pugatchconsilium

BUILDING THE BIOECONOMY 2016

Examining National Biotechnology Industry Development Strategies Globally

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

CONTENTS

LIST OF ABBREVIATIONS

ANVISA	Brazilian National Health Surveillance Agency
CLs	Compulsory Licenses
EEU	Eurasian Economic Union
EPA	US Environmental Protection Agency
FDA	US Food and Drug Administration
FDI	Foreign direct investment
GCP	Good Clinical Practices
GMP	Good Manufacturing Practices
GM	Genetically Modified
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
PCT	Patent Cooperation Treaty
PRO	Public Research Organization
RDP	Regulatory Data Protection
R&D	Research and Development
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

2016 marks the third year and third edition of *Building the Bioeconomy Examining National Biotechnology Industry Development Strategies*. Commissioned by the Biotechnology Industry Organization and authored by Pugatch Consilium this series of reports seek to provide an overview of those national innovation strategies, policies and best practices that have been successful in creating an environment in which biotechnologies and biotechnological innovation can flourish.

This year *Building the Bioeconomy* has grown from thirteen economies to sixteen, adding Colombia, Israel and Japan. As in previous editions the sample of economies is geographically and economically diverse with a mix of high-income mature OECD economies and middle income and emerging markets.

Building the Bioeconomy takes into account the specific requirements of the biotechnology sector, how biotech R&D takes place and what policies economies that have been successful in fostering biotechnology innovation have pursued. The overall purpose is to provide an overview of some of the best practices in place internationally that support and enhance biotechnology inputs and outputs. The point of reference for this assessment is the development of a globally competitive sector; economies 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.

A key feature of the report series is the identification of those factors and policies that enable biotechnology innovation. Based on the existing literature and experience of those economies that have been successful in building an advanced biotech capacity it is possible to piece together a set of principles and factors which, evidence suggests, are enablers of biotechnology innovation. We call these the seven enabling factors for biotechnology innovation. The table on the following page provides an overview of these factors and definitions for each.

As with previous editions of *Building the Bioeconomy* this report is accompanied by an Annex. This Annex contains a detailed discussion of each enabling factor included in this report for each of the sampled economies. It is a reference tool and can be read in conjunction with this, the main report.

The Biotech Policy Performance Measure – Overall results

Last year a key new feature of *Building the Bioeconomy* was the Biotech Policy Performance Measure. This tool (the 'Measure') provided readers a quick overview of a given economy's policy framework and performance in relation to the other economies sampled. The Measure assessed the existence and performance of some of the most important elements for each of the seven enabling factors used to map a given economy's biotechnology policy framework. This year the Biotech Policy Performance Measure has been expanded to now also take into account biotech outputs. Indicators on biotechnology outputs cover a broad spectrum ranging from levels of total clinical trial activity, clinical trials for biologics, scientific output, biotechnology crops under cultivation, venture capital attractiveness, biotechnology patenting, rates of university patenting, to biopharmaceutical product launches.

All in all there are now 21 indicators in total (10 policy inputs and 11 outputs) that together provide a full and detailed measure of the complete biotechnology environment for a given economy. As can be seen below the Biotech Policy Performance Measure *Building the Bioeconomy 2016* provides a clear and empirical link between the types of policies that countries have in place and real biotechnology outputs.

Seven enabling factors for biotechnology innovation

Key enabling factors	Explanation
Human capital	A basic and fundamental building block for the biotech sector is the availability of high skilled and technically trained human capital. Without the right human capital it is virtually impossible to create the conditions in which biotech innovation can take place.
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. Without the necessary laboratories and clinical research facilities biotechnology R&D would be next to impossible.
Intellectual property protection	IPRs (including patents and regulatory data protection) 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.
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.
Technology transfer	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.
Market and commercial incentives	Market and commercial incentives range from general R&D incentives to specific policies aimed at biotech sectors such as pricing and reimbursement policies for biopharmaceuticals. For the biopharmaceutical sector incentives determined by pricing and reimbursement systems for medicines and health technologies can have a profound impact on commercial and market incentives for innovation in health and biotech R&D.
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.

Measuring Policy Inputs and Biotech Outputs: The Biotech Policy Performance Measure

Policy Inputs	India	Turkey	Colombia	Russia	Mexico	Brazil	China	South Africa
Human capital	Challenging	Challenging	Challenging	Mixed	Challenging	Challenging	Mixed	Challenging
Infrastructure for R&D	Challenging	Challenging	Challenging	Mixed	Challenging	Mixed	Mixed	Challenging
Intellectual property protection	Challenging	Challenging	Mixed	Mixed	Mixed	Challenging	Challenging	Challenging
The regulatory environment	Challenging	Challenging	Mixed	Challenging	Mixed	Mixed	Challenging	Mixed
Technology transfer frameworks	Challenging	Mixed	Challenging	Challenging	Challenging	Mixed	Attractive	Mixed
Market and commercial incentives	Challenging	Challenging	Challenging	Challenging	Challenging	Challenging	Challenging	Challenging
R&D tax incentives	Attractive	Attractive	Mixed	Mixed	Mixed	Mixed	Mixed	Mixed
Legal certainty (including the rule of law)	Mixed	Challenging	Mixed	Challenging	Challenging	Mixed	Challenging	Mixed
Biotech Outputs								
Scientific publications by population	Struggling to compete	Mixed	Struggling to compete	Mixed	Struggling to compete	Mixed	Struggling to compete	Highly competitive
Quality of academic publications	Struggling to compete	Mixed	Not available	Struggling to compete	Mixed	Struggling to compete	Struggling to compete	Mixed
Clinical trials per capita	Struggling to compete	Mixed	Struggling to compete	Struggling to compete	Struggling to compete	Mixed	Struggling to compete	Mixed
Clinical trials for biologics, 2010-2015, per capita	Struggling to compete	Struggling to compete	Mixed	Mixed	Struggling to compete	Struggling to compete	Struggling to compete	Mixed
Early phase (Phase I and II) Clinical trials for biologics, % of total CTs, 2010-2015	Highly competitive	Struggling to compete	Struggling to compete	Struggling to compete	Struggling to compete	Mixed	Highly competitive	Mixed
Biotechnology triadic patenting, share of global total average 1999-2012	Mixed	Struggling to compete	Struggling to compete	Mixed	Struggling to compete	Mixed	Mixed	Struggling to compete
Biopharma product launches, % available in country within 5 years of global product launch, 1983-2000	Struggling to compete	Struggling to compete	Mixed	Struggling to compete	Highly competitive	Mixed	Not available	Mixed
National % share total number of patents from top 50 PCT applicants: universities, 2014	Struggling to compete	Struggling to compete	Struggling to compete	Struggling to compete	Struggling to compete	Struggling to compete	Highly competitive	Struggling to compete
Biotechnology crops, hectares under cultivation, % of total 2015	Highly competitive	Struggling to compete	Mixed	Struggling to compete	Mixed	Highly competitive	Mixed	Mixed
Biopharmaceutical Competitiveness Index (BCI) Survey, 2015 Ranking	Mixed	Struggling to compete	Struggling to compete	Struggling to compete	Mixed	Struggling to compete	Struggling to compete	Mixed
Venture Capital & Private Equity Country Attractiveness Index, Economy Ranking	Mixed	Mixed	Struggling to compete	Struggling to compete	Struggling to compete	Struggling to compete	Mixed	Struggling to compete

Measuring Policy Inputs and Biotech Outputs: The Biotech Policy Performance Measure (cont.)

Policy Inputs	Malaysia	Israel	Japan	Singapore	Korea	Switzerland	UK	US
Human capital	Mixed	Attractive	Attractive	Attractive	Attractive	Attractive	Mixed	Mixed
Infrastructure for R&D	Mixed	Attractive	Attractive	Mixed	Attractive	Attractive	Mixed	Attractive
Intellectual property protection	Mixed	Mixed	Attractive	Attractive	Attractive	Attractive	Attractive	Attractive
The regulatory environment	Mixed	Mixed	Attractive	Attractive	Attractive	Mixed	Attractive	Attractive
Technology transfer frameworks	Challenging	Attractive	Attractive	Attractive	Attractive	Attractive	Attractive	Attractive
Market and commercial incentives	Challenging	Mixed	Mixed	Mixed	Challenging	Mixed	Mixed	Attractive
R&D tax incentives	Attractive	Attractive	Mixed	Mixed	Mixed	Mixed	Attractive	Mixed
Legal certainty (including the rule of law)	Mixed	Not available	Attractive	Attractive	Attractive	Not available	Attractive	Mixed
Biotech Outputs								
Scientific publications by population	Struggling to compete	Highly competitive	Mixed	Mixed	Mixed	Highly competitive	Highly competitive	Highly competitive
Quality of academic publications	Not available	Highly competitive	Mixed	Not available	Mixed	Highly competitive	Highly competitive	Highly competitive
Clinical trials per capita	Mixed	Highly competitive	Mixed	Highly competitive	Mixed	Highly competitive	Highly competitive	Highly competitive
Clinical trials for biologics, 2010-2015, per capita	Mixed	Highly competitive	Mixed	Highly competitive	Mixed	Highly competitive	Highly competitive	Highly competitive
Early phase (Phase I and II) Clinical trials for biologics, % of total CTs, 2010-2015	Struggling to compete	Mixed	Mixed	Mixed	Highly competitive	Mixed	Highly competitive	Highly competitive
Biotechnology triadic patenting, share of global total average 1999-2012	Struggling to compete	Mixed	Highly competitive	Mixed	Highly competitive	Highly competitive	Highly competitive	Highly competitive
Biopharma product launches, % available in country within 5 years of global product launch, 1983-2000	Struggling to compete	Struggling to compete	Mixed	Mixed	Highly competitive	Highly competitive	Highly competitive	Highly competitive
National % share total number of patents from top 50 PCT applicants: universities, 2014	Struggling to compete	Mixed	Highly competitive	Mixed	Highly competitive	Mixed	Mixed	Highly competitive
Biotechnology crops, hectares under cultivation, % of total 2015	Struggling to compete	Struggling to compete	Struggling to compete	Struggling to compete	Struggling to compete	Struggling to compete	Struggling to compete	Highly competitive
Biopharmaceutical Competitiveness Index (BCI) Survey, 2015 Ranking	Not available	Mixed	Mixed	Highly competitive	Highly competitive	Highly competitive	Highly competitive	Highly competitive
Venture Capital & Private Equity Country Attractiveness Index, Economy Ranking	Mixed	Mixed	Highly competitive	Highly competitive	Mixed	Highly competitive	Highly competitive	Highly competitive

Key findings

Building on the discussion of the seven enabling factors, global biotechnology developments in 2015 and the results of the Biotech Policy Performance Measure *Building the Bioeconomy* findings can be grouped around three key take-home messages.

