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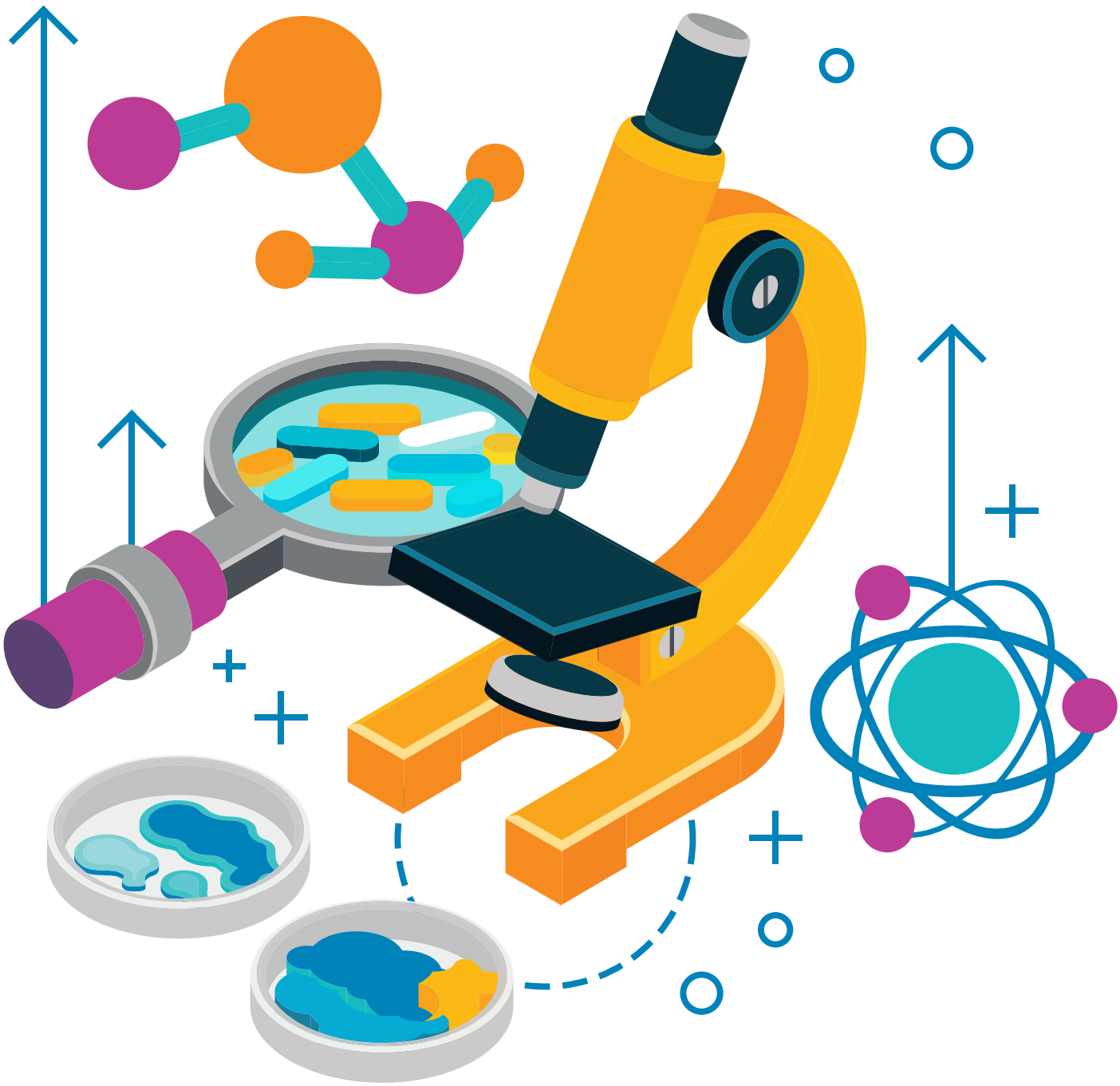

BUILDING THE BIOECONOMY 6TH EDITION

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

TABLES AND FIGURES

LIST OF ABBREVIATIONS

AMNOG	Pharmaceuticals Market Reorganization Act (Germany)
ASEAN	Association of Southeast Asian Nations
ATU	Temporary Use Authorization (France)
BCI	Biopharmaceutical Competitiveness and Innovation
BERD	Business Expenditure on R&D
CEA	Cost Effectiveness Analysis
CRISPR	Clustered Regularly Interspaced Short Palindromic Repeats
CSP	Certificate of Supplementary Protection
DRA	Drug Regulatory Authority
EC	European Commission
ECJ	European Court of Justice
EMA	European Medical Agency
EU	European Union
FAS	Federal Anti-monopolistic Service (Russia)
FDA	US Food and Drug Administration
FDI	Foreign Direct Investment
GDP	Gross Domestic Product
GE	Genetically Engineered
GM	Genetically Modified
GMO	Genetically Modified Organism
HTA	Health Technology Assessment
ICT	Information and Communications Technology
IP	Intellectual Property
IPI	International Pricing Index
IPRs	Intellectual Property Rights
IRP	International Reference Pricing
KORUS	Korea-US Trade Agreement
MoH	Ministry of Health
NAFDAC	National Agency for Food and Drug Administration and Control (Nigeria)
NAFTA	North Atlantic Free Trade Area
NDA	New Drug Authorization

LIST OF ABBREVIATIONS (cont.)

NME	New Molecular Entity
OECD	Organization for Economic Co-operation and Development
P&R	Pricing and Reimbursement
PhRMA	Pharmaceutical Research and Manufacturers of America
PMP	Price Maintenance Premium
PPP	Purchase Power Parity
PRO	Public Research Organization
PTE	Patent Term of Extension
RDP	Regulatory Data Protection
R&D	Research and Development
SDGs	Sustainable Development Goals
SMEs	Small and Medium Enterprises
SPC	Supplementary Patent Certificate
STI	Science, Technology and Innovation
TCC	Therapeutic Class Comparison
USMCA	US-Mexico-Canada Agreement
VC	Venture Capital
WHO	World Health Organization
WIPO	World Intellectual Property Organization
WTO	World Trade Organization

EXECUTIVE SUMMARY

2019 marks the sixth edition of the *Building the Bioeconomy* series. Since 2013 it has taken the pulse of biotechnology policy frameworks by looking at their developments and overall performance in some of the major economies around the world. The overriding goal of this exercise has been to identify how successful biotechnology sectors can be built and sustained.

