infrastructure and incentives to conduct research. In particular there are barriers in the regulatory, market and commercial environment which are detailed below.[180] This is reflected in the number of clinical trials conducted in China which is on an absolute and per capita basis small. China currently has 4,793 registered trials in operation.[181]

In terms of direct government funding for science and technology 2012 figures show that central government spending was just over USD36 billion.[182] However, of this less than 15% went towards basic research.[183] Indeed, compared with more mature markets China spends proportionately less of its total R&D budget on research and translational research. Estimates by Battelle and *R&D Magazine* suggest that funding for basic and applied research is less than a quarter of total R&D spending. In contrast in Europe and the US the proportion is well over a third of the total.[184]

Intellectual property protection

Although improving, the protection of IP and enforcement of IPRs in China has long been a challenge to innovators. In particular, while China has some of the legal and regulatory framework to protect IP, the enforcement of IPRs has long been difficult with the counterfeiting of goods (including pharmaceuticals) rife.

As a WTO member China offers standard 20 year patent protection. However, while this protection has been available for biopharmaceuticals the patent examination practice and basis for awarding patents has been out of line with international best practices. First, with regards to biologics the scope of patent protection is narrower in China than in other countries. As a result, it is possible to gain patent protection for only small changes to protein sequences which in other jurisdictions would not be granted.[185] Second, patent examiners commonly require a significant amount of biological data, with examinations often ending in the denial of patents for pharmaceutical products and technologies that have been granted in other jurisdictions. Recent steps, including a change in the interpretation of patent examination guidelines to allow for supplementation of data during patent prosecution, may help resolve this.

Under its WTO commitments and article 35 of the regulations implementing the Drug Administration Law China offers regulatory data protection for submitted test and clinical data for pharmaceutical or agricultural chemical products which utilize new chemical entities. However, it is not clear whether this period of exclusivity also applies to biologics.[186]

The regulatory environment

China's regulatory capabilities are expanding and evolving although a number of challenges remain for all biotech sectors. For example, in the biopharmaceutical space the Chinese drug regulatory authority, the SFDA, has by comparison to many middle income countries a relatively elaborate and detailed regulatory structure in place.[187] Still, a number of barriers remain. First, there is currently no biosimilar pathway in China.[188] Existing regulatory requirements do not consistently condition marketing approval on the submission of complete clinical trials test data showing biosimilarity.[189] Consequently, the regulation of non-innovative biologics is not in line with international best practices. Second, current regulatory requirements and procedures for clinical trials are by international comparisons onerous and delay product registration. Finally, there are also challenges in existing pharmacovigilance programs with reporting requirements for ADRs by manufacturers being an area in need of reform and enforcement.[190]

With regards to agricultural biotechnology the Ministry of Agriculture and the National Biosafety Committee are responsible for the regulation and approval of imported agricultural GM products and/or the domestic production of GM products in China.[191] However, for this sector there are a number of regulatory related barriers to market entry. They include: the requirement that a product must be registered and approved in the country of export prior to an application for approval can be made in China; and a requirement that import applications include viable seeds.[192] The latter requirement has raised concerns among manufacturers about the protection of their IP.[193]

Finally and more broadly, since the mid-2000s, China has introduced and implemented a range of policies making access to the Chinese market conditional on the sharing of technology and IP with domestic entities. These policies include the transfer of proprietary technologies in procurement, joint ventures, and standardization processes; local manufacturing requirements; and limitations on investment by foreign entities, without guarantee they will be protected from unauthorized disclosure, duplication, distribution, and use. Although some policies have been revoked at the central level at the provincial and local level these policies are still in place and continue to be introduced.

Technology transfer

With regards to technology transfer and IP commercialization, Chinese universities have been encouraged since the mid-1980s to manage and use inventions produced by their researchers, although formal ownership was retained by the state. This was changed through a number of reform initiatives culminating in the 2002 "Opinion on Exerting the Role of Universities in Science and Technological Innovation".[194] Combined with the overall growth and development of the Chinese economy, the result of this relative freedom for universities and researchers to pursue commercial ventures has been a sharp increase in university patenting, patent and technology transfers and number of spin-offs. University patenting has increased dramatically and been a major contributor to China's rise as one of the world's top patenting nations. In 2006, resident university patent applications totaled 17,312, representing just under 15% of total resident applications.[195] Since 2000, university patenting has increased by almost 50% per year. Technology transfer has also increased. The number of patent transfers rose from 298 in 1999 to 532 in 2002. During the same period technology transfers also increased from about 4,000 to 5,600.[196] In addition, university spin-offs have increased in large part due to an incentive structure that allows researchers to retain at least 50% of income from commercialized technologies.[197]

Nevertheless there remain important challenges. First, many Chinese universities and research institutes have explicitly had a policy of promotion and evaluation based in part on number of patent applications. According to some studies patenting has become a substitute for peer-reviewed publications.[198] Second, there is still a lack of experience and tradition with regards to commercialization activities especially in the life sciences. According to industry sources Chinese universities and research institutions (with a few exceptions) do not have the institutional and professional experience to fully commercialise their research.[199]

Market and commercial incentives

With regards to the biopharmaceutical market relatively strict reimbursement policies have limited the number of biological drugs available on the market. For example, the National Reimbursement Drug List does not include any monoclonal antibodies (used for example in cancer treatment) and there is also limited availability on provincial drugs lists.[200]

More generally, China does have a number of tax incentives in place to encourage R&D and high technology manufacturing. For example, since 2010 a R&D tax credit is in place and special, reduced rates of corporation tax and VAT are available for qualifying high-technology enterprises.[201]

Legal certainty (including the rule of law)

The Chinese legal environment can be challenging generally and for specific industries and sectors. Legal redress, enforcement of contracts and administrative justice can be difficult and inconsistently available or applied. In the 2013-14 *Global Rule of Law Index* China was ranked 76th out of 99 countries.

India

Human capital

Indian universities are not part of the top ranked universities in the world. For example, in the 2013-14 *Times Higher Education* rankings no Indian university is ranked in the top 200 universities generally or in the top 100 universities for life sciences.[202] Looking at academic publications India is ranked 11th on the total number of academic papers published in Thomson Reuters-indexed journals from January 2001 through August 31, 2011.[203] However, looking at citations per paper – which implies impact of academic work – India is ranked outside of the top 20 with 5.9 citations per paper.[204]

In terms of number of researchers per million population India is not a top performer.[205] There is a paucity of data but the most recent figures from the World Bank (2005) show that India had 135 researchers per million population.[206] This is the lowest rate among the BRICS and significantly behind other developed OECD economies.

Infrastructure for R&D

On an absolute basis India is a relatively big investor in research and development on par with spending in Italy, Spain, Brazil and Canada.[207] In 2007 Indian gross domestic R&D spending totalled USD24.3billion at PPP.[208] However, on a per capita basis and as a percentage of GDP Indian R&D spending is low. 2007 figures show total R&D expenditure at 0.76% of GDP.[209] This is significantly behind the other BRIC economies and mature OECD economies. Moreover, the majority of this R&D is government funded at 66% which is the inverse to spending patterns in other countries.[210]

Looking at rates of general as well as biotechnology specific patenting as an indicator of R&D activity, India is more competitive in some areas than others. For example, examining high-quality patents filed under triadic patenting, Indian residents filed 27 such patents in 2010 out of a global total of 3,017.[211] In the biotechnology field Indian inventors filed 70 patents under the PCT route in 2011 which compares favorably with both Russia and Brazil.[212]

In terms of biotech infrastructure and R&D capacity, the Department of Biotechnology has through its policy initiatives expanded and increased India's biotech capacity and infrastructure. For example, through the Biotechnology Industry Partnership Programme partnerships have been developed and agreements signed with close to 100 companies with a budget of INR8 billion (797 crore).[213] Similarly, the Small Business Innovation Research Initiative provides grants to SMEs with 134 such projects being funded since 2007.[214] In both these programs the private sector financial contribution has been significant.