Take-home message 1: Inputs = Outputs

The expansion of the Biotech Policy Performance Measure to now also take into account biotech outcomes helps clearly illustrate the direct link between creating a positive enabling environment with real-world biotech outcomes. Perhaps the most important finding of the 2016 edition of *Building the Bioeconomy* is that economies that have weak enabling environments – and perform worse relative to other economies on the ten indicators relating to policy inputs – tend also to have lower biotechnology outputs. The 2016 Biotech Policy Performance Measure shows economies that have the right policy framework and create positive, incentive based environments around the seven enabling factors tend to be much more successful in achieving strong biotechnology outputs.

Take-home message 2: Erecting localization barriers and mandating local production does not translate into greater levels of innovation

The desire to attract greater flows of foreign direct investment (general as well as biotech specific) has promoted a growing number of countries to launch ambitious policies seeking to "localize" innovation and economic activity. While active government efforts to increase attractiveness to domestic and international investment are nothing new, in a growing number of countries these localization policies seek to mandate or coerce local economic activity and investment through in fact raising localization barriers. Over the last 5-10 years policies and barriers aimed at nurturing local industries in the place of more non-discriminatory incentive-based approaches have steadily increased. Numerous financial and trade bodies, including the European Central Bank, have documented a recent trend toward use of trade barriers, particularly non-tariff or indirect tools, that have the goal of discriminating against imported goods and boosting local industrial sectors. A number of economies in the *Building the Bioeconomy* sample have erected there barriers with the goal of developing their biotech capacity. Yet these policies are

often self-defeating. Economies that tend to impose local content requirements or domestic manufacturing requirements in an effort to boost local technical capacity often see less investment and less innovation – in biotechnology as well as in other sectors. For example, a number of countries mandate the conduct of clinical trials as a condition of market registration. These requirements for additional local clinical trials are often based on industrial policy and efforts to build local research capacity. They form part of broader policies seeking to localize biopharmaceutical R&D through mandatory requirements. In China, for instance, since 2014 in order to obtain market authorization for higher-risk (Class III) medical devices local clinical trials must be conducted. Similarly in Russia since 2010 under Federal Law N.61 "On Circulation of Medicines" there is an obligation to conduct local clinical trials in Russia by all companies (including foreign ones) as a condition of the registration of medicine.

Yet the evidence presented in the Biotech Policy Performance Measure shows clearly that those economies that embrace open, transparent policies centred around the seven enabling factors achieve much higher levels of actual biotechnology outputs. The findings in the Measure suggest that the best way to 'localize' innovation is to offer open and positive incentives.

Take-home message 3: The necessity for holistic policy reform

Finally, while many economies can have strengths and successes on some enabling factors and some outputs, the countries that achieve success across the board are those that are able to introduce policies and reforms that cut across all enabling factors.

For example, while Brazil remains a world leader in biotechnology crops and biofuels production, in the biopharmaceutical sector it lags behind. A challenging environment across factors relating to its regulatory environment, protection of IP and market and commercial incentives have resulted in Brazil having low levels of clinical research activity absolutely and for biologic products. Of note is that in many cases the incentives used to spur investment and innovation in the ag-bio and biofuels fields –including providing a ten year term of RDP for fertilizers and agrochemical products – have not been put in place for the biopharmaceutical sector.

Indeed, from a policy perspective a critical take-away message from this report is that these factors work together. Economies that have been successful in developing and building a world-class R&D environment for all biotech sectors have had to pursue policies across **all** seven enabling factors.


NUNC

1 INTRODUCTION

2016 marks the third year and third edition of *Building the Bioeconomy Examining National Biotechnology Industry Development Strategies*. Commissioned by the Biotechnology Industry Organization and authored by Pugatch Consilium this series of reports seek to provide an overview of those national innovation strategies, policies and best practices that have been successful in creating an environment in which biotechnologies and biotechnological innovation can flourish.

The analysis and policy mapping of *Building the Bioeconomy* is built around seven enabling factors for biotechnology development 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). Together these factors create the conditions that through international experience have over the years given countries and policymakers the best chance of having success in developing their biotech capacity and promoting biotech innovation.

Although it has only been a few short years since the launch of the *Building the Bioeconomy* series the importance of biotechnologies to global economic development has only grown more pronounced. Several of the world's biggest and fastest growing economies have launched new or updated national plans or strategies to promote the growth of this sector. India and South Africa have both outlined ambitious and detailed national biotechnology policy plans over the last two years and in the publication of its 13th Five-year Plan in March 2016 China recommitted to the biotechnology sector by designating it as a 'strategic industry'.[1] And recent estimates of the value of the three major biotechnologies (biopharmaceuticals, biotech crops and industrial biotechnology) place their contributions at about 2% of GDP in the US.[2]

Looking at individual biotech sectors the trajectory is also upwards. In 2015 the total acreage of biotechnology derived crops stayed roughly the same as in 2014 at just under 180million hectares of biotech crops under cultivation.[3] Yet viewed over the past two decades the commercial cultivation of biotech crops has increased by a factor of over 100 growing from 1.7million hectares in 1996 to close to 180million in 2015. Similarly, the pace of innovation and commercialization of new biopharmaceuticals remains at record levels. In 2015 the US FDA approved a record 45 NME and BLA products; the highest rate over the last decade.[4] Significantly, a growing portion of these approval were for biologic medicines and therapies.

1.1 Covering more economies and comparing policy inputs vs. real-world biotechnology outputs – How *Building the Bioeconomy* is evolving

More economies covered

This year *Building the Bioeconomy* has grown from thirteen countries to sixteen, adding Colombia, Israel and Japan. As in previous editions the sample of economies is geographically and economically diverse with a mix of high-income mature OECD economies and middle income and emerging markets. The sample of economies is intended to reflect a range of key economies in terms of geography and income level. Using the World Bank's classification system,[5] *Building the Bioeconomy 2016* comprises 8 high-income economies (two of which, Singapore and Russia, are not OECD members), 7 upper-middle-income economies and 1 lower-middle-income economy. Table 1 groups the economies sampled according to their World Bank defined income levels.

Table 1 *Building the Bioeconomy 2016*, sampled economies by World Bank classification

High-income economies	Upper-middle-income economies	Lower-middle-income economies
Israel, Japan, Korea, Russia, Singapore, Switzerland, UK, U.S.	Brazil, Colombia, China, Malaysia, Mexico, South Africa, Turkey	India

Source: World Bank (2016)[6]

Measuring the immeasurable? How do policy inputs affect real world biotech outputs?

Last year a key new feature of *Building the Bioeconomy* was the Biotech Policy Performance Measure. This tool (the 'Measure') provided readers a quick overview of a given economy's policy framework and performance in relation to the other economies sampled. The Measure assessed the existence and performance of some of the most important elements for each of the seven enabling factors used to map a given economy's biotechnology policy framework. Questions the Measure sought to quantify and or assess included:

- What were the levels of advanced human capital in a given economy?
- How much did economies invest in R&D as a percentage of GDP?
- What was the regulatory framework like for the major biotech sectors? Was it in line with international best practices and standards?
- What was the IP environment like in a given economy? Did the economies sampled offer biopharmaceutical specific IPRs such as RDP and patent term restoration? Were biotech innovator able to obtain adequate protection for their IP and proprietary technologies created?

Yet while adding concrete empirical data on individual economies' performance to the international discussion on biotechnology policy frameworks, in many respects last year's Measure did not fully address the other side of the ledger, that is, indicators relating to biotechnology outputs or results.

This year the Biotech Policy Performance Measure has been expanded to now also take into account biotech outcomes. Indicators on biotechnology outputs cover a broad spectrum ranging from levels of total clinical trial activity, clinical trials for biologics, scientific output, biotechnology crops under cultivation, venture capital attractiveness, biotechnology patenting, rates of university patenting and biopharmaceutical product launches.

All in all there are now 21 indicators in total (10 policy inputs and 11 outputs) that together provide a full and detailed measure of the complete biotechnology environment for a given economy.

As with the previous edition of the Measure the purpose here is not to 'score' or benchmark individual countries to a pre-determined set of criteria. Rather, the purpose of the Measure is to give readers (and the economies mapped) an idea of how a sample of their policy inputs (for each enabling factor), firstly, compares with the same policy inputs for the other economies sampled and, secondly, what type of actual biotech outcomes the individual inputs in a given economy actually translate into. Full details of the methodology and the findings of the Measure are included below in section 4.

Annex

Finally, it is worth noting that just as for previous editions of *Building the Bioeconomy* this report is accompanied by an Annex. This Annex contains a detailed discussion of each enabling factor included in this report for each of the sampled economies. It is a reference tool and can be read in conjunction with this, the main report.

1.2 Report overview

Building the Bioeconomy takes into account the specific requirements of the biotechnology sector, how biotech R&D takes place and what policies economies that have been successful in fostering biotechnology innovation have pursued.

The overall purpose is to provide an overview of some of the best practices in place internationally that support and enhance biotechnology inputs and outputs. The point of reference for this assessment is the development of a globally competitive sector; economies 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. It identifies key enabling policy input factors ranging from human capital, R&D infrastructure, protection of IP, the regulatory environment, availability of technology transfer frameworks, market and commercial incentives and rule of law. To illustrate the importance of these policy inputs to generating actual, measurable biotech outcomes through the Biotech Policy Performance Measure *Building the Bioeconomy 2016* provides a clear and empirical link between the types of policies that countries have in place and real results.

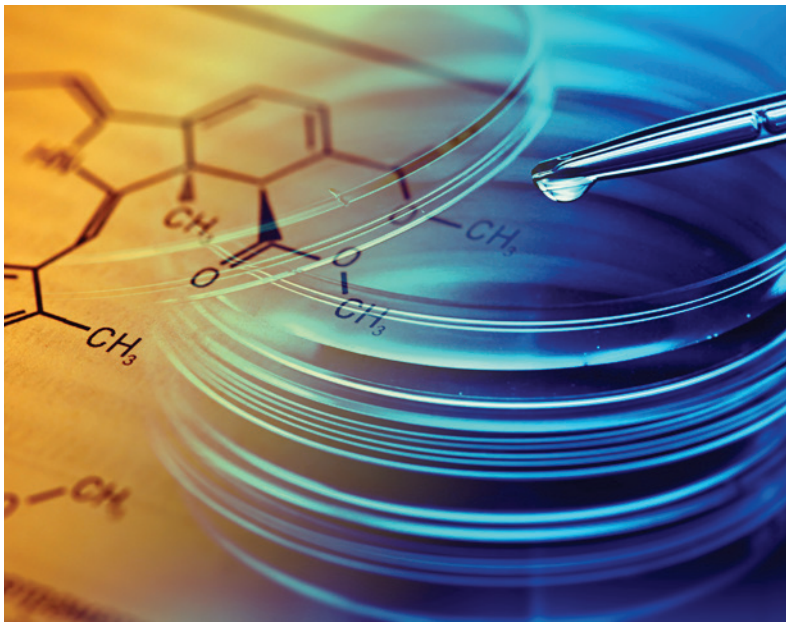
In addition to this Introduction the paper contains the following sections.