Seven enabling factors for biotech success

The analysis and policy mapping of *Building the Bioeconomy* is built around seven enabling factors for biotechnology development. The factors range from the institutional and eco-system level (such as levels of tertiary education, technical skill 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 give countries and policymakers the best chance of having success in developing their biotech capacity and promoting biotech innovation.

The below table provides an overview of these factors and a brief description of each.

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 incentivize 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 commercializing 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.

A wider sample of national biotech policies

This edition of *Building the Bioeconomy* expands the analysis by one-third – from 33 to 44 of the world's major economies and aspiring biotech pioneers. The below table lists the 44 countries included in this year's report according to World Bank income level with the 11 new countries highlighted in bold.

Key findings and Biotech Policy Performance Measure results

First featured in 2015, the Biotech Policy Performance Measure (the "Measure") is an empirical tool that directly compares economies' policy inputs with real-life biotech outputs. This year the Measure examines a total of 30 indicators with two new indicators having been added to this edition of *Building the Bioeconomy*. These indicators are divided between 18 measures of policy inputs (as in previous editions related to the seven enabling factors listed above) and 12 indicators of biotechnology outputs. Together these indicators provide a rich and detailed measure of the biotechnology environment for a given economy. Below are the overall results for the Biotech Policy Performance Measure. Economies move from top to bottom in the figure from those that have the most attractive policy environments and accompanying high levels of biotechnology outputs to those that have the most challenging environments for both policy inputs and biotech outputs. (A full set of tables with results for each indicator and inputs and outputs for each economy is provided in the accompanying Annex.)

Building the Bioeconomy 2019 44 economies by World Bank income group

Lower-middle-income economies	Upper-middle-income economies	High-income economies	High-income OECD Members
Egypt	**Algeria**	Argentina	Australia
India	Brazil	Saudi Arabia	**Canada**
Indonesia	China	Singapore	Chile
Kenya	Colombia	Taiwan	Denmark
Nigeria	Costa Rica	UAE	Finland
Philippines	**Ecuador**		**France**
Vietnam	Malaysia		**Germany**
	Mexico		Ireland
	Peru		Israel
	Russia		Japan
	South Africa		**Lithuania**
	Thailand		New Zealand
	Turkey		**Netherlands**
			Norway
			South Korea
			Sweden
			Switzerland
			UK
			US

The Biotech Policy Performance Measure – Overall results

Looking at the above indicators, the addition of 11 new economies (a growth of 33% in the sample size) only strengthens the overall message of previous editions of the Measure: **Inputs equal outputs**. There is a strong and sustained link between creating a positive enabling policy environment and achieving real-world biotech outcomes. 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.

Another important take-away from the Measure is that **there is no shortcut** to building a conducive biotech policy environment. Each economy has its own strengths, which it can leverage to enhance its attractiveness vis-à-vis other markets. Some – such as many Latin American countries – are blessed with rich and varied ecosystems that provide a strong starting point for biotechnological innovation and R&D. Others – such as Algeria and Norway – have benefitted from the inflow of revenues from natural resources. But relying only on intrinsic strengths cannot alone deliver the expected economic and social benefits of biotechnologies. Small economies with limited natural resources such as Israel, Denmark, Ireland and Singapore have had to rely more on ingenuity, creativity and getting their incentives right to create an enabling environment for innovation.

Conclusions and recommendations

For six years, this report has reflected on how the right policies can help build thriving biotech sectors. This edition of *Building the Bioeconomy* again makes it clear that the countries that stand the best chance of enjoying the fruits of biotechnology innovation are the ones where forward-looking regulations act to encourage, and not hinder, innovation. Based on the analysis and mapping of the national innovation systems and biotechnology policies and enabling factors in place in the 44 countries sampled it is possible to piece together five universal recommendations.

They are:

1. **Create a national blueprint or plan of action** – The existence and creation of a blueprint or national biotechnology strategy can be a powerful tool in creating a vision and setting a goal for national aspirations. There are many ways in which governments can provide leadership and direction for the building of biotechnology capacity. By and large most countries studied in this paper have directly or indirectly targeted biotechnology as a technology and industry of strategic importance to national economic development and growth. But not all 44 of the sampled countries have developed national blueprints or plans for developing the sector.

2. **Execute** – A national blueprint or plan of action is a necessary starting point for all aspiring biotech nations, but it is only the first step. Once it has been formulated and drawn up it must be implemented. Building a bioeconomy is not a short-term proposition. It takes long term planning, patience and commitment. But where many countries fall short is in their ability and efforts to move from a planning phase to actually implementing and applying the necessary policies. This is where the hard work begins.

3. **Measure performance** – The measuring of performance and the creation of key performance indicators is critical. Without an understanding of whether or not implemented policies are actually working it is impossible to properly evaluate whether any progress is being made.

4. **Recognize and use existing best practices** – Although no two countries are the same and all face different circumstances, countries can learn from the experiences of each other.

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

1 INTRODUCTION

In 2015 the international community through the United Nations agreed to a new socio-economic blueprint – the "2030 Agenda", including 17 Sustainable Development Goals and 169 targets.[1] Some targets are societal in nature: they tackle basic needs, access to services and poverty, and relate to human well-being. Others focus on economic development and wealth creation. And there are also important targets relating to the environment and resource security, health ecosystems and climate change. It is an ambitious set of holistic global goals and aspirations.

1.1 Rising to the challenge – biotechnologies for sustainability

From a biotech perspective it is amazing to think how biotechnology as such and the many different biotechnologies are critical to achieving these goals.[2] Biotechnologies provide in the health space new medical therapies and treatments (e.g. immunotherapy and gene therapy), more effective diagnostics, speedier and more targeted vaccine production and personalized medicine. For agricultural production biotech can help produce crops resilient to extreme environments caused by climate change, improve yields and nutritional value. In industrial development, biotechnology can not only reduce costs for the production of many human essentials but also reduce the environmental footprint for a given level of production through for instance the development of new environmentally friendly fuels and sources of energy.[3] As an application of biology for the benefit of humanity and the environment, sustainability is intrinsic to biotechnologies. Exploiting the role of biotechnologies as a long-term lever of sustainable and inclusive growth is both an imperative and an opportunity.