However, while these initiatives are promising they are still quite small. Relatively speaking India does not have an advanced R&D

infrastructure and does not attract the type of investment required to build this capacity. Looking for example at biopharmaceutical investment and R&D funding by multinationals, the percentage of R&D budgets being spent in India is small. In 2010 India attracted USD0.7 billion in pharmaceutical R&D and USD0.8 billion in 2011.[215] The main investors in biopharmaceutical R&D in India are domestic generic companies. However, a significant proportion of their investments are not in developing new innovative products and technologies but on developing generic drugs.[216]

Similarly, when looking more specifically at the advanced manufacturing and R&D facilities required for biologics, the latest survey evidence suggests that India's attractiveness has dropped since 2012.[217] Levels of clinical trials are also quite low on both a relative and absolute basis. As of 2014 2,407 clinical trials were being conducted in India.[218] This is behind all other BRICS as well as more mature economies such as Korea.

Intellectual property protection

The protection of IP and enforcement of IPRs in India has long been a challenge to innovators. Although India provides standard patent protection under TRIPS recent policies have undermined the actual availability of this protection. For example, patent protection in India has not been awarded to products that enjoy protection in most countries around the world. At the time the Indian Supreme Court denied a patent for Novartis' Glivec, the drug enjoyed patent protection in nearly 40 countries including other BRICS like China and Russia.[219]

Indian patent law has in place an additional requirement to the international norms of patentability that goes beyond the required novelty, inventive step and industrial applicability requirements. Under Section 3(d) of the Indian Patent Act, there is an additional "fourth hurdle" with regards to inventive step and enhanced efficacy that limits patentability for certain types of pharmaceutical inventions and chemical compounds. This has led to a number of patent revocations in recent years. India has also made use of the threat and actual issuing of compulsory licenses for biopharmaceutical products. Since 2006 India has been involved in almost half of all major international CL disputes. In 2012 Bayer was instructed by the Indian patent office to agree to have Bayer's cancer drug, Nexavar, duplicated by a local generic company through a CL. With regards to patent revocations Roche in 2012 had its patent for the hepatitis C drug, Pegasys, retracted by the Intellectual Property Appellate Board of India due to a simple design that could be copied rather easily by competitors. Similarly, the Delhi Patent Office also revoked the patent for the drug Sutent in 2012. This revocation was in response to a post-grant opposition and based on an alleged lack of inventive step. The drug is currently under patent in the US.[220]

Furthermore, India does not offer regulatory data protection for clinical test data submitted during market authorization applications.

With regards to ag-biotech India's current legal framework on the protection of plant varieties differs from international best practices as found with the International Union for the Protection of New Varieties of Plants. Specifically, requirements relating to the submission process, compulsory deposit of parental lines to a public gene bank, and potential claims of benefit sharing and compensation if crop performance is less than expected make this framework less attractive than in other countries.[221]

The regulatory environment

India's regulatory environment faces a number of critical challenges, to begin with biopharmaceuticals. To begin with biopharmaceuticals. The availability of counterfeit and substandard medicines is by many estimates the highest in the world. For instance, in 2008 the OECD estimated that 75% of the world's total supply of counterfeited and/or substandard drugs came from India.[222] Indian drug regulations have not been developed in a centralized and deliberate fashion. There exists no equivalent to the Chinese SFDA, the US FDA or the EU's EMA. Instead, authority over medicines and pharmaceutical drugs is spread out over various layers of the Indian

central government and state governments. On many critical issues of quality and safety regulations, there is divided authority between Central Government and the governments of individual Indian States. For example, while the CSDC is charged with laying down standards of drugs and approving new drugs, State governments have the responsibility for approving drug formulations. That is, State governments approve what substances (for example, excipients in generic drugs) go into the manufacturing process and medicines. Similarly, while the central authorities are responsible for regulating clinical research and the testing of drugs in Central Drug Labs, they are only in charge of approving licenses for the manufacture of specific categories of drugs: blood banks, large volume parenterals and vaccine and sera. State governments hold responsibility for, firstly, the majority of licensing of drug manufacturing and sales; secondly, licensing drug testing laboratories; and, finally, pre- and post- licensing inspection. State governments have the ultimate responsibility when it comes to ensuring that good GMP practices and safety and quality procedures are in place and are being followed by manufacturers, sellers and distributors of medicines and pharmaceuticals. While some state governments have good inspection methods and rates, others do not. Standards invariably vary and with it the quality and safety of medicines in India.[223]

With regards to agricultural biotechnology the current regulatory structure involves both central government institutions and state governments.[224] At the central level the Genetic Engineering Appraisal Committee is responsible for product approval for imports of biotech products and commercialization. State governments are involved in the regulation of field trials in their respective states by the need to consent to trials taking place. Since 2011 no applications for field trials or commercialization have been approved by the Genetic Engineering Appraisal Committee. Attempts have been made to create a centralized biotechnology and biosafety authority replacing the existing structure. This was first pronounced in the 2007 National Biotechnology Plan and was reiterated in the draft 2014 plan.[225]

India introduced biosimilar guidelines in 2012. These guidelines incorporate elements of the pathways in place in the US and EU. However, a key difference is the lack of market exclusivity provided through regulatory data protection.[226] Moreover, prior to the publication of these guidelines India had approved a number of non-innovative biologics under its old regulatory structure.[227]

Technology transfer

Technology transfer in India is still in many respects at the early stages. While universities and public research organizations are much more prolific than they were in the past, the successful transfer of technologies is still relatively low. For example, measured by university patent applications under the PCT by a range of middle- and low-income countries between 1980 and 2010, India had a share of 7%.[228] This puts India in third place, just behind Brazil at 8%, but far below China, which dominates patenting by middle- and low-income countries at 64% of the total.[229] However, with regard to public research organizations, India is much closer to China's share, measured as a percentage of the total PCT university patent applications for low- and middle-income countries. Between 1980 and 2010, India had a share of 36%, just under China's 41%.[230] The majority of these patent applications were tied to just one organization: the Council of Scientific and Industrial Research. This Council was the largest domestic patentee and has since the early 1990s accounted for 80% of public sector patents.[231]

As these figures suggest, technology transfer and university patenting rates are still relatively low. Indeed, very few Indian universities have functioning TTOs. The institutions with the most advanced and developed technology transfer capabilities are the Indian Institutes for Technology. The institutes in Madras and Mumbai have technology and start-up incubators in place and have produced a growing number of start-ups in the past few years.[232] To encourage greater rates of technology transfer and commercialization India has since the mid-2000s explored developing its own private-public technology transfer framework, the Protection and Utilisation

of Public Funded Intellectual Property Bill, introduced in 2008.[233] Although a step in the right direction the draft bill contained a number of potentially challenging aspects. This includes uncertainties over ownership of the IP generated and the Government's ability to refuse title to the IP on grounds of a "public interest" case which was not adequately defined.[234] The bill was reported out of committee in 2010, but actual legislation is still not in place. In fact introduction and passage of the bill and corresponding legislation is included in the draft 2014 National Biotechnology Plan.[235]

Market and commercial incentives

With regards to the biopharmaceutical market relatively strict price controls are in place for drugs and pharmaceuticals available through the National List of Essential Medicines. New price calculations through a Drug (Prices Control) Order were released by the National Pharmaceutical Pricing Authority in May 2013.[236] These calculations expand the number of biopharmaceuticals subject to price controls to 652.[237]

Legal certainty (including the rule of law)

The Indian legal environment presents a number of challenges. Legal redress, enforcement of contracts and administrative justice are not always available or consistently applied. In the 2013-14 *Global Rule of Law Index* India was ranked 66th out of 99 countries. A wide-spanning anti-corruption law, the *Lokpal Act*, was passed in 2013 with high hopes for reducing corruption and graft.[238]