Section 2 describes the rationale and up-to-date thinking that underpin national biotechnology strategies. The section focuses on outlining the seven enabling factors identified as being critical to creating an enabling environment for biotech innovation and putting in place the right 'hardware' and 'software' policies.

Section 3 examines the state of biotechnology in 2016 across the sampled economies. What were the major developments globally and in the sampled economies over the last year? This section zooms in on some of the key policy challenges that have emerged over the last few years, in particular the erection of localization barriers and the weakening of IP standards in many aspiring biotech markets.

Section 4 describes the expansion of the Biotech Policy Performance Measure and the creation of an inputs vs outputs matrix for the 16 economies included in this year's edition.

Section 5 provides concluding thoughts and ties together the data, information and performance review of the preceding sections.



2 ENABLING BIOTECHNOLOGY INNOVATION – GETTING BOTH THE 'HARDWARE' AND 'SOFTWARE' RIGHT

How do you best encourage biotechnology innovation and R&D? Which factors and policies should governments and policymakers focus on?

2.1 Seven enabling factors for biotechnology innovation

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, economy or region is different. Depending on the structure of a particular economy and levels of overall socio-economic development, different economies have greater or lesser needs in specific policy areas.

Based on the existing literature and experience of those economies that have been successful in building an advanced biotech capacity it is possible to piece together a set of principles and factors which, evidence suggests, are enablers of biotechnology innovation. We call these the seven enabling factors for biotechnology innovation.

While each factor is mostly described independently in the academic literature and studies by the OECD, WIPO and other international institutions, taken together these enabling factors are likely to create an environment conducive to biotech innovation. They cover areas ranging from basic scientific skills and capabilities to the more complex and biotech specific such as clinical and technical regulations. Yet while these factors can be viewed in isolation, from a policy perspective a critical take-away message is that these factors work together: economies that have been successful in developing and building a world-class biotechnology industry have had to pursue policies in **all** seven areas. For example, many economies can have a strong scientific and research base, yet if the relevant technology transfer framework, incentives and culture is not in place to spur researchers into commercializing their research than these human resources will not translate into new biotechnology-based products.

The following pages provides a more detailed description of each enabling factor, its importance in contributing to an environment that encourages and promotes biotech innovation and research, and the types of indicators that can be used to measure and gauge the presence of each factor in a given economy.

Human capital

The first factor is human capital. 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.[7] 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.[8] Moreover, in terms of rates of innovation a 2010 study found that sectors which maintain a relatively high share of highly-skilled employees, such as the science-based industries, engage in more innovative activity.[9] Indeed, high-skilled and technically trained human capital is one of the most fundamental features that successful biotech innovation is reliant upon.

Table 2 Seven enabling factors for biotechnology innovation

Key enabling factors	Explanation
Human capital	A basic and fundamental building block for the biotech sector is the availability of high skilled and technically trained human capital. Without the right human capital it is virtually impossible to create the conditions in which biotech innovation can take place.
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. Without the necessary laboratories and clinical research facilities biotechnology R&D would be next to impossible.
Intellectual property protection	IPRs (including patents and regulatory data protection) 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.
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.
Technology transfer	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.
Market and commercial incentives	Market and commercial incentives range from general R&D incentives to specific policies aimed at biotech sectors such as pricing and reimbursement policies for biopharmaceuticals. For the biopharmaceutical sector incentives determined by pricing and reimbursement systems for medicines and health technologies can have a profound impact on commercial and market incentives for innovation in health and biotech R&D.
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.

Yet while having sufficient numbers of science and technology graduates is in itself essential, ensuring that the degrees are of a high quality is of equal if not more importance. For example, while a number of emerging markets score relatively highly on the OECD PISA test and have large numbers of research scientists, their skills are not always adequate to the development of innovative and cutting edge technologies.[10] In order to promote innovation, the researchers and scientists that make up the human capital must be set in an environment which provides scientific as well as commercial opportunities.[11] Indeed, as discussed below economies that have invested in developing technology transfer pathways to enable and encourage successful academic-industry transfers have generally succeeded in promoting general rates of high-tech innovation as well as biotechnology innovation.[12]

Human capital refers to and can be measured by a range of indicators including: higher education rankings; life science and medical college rankings; number of researchers in R&D and general levels of researchers and scientists in the population.

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.[13] Without the necessary laboratories and clinical research facilities biotechnology R&D would be next to impossible. The importance of investing and building adequate infrastructure is highlighted by, for example, the OECD and member economies in their *Science and Technology Outlook* series.[14]

What types of policies are in place to encourage the building of facilities and initiatives? Governments and countries can support the building of R&D infrastructure through direct government funded and operated facilities and also through public-private partnership. For example, as discussed in the Annex, a key part of Singapore's emergence as a biopharmaceutical global leader was its sustained commitment to building world-class infrastructure and R&D facilities including public sector investment of over USD2 billion since 2000.[15] In other countries too, R&D partnerships and investments have been critical. For example, the multiple public-private partnerships between the public sector, Boston-based universities and research centres and pharmaceutical companies has led to the development of the Boston technological hub as an international leader in the field of biomedical innovation.[16]

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; public and private biotech R&D expenditure (where available); and overall life science investment levels.

Intellectual property protection

The third enabling factor is the protection of IP. Always a controversial field (particularly in relation to biopharmaceutical innovation) yet the economic and empirical evidence built up over the last few decades strongly suggests that overall IPRs tend to have a positive impact on economic activity, especially for high-tech industries and on rates of FDI.[17]

Over the last decade a number of empirical studies have been published on the positive and cumulative economic effects of IPRs. In particular, there is a growing body of evidence suggesting a positive link between the strengthening of IPRs and economic growth and development, job creation, technology transfer, and increased rates of investment and innovation. For example, comparing WTO members (that is, signatories to the TRIPS Agreement) with non-members, a 2003 OECD study found that overall IPRs tend to have a positive impact on FDI with WTO members generally enjoying higher levels of FDI than non-members.[18] The authors found that with the exception of least developed countries, which may not yet have implemented the TRIPS Agreement due to transition period allowances, WTO members have higher levels of FDI than non-members. Léger used regression analysis to determine that IP protection is one of the most influential factors on innovation in both developing and industrialized countries.[19] Similarly, the OECD's Cavazos et al looked at R&D expenditure and technology transfer as well as FDI and found that a 1% change in the strength of a national IP environment (based on a statistical index) is associated with a 2.8% increase in FDI in-flows, a 2% increase in service imports and a 0.7% increase in domestic R&D.[20] Finally, looking at the US Pham found that IP-intensive industries generated one-third of total US economic output.[21]

IPRs are historically of real importance to the biotech and biopharmaceutical innovation process.[22] 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. 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 incentives 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 finds that the combination of market exclusivity and income from patent protection drives private investment in innovation, which contributes to new drug development.[23] Older studies have estimated that between 60-65% of pharmaceutical products would not have been introduced or developed in the absence of patent protection.[24]

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.[25] 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.[26]

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.[27] 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 and EMA, on ensuring that international manufacturers and non-US manufacturing adheres to their standards, the establishment of foreign offices and increased inspections of foreign manufacturers and suppliers.[28] The 2012 Food and Drug Administration Safety and Innovation Act (FDASIA) serves as a good example of legislation which expands the drug regulator's authority in order to "address the challenges posed by an increasingly global drug supply chain".[29] One prominent measure within this law is the FDA's extended authority to perform administrative detention of any drugs which are suspected as adulterated or misbranded, "until FDA has had time to consider what action it should take concerning the drugs, and to initiate legal action, if appropriate".[30] In addition, the FDA has issued guidelines on the "Circumstances that Constitute Delaying, Denying, Limiting, or Refusing a Drug Inspection", as well as established higher penalties for adulterated and counterfeit medicines.[31]

For biopharmaceuticals 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.[32] Regulatory certainty and transparency is also an important factor affecting rates of general and biotech specific innovation. Long regulatory delays and barriers can stand in the way of translating scientific and academic research into fully commercialized products.

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 constitutes the fifth factor and 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.[33] 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.[34] 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 Commercialization Act in 2003. 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 marketplace 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 from 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.[35]

These 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.[36] Indeed, *The Economist* called Bayh-Dole "possibly the most inspired piece of legislation to be enacted in America in the last half-century".[37]

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 other economies 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.[38]

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 which may need to be registered with government agencies and/or subject to regulation.

It is also worth highlighting that economies with successful technology transfer frameworks in place and accompanying high levels of activity also see significant economic benefits with direct and significant contributions to economic output and employment. For example, using eighteen years of data from the annual AUTM survey a 2015 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 USD282-1,180 billion (measured in 2009 USD).[39] Contributions to GDP were equally significant estimated at between USD130-518 billion (measured in 2009 USD).[40] In addition, this study found that this licensing activity was also a major contributor to the American jobs market, responsible for between 1.1million-3.8million person years of employment. The latest figures from the AUTM survey show how licensing revenue and technology transfer is continuing to grow in the US and presents an important income stream for higher education institutions. Results from the latest available survey (published in 2015) show that executed licenses grew by 4.5% year on year, almost 1,000 new commercial products were created (representing an increase of over 34% from the previous year) and over 6,000 new patents were issued.[41]

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 technology transfer offices which employ IP experts and marketing professionals; industry oriented scientists; entrepreneurs and companies seeking seed technologies to license from a university and then develop; governmental grants to support the process; a strong national IP system that allows a university/academic institution to protect and license its inventions; and developing a culture of entrepreneurship.[42]

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

The sixth enabling factor is market and commercial incentives which are provided as a means of encouraging R&D and enabling access to new technologies. These range from general R&D incentives to specific policies aimed at biotech sectors such as pricing and reimbursement policies for biopharmaceuticals.

R&D incentives can be various tax incentives, credits, deductions, lower rates of taxation for specific forms of income (e.g. income derived from IP assets such as patent box schemes) and/or direct support mechanisms such as grants and subsidies for R&D activities. In some countries R&D tax incentives are in place that target biotechnologies and/or biopharmaceutical innovation.

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 economies. Many health systems have also adopted advanced systems of pharmaco-economic and cost-effectiveness analysis and comparisons. In other more diversified health 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.[43] 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.[44]

Legal certainty (including the rule of law)

And finally, the seventh enabling factor is legal certainty, which is crucial to commercial and business activities.[45] 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.[46] Economies 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 economy can be mapped through existing international indices such as the World Justice Project's *Rule of Law Index*.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3 THE STATE OF GLOBAL BIOTECHNOLOGY 2016 – A LANDSCAPE ANALYSIS

This section provides a discussion of the major developments in the global bioeconomy in 2015. It examines key international trends, major policy shifts and announcements from a selection of the 16 economies included in *Building the Bioeconomy*. The purpose of this section is not to detail every policy development in each of the 16 economies. (A full discussion of each individual economy and biotechnology developments during 2015 is provided in the accompanying Annex.) Rather, the purpose is to highlight key global trends and in particular areas where the policy environment for biotech innovators still remains challenging.