1.2 Objectives of the 2019 edition of *Building the Bioeconomy*

2019 marks the sixth edition of the *Building the Bioeconomy* series. Since 2013 it has taken the pulse of biotechnology policy frameworks by looking at their developments and overall performance in some of the major economies around the world. The overriding goal of this exercise has been to identify how successful biotechnology sectors can be built and sustained. In addition to mapping policy trends and monitoring changes, the last few editions of the report have also assessed how different economies are achieving their stated biotech goals. This is done through the Biotech Policy Performance Measure (the "Measure"), a comparison of economies on 30 policy inputs and biotech outputs showing how individual economies' policy environments affect their success or failure in creating thriving biotech sectors.

1.3 Enabling factors for biotech success

Designing an environment that is conducive to the innovation, research, commercialization and marketing of biological products and technologies is not an exact science. Different countries have greater or lesser needs in specific policy areas. Still, most countries that have been successful in creating an environment conducive to biotech innovation share some key enabling factors.[4]

The analysis and policy mapping of *Building the Bioeconomy* is built around seven enabling factors for biotechnology development. The factors range from the institutional and eco-system level (such as levels of tertiary education, technical skill 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 give countries and policymakers the best chance of having success in developing their biotech capacity and promoting biotech innovation.

Below Table 1 provides an overview of these factors and a brief description of each.

TABLE 1 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.
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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.

1.4 A wider sample of national biotech policies

This edition expands the analysis from 33 to 44 of the world's major economies and aspiring biotech pioneers, providing a larger sample to examine the main global trends and developments. On the next page Table 2 lists the 44 countries included in this year's report according to World Bank income level with the 11 new countries highlighted in bold.

1.5 Report overview

In addition to this Introduction this report consists of three sections.

Section 2 provides a thematic analysis and overview of the past year in biotechnology. It identifies the main challenges for biotech development across the countries analyzed. What are the main constraints for biotech innovators? Are recent policy

initiatives helping or hindering faster technological advances?

Section 3 zooms in on the 11 economies added to this year's edition. For each of them, the section briefly presents the policy framework for innovation and biotechnology: What is the role of innovation in the country's economy? Is a biotechnology vision or strategy in place? Which biotech sectors are seen as holding the greatest potential?

Section 4 describes the Biotech Policy Performance Measure. It explains the 30 indicators used and provides an overview of the underlying data that feeds into the Measure. What do the results of the Measure tell us about best practices for enabling biotech innovation in the 44 economies sampled? What can these economies learn from it and what does it mean for other economies not included in *Building the Bioeconomy* but aspiring to develop their biotech capacity? (The full results including all the underlying data for each of the 30 indicators for each economy is included in an accompanying Annex).

Section 5 ties together the analysis and data-based insights of the preceding sections and presents the main conclusions from six years of the *Building the Bioeconomy* series.

TABLE 2 *Building the Bioeconomy 2019* 44 economies by World Bank income group

Lower-middle-income economies	Upper-middle-income economies	High-income economies	High-income OECD Members
Egypt	**Algeria**	Argentina	Australia
India	Brazil	Saudi Arabia	**Canada**
Indonesia	China	Singapore	Chile
Kenya	Colombia	Taiwan	Denmark
Nigeria	Costa Rica	UAE	Finland
Philippines	**Ecuador**		**France**
Vietnam	Malaysia		**Germany**
	Mexico		Ireland
	Peru		Israel
	Russia		Japan
	South Africa		**Lithuania**
	Thailand		New Zealand
	Turkey		**Netherlands**
			Norway
			South Korea
			Sweden
			Switzerland
			UK
			US

Source: World Bank (2018)

2 THE STATE OF GLOBAL BIOTECHNOLOGY IN 2019

The last twelve months have been an active time in the international biotech community. In terms of news headlines, the main came from China in November 2018 with the announcement by Chinese scientist He Jiankui that he had used gene editing technology on human embryos.[5]

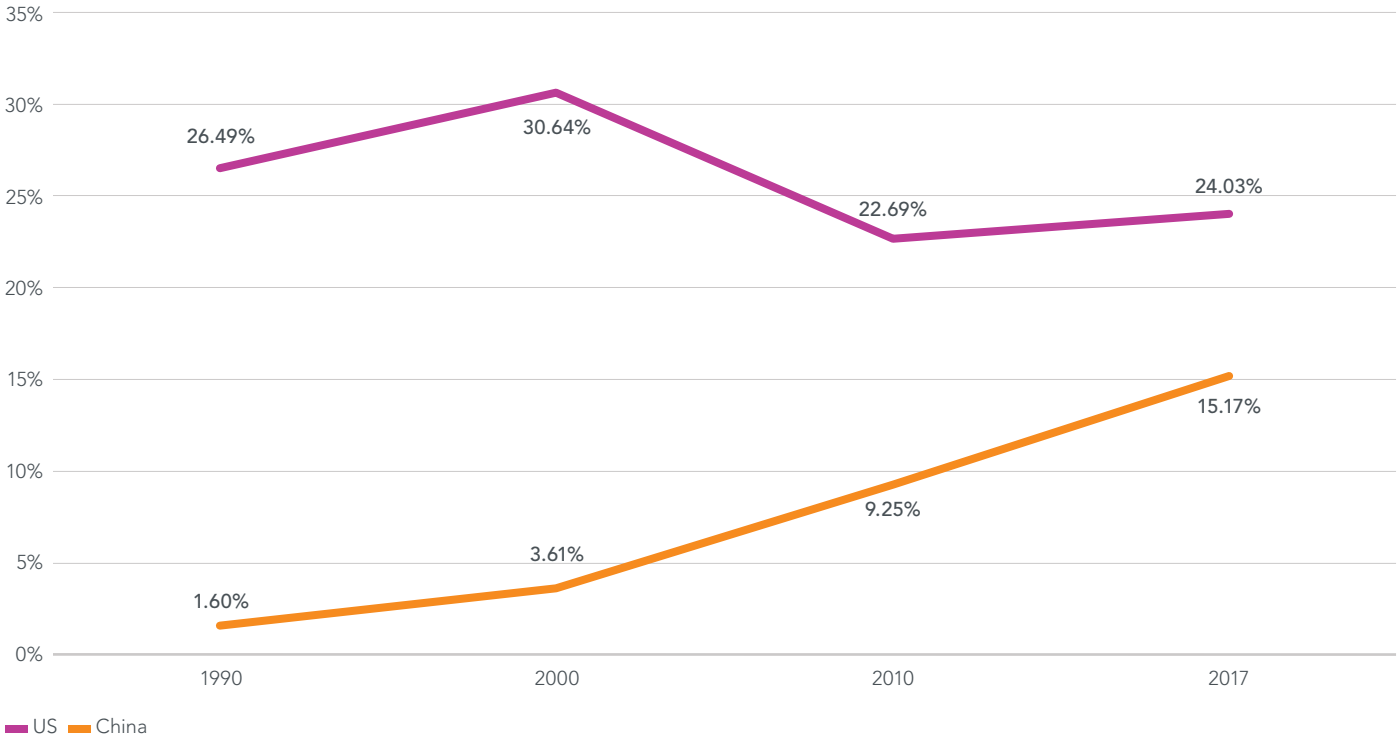
This claim has yet to be independently verified and the bulk of the scientific community – internationally and in China – have condemned the purported research. Whether or not He was successful, his claim has brought to the forefront some of the most critical ethical considerations and discussion on the use and application of genetic engineering techniques on humans.