Korea

Human capital

Korean universities are relatively well regarded, particularly in the biomedical and life science fields. For example, in the *Times Higher Education* rankings the Seoul National University and the Pohang University of Science and Technology (Postech) are respectively ranked 80th and 83th in the life sciences ranking.[239] As a percentage of the total population in the age group 25-64 that has attained some level of tertiary education, Korea had a 2011 rate of 40% which is above the OECD average of 32%.[240] In terms of the life sciences, Korea had 12,466 life sciences graduates in 2011 which is an increase of 136% since 2000.[241]

In terms of number of researchers in full-time equivalent Korea had 288,901 in 2011 the latest year for which OECD figures are available.[242] Looking at the number of researchers in relation to the total work force, Korea was ahead of the OECD average of 7.7. In 2011 Korea had 11.9 total researchers in full-time equivalent per thousand of total employment.[243]

Infrastructure for R&D

Korea is a leading investor in research and development. In 2011, Korean gross domestic R&D spending totalled roughly USD60 billion at PPP.[244] In absolute terms this represents a world-leading number (5th place). When measured as a percentage of GDP 2012 figures show R&D spending at 4.36%.[245] This is the highest figure in the OECD.[246] Korean R&D spending is largely made up of private sector and industry spending. The latest data from 2011 show industry expenditure on R&D at 74% of the national total.[247] Biotech R&D accounted for 2.72% of overall industry R&D spending.[248]

Korea has quite advanced medical and biomedical research facilities. As mentioned, two of its life science and medical universities are ranked in the global top-100. Also indicative of the competitive clinical environment is the high level of clinical trials. Korea currently has 5,241 clinical trials in operation.[249]

Korean patenting activity is substantially higher than other larger countries. Looking at high-quality patents filed under triadic patenting, the Korean share of the global total is 4.00% at 2011 figures.[250] More significantly, Koreans have a high level of patenting intensity: between 2007 and 2009 40 patents were filed per million people.[251] This was slightly above the average rate of 38 in the OECD. With regards to biotechnology patenting activity in 2011 the number of patents filed by Korean residents under the PCT was 477.[252]

Pharmaceutical research by the Korean pharmaceutical industry made up 2.26% of total R&D expenditure at KRW863 million in 2011.[253] The share of biopharmaceutical products as a total percentage of pharmaceuticals went up from 6.5% in 2007 to 9.3% in 2010.[254] In 2009, it was estimated that there were more than 600 biotechnology companies in Korea. Of these, 61% operate in biopharmaceuticals with the remaining being dedicated to areas such as bio-foods, bio-chemicals, bio-environments, bio-energy and resources, bio-process and bio-equipment, and bio-electronics and bio-informatics.[255]

Biotech R&D is receiving a huge boost from the 2010 "Life Industry 2020 Development Strategy". Under this program the Korean Government will invest approximately USD6.5 billion over 10 years in building up life sciences infrastructure.[256]

Venture capital in Korea is relatively well-established. In particular, the percentage of GDP going to both early and late stage venture capital investment was one of the highest in the world at 0.054% of GDP in 2011.[257] However, Korea could be more attractive as a VC market. According to the IESE 2013 VC and PE Attractiveness Index, Korea is outside the top-10 in the world (ranked 15th).[258]

Intellectual property protection

Overall, Korea has a strong system of protecting IP and enforcing IPRs. Korea provides a standard 20 year term of protection for patents as well as a 5 year term of patent restoration for pharmaceuticals. In conjunction with the US-Korea Free Trade Agreement, Korea also introduced a 5 year regulatory data protection period similar to that in the US.

Korea introduced legislation relating to the development of orphan drugs in 2003. Incentives include marketing rights for 6 years and nationally funded research programs along with support from the Ministry of Family Affairs, Health and Welfare and the Korean Centers for Disease Control and Prevention to encourage the research and development of orphan drugs.[259]

Still, there remain some important challenges. For example, with regards to biopharmaceutical patents Korean patent law and examiners require vast amounts of pharmacological data to be submitted in the original patent application, not, as is the more common international practice, of submitting such data during either patent prosecution or post-grant validity proceedings.[260]

There also remains uncertainty over the implementation of the patent linkage system agreed between the US and Korea. Specifically, the requirements on innovators to provide lengthy descriptions of the patent and patent claims in question raises uncertainty for innovators and generics alike.[261]

Finally, there are some challenges with regards to the enforcement of IPRs, particularly patent rights. For example, rights-holders cannot apply directly to Korean customs authorities for the suspension of suspected patent infringing goods entering Korea as they can with copyright and trademark infringing goods. Instead, an application must be lodged with the Korean Trade Commission which can order a suspension. Evidence suggests that the Commission has investigated relatively few such applications and that, consequently, the patent enforcement environment in Korea could be improved.[262]

The regulatory environment

Korea has a relatively strong clinical and regulatory environment. For biopharmaceuticals the Ministry of Food and Drug Safety (formerly the Korean Food and Drug Administration) is responsible for the authorisation and safety supervision of pharmaceuticals. The agency is highly regarded internationally and has been recently praised by the FDA.[263] Korea introduced a biosimilar pathway in 2009.

Korea has ratified the Cartagena Protocol on Biosafety in 2007 and implemented this through the Living Modified Organism Act in 2008. Imports of biotech grains as well as genetically engineered animals are regulated under this Act. Korea does not commercially produce any biotech crops and most research is still at the laboratory stage.[264] Further, commercialization is expected to take some extra time, as it will be entirely dependent on getting Korean farmers

to first recognize the benefits and adopt this technology.[265] Public attitudes towards biotech are somewhat contradictory. The public is favourable to the use of biotechnology in human and animal research and in the treatment of disease, while they tend to have negative views towards the use of biotech in the production of food. As a consequence, the majority of public funding for biotechnology R&D is directed towards non-agricultural projects in the fields of biomedicine, stem cell research, cloning, and gene therapy.[266]

Technology transfer

Korea early on recognized the importance of closer working relations between universities and businesses in building an innovation and knowledge based economy. The legislative framework has been changed, with new laws and regulations introduced to encourage technology transfer, commercialization and collaboration between universities and businesses.[267] These include the 2000 Technology Transfer Promotion Act as well as more recent laws such as the Technology Transfer and Commercialization Promotion Act. These acts provide direct support, opportunities and incentives for universities and research institutions to engage in technology transfer and commercialization activities. This includes support for tech transfer infrastructure, financial support through investment and loans to help small and medium enterprises and concessions with regards to state property and IP. There are also legal provisions for facilitating international cooperation and mutual tech transfer and commercialization between national and foreign governments, enterprises, colleges and universities, research institutes, and organizations.[268] Since the early 2000s and the initial interest in developing technology transfer Korea has seen a steady growth in university licensing income and patent rates.[269]

There are also a range of schemes in place in order to improve knowledge flow and commercialization from public sector research. Examples include the Technology Holding Company system (which seeks to promote spin-offs of venture capital businesses from universities and research institutes); the Leaders in Industry-University Programme and the Brain Korea Programme, which are aimed at promoting collaboration between industry and academia.[270]

Examples of government tech transfer institutions include the Korea Institute for Advancement of Technology which is a public institute founded in 2009. Its activities include developing a national technology strategy, supporting technology transfer and commercialization, and fostering international technological cooperation. In 2012, the institute had an annual budget of USD1.17 billion and 257 employees.[271]

Market and commercial incentives

Korea has relatively strict biopharmaceutical pricing and reimbursement policies in place. A positive list system was introduced in December 2006. Price negotiations are used for drugs and pharmaceuticals available through basic insurance. There have been cuts for a number of years and cost containment policies are in place.[272]