In many respects the main lesson from 2015 is that while more and more economies are looking to the biotechnology field as a future engine for economic growth and development, at the same time many are embracing policies that tend to be counterproductive. Specific examples include the increased and wide-spread use of mandatory localization policies, trade barriers and the weakening of standards of IP protection including through the issuing of compulsory licenses.

3.1 Investment and growth

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. In fact, the OECD predicted that by 2030 biotechnology could make up to 2.7% of member state GDP.[47] Yet while 2030 is still close to a decade and a half away examining the most recent estimates of biotech's economies contribution and this figure may already have been reached.

Earlier this year an estimate of the total revenues of the three main biotech sectors was published in *Nature Biotechnology*.[48] Looking at US sales figures for biologic drugs, GM crop revenues and a host of industrial biotech products (biofuels, biochemical, biologics feedstock etc.) the author provided a detailed estimate of the direct economic contribution the main biotech sectors make to US national output. Using 2012 data the article found that total direct biotechnology contributions to the American economy in amounted to between USD324-374 billion. This translate to between 2-2.2% of total GDP. It should be noted, as the author does, that this estimate is conservative and does not include any multiplier effect. Furthermore, it also does not factor in broader definitions of the bio-based economy which expands the value of bioeconomic activities to significantly higher proportions of national and international economic output.[49]

Although it is difficult to extrapolate and apply this estimate for the US to the contribution of biotechnologies globally – America is, after all, the most advanced and prolific user and generator of biotechnologies globally – this estimate nevertheless provides a clear indication that at least some countries are almost a full fifteen years ahead of schedule in being fairly close to the OECD's projected estimate for 2030. So in this sense the bioeconomy, per the OECD's definition, is close to being fully developed.

Indeed, looking at rates of investment and growth of individual biotechnology sectors in the US and beyond it is clear that biotechnology continues to grow and perform strongly. In fact, in many respects 2015 turned out to be a banner year. In the US venture capital investment in life sciences based biotechnology increased significantly to

over USD7 billion, up by 17% over 2014 figures.[50] Overall biotechnology venture capital investment was the second largest sector invested in accounting for 13% of total 2015 venture capital investment.[51] Significantly, a growing portion of this investment was early stage capital. For example, in the second quarter of 2015 out of the total USD2.3 billion venture capital invested in biotechnology, close to two-thirds went towards early stage entities.[52] Out of this about half – or USD733 million – was invested in start-ups receiving venture capital for the first time.[53]

The strong performance in the US was matched by equally impressive levels of venture capital investment in Asia and Europe. Estimates for 2015 published in *Nature Biotechnology* suggests the amount of venture capital raised for biotechnology investment in Asia, for instance, almost tripled, growing from USD322 million in 2014 to USD930 million.[54]

The strong growth in overall levels of investment and private capital allocation to biotechnologies was matched by strong levels of growth and expansion in the three major biotechnology sectors.

For example, as noted above, looking at ag-bio, the number of hectares under cultivation globally in 2015 stayed roughly the same as in 2014 at just under 180million hectares of biotech crops under cultivation.[55] Yet this overall number masks some important regional and national changes. For example, in Brazil the number of hectares under cultivation increased from 42.2million hectares in 2014 to 44.2 million hectares.[56] While in the US this dropped from 73.1million hectares to 70.9million hectares.[57] Nevertheless looked at over a longer time period over the past two decades the commercial cultivation of has increased by a factor of over 100 growing from 1.7million hectares in 1996 to close to 180million in 2015.[58]

Zooming in on biofuel production the last few years has seen a similar story of increased output and capacity. The latest available figures from BP's annual energy review shows that total global biofuels production increased substantially from 65,928 thousand tonnes of oil equivalent in 2013 to 70,792 thousand tonnes in 2014.[59] This was an increase of 7.4%. Yet, just as with ag-bio production this global figure masks considerable regional and national variation. For instance, while production by the two global leaders – US and Brazil – grew by a relatively modest 5.6% and 5.5% respectively, a number of smaller economies made significant jumps in production.[60] Argentina, for instance, boosted biofuels output by over 30% and in 2014 accounted for 3.6% of global production. Similarly, Indonesia managed to increase its level of output by over 40% accounting for 3.5% of global output.[61]

A similar picture emerges when looking at rates of technology transfer and partnerships in the life sciences sector. Data on preclinical partnerships in 2015 in the US (where the best information is available) shows that the number of partnerships stayed roughly the same as in 2014 at 236 deals.[62] These deals were spread out among various universities and research institutes with the largest number of partnerships between the University of Texas (12 deals) and University of California (8 deals). Of note is that both the University of Texas and University of California are also world leaders at rates of university patenting.[63] In WIPO's Annual PCT review the University of California is ranked as the number one patenting university in the world with 413 applications for 2014.[64] The University of Texas is ranked third with 154 patent applications.[65] While the figures from WIPO is not technology specific it is likely that a large number of these patent applications are in the biotechnology and life sciences field.

3.2 Localization barriers and weakening standards of IP – A challenging policy environment in 2015

Although many of the headline figures and data on the growth and economic contribution of the bioeconomy and biotechnologies is positive, looking at the biotechnology policy environment the picture is mixed.

On the one hand a growing number of emerging economies are making the development of the biotech sector a national and strategic priority. Yet while many positive policy commitments and announcements have been made over the course of 2015, elsewhere the policy environment has

actually deteriorated. In many cases economies are embracing policies built on protectionism and the weakening of property rights.

For example, in a positive step China in its latest 5-year plan reiterated its view of biotechnology as a strategic sector. Building on and reiterating some of the objectives of the 2006 "Medium- and Long-term Plan for Science and Technology Development 2006-20", China's latest five-year plan strengthens the country's focus on innovation with an additional emphasis on "biological technology." According to the plan, approved on 16 March 2016, China will increase science and technology investment by 9.1% to CNY271 billion (USD 41 billion) in 2016.[66] As already included in the 2006 Plan, R&D funds are expected to reach 2.5% of GDP by 2020, up from 2.05% in 2014.[67] Science and technology innovation is to be achieved by strengthening basic research and re-innovation of existing technologies.[68] Funding for basic research is also expected to rise from 5% to 10% of total R&D spending by 2020.[69] In addition, the new five-year plan promises to better protect IP; create new innovation clusters, national laboratories and market-oriented research institutions; empower universities to decide more autonomously on their research and funding as well as help organise international scientific programs.[70]

Yet looking outside these commitments in the 5-year plan, China's policy environment has not improved. This can be seen in four major areas.

First, the Ministry of Commerce issued a new Foreign Investment Law that, generally speaking, appears to undermine WTO rules, including the national treatment principle.[71] In certain areas, investors must obtain administrative approval prior to investment, while in other areas instead of pre-approval investors must submit detailed annual reports. The law also requires certain companies (such as those operating in a joint venture with a local company) to restructure to meet certain local requirements. Similarly for biopharmaceuticals through the "Technical Guideline for the Research, Development and Evaluation of Biosimilars" only locally produced drugs (including biologics) benefit from the exclusivity protection through a "monitoring period" (akin to RDP).[72]

Second, the 2015 State Council circular put forward a new definition for "new drugs" that is stricter than the current one and requires an extensive level of investment – first global launch in China – in order to benefit from a range of existing advantages. Specifically, the current definition of new drug comprises drugs already marketed elsewhere but not yet in China. In contrast, under the new rules only drugs not yet marketed anywhere in the world will be considered as "new" in China, and thus qualified for certain benefits such as the five-year monitoring period. Moreover, under new biosimilar legislation, biologics reportedly must not only have the first worldwide launch in China but also be produced there in order to qualify for the 5 year marketing exclusivity.[73]

Third, new official tax guidance will reportedly reinforce requirements for stringent transfer pricing tax schemes requiring a higher amount of global value chain profits from multinational companies to be conducted and "booked" in China (including transfer and "enhancement" of IP) as well as greater tax presence in China (for instance, requiring a subsidiary in China in order to market in the country).[74]

Finally, cost containment measures designed to make medicines more accessible for patients have

largely hindered innovative drugs from entering the Chinese market. In a bid to reduce drug prices and in stark contrast with international practice, State Council Opinion N. 44 of August 2015 links new drug registration to a price commitment by innovators, whereby the post-marketing sales price in China should be equal or lower to the one in their originating country or neighboring markets comparable to China.[75] Considering pricing when deciding about approval threatens to distort scientific with budgetary considerations, and could set a negative example for other countries. In addition, this technical barrier would hinder access by Chinese patients to life-saving treatments and greatly degrade the Chinese innovation environment. An implementing measure is currently being drafted, and is expected to expand the scope of the price commitment to imported drugs first registered on the Chinese market.

Similar developments can be seen in India. On the one hand in a welcome and positive development the Indian Government in 2015 finalized its *National Biotechnology Development Strategy*, 2015-2020 and continued to build on its economic development goals laid out in the *Make in India* plan.[76] The *Strategy* sets the goal of India becoming a bio-manufacturing global hub and making biotech the new success story of its economy after the IT sector.[77] It also places a considerable emphasis on strengthening technology transfer and encouraging greater levels of commercialization of nascent biotechnologies. By increasing technology transfer capacities, improving human capital and strengthening the regulatory environment, the *Strategy* ambitiously aims to multiply the value of the Indian biotech sector up to USD100 billion by 2025, up from the current USD7 billion.[78]

Yet just as in China biotechnology innovators face steep hurdles in India.