More broadly, developments in international politics during the course of the year have the potential to have a major impact on virtually all biotechnologies and sectors. Perhaps most important of all is the trade dispute and trade negotiations between the **US** and **China**.

2.1 The story of the early 21st century: The rise of China

Apart from the fall of the Soviet Union arguably the most important geopolitical development of the past three decades has been the economic development and growth of China. As a share of aggregate global GDP China's economy in 1990 was a little bit bigger than Sweden's and constituted roughly 1.6% global output.[6] While American economic output as a share of global GDP has largely stood still, as Figure 1 illustrates below the growth of China over the last 30 years has been breathtaking. By 2017 China's economic output was second only to the US and made up over 15% of global GDP.

FIGURE 1 % share of global GDP, Current USD, 1990-2017, China and United States[7]



In just over one generation China has transformed itself – and the global economy – from a primarily agrarian economy to a global exporting powerhouse. In 2017 China was the largest trading nation in the world, Chinese exports totalled USD 2.22trillion and its trade surplus was over USD 400billion.[8] China's growth and socio-economic transformation have had a profound domestic impact: millions of Chinese have been lifted out of poverty. Its international impact has been heightened as it has coincided with deep structural changes to the global economy. Today's global economy is inter-linked, inter-dependent and open for business in a way that it was impossible logistically, politically or financially a generation ago. Indeed, the sum of the technological, cultural, political and socio-economic changes of the last three decades amounts to what is truly a paradigm shift. In 1990 the internet was not a commercially or publicly available entity. The Soviet Union, although crumbling, was still the world's second most important geopolitical bloc and one of its largest economies. Just-in-time manufacturing and the use of international supply chains were not industry standards and are now the bases for much of modern commerce. At the heart of all these changes have been China's development and growing importance within the global economy.

2.2 The future of global trading relations: Effective market access and the protection of IP

Market access and the protection of IP lie at the heart of the current trade dispute between the US and China. Chinese policymakers have long recognized the need to shift domestic economic activity away from low added value industrial production into higher value knowledge-creation and high-tech, advanced manufacturing and R&D. Successive Chinese administrations have emphasized the need for investing in R&D capacity, technology development, human capital and incentivizing innovation. Specific policies and plans range from the *Five-Year Plans* to plans for *Science and Technology Development* to the more recent *Made in China 2025*. Underlying many of these policies and plans is a focus on local technology acquisition and development. For example, there are a number of barriers in place for licensing agreements and entry into China that both directly and indirectly require localization in order to access the market. Examples of such policies include joint ventures and technology transfer deals, whereby technology intensive industries trade technology for market access or government entities favor foreign suppliers that provide training services or transfer of know-how. These agreements have been common practice in China for several years, despite being prohibited by the WTO.[9] One illustration of this is the fact that while a specially reduced corporation tax of 15% (compared to 25%) is in place for high-tech companies, foreign entities must transfer ownership of their IP to a local entity in order to qualify.[10] In addition, licensing of foreign IP to local entities is subject to wide flexibilities on the local entities' part, including the ability to make improvements or reverse engineer the licensed asset without any ownership on the part of the foreign rights holder.[11] In the context of standard setting, there is also a trend toward greater administrative involvement in determining patent licensing terms and the ability to secure relief from infringement. Although some policies have been revoked, many of these policies are still in place and continue to be introduced. At the heart of this policy has been the lure of the enormous potential of the Chinese market. While all high-technology sectors have been affected by these policies, biotechnology in particular has been a focus of Chinese policymakers. China has in various policies outright or indirectly sought to link access to the Chinese market with more favourable terms and/or restrict foreign competition for domestic producers. For example, with respect to agriculture and production of biotech crops, severe restrictions of access to the Chinese market have hampered trade between the US and China. The Chinese Ministry of Agriculture and the National Biosafety Committee are responsible for the regulation and approval of imported agricultural GM products and/or the domestic production of GM products in China.[12] The regulatory pathway to commercialization has not been easy to navigate either for international or Chinese innovators as there are a number of regulatory-related barriers to market entry. They include: the requirement that a product must be registered and approved in the country of export prior to an application for approval can be made in

China; and a requirement that import applications include viable seeds.[13] The latter requirement has raised concerns among manufacturers about the protection of their IP.[14] Perhaps most damagingly of all are the long delays in market approval for biotech events and products. A 2018 report suggested that these delays in Chinese approval times had cost the major biotech crop producers in the world (US, Brazil and Argentina) billions of dollars in potential lost sales share.[15] The direct and indirect negative impact on the American economy was an estimated USD 14.8billlion in economic output.[16] Similarly, for the biopharmaceutical sector Chinese policymakers have sought to make market access and IP protection contingent on early product launches and investment into the Chinese market. For example, in 2016 *The Work Plan for the Reform of Chemical Drug Registration Categories* introduced a definition for "new drugs" that required an extensive level of investment – first global launch in China – in order to benefit from a range of existing advantages. Under the proposed policy only drugs not yet marketed anywhere in the world would be considered as "new" in China, and thus qualified for certain benefits such as a five-year "monitoring period" (i.e. akin to RDP).[17] Out of around 350 drugs approved in 2014, only 2.9% were drugs that had not been marketed anywhere in the world and none were the more advanced biological drugs.[18] Moreover, under proposed 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 five-year marketing exclusivity.[19] While these policies were never fully implemented, as is detailed below China is now proposing similar measures and conditions with respect to periods of patent term restoration.