Korea offers tax reductions for investments in sectors involving high technology that fulfil the following requirements: (1) the technology shall have a profound economic or technological impact on the national economy, and be essential to improving the industrial structure and strengthening industrial competitiveness; (2) the technology shall have been introduced to the country less than 3 years prior, or shall be economically and technologically superior to already introduced technologies even though it was introduced more than 3 years ago; and (3) most of the processes using the actual technology shall be carried out domestically. The products and technology items falling under the above category are listed by the Ministry of Strategy and Finance.[273]

Legal certainty (including the rule of law)

The Korean legal environment is generally considered stable and certain. Legal redress, enforcement of contracts and administrative justice are generally available and viewed as effective. Korea ranked 14th overall in the WJP *Rule of Law Index* 2014 and was among the most improved countries during the past year.[274]

Russia

Human capital

Russian universities are not widely recognized in international rankings. For example, no Russian university is included on the 2013/14 *Times Higher Education* rankings, both generally and in terms of the life sciences. Looking at academic and research publications, the number of scientific and technical journal articles published in Russia has dropped since 2000. Data from the World Bank shows that for the latest available year (2009) only 14,106 articles were published, while in 2000 the number was 17,180.[275] This is in contrast to other major emerging economies which all experienced at least a two-fold increase during the same period. Russia has also seen little growth in the number of science and engineering graduates, particularly in the life sciences. During 2001-2010, the number of doctoral degrees in natural sciences and engineering remained about 10,000, which is on par with Germany and the UK, but lower than China and the US.[276]

However, Russians have traditionally had a high level of enrolment in tertiary education. As a percentage of the total population in the age group 25-64 that has attained some level of tertiary education, Russia had a 2011 rate of 53%, which is higher than any OECD country and well above the OECD average of 32%.[277] Similarly, although the number has dropped somewhat in the last decade, Russia has a high number of researchers in the population. The latest data (2010) from the World Bank shows that Russia had 3,092 researchers per million people, in comparison to 703 in Brazil and 863 in China (in 2009).[278]

Moreover, one of the aims of the 2020 Strategy is, apart from existing public research institutions, to build world class science and technology universities. Programs and funding have focused on creating a network of 27 research universities and attracting leading international scientists.[279] In addition, the Innovative Universities program provides grants to close to 60 Russian universities for strengthening and training infrastructure and staff.[280]

In terms of biotech specifically, although not included on certain leading rankings such as the Milken Institute's biotechnology publication and patent rankings, Russia ranks 13th out of 147 countries on the Thomson Reuters "Essential Science Indicators", with over 265,000 publications in accredited journals over the period 2001-2011.[281]

Infrastructure for R&D

Among developing countries, while Russia is a significant investor in research and development, important gaps exist. In 2012, gross domestic R&D spending totaled USD37.8 billion at PPP.[282] Nevertheless, although in absolute terms this is a fairly high number relative to other emerging economies (with the exception of China), when measured as a percentage of GDP Russia's spending on R&D appears to be much lower. 2012 figures show R&D spending as a percentage of GDP at 1.12%.[283] This is well behind Brazil (1.16%) and China (1.98%) as well as the OECD average of 2.40%.[284] Russian R&D spending is largely made up of government spending – the latest data from 2012 show government expenditure on R&D at 67.8% of the national total, while industry expenditure was at only 27.2%.[285] However, among government-funded R&D only 9.3% is performed by universities, reflecting the emphasis on basic research conducted in public research institutions as opposed to academic institutions.[286] According to 2011 OECD data, biotechnological R&D accounted for only a small percentage of business enterprise R&D (under 1%).[287] In relation to government and higher education R&D expenditure, though somewhat higher biotech R&D still only represented a little over 7% of total government and higher education sectors R&D spending.[288]

Russian patenting activity has remained at a relatively low level for the last decade. Looking at high-quality patents filed under triadic patenting, the Russian share of the global total is 0.11% at 2011 figures.[289] With regards to biotechnology patenting activity in 2011 the number of patents filed by Russian residents under the PCT was 38, very low in comparison to developed countries and key emerging economies such as China (with 443 biotech patents filed in 2011).[290]

Russia's biomedical and biotechnological R&D capabilities are in the initial stages of development. Despite the market potential in Russia and the government's desire to attract investment in R&D in recent years, these factors have not yet generated significant investment in biotech R&D in Russia. For example, the biopharmaceutical space has seen a few large investments by international research-based companies, such as in the St. Petersburg pharmaceutical 'cluster', as well as a special fund of RUB500 million – RUB1.5 billion devoted to bio-clusters and biotech start-ups established by the Russian Venture Company, a government fund of funds.[291] However, on the whole significant challenges remain in terms of incentives for foreign companies with R&D capabilities and know-how to invest in facilities and conduct biopharmaceutical R&D in Russia. In particular, government policies providing preferential treatment to domestic manufacturers and locally-produced products, which are detailed in below sections, have made it difficult for companies to establish more than manufacturing and production facilities in Russia. For instance, the number of clinical trials conducted in Russia is still on an absolute and per capita basis fairly small. Russia currently has 2,661 registered trials in operation.[292]

One significant effort to attract and stimulate investment in R&D is the Skolkovo Innovation Center outside of Moscow, including a planned 'biomedical cluster' and R&D center involving international and local scientists, companies and venture capital funds. In the early stages of development, the cluster has reportedly established strategic partnerships with over 100 companies including Johnson & Johnson and EMC and several world-class research universities.[293] In terms of the entire Innovation Center, partners have committed to R&D centers worth USD 420million and involving over 1,100 researchers.[294]

Russia has a number of tax incentives in place to encourage R&D and high technology manufacturing. For example, since 2008 all funding towards R&D projects is exempt from taxes.[295] In addition, companies located in one of Russia's Special Economic Zones (St. Petersburg, Tomsk and outside Moscow) as well as in the Skolkovo Innovation Center are exempt from property and land taxes for a 5 year term and pay a reduced rate of income tax.[296]

Intellectual property protection

Russia's environment for the protection of IP and enforcement of IPRs has improved in the last few years but on the whole continues to act as a deterrent for innovators. Although a signatory to several key IP-related international treaties including the TRIPS Agreement, Russia's legal and regulatory framework for the protection of IP, as well as enforcement of IPRs in practice, in many ways still falls short of its commitments.

As a WTO member Russia offers a standard 20 year patent protection term. However, while the protection has been available for biotechnological and biopharmaceutical inventions (with the exception of biological processes), the actual protection afforded to biopharmaceutical inventions is at times uncertain.[297] For example, there is no guarantee that the drug regulator will not approve a biosimilar product for market despite an active patent on the reference biopharmaceutical, and remedies through the judicial system are slow and ineffective.[298]

Under its WTO commitments and article 18.6 of the Law on the Circulation of Medicines, Russia offers 6 years of regulatory data protection for submitted test and clinical data for medicinal products.[299] However, it is not clear whether this period of exclusivity applies to biologics as well as how the protection would actually be applied to biosimilar applications for market authorization in a way that ensures that this protection is not violated.

The regulatory environment

Russia's regulatory system is evolving towards a system in line with international standards but a number of challenges remain for many biotech sectors.

First, the market approval process in relation to biopharmaceuticals is quite onerous and lacks transparency. There are currently no specific regulations for registering both biologics and biosimilars in Russia. The registration process is the same for chemical-based and

biologic products, and higher standards for the approval of biosimilars are not necessarily applied. Moreover, since 2010 registration of biopharmaceuticals is dependent on the submission of locally-conducted clinical trial data. These factors have resulted in significant registration delays and costs for foreign innovative companies.