For instance, the protection of IP and enforcement of IPRs in India has long been a challenge to innovators. And while 2015 did not see a material change in the environment for innovators, a number of positive steps were taken by the new Indian Government in particular by Prime Minister Modi himself. These include hiring more examiners to reduce the application backlog,

improved anti-piracy efforts and passing the Bill on Commercial Courts, Commercial Division and Commercial Appellate Division of High Courts. In what is somewhat of a missed opportunity a *National Intellectual Property Rights (IPR) Policy* was finally unveiled by the Department of Industrial Policy and Promotion in May 2016.[79] The IP policy contains seven objectives each with proposed policy measures: IPR awareness, generation of IPRs, legal and legislative framework, administration and management, commercialization of IPR enforcement and adjudication, and human development. The document emphasizes the need for a balanced approach between IP and the need to protect public interest. It also aims to spread awareness among public about IP rights to promote innovation and calls for renewed enforcement efforts.[80] As such, Indian research-based pharmaceutical companies welcomed it as a first step to foster innovation culture.[81] Positive aspects include centralizing the patent regime under DIPP and improving co-ordination between the federal and state level on compliance.[82] However, the text fails to address the main concerns over IP protection. The Government retains the prerogative of issuing compulsory licenses, as *"India will continue to utilise the legislative space and flexibilities available in international treaties and the TRIPS Agreement."*[83] The policy does not open debate over data exclusivity, patent linkage and patent-term extension, nor on Section 3(d) of Indian Patent Act.[84] It also fails to introduce specialized IP courts, as included in a previous draft of the text.[85]

Other major economies are also sending mixed messages through their policy choices. For example, home to one of the world's most biodiverse environments – hosting close to 10% of global biodiversity – the biotechnology sector is increasingly a strategic priority of the Colombian Government. Over the last half-decade Colombia has put in place a number of policies and positive incentives to promote greater activity and innovation across a range of biotech sectors from ag-bio, industrial biotechnology, biopharmaceuticals and cosmetics. In 2011 the National Council for Economic and Social Policy and National Department of Planning released a framework for the commercialization and development of biotechnologies, *Policy for the Commercial Development of Biotechnology for the Sustainable Use of Biodiversity*.[86] The initiative seeks to improve the investment environment in the area of biotechnology in order to draw greater private and public investment in commercial development within the sector. It targets a wide range of biotech sectors including cosmetics, biopharmaceuticals, food and agriculture. And biotechnology figures heavily in current government industrial and innovation plans, particularly the 2014-2024 National Program for Sustainable Bio-Trade. Most recently in a positive step to improve the attractiveness of carrying out clinical research in Colombia in March 2016 the Colombian DRA INVIMA introduced a reduction in approval of clinical trials, with the new timeframe for approval to be streamlined and set to drop considerably with a target of 60 days. Clinical trial approval will be streamlined through simultaneous review of research protocol with quality control evaluations of the drug being tested.[87]

Yet in other areas Colombia is seeking to or has put in place policies that greatly reduce the incentives for investment and biotechnology innovation. For example, the National Development Plan 2014-2018 introduces a number of problematic measures affecting several enabling factors for biotech innovation. Article 70 widens the basis for the issuing of compulsory licenses in a manner that goes beyond the TRIPS Agreement, Article 31 and the 2001 Doha Ministerial Declaration and subsequent General Council decision concerning Paragraph 6. The provision allows the Ministry of Health to define public health emergencies broadly and to actively seek out compulsory licenses, allowing for grounds outside extreme circumstances including industrial or commercial objectives, to play a role in the issuing of compulsory licenses. In addition, Articles 70 and 72 of the National Development Plan link two distinct and independent processes with regulatory approval of biopharmaceuticals: patent examination and pricing decisions. Article 70 allows the Ministry of Health to participate in the patent review process by the Ministry of Industry. This allows non-legal and in some cases subjective criteria to be factored into decisions on whether to grant a biopharmaceutical patent, rather than

examination solely by patent specialists and officials based on established legal and technical criteria. Article 72 of National Development Plan links approval of biopharmaceuticals with pricing decisions. Specifically pricing decisions must be made as part of the market approval process, which in most countries is a separate process and only takes place based on scientific and technical determinations, independent of pharmacoeconomic or political considerations. Similarly, on the regulatory side, decree 1782 from 2014 established a "third" pathway for the approval of biologic medicines applicable to so-called "non-comparable" biosimilars. This represents an unprecedented abbreviated pathway for registration of non-comparable products, which is inconsistent with WHO or FDA standards and could result in the approval of medicines that are not safe and/or effective. In contrast to the Full Dossier Route (for originators) and the Comparability pathway (pathway for biosimilars) found in WHO guidelines, which require both non-clinical and clinical data to be submitted, the "Abbreviated Comparability Pathway" as described in the decree allows for an expedited approval of non-comparable products without adequate controls or any clarity regarding how the safety or efficacy of a product approved via this pathway will be evaluated and ensured.

Finally, echoing these legislative developments the Ministry of Health and Colombian Government has recently been actively considering (on the basis of a recommendation of an internal committee) the issuing of a compulsory license on the oncology drug Glivec on grounds of high prices.[88] In a number of interviews the Minister of Health made clear that the driving reason for the potential over-riding of the existing patent for Glivec was the issue of cost. In May 2016 the Minister was quoted in the *Wall Street Journal* as saying that: "Technological pressure and high drug prices have brought the health-care system to a financial crisis…Colombia is a paradigmatic case of a middle-income country, with a growing health system and with rising expectations from its middle class, which cannot pay high prices for new drugs."[89]

At the time of research the Colombian Government had issued a "public interest declaration" which would allow the authorities the right to unilaterally reduce the price of Glivec.[90] Although a different mechanism from the issuing of a compulsory license this unilateral reduction in price in effect constitutes an infringement of the property rights of the rights-holder and creator of Glivec, Novartis.

Other economies have also introduced new policies that make the environment for biotechnology innovators more challenging. Here too an emphasis on creating localization barriers and conditioning market access on local content requirements can be seen. For example, In November 2015, the Russian Government adopted Resolution No. 1289 "On Restrictions and Conditions of Access of Foreign Essential Medicines to State and Municipal Tenders", which introduces a direct import ban within the procurement system. Access to state purchases of imported medicines will not be allowed when (at the time supplies are requested) at least two generics produced within the EEU are available for a given INN. Foreign manufacturers will only be able to participate in a public tender in cases where fewer than two bids from EEU manufacturers have been submitted. In addition Decree 1125/2015[91] made the National Immunobiological Holding Company owned by state Corporation Rostech the sole provider of immunobiological products for state needs for the period 2015-2017.[92] A similar monopoly expected to benefit Rostech's subsidiary has been proposed for insulin.[93]

Yet while the policy record is mixed in many economies big and small – with a particular emphasis on localization barriers and rolling back property rights – it should also be noted that there are positive examples of economies that have full-heartedly embraced structural reforms and succeeded in both developing and boosting their bioeconomies.

3.3 From international outlier to best in class – How Israel has developed into a biopharmaceutical pioneer

While the discussion in the preceding sub-section has focused on the many challenges and mixed policy records in a growing number of economies, there are also positive examples of economies that

have focused on creating a positive, incentives based enabling environment.

For example, though the biotechnology sector is still relatively young one of the new additions to *Building the Bioeconomy* this year, Israel, has seen a surge in enabling policies and incentives in the last 15 years which has led to record growth of the biotech sector in Israel.[94]

For many years, Israel's biotech sector consisted mainly of research organizations and early stage companies focused on licensing out technologies, with little development and commercialization of biotechnologies in Israel. A dedicated effort to improve enabling policies and incentives has taken place since 2000, when the Office of the Chief Scientist issued a "Bio-Plan" for Israel for the decade to 2010.[95] Among its key recommendations, the plan called for greater funding for early and later phase biotech companies, increased collaboration between industry and universities and PROs, and a strengthening of the regulatory framework and capacity. Since then the Israeli government has taken a number of additional measures aimed at achieving these targets, including within the Office of the Chief Scientist's wider innovation policy and annual R&D budget.

Apart from a significant strengthening of funding for innovation more broadly, the Israel venture capital market is quite healthy, with a large number of venture capital companies targeting biotech and biomedical innovation.[96] This includes, for instance, a new USD100 million Israel Biotech Fund launched in 2015 focused on biopharmaceuticals.[97] As part of a broader effort to establish technology incubators, a special focus has also been placed on creating and supporting bioclusters, such as RAD BioMed, that provide R&D infrastructure and scientific and business support and capacity building to local start-ups.[98]

A major shift in technology transfer towards the biotech and biomedical field has also taken place. Technology transfer is well established in Israel, with over 10 tech transfer offices and companies present at the major universities and research institutions for over 50 years. Israel's technology transfer model is similar to the American Bayh-Dole framework but based on largely independent and corporate-style offices heavily focused on generating royalties and creation of new companies. By and large this model has been widely successful: Israeli technology transfer offices in Israel are very active with an estimated average of 150 new licensing deals, 15 start-ups and NIS1.5 billion (USD400 million) in royalties per year.[99] Indeed, two technology transfer offices in Israel, Yissum from the Hebrew University and Yeda from the Weizmann Institute, are ranked among the top tech transfer offices worldwide.[100] Reflecting wider emphasis on and growth of the biotech sector in Israel, today much of this activity targets biotechnology; for instance, around 60% of Yeda's portfolio focuses on biotechnology.[101]

Another area in which Israel has made significant strides in the context of its biotechnology innovation strategy is IP protection. Israel has historically had a difficult IP environment, particularly in relation to biopharmaceuticals (noted in the USTR's Special 301 Report for several years), however following a 2010 Memorandum of Understanding with the US, Israel carried

out significant improvements in key areas of biopharmaceutical IP protection. Specifically, in 2011 the RDP term for chemical drugs was increased to 6 years from the date of registration in Israel or 6.5 years from the date of registration in one of the recognized drug regulatory authorities (primarily the FDA and EMA); although this term is not currently applied to biologics.[102] 2012 and 2014 amendments to patent legislation introduced several additional improvements, such as patent term restoration, speedier review and publication of patent applications (the latter, after 18 months from the date of application) and legal remedies in case of infringement cases during the early publication period.[103]

In the context of these and other policy improvements, the biotechnology sector in Israel has expanded significantly. Today, around 80% of the sector is focused on biomedical R&D, with emphasis on biopharmaceuticals and diagnostics, including tissue engineering, cell therapy, immunotherapy and vaccines.[104] Bioinformatics also represents a growing field in Israel, due in part to a historically strong emphasis and success in the field of information and communication technologies, with a significant number of partnerships between local bioinformatics companies and multinational biopharmaceutical companies.[105]

As the most advanced biotech sector in Israel, a dynamic innovative biopharmaceutical and biomedical sector has sprouted up alongside its traditionally generic biopharmaceutical sector (while not detracting from the latter's global competitiveness). According to the OCS 2015 Innovation Report, the number of life sciences companies in Israel has increased by more than five times in the past 15 years (from 200 in the late 1990s to around 1,100 in 2015) and the sector represents around 18% of total exports.[106] Today at least 40% of the total biopharmaceutical sector includes companies involved in biopharmaceutical discovery, development and delivery (with 22% engaged in drug discovery).[107] Despite the market's relatively small size Israel hosts 17 local subsidiaries of research-based multinational biopharmaceutical companies.[108] In addition to their traditional involvement in importing and marketing of their products, multinational research-based companies are also active in R&D activities and play a critical role in cooperating with local firms and creating a vibrant innovation start-up platform.[109] Israel also has one of the highest per capita rates of clinical trial activity worldwide, with close to 700 trials hosted to date per million population and a large portion of these for more complex and cutting edge early phase trials.[110] Moreover, today the biomedical sector not only continues to play a role in many cutting edge treatments (with contributions from Israeli-developed technologies to a number of recent "blockbuster" biopharmaceuticals estimated at around 25%), but is also leading the development and marketing of cutting edge treatments, such as the Israeli company Protalix's BioTherapeutics plant cell-based enzyme replacement therapy for Gaucher disease.[111]

3.4 Section summary

The Bioeconomy in 2015 has not stood still. On the one hand a growing number of economies are embracing the potential that biotechnologies can bring to their socio-economic development. Yet on the other hand policy challenges persist and economies seeking to build and develop their biotechnology capacity are increasingly embracing policies, such as limiting protection for biopharmaceutical IPRs and mandatory localization policies, that have not been successful in generating sustained levels of biotechnology growth and innovation. The next section will illustrate the negative impact these policies can have through the findings of the Biotech Policy Performance Measure; an empirical tool that directly compares economies' policy inputs with real-life biotech outputs.