Yet these trading challenges are not unique to China. As the following sub-section details, biotechnology entrepreneurs and innovators face similar issues of effective market access and protecting their IP in many of the world's biggest markets.

2.3 One step forward, two steps back…

Looking at the seven enabling factors identified in the *Building the Bioeconomy* series, it is clear that one of the major challenges facing policymakers is a lack of coordination and holistic thinking. Simply put policy reform efforts in one policy area are often counter-balanced or cancelled out by negative action in other areas.

For instance, on the one hand, many countries are moving ahead with positive reform efforts in the space of speeding up drug marketing approvals and R&D tax incentives. As was noted in last year's *Building the Bioeconomy*, in many countries drug regulators are responding to the rapid pace of innovation and unmet medical need by introducing accelerated and/or abbreviated market approval pathways. This trend has continued in some major economies during 2018, most notably in **China**. During 2018 China agreed to accept trial data from other countries for drug marketing procedures, putting an end to a burdensome, time-consuming and expensive requirement to enter the Chinese market.[20] It also streamlined trial approval procedures setting a 60-day approval target.[21] In a further move to make foreign drugs more rapidly available to Chinese patients, the National Medical Products Administration established a "special channel" for the review and approval of new drugs approved and marketed in the US, EU, or Japan in the past 10 years, but not yet approved in China.[22] To this effect, the first *Catalogue of Urgently-Needed Overseas Pharmaceuticals* contains 40 drugs for rare and life-threatening diseases for which no treatment is available or with a demonstrated clinical advantage. Through this special channel, the timeline for technical review will be shortened to three months for orphan drugs and to six months for treatments of life-threatening diseases.[23] More generally, improvements to approval procedures have continued, and since 2017 China has approved a record number of innovative foreign drugs. Finally, the Chinese government has, starting from March 2019, introduced a new preferential 3% VAT rate (versus a standard rate of 16%) for 21 medicines and 4 drug substances used to treat rare diseases.[24]

Similarly, more countries are attempting to enhance their competitiveness by introducing new R&D tax benefits or improving the schemes already in place, often in the framework of reforms to bring them in line with OECD BEPS requirements.[25] Of the economies sampled in the *Building the Bioeconomy* series, in 2018 significant improvements were registered in Singapore, who raised its tax deduction rate and introduced a patent box regime – as did Switzerland.[26] And since the first quarter of 2019 a new R&D tax scheme is also available to businesses in New Zealand.[27] Also Germany, who has traditionally relied on direct funding, is planning to introduce R&D tax breaks to reach its target of allocating 3.5% of GDP to R&D.[28]

Nevertheless, despite important reforms such as these, many countries continue to introduce negative policies and raise barriers with respect to two areas in particular: i) market and commercial incentives, especially for biopharmaceutical products; and ii) the protection of IP.

2.4 Cost control at all costs? Developments in biopharmaceutical pricing policies

Pharmaceutical pricing and reimbursement (P&R) policies are perhaps the most common set of policies used by payers (government or private) to control the cost of biopharmaceuticals. P&R policies are used in all types of health care markets, whether they be OECD countries with sophisticated and well-developed health systems or emerging and developing markets where, in many cases, the health system is still being built. The growing need for specialty drugs – estimated at one third of total drug spending globally in 2016[29] – and availability of new, life-saving treatments add pressure on healthcare systems that are already grappling with other long-term structural factors such as ageing populations. These pressures require long-term strategic and holistic thinking and a concerted policy approach taking into consideration all parts of the health system. Unfortunately, in many countries payers are not engaging in systematic and holistic health system evaluation and reform. Instead, much of the effort is aimed at cutting spending on the perceived high cost of new medicines. This theme has become particularly pronounced over the last

eighteen months, when health systems that have traditionally valued biopharmaceutical innovation appear to be shifting focus embracing cost control policies that risk leading to less innovation and fewer new products.

Innovation strongholds playing with fire

In the US the cost of biopharmaceuticals is again at the top of the policy agenda. Over the course of 2018 the Trump administration has introduced a number of reform initiatives aimed at lowering the cost of prescription medicines. In February 2018 the Council of Economic Advisers (CEA) released *Reforming Biopharmaceutical Pricing at Home and Abroad*, an analysis of the global biopharmaceutical market. A few months later President Trump and the Department of Health and Human Services also announced a set of reforms in the blueprint document *American Patients First*. And in October 2018 the administration announced a plan to build an "International Pricing Index". This Index would seek to align Medicare payments for physician administered drugs under the program with the prevailing prices in 14 countries, some of which with a significantly lower purchasing power (e.g. Greece, Czech Republic) than the US.[30] Given the experiences of other countries and the use of international reference pricing, it is more likely than not that the introduction of such a mechanism on the American market would have a deep and negative impact on long-term innovation and R&D. It is worth noting that one of the strongest drivers of biopharmaceutical innovation in the US has been the existence of a relatively free market in the pricing of pharmaceuticals. While the price of prescription medicines is a hot button issue for the public and elected representatives, the overall context of pharmaceutical pricing and health care access is often overlooked. To begin with, one fact often ignored in this debate is that as a proportion of overall health care spending, expenditure on prescription drugs represents a relatively small share of health care spending in the US at around 12% of total spending according to the OECD.[31] Similarly, the US has by far the highest availability of new and innovative products, being the first country of launch for the vast majority of new and innovative medicines. For example, IMS Health looking at the availability of new molecular entities (NMEs) in different countries between 2008-2014 found that, out of 154 NMEs introduced, 104 were available in the US; the second highest penetration rate was in Germany, where only 82 products had been introduced, 22 less than in the US.[32] Looking specifically at the 16 countries used in the IPI proposal, the US Chamber of Commerce has noted that over the past seven years, 32 fewer drugs were available for the treatment of cancer in these countries.[33] Finally, the vast majority of global medical and biopharmaceutical innovations

currently take place within the US and a handful of EU countries (Denmark, Germany, France, Switzerland etc.). Looking at historical data on global NCEs developed by firm nationality for the two decades between 1982-2003, Grabowski et al show that out of the 919 NCEs analyzed only 20 (or just over 2%) were developed outside the US, EU and Japan.