Second, with regards to agricultural biotechnology several challenges exist. The Ministry of Agriculture is responsible for the regulation and approval of agricultural GM products. Up until July 2014, only imported GM crops may be registered and marketed; this represents a *de facto* ban on cultivation of GM seeds and products in Russia.[300] However, effective July 1, 2014, all GM organisms and GMO-containing crops may be authorized for market. Still, this pathway will have to go through a process of implementation and industry sources expect the registration process to take 2-3 years initially.[301] In addition, technical regulations governing the Eurasian Customs Union, of which Russia is a member, that came into force in 2013 require all food products with over 0.9% of GM lines to be labeled as such.[302]

Nevertheless, both the Russian government and Russian policymakers are considering reversing this approach and tightening controls on GMOs. The Ministry of Agriculture is conducting a review of existing regulations on GMOs in light of international practices which the government considers to be more stringent than in Russia.[303] Also, amendments to the Law On Safety and Quality of Alimentary Products that would ban local production and some imports of GMO-containing foods have been submitted to both houses of parliament as of February 2014.[304]

One positive step involves efforts to ensure all biopharmaceutical, biomedical and microbiology production facilities comply with Good Manufacturing Practices (GMP). Although still in the process of implementation – the deadline for compliance is now reportedly set at 2016 – mandatory GMP and similar international standards in the regulatory process will help drive improvements to R&D and manufacturing sites in Russia, enabling further innovative activities by both multinational and local companies.[305]

Technology transfer

The central legislative framework for technology transfer in Russia is somewhat unique in that it focuses mainly on enterprise partnerships as opposed to patenting and licensing agreements as platforms for technology transfer. Federal Law 217-FZ on the Commercialization of University Research (2009) provides universities with the exclusive right to market their research through launching their own SMEs or obtaining stock in companies that rely on their research. Specifically, Law 217 requires that universities have at least a 25-33% share in spin-offs, depending on the type of company, in exchange for the right to use the university invention.[306]

In 2010, the Russian government also approved Decree 218 "On measures of state support for the development of cooperation of Russian higher education institutions and organizations implementing complex projects on high-tech production".[307] The measure provides competitive subsidies (up to RUB100 million) to high-tech companies seeking to establish R&D and manufacturing facilities in Russia that would be operated jointly with a Russian university.[308] In 2010-2012, a total of RUB19 billion was allocated to the initiative. In return the university obtains equity in the company equal to the amount of the subsidy. At least 20% of the funds are required to go towards R&D.

Private efforts at technology transfer are also ongoing, including the Russian Technology Transfer Network, which involves 60 R&D organizations and innovation centers and is aimed at linking potential academic and industry partners including from the biotech and biomedical sectors.[309]

Data on patenting activities by universities and public research organizations confirms that patenting has not been a priority for Russian publicly funded research institutions; as of 2011 Russia represented only 4% of PCT applications by universities and 2% of public research organizations among middle-income and selected low-income countries.[310] However, reflecting the emphasis on direct university participation in spin-offs, joint university-firm PCT applications represent a relatively large

portion of total university applications in comparison with other leading countries. At 30% of total university PCT applications, Russia is on par with China and only behind Japan vis-à-vis other high and middle-income countries.[311]

Market and commercial incentives

With regards to the biopharmaceutical market in the last few years Russia has introduced several policies that provide preferential treatment to local companies at the expense of foreign companies. Broadly speaking, the Pharma 2020 Strategy has as one of the key goals to increase local companies' share of the total biopharmaceutical market value to 50% by 2020 (in 2012, the share was about 20%). Several measures, including the 2010 Law on Circulation of Medicines, introduce a range of conditions intended to drive local manufacturing of pharmaceuticals.

These conditions effectively represent indirect requirements for foreign companies to invest in local production in order to gain access to the market. For example, local products are given an up to 15% higher price in government tenders. In addition, in cases where two or more local manufacturers are registered for the same molecular entity, a proposed measure would restrict state purchases to locally produced drugs. In terms of pricing, for products on the Essential Drugs List locally manufactured drugs are annually adjusted for inflation, whereas prices are frozen on imported products. A policy that would introduce import tariffs on off-patent products if a stage is reached where market demand can be fully be satisfied with locally produced medicines has also been discussed.

As mentioned, these policies on their own are inadequate to attract FDI in the biopharmaceutical sector, with many other framework conditions discussed above lacking in Russia. Instead, such policies mainly represent barriers to entry for many multinational research-based companies.

Legal certainty (including the rule of law)

The Russian legal environment can be challenging and several barriers exist. Problem areas include corruption in the government and judicial system, civil conflict and protection of property rights and privacy. In the 2013-14 *Global Rule of Law Index* Russia was ranked 80th out of 99 countries.[312]

Singapore

Human capital

The National University of Singapore is generally highly regarded, particularly in the biomedical and life sciences. For example, in the 2013-14 *Times Higher Education* rankings it ranked 26th overall and 31st for the life sciences.[313] Looking at some biotech specific indicators linked to higher education Singapore does well. For example, according to the Milken Institute's 2006 "Biotech Patent Rankings" the National University of Singapore was in the lower quintile at 76th place.[314]

In terms of the number of researchers in full-time employment, Singapore in 2011 had over 32,000 researchers, scientists and engineers (excluding full-time postgraduate research students).[315] Out of this number, 26% of those employed had obtained doctoral degrees and 24% had obtained Master's degrees.[316] Looking at the proportion of researchers in relation to the total work force Singapore has one of the highest rates in the world. In 2011 Singapore had 10.4 total researchers in full-time equivalent per thousand of total employment.[317] This is considerably higher than the OECD average of 7.7.

Infrastructure for R&D

Singapore is a big investor in research and development. In 2011, gross domestic R&D spending in Singapore totalled USD7.1 billion at PPP.[318] Measured as a percentage of GDP 2011 R&D spending was 2.23%.[319] Internationally, this is just below the 2012 OECD average of 2.40%, and still behind the biggest R&D spenders such as Korea and Israel.[320] R&D spending in Singapore is made up slightly more of the private sector than government. The latest data from 2011 shows industry expenditure on R&D at 55.3% of the national total.[321]

Singapore's innovation infrastructure and services is extremely well developed. The Government's One North infrastructure initiatives, which comprise R&D facilities, campuses for new higher education institutions, living amenities for researchers and offices for VCs and IP law firms, have been extremely successful and are highly regarded internationally.[322] The initiative consists of two major research hubs or clusters. Biopolis is the biomedical hub and Fusionopolis is aimed at ICT, engineering and the physical sciences.

Looking at high-quality patents filed under triadic patenting, the share of the global total is 0.17% at 2011 figures which is considerably higher on an absolute and per capita basis than many OECD economies as well as the BRICS.[323] With regards to biotechnology patenting activity in 2011 the number of patents filed by Singaporean residents under the PCT was 64.[324]

Biomedical research makes up a substantial part of the overall R&D expenditure in Singapore. In 2011 Biomedical Sciences R&D accounted for SGD1,509 million of which SGD573.8 million came from the private sector and SGD 935.2 million from the public sector.[325]

Singapore's high level of biomedical R&D capability is also illustrated by the number of researchers and scientists employed in the biomedical sector. In 2011 biomedical researchers and scientists (private and public sectors including in A*STAR) made up 22% of the overall number of researchers and scientists.[326]

Biopharmaceutical R&D has been supported by public-private partnerships promoted by A*STAR in order to accelerate drug discovery and development. Some concrete results and examples include Bayer Healthcare partnership with five research institutions in Singapore in order to set up a new Translational Oncology Network to target R&D aimed at the growing cancer burden in Asia.[327] There is also the example of Menicon which developed the world's thinnest one-day disposable contact lens in Singapore.[328]

Singapore is an attractive market for venture capital and private equity. According to the IESE 2013 VC and PE Attractiveness Index, Singapore ranked 5th.[329]

Intellectual property protection

Singapore has a robust system of IPRs. Standard patent terms are issued for 20 years and Singapore also provides for a five-year patent term extension.[330] In addition, Singapore offers a five year term of regulatory data protection.