4 POLICY INPUTS AND BIOTECH OUTPUTS – COMPARING PERFORMANCE

Last year *Building the Bioeconomy* measured a given economy's policy framework and performance in relation to the other economies sampled through. This year the Biotech Policy Performance Measure has been expanded to now also take into account actual, real-world biotech outcomes. How does the policy environments affect biotechnology outputs?

4.1 Expanding the Biotech Policy Performance Measure

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 sustained investment, the right polices and persistence. Last year's edition of *Building the Bioeconomy* featured a new component: a Biotech Policy Performance Measure. This tool (the "Measure") provided readers a quick overview of a given economy's policy framework and performance in relation to the other economies included in the report. The Measure included some of the most important elements for each of the seven enabling factors described in the preceding section.

This year the Biotech Policy Performance Measure has been expanded to now also take into account biotech outcomes. Indicators on biotechnology outputs cover a broad spectrum ranging from levels of total clinical trial activity, biologics clinical trials, scientific output, GM crops under cultivation, venture capital attractiveness, biotechnology patenting, rates of university patenting, biopharma product launches and so forth.

All in all there are now 10 policy inputs and 11 outputs that together provide a full and detailed measure of the complete biotechnology environment for a given economy.

As with the previous edition of the Measure the purpose is not to benchmark individual countries to a pre-determined set of criteria. Rather, the purpose of the Measure is to give readers (and the economies mapped) an idea of how a sample of their policies inputs (for each enabling factor), firstly, compares with the same policy inputs for the other economies sampled and, secondly, what type of actual biotech outcomes these policy inputs translate into.

4.2 Policy inputs

The Biotech Policy Performance Measure consists of two distinct halves: policy inputs and biotech outputs. Policy input indicators are drawn from the seven enabling factors and are by and large the same as those indicators included in last year's Measure. These are indicators that provide a sense of a given economy's policies and direction under each of the enabling factors. There are 10 indicators in total – 5 quantitative and 5 qualitative – from all seven enabling factors. On the next page Table 3 shows the 10 indicators for each of the 7 enabling factors.

The indicators in factors 1, 2 and 7 are quantitative measuring key elements of a given economy's policy framework as it relates to human capital, R&D infrastructure and its legal environment. With the exception of an economy's biopharmaceutical IP environment as ranked by the US Chamber of Commerce's International IP index in factor 3, all other indicators in factors 3, 4, 5 and 6 are more qualitative in nature assessing the policy environment for a given indicator.

All indicators (quantitative and qualitative) are based on the information and data collected, analysed and presented in this report and the accompanying Annex.

Table 3 Biotech Policy Performance Measure, policy input indicators

Factor 1: Human capital	**Factor 5: Technology transfer frameworks**
• Number of researchers per capita compared to sample average	• Frameworks in place
Factor 2: Infrastructure for R&D	**Factor 6: Market and commercial incentives**
• R&D spending % of GDP	• Biopharmaceutical pricing and reimbursement policies • R&D tax incentives
Factor 3: Intellectual property protection	**Factor 7: Legal certainty (including the rule of law)**
• Availability of Regulatory Data Protection • Availability of Patent Term Restoration • US Chamber IP Index 2016 Life Sciences Score 2016, standardized to %	• World Justice Project 2015 Rule of Law Index ranking
Factor 4: The regulatory environment	
• Existence of regulatory framework and efficiency	

4.3 Biotech outputs

As mentioned, the second half of the Biotech Policy Performance Measure relates to biotechnology outputs. Just as with assessing inputs, measuring biotechnology outputs is a difficult task. There are challenges with both defining what constitutes an actual biotech output as well as finding empirical evidence that is comparable for all the economies sampled. Nevertheless, it is possible to identify 11 indicators that together provide a snapshot of a given economy's biotechnology outputs. On the following page Table 4 shows the 11 indicators measuring biotechnology outputs.

As can be seen from Table 4 many of these indicators relate directly to a given form of biotechnology. These include, for example, rates of clinical research on biologic medicines or number of hectares of biotechnology crops under cultivation. Other indicators are more general and not biotechnology specific. For example, the data for rates of university patenting is not biotech specific. Still, this measure provides a good indication of the propensity of higher education institutions in a given economy to seek to patent their technologies. Each of the 11 indicators is described below together with its source and the number of *Building the Bioeconomy* countries which the data set covers.

Indicator 1: Scientific publications standardized for population

This indicator measures the number of scientific and technical journal articles published from a given economy.[112] This data provides an indication of a given economy's overall level of scientific and academic proficiency and output. This indicator is not biotechnology specific but covers all major forms of scientific and technical fields.[113] The data is collected by the World Bank and forms part of its World Development Indicators.

The number of scientific publications has been standardized for population to provide a more accurate reflection of scientific publishing intensity in a given economy regardless of population size.

This data set includes all of the economies sampled in *Building the Bioeconomy 2016*.

Indicator 2: Quality of academic publications

This indicator examines the quality of scientific publications. This data is collected by the OECD and measures the percentage of scientific publications among the world's 10% most cited.[114]

This data set includes all of the economies sampled in *Building the Bioeconomy 2016* except Colombia, Malaysia and Singapore.

Table 4 Biotech Policy Performance Measure, biotech outputs

- Scientific publications standardized for population
- Quality of academic publications
- Clinical trials per capita
- Clinical trials for biologics, 2010-2015, per capita
- Early phase (Phase I and II) clinical trials for biologics, % of total clinical trials for biologics
- Biotechnology triadic patenting, share of global total average 1999-2012
- Biopharmaceutical product launches, % available in country within 5 years of global product launch, 1983-2000
- National % share, total number of patents from top 50 PCT applicants: universities, 2014
- Biotechnology crops, hectares under cultivation, % of total 2015
- Biopharmaceutical Competitiveness Index (BCI) Survey 2015 Ranking
- Venture Capital & Private Equity Country Attractiveness Index, Economy Ranking

Indicator 3: Clinical trials per capita

This indicator provides an overview of the biopharmaceutical clinical research environment in a given economy. Specifically, it provides the absolute number of clinical trials taking place (or having taken place) in a given economy as collated and registered on the website ClinicalTrials.gov; a website maintained by the National Library of Medicine at the National Institutes of Health in the US.

As with other indicators the total number of trials has been standardised to population to provide a more accurate reflection of levels of clinical research intensity in a given economy regardless of population size.

This data set includes all of the economies sampled in *Building the Bioeconomy 2016*.

Indicator 4: Clinical trials for biologics, 2010-2015, per capita

This indicator examines the amount of recent clinical research focusing on biologic medicines. Specifically, it provides the number of clinical trials on biologic medicines taking place (or having taken place) in a given economy as collated and registered on the website ClinicalTrials.gov between 2010-2015. Examining rates of clinical research specific to biologics is a good indicator of a given economy's technical capacity and proficiency in complex biotech innovation. Given the size, complexity and inherent instability of a biologic, the R&D process requires a considerable level of stability and technical capacity. The testing of a biologic drug candidate's safety and efficacy within a clinical trial necessitate a highly-controlled environment, where: the transportation and storage of the drug are controlled; the trial protocols are strictly adhered to; and patients are monitored carefully.

As with other indicators the total number of biologic trials has been standardised to population to provide a more accurate reflection of levels of biologics clinical research intensity in a given economy regardless of population size.

This dataset includes all of the economies sampled in *Building the Bioeconomy 2016*.

Indicator 5: Early phase (Phase I and II) clinical trials for biologics, % of total clinical trials for biologics 2010-2015

This indicator focuses on early phase clinical research on biologic medicines between 2010-2015. Early phase trials are the most scientifically advanced and represent the most innovative and riskiest phases of the clinical development process.

This dataset includes all of the economies sampled in *Building the Bioeconomy 2016*.

Indicator 6: Biotechnology triadic patenting, share of global total average 1999-2012

This indicator examines levels of triadic patenting and an economy's share of the global number of biotechnology patents between 1999-2012. Triadic patenting is generally considered to be the best indicator of the perceived overall value and quality of a patent. The patent application is filed in three separate locations and filing costs are quite

high. The three major patenting offices in which protection is sought are: the European Patent Office, the US Patent Office and the Japanese Patent Office.

This data is collected from the OECD.[115] This dataset includes all of the economies sampled in *Building the Bioeconomy 2016*.

Indicator 7: Biopharmaceutical product launches, % available in country within 5 years of global product launch, 1983-2000

This indicator compares relative levels of biopharmaceutical product penetration in the sampled economies. Specifically, it looks at the percentage of products available in a given economy within five years of first global launch. The data is drawn from a 2014 National Bureau of Economic Research working paper and is in turn based on national product approval rates in 76 individual economies including all of the economies sampled in *Building the Bioeconomy 2016* except China.[116]

Indicator 8: National % share total number of patents from top 50 PCT applicants: universities, 2014

This indicator examines rates of university PCT patenting as collected and published by WIPO.[117] Specifically, it looks at in which countries the world's 50 most prolific PCT patenting universities were based. To obtain a weighted share for each economy included in *Building the Bioeconomy 2016* the total number of PCT patents applied for by universities from each economy included in the top-50 was divided by the total number of patents applied for in 2014 by all 50 universities.

The underlying data includes all of the economies sampled in *Building the Bioeconomy 2016*.

Indicator 9: Biotechnology crops, hectares under cultivation, % of total 2015

This indicator compares levels of biotechnology derived crops in the sampled economies.[118] Data on hectares of biotechnology crops under cultivation are collected by the International Service for the Acquisition of Agri-biotech Applications and published annually. The number of hectares of biotech crops under cultivation is a good indicator of the level of biotechnology derived agricultural products in a given economy.

This data set includes all of the economies sampled in *Building the Bioeconomy 2016*.

Indicator 10: Biopharmaceutical Competitiveness Index (BCI) Survey, 2015 Ranking

This indicator compares economy's relative attractiveness to biopharmaceutical investment and innovation as viewed by executives on the ground in a given economy and captured in the BCI survey.[119] The BCI Survey examines the entire ecosystem in which biomedical innovation takes place from scientific capabilities and infrastructure; to state of the clinical environment; quality and efficiency of biomedical manufacturing and logistics operations; the biomedical regulatory framework (including the protection of intellectual property); healthcare financing; and overall market and business conditions. Using statistical analysis respondents' answers are translated into a quantitative score, which is used to benchmark economies' performance and overall attractiveness for investment. The BCI Survey is conducted by Pugatch Consilium, an international research consultancy and commissioned by PhRMA.