While in the US these discussions are only at the early stages, other countries that have traditionally been viewed as leaders on global innovation are embracing even harsher policies of biopharmaceutical cost-containment. An increasingly challenging pricing environment is tarnishing **Japan**'s status as a biopharmaceutical innovator. Specifically, the Central Social Insurance Medical Council (*Chuikyo*) has significantly restricted access to the Price Maintenance Premium (PMP), a scheme that recognizes the contribution of innovative drugs to patients and to the health system. The new PMP criteria introduce what is in effect a localization premium. Products and companies are prioritized on the basis of local research conducted with evaluation parameters including the number of recent local clinical trials, drug launches in Japan and 'Sakigake' status. Almost one in three patented drugs lost the PMP under the new criteria, particularly foreign ones.[34] Since it was introduced in 2010 the PMP has been fundamental to reforming Japan's P&R environment. It has resulted in more innovative drugs being introduced onto the Japanese markets and cuts in market approval times.[35] Furthermore, the *Chuikyo* has revised its pharmacoeconomic system of analysis through the use of a revised HTA methodology. Health technology assessment is an important tool of analysis and can assist payers to understand and make decisions on resource allocation.

However, any pharmacoeconomic system relies on the underlying assumptions and evaluation criteria. The new HTA system in Japan is based around a fixed QALY threshold of JPY5 million (circa USD 45,000), to be raised by 50% for orphan, pediatric and anti-cancer drugs.[36] Only drugs used uniquely for pediatric conditions or rare diseases with no current treatment will be exempted from the HTA.[37] At the time of research it was not clear the extent to which this QALY threshold would be applied and if there would be any discretion for medicines priced higher but providing a concomitant therapeutic benefit. During the initial trial period of the new HTA criteria a number of products saw substantial price cuts.

Another high-income market that has recently proposed measures directly aimed at reducing innovative drug prices is **Canada**.[38] Canada has introduced a proposal to change the fundamental basis of the Patented Medicine Prices Review Board (PMPRB) evaluation and the setting of prices for patented medicines.[39] Traditionally the PMPRB monitors and sets the price of patented medicines judging whether a price is "excessive" for new and existing patented drugs. The PMPRB has used a two-step process to set and review prices for new patented drug products including a "Scientific" and "Price" review. The purpose of the scientific review process is to establish the "level of therapeutic improvement of a patented drug product", an assessment made by the Human Drug Advisory Panel. With respect to pricing levels and what was judged to be an "excessive" price, the level of therapeutic improvement determined the pricing methodology and point of comparison, which includes international reference pricing (IRP) price comparisons with drugs of the same therapeutic class (TCC test). The new proposal would fundamentally change the evaluation process: it would change the pricing methodology and points of comparison, including expanding the basket of countries used in the IRP process. The change of this mandate and pricing system is likely to have a substantial negative impact. Industry estimates that the change of reference countries for IRP alone could result in a 10-15% price reduction, while overall the reform could slash prices of innovative drugs by at least 20%.[40]

Local preferences and mandatory localization requirements

Another economy that stands out for its strict cost-containment policies is **Korea**. On the one side, Korea continues to allocate considerable funds to R&D and improve the regulatory environment, most recently with the announcement of a 'regulatory sandbox' for innovative industries.[41] On the other, it has in place a strict P&R system applicable primarily to innovative products.[42] Mandatory price cuts have been instituted through a therapeutic reference pricing system that places innovative and generic drugs in the same basket, with prices set based on the average price in the basket.[43] The innovative or therapeutic value of a given product is not factored into the price.[44] As a result of such punitive system, over the past four years, the price for patented medicines in Korea has fallen by an average of 17%, which is two times lower than the average OECD countries average drug price cut rate of 9%.[45] Between 2007 and 2012, ten new drugs for advanced-stage or rare diseases became non-reimbursable despite the fact that they were clinically useful and lacked alternatives.[46] Over the last few years Korea has introduced a number of changes to its pricing and reimbursement policies that favor local manufacturers and penalize foreign companies. The *Reform Plan for Reimbursement Prices of Biopharmaceuticals and Global Innovative Pharmaceuticals*, presented in June 2016, grants price preference to locally developed innovative drugs. The Plan increases by 10% the prices of biosimilars tested in local trials and developed by companies designated as innovative (mostly Korean) or jointly developed with a Korean firm.[47] Only two out of the 47 biopharmaceutical drugs designated as innovative are by foreign companies, although many more invest in local clinical trials.[48] Companies designated as innovative receive special tax benefits, preferential governmental research funding and postponement of drug price discounts.[49] In the revised South Korea – US (KORUS) agreement reached in September 2018, Korea committed to create a level playing field for local and foreign drugs, granting access to the 10% price increase foreseen by the Premium Pricing Policy for Global Innovative New Drugs to all drugs, irrespective of their origin.[50] Currently, one of

the requirements is that the new drug must be released in Korea before being released in other markets, thus discriminating against non-Korean manufacturers.[51]

Another, more blatant case of preferences for local drugs in P&R policies is **Turkey**. More – and more targeted – localization measures for the biopharmaceutical sectors have been put in place in a bid to implement localization targets. Such key policies include import substitution,[52] procurement preferences and pricing and reimbursement preferences for local products, but also product registration preferences and local GMP certification. Most recently, Turkey's *New Economy Program 2019-2021* continues the policy of localization and of targeting import-intensive industries and increasing domestic production with the view of lowering the current account deficit and over the long term develop Turkey's technological and export capacities.[53] In addition to the above-mentioned policies, the government has committed to provide direct and tax incentives for the local manufacturing of 20 drugs relying on foreign know-how.[54] In reply to this large set of mandatory localization and tech transfer requirements, the EU initiated in April 2019 a dispute at the WTO, claiming that these measures violate Turkey's WTO obligations to treat foreign companies on equal footing with domestic ones, and to protect the intellectual property of foreign companies.[55]

2.5 Growing headwinds for IP protection

As highlighted in previous editions of *Building the Bioeconomy*, the twin factors of, one, the growing importance of biotechnologies to economic growth and development and, two, the rising cost of many of these technologies mean biotechnology innovators are increasingly seeing their IP rights encroached and curtailed in. This is especially the case for biopharmaceutical rights-holders. International experience and the basic economics of the biopharmaceutical industry show how critical IP rights are to incentivize and support the research and development of new medical technologies and products.[56] In particular patents and other forms of exclusivity for biopharmaceuticals, such as regulatory data protection (RDP) 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 drugs, products and therapies. Yet, regulators globally – even those who have so far benefitted to large amount of R&D investment thanks to their IP regime – are tinkering with IP rights, unduly interpreting the meaning of IP exceptions and making them an instrument to achieve other policy objectives, such as reducing the 'drug lag'.