Additionally, Singapore introduced legislation relating to the development of orphan drugs in 1991, which includes marketing exclusivity and subsidies as incentives for orphan drug development.[331]

The regulatory environment

Singapore has a strong clinical and regulatory environment administered by the Health Sciences Authority. For biopharmaceuticals the Health Products Regulation Group is responsible for the authorisation and safety supervision of pharmaceuticals. Additionally, this agency is responsible for clinical trials in Singapore. The agency is highly regarded and is involved in the regulation of western medicinal products as well as Chinese proprietary medicines and cosmetic products.[332] However, generally speaking the regulatory authorities in Singapore require new products and technologies to be approved in other jurisdictions prior to approval in Singapore.[333]

GM foods are regulated by the Genetic Modification Advisory Committee. This committee regulates the import and commercialization of biotech products and services. Singapore's regulations are science-based and the registration process is generally viewed as efficient. Approval for food imports (GM and non-GM) is contingent on the product having been approved as safe in the exporting country.[334]

Technology transfer

Singapore has a strong tradition of technology transfer with governmental bodies as well as academic institutions being closely involved in transfer activities. For example, the Biomedical Sciences Industry Partnership Office liaises

between universities, public research institutes and industry. It promotes partnerships and links commercialization partners with public sector research.[335]

Singapore's main bioclusters host domestic and international firms and biomedical research institutions and are integrating governmental R&D bodies. Technology transfer is also being promoted and is made accessible by the close proximity of these bioclusters to the Singapore Science Park and the National University of Singapore.[336] In 2011, Singapore set up the Intellectual Property Intermediary to help local enterprises enhance innovation capacity through technology transfer. This initiative is backed by collaboration and support from the Government. From 2011 to 2012, the IPI had engaged 95 companies.[337]

From the technology transfer office administered by the National University of Singapore, over 700 patent applications, 84 licensing agreements and equity in lieu of royalties reaching USD4.85 million had been managed from the period of its inception in 1990 till the mid-2000s.[338]

Market and commercial incentives

With regards to the biopharmaceutical market this is relatively free with government subsidies in place only for pharmaceuticals included on the Standard Drug List.

Singapore offers a generous R&D tax credit of up to 400% on qualifying R&D expenditure.[339] The majority of this relief is available on R&D performed in Singapore.

Legal certainty (including the rule of law)

The legal environment in Singapore is considered stable and certain. Legal redress, enforcement of contracts and administrative justice are generally available and viewed as effective. Singapore is ranked 10th on the *Global Rule of Law Index* of the World Justice Project 2014.[340]

Switzerland

Human capital

Swiss universities are generally highly regarded, particularly in the biomedical and life sciences fields. For example, in the *Times Higher Education* rankings the Swiss Federal Institute of Technology Zürich is ranked 14th overall and 15th in the life sciences.[341]

Moreover, looking at some biotech specific indicators linked to higher education Swiss universities are prominent. For example, with regards to publications in the biotech sector according to the Milken Institute's "Biotechnology Publication Ranking" compiled in 2006, three Swiss universities were in the top fifty.[342] And according to their "Biotech Patent Rankings" Switzerland had one university (Zurich University) in the top 100 at 83rd place.[343]

As a percentage of the total population in the age group 25-64 that has attained some level of tertiary education, Switzerland had a 2011 rate of 35% which is slightly above the OECD average of 32%.[344] In terms of the life sciences, Switzerland had 1,830 life sciences graduates in 2011 which is an increase of over 100% since 2000.[345]

In terms of number of researchers in full-time equivalent Switzerland had over 25,000 in 2008 the latest year for which OECD figures are available.[346] Looking at the number of researchers in relation to the total work force, Switzerland was behind the OECD average of 7.7. In 2008 it had 5.5 total researchers in full-time equivalent per thousand of total employment.[347]

Infrastructure for R&D

Switzerland is a leading investor in research and development. In 2008, Swiss gross domestic R&D spending totalled USD10.5 billion at PPP.[348] While in absolute terms not a world-leading number Switzerland has a relatively high level of R&D spending when measured as a percentage of GDP. 2008 figures show R&D spending as a percentage of GDP at 2.87%.[349] Internationally, this is higher than the OECD average of 2.40%, but still behind the biggest R&D spenders such as Korea and Israel.[350] Swiss R&D spending is largely made up of private sector and industry

spending. The latest data from 2008 show industry expenditure on R&D at 68% of the national total.[351] According to the Swiss biotech industry, biotech R&D accounted for 13% of overall industry R&D spending.[352]

Switzerland has quite advanced medical and biomedical research facilities. As mentioned, one of its life science and medical universities is ranked as among the best in the world. Switzerland punches above its weight in terms of clinical trials and currently has 3,412 in operation.[353]

Swiss patenting activity is substantially higher than other larger countries. Looking at high-quality patents filed under triadic patenting, the Swiss share of the global total is 1.59% at 2011 figures.[354] More significantly, the Swiss have one of the highest levels of patenting intensity in the world: between 2007 and 2009 115 patents were filed per million people.[355] This was one of the highest rates in the OECD, well above the average of 38. With regards to biotechnology patenting activity in 2011 the number of patents filed by Swiss residents under the PCT was 131.[356]

Biomedical research makes up a substantial part of overall R&D expenditure. Led by its two dominant national champions, Roche and Novartis, R&D expenditure by the Swiss pharmaceutical industry made up over one-third of total private sector R&D expenditure at CHF4.6 billion in 2008.[357] This was the fourth highest total pharmaceutical R&D expenditure in Europe just behind the UK, France, and Germany.[358] Biopharmaceutical research represents a large share of the Swiss economy with pharmaceutical exports for 2011 estimated at an excess of USD40 billion.[359] Switzerland's high level of biomedical R&D capability is also illustrated by over 35,000 people with direct employment in the industry and an estimated further 120,000 in related and downstream industries.[360] While there are a number of SMEs and smaller Swiss biomedical manufacturers the industry is dominated by Roche and Novartis. Both companies employ over 10,000 staff each and invest either the majority or a large portion of their R&D expenditure in Switzerland. Novartis, for instance, spent over half of its total R&D budget of EUR5.1 billion in Switzerland.[361] Roche spent just under EUR2 billion of its total global R&D expenditure in Switzerland.[362]

In terms of public funding, the Swiss National Science Foundation provided CHF755 million in funding for basic research in 2012.[363] 41% of this was dedicated to biological and medical research.[364] Out of this close to 60% was for basic biological and medical research.

Venture capital in Switzerland is relatively well-established. In particular, the percentage of GDP going to early stage venture capital investment was the highest in the world at close to 0.06% of GDP in 2008.[365] Switzerland is also an attractive VC market. According to the IESE 2013 VC and PE Attractiveness Index, Switzerland ranked 10th.[366]

Intellectual property protection

Switzerland has a very strong system and history of IPRs. Switzerland is a member of the EPO and a signatory party to the European Patent Convention. Standard patent terms are issued for 20 years. Switzerland also provides a Supplementary Protection Certificate (SPC) of five years.[367] RDP is also available at a 10 year term.

Switzerland introduced legislation relating to the development of orphan drugs in 2006. This is similar to Regulation 2000 operating within the EU. Incentives include scientific advice and tax relief on qualifying expenditures.[368]

The regulatory environment

Switzerland has a strong clinical and regulatory environment. For biopharmaceuticals the drug regulatory authority Swissmedic is responsible for the authorisation and safety supervision of pharmaceuticals. The agency is highly regarded internationally.[369]

With regards to the use of biotechnology in agriculture the Swiss public in 2005 voted for a five-year moratorium on the use of GM crops in Switzerland.[370] This was later extended by the Swiss Parliament in 2010 to the end of 2013 and was recently extended again till 2017. The extensions come despite a number of scientific reports being commissioned by the Swiss

Government finding that GM crops present no clear danger to human or plant health.