This data set includes all of the economies sampled in *Building the Bioeconomy 2016* except Malaysia.

Indicator 11: Venture Capital & Private Equity Country Attractiveness Index, Economy Ranking

This indicator compares economies relative attractiveness to venture capital and private equity.[120] The *Venture Capital & Private Equity Country Attractiveness Index* is compiled by the IESE and EMLYON business schools and examines factors from general rates of economic activity to the taxation environment, investor protection mechanisms, size and liquidity of existing capital markets and other relevant factors.

Availability of venture capital and private equity funding is of considerable importance to

biotechnology innovation and commercialization as many biotechnologies begin as nascent ideas within a start-up, smaller company or university. Figures from the National Association of Venture Capital suggests that in the US (the largest venture capital market in the world) biotechnology investments accounted for 13% of the close to USD60 billion invested in 2015.[121]

This dataset includes all of the economies sampled in *Building the Bioeconomy 2016*.

4.4 Green, yellow and red – Traffic light classification system

Each economy's performance is classified according to three categories of classification for both indicators relating to policy inputs and biotech outputs:

1. Attractive (Policy inputs)/Highly Competitive (Biotech outputs)

2. Mixed

3. Challenging (Policy inputs)/Struggling to compete (Biotech outputs)

Quantitative indicators for both policy inputs and biotech outputs compare economies to one another based on relative performance. The top third of the economy sample is classified as "Attractive" or "Highly Competitive". The middle third of the economy sample is classified as "Mixed". And, finally, the lower third of the economy sample is classified as "Challenging" or "Struggling to Compete".

Based on the discussions in previous sections on the desirability and necessity of each of the seven enabling factors to stimulate innovation in the biotechnology sector economies with higher levels of the measured indicators (for instance, R&D spending) translates into a higher classification.

Qualitative indicators are based on a normative assessment of the desirability of the remaining enabling factors. For example, for Enabling Factor 3: Intellectual Property Protection, the availability of such IPRs as regulatory data protection and patent term restoration are viewed as attractive.

Similarly, the indicator included in Enabling Factor 4: The Regulatory Environment examines the existence and efficiency of the regulatory structure in a given country. This incudes, for instance, the speed of market authorization for biotechnology products; patent office backlogs; the existence and efficiency of an ag-bio framework; the existence of a biosimilars pathway in line with international standards; and other key regulatory elements discussed in this report and accompanying Annex.

Significantly, as is discussed in the following sub-section 4.5 the relationship between policy inputs and biotech outputs is strong; economies that tend to have stronger environments with all enabling factors in place tend also to see higher levels of biotechnology outputs.

4.5 The Biotech Policy Performance Measure – Overall results

On the following two pages Table 5 shows the overall results for the Measure. Economies move from left to right in the tables from those economies that have the most challenging environments to those with the most attractive and highest levels of biotechnology outputs.

The top half of the table displays each economy's classification for the policy inputs under the seven enabling factors. The lower half of the table shows economies' performance with regards to biotech outputs. Three things stand out from this table.

First, it is clear that economies that have weak enabling environments – and perform worse relative to other economies on the indicators relating to policy inputs – tend also to have lower biotechnology outputs. In this sense the 2016 Biotech Policy Performance Measure strongly suggests that having the right policy framework in place is fundamental to achieving strong biotechnology outputs. Looking at the above results economies including India, Turkey and Colombia either do not have all the enabling factors in place or have relatively weak levels compared to other economies. For instance, all three economies have low levels of human capital and R&D infrastructure as measured by number of R&D researchers and general R&D

Table 5 Biotech Policy Performance Measure – Overall results

Policy Inputs	India	Turkey	Colombia	Russia	Mexico	Brazil	China	South Africa
Human capital	Challenging	Challenging	Challenging	Mixed	Challenging	Challenging	Mixed	Challenging
Infrastructure for R&D	Challenging	Challenging	Challenging	Mixed	Challenging	Mixed	Mixed	Challenging
Intellectual property protection	Challenging	Challenging	Mixed	Mixed	Mixed	Challenging	Challenging	Challenging
The regulatory environment	Challenging	Challenging	Mixed	Challenging	Mixed	Mixed	Challenging	Mixed
Technology transfer frameworks	Challenging	Mixed	Challenging	Challenging	Challenging	Mixed	Attractive	Mixed
Market and commercial incentives	Challenging	Challenging	Challenging	Challenging	Challenging	Challenging	Challenging	Challenging
R&D tax incentives	Attractive	Attractive	Mixed	Mixed	Mixed	Mixed	Mixed	Mixed
Legal certainty (including the rule of law)	Mixed	Challenging	Mixed	Challenging	Challenging	Mixed	Challenging	Mixed
Biotech Outputs								
Scientific publications by population	Struggling to compete	Mixed	Struggling to compete	Mixed	Struggling to compete	Mixed	Struggling to compete	Highly competitive
Quality of academic publications	Struggling to compete	Mixed	Not available	Struggling to compete	Mixed	Struggling to compete	Struggling to compete	Mixed
Clinical trials per capita	Struggling to compete	Mixed	Struggling to compete	Struggling to compete	Struggling to compete	Mixed	Struggling to compete	Mixed
Clinical trials for biologics, 2010-2015, per capita	Struggling to compete	Struggling to compete	Mixed	Mixed	Struggling to compete	Struggling to compete	Struggling to compete	Mixed
Early phase (Phase I and II) Clinical trials for biologics, % of total CTs, 2010-2015	Highly competitive	Struggling to compete	Struggling to compete	Struggling to compete	Struggling to compete	Mixed	Highly competitive	Mixed
Biotechnology triadic patenting, share of global total average 1999-2012	Mixed	Struggling to compete	Struggling to compete	Mixed	Struggling to compete	Mixed	Mixed	Struggling to compete
Biopharma product launches, % available in country within 5 years of global product launch, 1983-2000	Struggling to compete	Struggling to compete	Mixed	Struggling to compete	Highly competitive	Mixed	Not available	Mixed
National % share total number of patents from top 50 PCT applicants: universities, 2014	Struggling to compete	Struggling to compete	Struggling to compete	Struggling to compete	Struggling to compete	Struggling to compete	Highly competitive	Struggling to compete
Biotechnology crops, hectares under cultivation, % of total 2015	Highly competitive	Struggling to compete	Mixed	Struggling to compete	Mixed	Highly competitive	Mixed	Mixed
Biopharmaceutical Competitiveness Index (BCI) Survey, 2015 Ranking	Mixed	Struggling to compete	Struggling to compete	Struggling to compete	Mixed	Struggling to compete	Struggling to compete	Mixed
Venture Capital & Private Equity Country Attractiveness Index, Economy Ranking	Mixed	Mixed	Struggling to compete	Struggling to compete	Struggling to compete	Struggling to compete	Mixed	Struggling to compete

Table 5 Biotech Policy Performance Measure – Overall results (cont.)

Policy Inputs	Malaysia	Israel	Japan	Singapore	Korea	Switzerland	UK	US
Human capital	Mixed	Attractive	Attractive	Attractive	Attractive	Attractive	Mixed	Mixed
Infrastructure for R&D	Mixed	Attractive	Attractive	Mixed	Attractive	Attractive	Mixed	Attractive
Intellectual property protection	Mixed	Mixed	Attractive	Attractive	Attractive	Attractive	Attractive	Attractive
The regulatory environment	Mixed	Mixed	Attractive	Attractive	Attractive	Mixed	Attractive	Attractive
Technology transfer frameworks	Challenging	Attractive	Attractive	Attractive	Attractive	Attractive	Attractive	Attractive
Market and commercial incentives	Challenging	Mixed	Mixed	Mixed	Challenging	Mixed	Mixed	Attractive
R&D tax incentives	Attractive	Attractive	Mixed	Mixed	Mixed	Mixed	Attractive	Mixed
Legal certainty (including the rule of law)	Mixed	Not available	Attractive	Attractive	Attractive	Not available	Attractive	Mixed
Biotech Outputs								
Scientific publications by population	Struggling to compete	Highly competitive	Mixed	Mixed	Mixed	Highly competitive	Highly competitive	Highly competitive
Quality of academic publications	Not available	Highly competitive	Mixed	Not available	Mixed	Highly competitive	Highly competitive	Highly competitive
Clinical trials per capita	Mixed	Highly competitive	Mixed	Highly competitive	Mixed	Highly competitive	Highly competitive	Highly competitive
Clinical trials for biologics, 2010-2015, per capita	Mixed	Highly competitive	Mixed	Highly competitive	Mixed	Highly competitive	Highly competitive	Highly competitive
Early phase (Phase I and II) Clinical trials for biologics, % of total CTs, 2010-2015	Struggling to compete	Mixed	Mixed	Mixed	Highly competitive	Mixed	Highly competitive	Highly competitive
Biotechnology triadic patenting, share of global total average 1999-2012	Struggling to compete	Mixed	Highly competitive	Mixed	Highly competitive	Highly competitive	Highly competitive	Highly competitive
Biopharma product launches, % available in country within 5 years of global product launch, 1983-2000	Struggling to compete	Struggling to compete	Mixed	Mixed	Highly competitive	Highly competitive	Highly competitive	Highly competitive
National % share total number of patents from top 50 PCT applicants: universities, 2014	Struggling to compete	Mixed	Highly competitive	Mixed	Highly competitive	Mixed	Mixed	Highly competitive
Biotechnology crops, hectares under cultivation, % of total 2015	Struggling to compete	Struggling to compete	Struggling to compete	Struggling to compete	Struggling to compete	Struggling to compete	Struggling to compete	Highly competitive
Biopharmaceutical Competitiveness Index (BCI) Survey, 2015 Ranking	Not available	Mixed	Mixed	Highly competitive	Highly competitive	Highly competitive	Highly competitive	Highly competitive
Venture Capital & Private Equity Country Attractiveness Index, Economy Ranking	Mixed	Mixed	Highly competitive	Highly competitive	Mixed	Highly competitive	Highly competitive	Highly competitive