After an informal agreement between the three main **EU** institutions was reached in February 2019,[57] legislation introducing an SPC manufacturing waiver is expected to receive final approval by the EU Council and enter into force in July 2019. Companies will be able to start manufacturing under the waiver from July 2022. Apart from the obligation to mark products produced under an SPC waiver for export as "export-only" and a general notification system, no other safeguard to protect against a possible diversion in the EU market of generics and biosimilars covered by an SPC has been included in the final text. Generic or biosimilar producers will need to notify regulators in the Member State where production will take place and the SPC holder three months before production begins. As noted in last year's edition of the *Building the Bioeconomy*, the overriding purpose of the SPC waiver is, by weakening IP protection for innovators, to provide European manufacturers of generic drugs and biosimilars a competitive advantage in global markets. Unfortunately, the Commission appears to have lost sight of the fact that IP incentives, including SPC protection, have been central to the success of Europe's research-based biopharmaceutical industry. The overall net effect of the SPC exemption may thus be a limited (if any) gain to the European generics industry and a weakening of the research-based industry through a direct loss of sales and a collective weakening of the global IP environment.[58]

In a similar vein, **Canada** has introduced provisions that completely undermine the spirit of recent positive reforms and the supposed strengthening of biopharmaceutical IP rights. Following the implementation of the Comprehensive Economic and Trade Agreement, Canada introduced

a new regulatory scheme allowing for some compensation for delays in obtaining marketing approval for biopharmaceutical products. The relevant amendments made to the Patent Act (sections 106-134) and implementing regulations published in the *Canada Gazette* provide a maximum restoration period of two years through a Certificate of Supplementary Protection (CSP) mechanism. While overall this is a positive step and an improvement, in Canada's biopharmaceutical IP environment there remain significant areas of concern. To begin with, under section 116(4) the Canadian government retains the right to reduce the term of protection at its discretion. Specifically, this sub-section states that: "the Minister may, if he or she is of the opinion that that person's [the rights-holder's] failure to act resulted in a period of unjustified delay in the process of obtaining the authorization for sale, reduce the term of the certificate when issuing it by the amount of that period." No further definition of what constitutes an "unjustified delay" has been provided in any of the relevant regulations, which leaves a broad scope for interpretation with the Canadian government. Moreover, the implementing regulations contain a 'Timely Submission Requirement' which sets a timeline for the submission of CSP applications based on the regulatory status of a given product in a set of 'prescribed economies'. The net effect is that the availability of a CSP is being made contingent on early market entry. Equally troublingly, the law also contains an export claw-out, with section 115(2) effectively exempting the infringement of CSP protection if the activity is for the purposes of exports. It is unfortunate that the law has undermined a positive and necessary incentive by limiting the actual protection afforded with these additional requirements and exemptions.

In a further blow to IP owners, in **India** the Delhi High Court in April 2019 dismissed the appeal of a 2017 ruling and authorized the export of generic versions of patented drugs "provided the seller ensures that the end use and purpose of sale/export is reasonably related to research and development".[59] The decision concerns sorafenib and rivaroxabin, two active ingredients used respectively for a proprietary cancer drug and blood thinner.[60]

And, as mentioned above, **China** is also pursuing reforms to its IP laws. In January 2019 China tabled *Draft Amendments to the Patent Law*, the fourth version of the draft presented since 2012.[61] The Draft Amendments propose to extend by 5 years the term of protection for patents to compensate for regulatory delays (PTE system).[62] They also propose to enhance available damages for patent infringement, including increasing statutory damages from 1 million to 5 million RMB Yuan (around 700,000 USD).[63] Yet, the proposed PTE system has important flaws: firstly, it applies only to innovative drugs marketed simultaneously in China and abroad, secondly, the draft limits the total effective term of the patent to 14 years after being placed onto the market.[64] At the time of research it was not clear what "simultaneous" would actually entail. Unfortunately, the new draft is silent on the patent linkage system proposed in 2017 (Circular 55), which could in the best case be left for administrative regulation.[65] As a first step in establishing a patent linkage mechanism, the Chinese FDA issued the *China Marketed Chemical Drug Catalogue*, a Chinese version of the *Orange Book* that contains information on both generic and patented products approved in China. Yet, since the system was presented in the 'Innovation Opinion' published October 2017, no implementing legislation has been adopted. The lack of protection from generic competitors is the main stumbling block for life sciences companies willing to enter the Chinese market. Prompt implementation of the proposed system is key to achieve greater investment and global competitiveness in this field. Finally, the 2018 draft *Pharmaceutical Data Exclusivity Implementing Rules* proposed to extend RDP to biologics, orphan and pediatric drugs. Yet, also this proposal disproportionally favors drugs first filed in China. The draft raises RDP to 12 years for new biologics and 6 years for new chemical entities (NCEs) from global launch, provided that the application is based on domestic clinical trials (or multi-center trials that include China).[66] If a drug is first approved overseas, a "drug lag" time will be deducted from the protection term. In case of applications based on overseas clinical data, protection is curtailed to 3 years for biologics and 1,5 years for NCEs.[67] This would severely limit the effectiveness of this incentive and protection mechanism. Under ongoing trade talks with

the US, the proposal to raise RDP to 8 years for biologics has been mulled.[68]