Technology transfer

Switzerland has a strong tradition of technology transfer with governmental bodies as well as academic institutions being closely involved in transfer activities. For example, the Commission for Technology and Innovation (KTI) has as one of its core goals to promote technology transfer between universities and industry. Here KTI uses physical and web-based platforms to link potential partners, support so-called "National Thematic Networks" (including the Swiss Biotech Association) and provide innovation mentors.[371]

Academic institutions and professionals have their own technology transfer association through swiTT (Swiss Technology Transfer Association).[372] The association provides support services and has its mission to help facilitate technology transfer between public institutions and private companies. A 2012 survey of 14 major universities and research institutions found that: "3,323 new research projects with economic partners were initiated; 519 invention disclosures were registered; 297 priority patent applications were filed; 174 license and option agreements were executed; and 62 start-up companies were created."[373]

Nevertheless, Switzerland faces some challenges. For example, like other European countries both the number of licenses agreed to and issued as well as licensing income is generally lower than in the US.[374] A 2008 survey of high performing academic institutions in Europe and the US found that the proportion of universities with high-income (EUR1 million+) vs lower income (EUR0-30,000) licensing revenue was inverse between the surveyed institutions: in the US the majority of surveyed institutions were most likely to have high licensing income while the European institutions were most likely to have lower levels of income.[375] Swiss institutions performed better than the European average but still appear to be behind the US.

Market and commercial incentives

With regards to the biopharmaceutical market relatively strict pricing policies are in place for drugs and pharmaceuticals available through basic insurance. There are consequently a limited number of market incentives for these products which total over 2,500 medicines.[376] However, for both supplementary insurance and all medicines not listed on the public reimbursement list there is free pricing and a relative free market.

In terms of tax credits, Switzerland offers only a moderate amount of R&D tax incentives. Overall its tax scheme is not very favourable in comparison to other OECD countries.[377] There are tax incentives in place for the use of biofuels. Qualifying biofuels are partially or wholly exempt from "mineral oil tax" which can make up a significant portion of the per litre cost of fuel.[378]

Legal certainty (including the rule of law)

The Swiss legal environment is generally considered stable and certain. Legal redress, enforcement of contracts and administrative justice are generally available and viewed as effective.

United States

Human capital

American universities consistently top world rankings in almost all subject fields and the US remains the top destination for foreign students.[379] In the life sciences the US dominates most rankings. For example, in the *Times Higher Education* 2013-14 rankings American universities make up 15 out of the top 20 universities in the life sciences sector.[380]

Moreover, looking at some biotech specific indicators linked to higher education American universities dominate. For example, with regards to publications in the biotech sector according to the Milken Institute's "Biotechnology Publication Ranking" compiled in 2006, US universities accounted for 46% of worldwide scientific biotech publications between 1998 and 2002.[381] Out of the top 20 universities 14 were American. Similarly, the Milken Institute

also found that American universities were the most prolific when it comes to biotechnology patenting. According to their "Biotech Patent Rankings" nine of the top ten performing universities were American.[382]

As a share of the total number of tertiary education students in the world the US has maintained its position as a world leader. In the latest year for which comparable data is available (2011) the US had a total of 70 million people in the age group 25-64 attaining some level of tertiary education.[383] Similarly, as a percentage of the total population in the age group 25-64 that has attained some level of tertiary education, the US has one of the highest rates in the world at 42%.[384]

Looking specifically at science and engineering the US produces the second largest number of natural science and engineering university graduates in the world at almost 250,000 per year.[385] While considerably less than China in which the total number of graduates has jumped from just under 240,000 in 1998 to over 1.1million in 2010, it is substantially higher than other countries like Japan, the UK and Korea.[386] Similarly, in the life sciences the US produced the highest number of graduates in the OECD at 109,023 for 2011.[387]

Furthermore, the US produces the highest number of doctoral degrees in science and engineering. In 2010 this was close to 33,000 degrees.[388]

In terms of number of researchers the US has the second highest total of researchers in full-time equivalent at close to 1.3 million researchers in 2011.[389] In relation to the total work force, however, the US is above the OECD average but behind countries such as Finland, Denmark and Israel. In 2011 the US had 8.8 total researchers in full-time equivalent per thousand of total employment.[390]

Infrastructure for R&D

The US is a leading investor in research and development. In 2011, US gross domestic R&D spending totalled USD429 billion at PPP.[391] This was the highest total rate in the world making up close to one-third of global total R&D spending. The US also has a relatively high level of R&D spending when measured as a percentage of GDP. 2011 figures show R&D spending as a percentage of GDP at 2.79%.[392] Internationally, this is higher than the OECD average of 2.40%, but still behind the biggest R&D spenders such as Korea and Israel.[393]

US R&D spending is largely made up of private sector and industry spending. The latest data from 2012 show industry expenditure on R&D at 59% of the national total.[394]

The US has some of the best and most advanced medical and biomedical research facilities in the world as indicated by the fact that the US has by far the highest absolute number of clinical trials in operation globally.[395] As of March 2014 close to 76,000 out of a global total of circa 163,000 clinical trials were being carried out in the US.[396]

American patenting activity is a substantial share of global patenting. Looking at high-quality patents filed under triadic patenting, the US share of the global total is the biggest at 29.35% at 2011 figures.[397] With regards to biotechnology patenting activity US residents file more biotechnology patents than any other country. In 2011 the number of patents filed under the PCT were 3,907 which was close to half of the OECD total.[398]

Government funding and support for biomedical and biotech R&D comes through both direct support and tax credits. (Direct support will be discussed here whereas support through R&D credits will be discussed below.) At the federal level the NIH is one of the main sources of funding for biotech and biomedical research in the United States. The NIH funds over 300,000 researchers at 2,500 universities, medical schools and research institutes in the US and abroad.[399] NIH's current budget is just over USD31 billion.[400] Historically, the NIH has allocated over 50% of its budget to basic fundamental research with translational and advanced research being pursued by biopharmaceutical and biomedical companies. Many commentators have noted that this has, by and large, been a successful combination.[401]

The US has a large number of biotech and

biomedical clusters. In particular, California and Massachusetts are home to a number of world-leading clusters. In California there are four major clusters that employ more than 20,000 people in biotech and biomedical research: the Bay Area, Los Angeles County, Orange County and San Diego County. Together these four areas employ over half of the 268,000 (2009 figures) Californians who work in the biomedical industry.[402] The total number of biomedical companies in the state is 2,244 with estimated revenues of USD114 billion.[403]

The Massachusetts biotech cluster, located primarily in the Greater Boston area, is one of the oldest biomedical clusters. The surrounding 122 colleges and universities and top research hospitals, as well as a healthy inflow of public seed money (via federal Small Business Innovation Research grants) and venture capital (it captures just over 18% of all US biotech VC investment) has contributed to the success of this region.[404] This cluster has grown to contain over 430 biotech companies.

Like many American states, both California and Massachusetts offer tax credits to biotech and biomedical companies as an incentive to both start up and run their businesses.[405]

Finally, the US is home to the largest private venture capital market in the world. While the market has decreased substantially since the pre-financial crisis highs of 2007, in 2013 the total size of venture capital investment in the US was USD29.4 billion.[406] Surveys and indexes of the top venture capital markets in the world frequently find the US as being the most attractive and dynamic place for venture capital investing. See for example the IESE's 2013 Venture Capital and Private Equity Country Attractiveness Index which ranked the US first in the world.[407]

Intellectual property protection

The US has one of the most sophisticated and elaborate forms of IP protection in the world. It offers standard patenting exclusivity of 20 years with data exclusivity provisions of up to 5 years for new chemical entities and 3 years for new indications of existing drugs.[408] Patent term restoration is also offered for up to a period of 5 years.

The US has a separate and distinct term of protection for biologics. The Biologics Price Competition and Innovation Act of 2009 (BPCIA) provides 12 years of data protection to biologics (i.e. 12 years until a biosimilar can be approved), with no filing of biosimilar applications for the first four years and an extra six months (added to both the four years and the 12 years) for submission of studies on paediatric use.