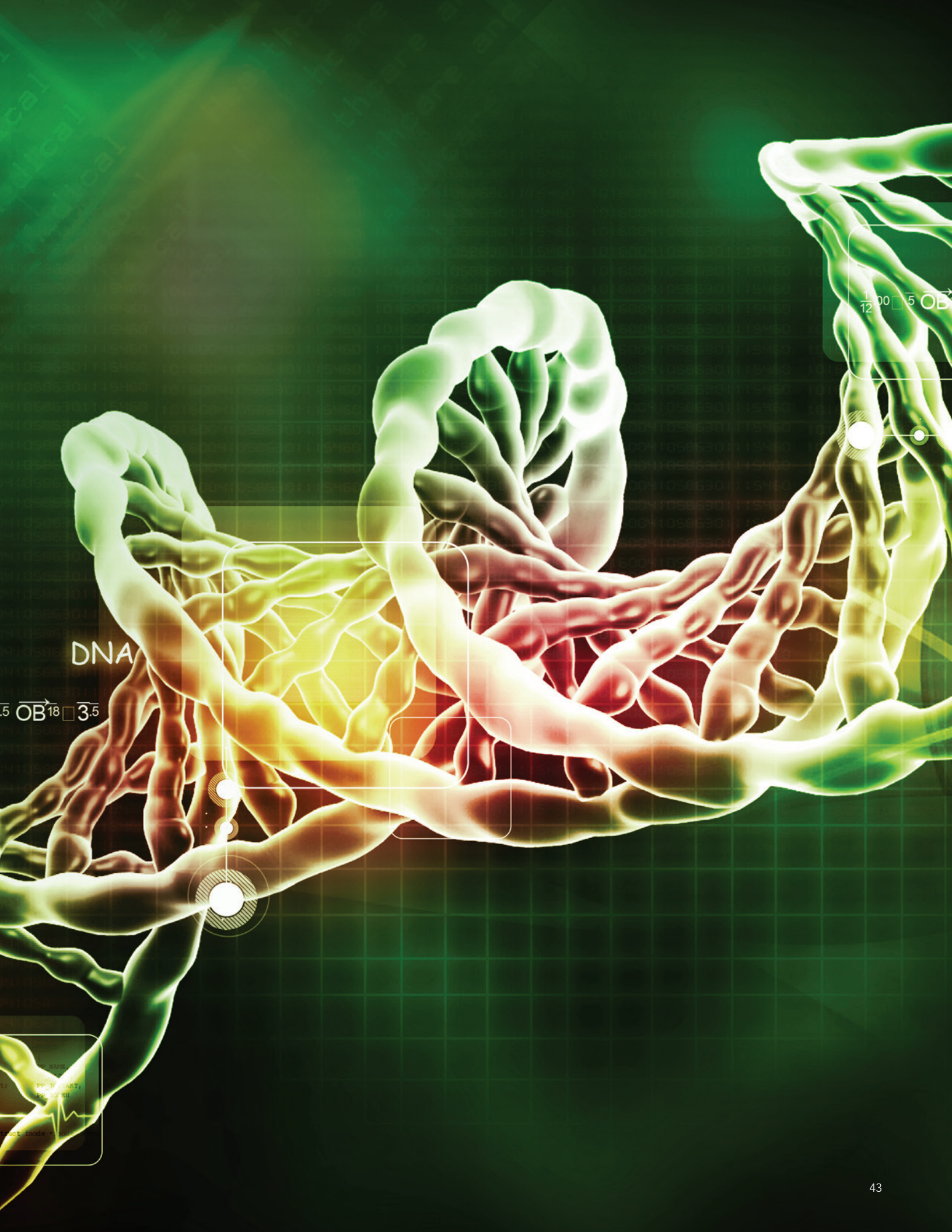
spending. Furthermore, India and Turkey face significant challenges in the IP and regulatory space. Conversely, economies that have strong and conducive enabling environments in place encompassing all seven enabling factors tend also to see high levels of biotechnology outputs. Traditionally strong centers for biotechnology innovation such as the UK, Switzerland and US are flanked by economies such as Singapore, Korea and Israel that over the last few decades in a concerted and holistic effort have reformed and successfully developed their respective biotechnology sectors.

Second, all economies have strengths and weaknesses. For example, even in the top performers who tend to have a strong policy framework and high levels of biotechnology outputs there are challenges. R&D tax incentives in the US are not as generous as in other markets. In fact, many economies that otherwise face steep policy hurdles – including India, Turkey and Malaysia – have in place relatively attractive R&D tax environments. Other economies tend to have strong outputs in some biotechnology sectors; with corresponding weaker policy frameworks in those biotech sectors which are weaker. For example, neither the UK nor Switzerland have particularly advanced ag-bio capacities. This is in large measure due to the lack of incentives, relevant regulatory framework and public opposition to the use of biotechnology crops. Conversely, Brazil has a strong and world-class regulatory framework for ag-bio – including providing a term of ten years RDP for fertilizers and agrochemical products – and is a world leader in the production of biotechnology crops.

Third, zooming in on biopharmaceuticals and clinical research the three output indicators relating to total levels of clinical research as well as specific to biologic medicines is highly concentrated. Traditional centers for biopharmaceutical R&D such as the US, UK and Switzerland together with Israel and Singapore have the highest levels of clinical trials across all three indicators. Conversely, the world's largest and fastest growing markets – including the BRICs, Turkey and Mexico – struggle to compete across these indicators with low levels of R&D activity. The only exception to this is early phase research in biologics where both China and India have relatively high levels relative to their total number of biologic trials. Yet while this is a net positive, it should also be noted that these figures for early phase trials have not been standardized to population nor do they reflect the overall levels of trial activity. For example, in the period analysed (2010-2015) India had a total of 69 phase I and II trials constituting 51% of the total number of biologics trials during this time period. Yet economies such as Israel, Switzerland and Japan had absolute number of early phase trials that matched or exceeded this number. But because of the higher levels of total biologic trials, as a percentage of this number their early phase trials was lower than India's.

In sum, although the results of the Biotech Policy Performance Measure show the great variety between economies and how each economy is unique and has individual strengths and weaknesses, the overall take-home message from the Measure is quite clear: **having the right policy framework in place is fundamental to achieving strong biotechnology outputs.**

Building on the preceding sections, discussion of the seven enabling factors, global biotechnology developments in 2015 and the preceding results of the Biotech Policy Performance Measure the following section provides a holistic assessment of all the data and evidence presented, tying together all the pieces and sections of this report into an overall set of conclusions and findings about the state of the bioeconomy in 2016 and going forward.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5 POLICY LESSONS FOR 2016 AND BEYOND

How do you succeed in building and developing a high-tech a sector as complex as biotechnology? Unfortunately there are no easy answers. Every economy is unique and has its own particular set of circumstances and starting points with regards to natural resources, socio-economic and demographic make-up as well as legal and cultural history.

Some economies such as Brazil and Colombia are blessed with high levels of biodiversity and have a natural starting point for biotechnological innovation and R&D. Other economies are not as fortunate. Small economies with limited natural resources such as Israel and Singapore have to rely more on ingenuity, creativity and the right policies in order to succeed.

The overriding purpose of the *Building the Bioeconomy* series over the past few years is not necessarily to provide a step-by-step guide to how to build a thriving bioeconomy. Instead, at its core, *Building the Bioeconomy* seeks to expound on those principles and factors that through international experience and empirical research have proved to be critical in developing a biotech capacity and incentivising biotech R&D. While encouraging innovation and building a biotech capacity is not an exact science, and different economies will have different needs, the seven enabling factors identified and explained in this series of papers provide a set of principles and areas of public policy governments and officials can take action and expect a positive outcome. Human capital; adequate R&D infrastructure; strong and targeted IP protection; transparent and effective regulations and administration; a technology transfer framework that encourages innovation and the translation of R&D into actual products and full commercialization; and a predictable and stable legal environment – these are all key factors and enablers of general and biotechnology-specific innovation.

Building on the preceding sections, discussion of the seven enabling factors, global biotechnology developments in 2015 and the preceding results of the Biotech Policy Performance Measure *Building the Bioeconomy* findings can be grouped around three key take-home messages.

Take-home message 1: Inputs = Outputs

The expansion of the Biotech Policy Performance Measure to now also take into account biotech outcomes helps clearly illustrate the direct link between creating a positive enabling environment with real-world biotech outcomes. Perhaps the most important finding of the 2016 edition of the Biotech Policy Performance Measure is that economies that have weak enabling environments – and perform worse relative to other economies on the ten indicators relating to policy inputs – tend also to have lower biotechnology outputs. The 2016 Biotech Policy Performance Measure shows economies that have the right policy framework and create a positive, incentives-based environment around the seven enabling factors tend to be much more successful in achieving strong biotechnology outputs.

Take-home message 2: Erecting localization barriers and mandating local production does not translate into greater levels of innovation

The desire to attract greater flows of foreign direct investment (general as well as biotech specific) has promoted a growing number of countries to launch ambitious policies seeking to "localize" innovation and economic activity. While active government efforts to increase attractiveness to domestic and international investment are nothing new, in a growing number of countries these localization policies seek to mandate or coerce local economic activity and investment through in fact raising localization barriers. Over the last 5-10 years policies and barriers aimed at nurturing local industries in the place of more non-discriminatory incentive-based approaches have steadily increased. Numerous financial and trade bodies have documented a recent trend toward use of trade barriers, particularly non-tariff or indirect tools, that have the goal of discriminating

against imported goods and boosting local industrial sectors.[122] As discussed above, a number of economies in the *Building the Bioeconomy* sample have erected there barriers with the goal of developing their biotech capacity. Yet these policies are often self-defeating. Economies that tend to impose local content requirements or domestic manufacturing requirements in an effort to boost local technical capacity often see less investment and less innovation – in biotechnology as well as in other sectors. For example, a number of countries mandate the conduct of clinical trials as a condition of market registration. These requirements for additional local clinical trials are often based on industrial policy and efforts to build local research capacity. They form part of broader policies seeking to localize biopharmaceutical R&D through mandatory requirements. In China, for instance, since 2014 in order to obtain market authorization for higher-risk (Class III) medical devices local clinical trials must be conducted.[123] Similarly in Russia since 2010 under Federal Law N.61 "On Circulation of Medicines" there is an obligation to conduct local clinical trials in Russia by all companies (including foreign ones) as a condition of the registration of medicine.[124]

Yet the evidence presented in the Biotech Policy Performance Measure shows clearly that those economies that embrace open, transparent policies centred around the seven enabling factors achieve much higher levels of actual biotechnology outputs. The findings in the Measure suggest that the best way to 'localize' innovation is to offer open and positive incentives.

Take-home message 3: The necessity for holistic policy reform

Finally, while many economies can have strengths and successes on some enabling factors and some outputs, the countries that achieve success across the board are those that are able to introduce policies and reforms that cut across all enabling factors. For example, while Brazil remains a world leader in biotechnology crops and biofuels production, in the biopharmaceutical sector it lags behind. A challenging environment across factors relating to its regulatory environment, protection of IP and market and commercial incentives have resulted in Brazil having low levels of clinical research activity absolutely and for biologic products. Of note is that in many cases the incentives used to spur investment and innovation in the ag-bio and biofuels fields –including providing a term of ten years RDP for fertilizers and agrochemical products – have not been put in place for the biopharmaceutical sector. Indeed, from a policy perspective a critical take-away message is that these factors work together. Economies that have been successful in developing and building a world-class biotechnology industry have had to pursue policies in for all seven enabling factors.


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