Most recently the 2011 patent reforms and the change from a first-to-invent to a first-to-file system of patenting were greeted by many innovators as a positive enhancement of existing patent protection.[409]

The importance of America's strong IP protection in encouraging biotechnology and biomedical innovation is illustrated by surveys of biomedical corporations and their leaders. For instance, when asked about the importance of IP protection, 98% of biomedical company CEOs in California stated that international and domestic IP protection were either somewhat or extremely important issues affecting their industry.[410]

The US also has strong and well-established orphan drug legislation which has promoted innovation and the development of several new orphan drugs. Between 1973 and 1983 fewer than 10 products treating rare diseases were produced; in the 16-year period following the introduction of the US Orphan Drug Act in 1983 over 200 products were introduced.[411] Similarly, the provisions for marketing exclusivity and tax incentives in the Orphan Drug Act are associated with a significant and sustained increase (69%) in new clinical trials for drugs treating rare diseases.[412]

Still, challenges remain even in the US. In particular in the biotech sector question marks have been raised over the patentability of basic biotech inventions due to the Supreme Court decisions in the 2013 *Molecular Pathology v Myriad Genetics* and 2012 *Prometheus Laboratories, Inc v Mayo Collaborative Services* cases. The former ruling has raised uncertainties over the patentability of DNA molecules that mimic naturally-occurring sequences as well as other patented products and technologies isolated from natural sources.[413] The latter ruling

has made the field of personalized medicines and the patentability of biotechnologies and products that make use of the application of natural laws highly uncertain.[414]

The regulatory environment

The American clinical and regulatory environment is highly regarded and internationally well recognised. With regards to the regulation of products and technologies developed using modern biotechnology, the Coordinated Framework for Regulation of Biotechnology is generally viewed as being successful. Since its announcement in 1986 the policy and subsequent sector-specific regulations are seen as having been instrumental in promoting the development of the American biotechnology industry and bringing a wide array of biotechnology products and technologies to consumers.

With regards to biopharmaceuticals the FDA sets and enforces rigorous standards of both GMP and GCL and frequently inspects drug manufacturing sites in the US and abroad. The agency also has an advanced system of pharmacovigilance. MedWatch is the FDA's Safety Information and Adverse Event Reporting Program. It serves both healthcare professionals and consumers. The international high standing of the FDA is most obviously reflected by its leading role in efforts to harmonise regulatory standards through the International Conference on Harmonisation. Moreover, the regulatory standards of the FDA are frequently emulated and recognised as a gold standard amongst clinicians, health economists and the academic community.[415]

Nevertheless, the FDA is not immune to criticism. Biomedical companies frequently point to deficiencies in the approval system and specifically time spent on approvals. Recent data suggests that FDA approval times have increased substantially. For example, for new molecular entities/new biologic agents the average number of months to approval has jumped by 28% from 14.68 months in the period 2003-7, to 18.85 in 2008.[416] Similarly, the average number of months to clearance of 510(k)s (an approval application for medical devices) has also increased from 3.14 months in 2003-7 to 4.45 months in 2010 – a jump of 43%.[417] And for pre-market approval (PMA) of medical devices the increase has been from an average time of 15.48 months in 2003-7 to 27.08 months in 2010; an increase of 75%.[418] According to local industry associations, these increases in processing times risk putting the US biomedical industry at a competitive disadvantage. Other regulatory agencies (particularly in Europe) have changed their approval processes with a view to attracting more manufacturers to both perform their clinical trials and launch their products there first. Indeed, in California the increase in FDA processing time was viewed as being a serious issue by a majority of biomedical CEOs. When asked to rate the influence of federal policy issues on the industry's ability to advance biomedical research, innovation and investment in California, the mandate, processes and resources of the FDA were listed as being of extreme importance by 80% or more of respondents. Furthermore, 80% of respondents listed the scope of the FDA mandate as being extremely important and 85% of respondents said FDA resources and/or processes were extremely important.[419]

With regards to the regulation of biotechnology crops, the USDA has in recent years taken steps to cut the approval time by half for petitions for nonregulated status for genetically engineered organisms including biocrops.[420] Approval times have increased from six months to three to five years since the mid-1990s. Key changes include streamlining internal USDA review processes, setting timeframes for the completion of specific review steps, and expedited internal review and decision-making procedures.[421] These changes were announced in 2012.

Technology transfer

One of the key drivers of American biotech innovation and commercialisation has been the success of technology transfer in the US. The Patent and Trademark Law Amendments Act of 1984 and 1986 (commonly referred to as the Bayh-Dole Act) and the Stevenson-Wydler Technology Innovation Act, which was later amended by the Federal Technology Transfer Act of 1986 and the Technology Transfer Commercialization Act in 2003 have all been instrumental in incentivizing technology transfer.

These laws gave institutions that received federal support (such as American universities, small businesses and non-profits) control and the rights to any resulting intellectual property of their inventions or research.

Studies have found a significant correlation between increased patenting activities at US universities following the Act. For example, a 2004 study found that university share of total patenting in the US increased from 0.69% of total patents at the time of legislation to just under 5% in 1996. Moreover, in a range of 117 industries (including drugs) the increase was from a decrease of 87% in 1969 to an increase of 1,648% in 1996.[422] Using fifteen years of data from the annual Association of University Technology Managers (AUTM) survey a 2012 study estimating the economic contribution of licensing activity by academic institutions found that in the US the contribution of academic licensing to gross industry output ranged from USD199-836 billion (2005 USD).[423] Contributions to GDP were equally significant estimated at between USD86-388 billion (2005 USD).[424] Even under the post-2007 adverse economic conditions, the positive effects of Bayh Dole are being felt. In 2012 university related patenting, licensing, and start-ups were still strong with over 22,000 patent applications filed, over 5,000 licenses executed, and 705 start-ups formed.[425]

Market and commercial incentives

By international standards, the US has a relatively free market in the purchase and sale of biopharmaceutical products. There are no national price regulations or national reimbursement agencies. Instead, private health insurers and public payers (such as Medicare, the Veterans Health Administration and Medicaid) negotiate prices with manufacturers and only indirectly set reimbursement limits and influence prescribing and patient usage through the use of formularies. Drug formularies (which often include therapeutic interchange or so-called switching mechanisms) and differential cost-sharing (such as tiered co-payments) are two of the more commonly used techniques to influence prescribing practices.

Arguably, one of the strongest drivers of biopharmaceutical innovation in the US has been the existence of this relatively free market in the pricing of pharmaceuticals. For example, a 2004 study of 11 OECD countries by the US Chamber of Commerce and the International Trade Administration found that under market conditions similar to those in the US, global R&D by biopharmaceutical corporations would increase by 11-16% and would result in the development of 3-4 new molecular entities annually.[426]

The US also provides a number of R&D tax credits, both at the federal and state level. The federal Research and Experimentation Tax Credit allows companies to claim a tax credit of between 14-20% of qualifying amounts.[427] This credit is not permanent and currently expired at the end of 2013. The Obama administration has proposed to both simplify and make permanent this rather convoluted and complicated credit.

In addition, 38 US states offer R&D tax credits at varying rates; Iowa, for instance, offers a credit of up to 6.5% of qualifying expenditure, which may be doubled for bioscience firms.[428] Many states also offer additional incentives and tax credits such as seed capital tax credits, state venture capital investments and state sales tax exemptions for R&D equipment.[429]

Legal certainty (including the rule of law)

The US legal environment is generally considered stable and certain. Legal redress, enforcement of contracts and administrative justice are generally available and viewed as effective. However, the US faces challenges as is reflected in its ranking on a number of international indices measuring the rule of law. In the 2014 *Rule of Law Index* the US ranked 19th.

NOTES

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