2.6 A ray of light? NAFTA 2.0

Historically trade agreements have been fundamental in setting international standards for the protection and enforcement of IP rights. TRIPS, NAFTA and numerous US and EU led bilateral agreements have helped improve the global IP environment and set a floor for rights-holders around the world. The agreement between the US, Mexico and Canada on a revised and substantially strengthened free trade pact in the United States-Mexico-Canada Agreement (USMCA) has the potential for setting a new standard for global biopharmaceutical IP rights.[69] NAFTA entered into force on January 1, 1994. At the time, it was widely considered as the first international trade agreement that included specific obligations to protect IP rights. Indeed, the NAFTA IP Chapter was the precursor to the TRIPS Agreement – considered by many to be the most comprehensive and ambitious multilateral agreement ever reached in the IP domain[70] – which was signed in 1995 and has been ratified by 164 economies. For a quarter of a century, NAFTA has stood as a model for a regional trade agreement. However, the economic relationships between nation-states are fundamentally different today than they were in the early and mid-1990s. Dramatic changes in technology and the structure and integration of the global economy require future trade agreements to be more comprehensive and detailed than preceding trade agreements. The USMCA provides the potential for a clear and forward-looking international benchmark on IP rights and would set not only an important precedent for future American trade agreements, but also provide a global standard for what IP protection in the 21st century should look like. Although chapter 20 of the Agreement covers all major IP rights, for biopharmaceuticals and the biotechnologies specifically the agreement contains numerous important provisions including:

– stronger pharmaceutical-related IP protection including:

  › Article 20.F.13: Protection of Undisclosed Test or Other Data; and Article 20.F.14: Biologics which provide a regulatory data protection terms of 5 years for new chemical entities (NCEs) and 10 years for biologics; and

  › Article 20.F.11: Patent Term Adjustment for Unreasonable Curtailment which provides a term of patent restoration for pharmaceutical products defined as "an adjustment of the patent term to compensate the patent owner for unreasonable curtailment of the effective patent term as a result of the marketing approval process"

– Article 20.I.1: Civil Protection and Enforcement; Article 20.I.2: Criminal Enforcement; Article 20.I.5: Confidentiality which provide more effective trade secret protection including criminal sanctions.

– Article 20.F.1: Patentable Subject Matter states clearly that with respect to biotechnology patentability patents shall be made available "at least for inventions that are derived from plants".

In addition to strengthening the provision of IP rights the USMCA's chapter 3 also contains specific provisions relating to biotechnology. Specifically, section B is dedicated to agricultural biotechnology and emphasizes "the importance of encouraging agricultural innovation and facilitating trade in products of agricultural biotechnology".

3 ZOOMING IN ON THE NEW COUNTRIES SAMPLED IN *BUILDING THE BIOECONOMY*

This year's edition of *Building the Bioeconomy* adds 11 new countries to the existing sample of 33 bringing the total number of countries included in the report to 44. The 11 new countries added are a good mix of middle-income and high-income OECD markets. This section discusses some of the key features of these countries' national innovation systems, their current biotech capacity and what they are individually doing to build and develop their biotechnology capabilities.

3.1 Laying the foundation: Algeria, Ecuador, Kenya, Nigeria and the Philippines

This year's edition adds a group of five non-OECD middle-income countries:

– **Kenya**, **Nigeria** and the **Philippines** (lower-middle income countries); and

– **Algeria** and **Ecuador** (middle-upper income countries).

When it comes to innovation and biotech policies, these economies share some common features. All are undertaking efforts to develop their national biotechnology sector as a way to move up the value chain and transition towards a knowledge economy, though only some have a dedicated biotechnology policy with clear objectives in place. In particular, Kenya and Nigeria have established a basic legal and institutional framework covering many of the key biotechnology issues. All are investing in research infrastructure, often with a flagship innovation hub or city built from scratch, such as Sidi Abdellah in Algeria,[71] Konza Technopolis in Kenya,[72] and Yachay City of Knowledge in Ecuador.[73] Yet, in general, limited resources (including human capital) and funding hinder their efforts to step up the quality and quantity of research.

Of note is how none of these five countries has recognized the role of IP as a key incentive to innovators. All lack fundamental IP standards, particularly with regard to patents and the enforcement of IP rights. In fact, Ecuador has been moving in the opposite direction than many emerging economies by significantly weakening its national IP environment generally and specifically as it relates to biopharmaceutical IP rights.

What is more, some of these countries are resorting to mandatory localization and manufacturing as a tool to develop their biotech industry.

Algeria has for several years imposed protectionist-style rules for how foreign firms may participate in the market, with the government actively pursuing an import substitution policy. The stated objective of these rules is to reduce imports, encouraging domestic production and maximizing technology transfer. Although largely emanating from the oil and gas industry, these policies run across various sectors and both directly and indirectly affect biotech innovators by imposing de facto localization requirements in return for market access. For example, on the basis of a pre-existing measure in the oil and gas sector, the 2009 Complementary Finance Law limits foreign investment to a minority stake (49% or below) in any industrial sector. The effect of this requirement is to impose a de facto localization requirement for foreign firms wishing to operate in Algeria directly or through licensing agreements. There are also rules targeting particular sectors. For example, the most stringent localization policies adopted in Algeria that target medicines specifically are outright import bans and quotas placed on biopharmaceutical products. Restrictions on drug imports have been in place since October 2008 and have been further expanded since then.

Nigeria's drug authority NAFDAC in 2019 presented a new requirement that foreign biopharmaceutical manufacturers re-registering their products partner with local Nigerian entities and/or commence local manufacturing of these products.[74] For these drugs, the renewal of marketing approval is subject to the presentation of plans for local manufacturing or partnership. Submitted plans will need to be implemented by the end of the renewed approval term.[75] At the time of research, it was not clear how the policy would be applied and the extent to which some manufacturers will be exempt. The new policy states that "The migration to local manufacturing will be limited to products the local manufacturers have capacity to produce".[76]

Finally, only the Philippines (and to a lesser extent Nigeria) has embraced agricultural biotechnologies, despite the potential positive impact in terms of food security for countries with limited arable land, such as Algeria, or needing food aid assistance, such as Kenya and Nigeria. An outright ban both on the import and cultivation of biotech crops is in place in Algeria and – as per art 401 of the Constitution – in Ecuador. Kenya has put in place an institutional and legal framework for the adoption of GE crops and is close to commercializing Bt Cotton for production;[77] yet, it has also banned the import of GE products since 2012. In Nigeria, on the other hand, Bt Cotton was commercialized in 2018, and other products are already at different stages of field and confined field trials.[78]

Country-by-country biotech overview

With a few exceptions, such as the Biotechnologies Research Center of Constantine,[79] biotech and general R&D represents a peripheral activity in **Algeria** in both the business and public sectors. Algeria does not currently have in place a clear biotechnology strategy or official policy.[80] Nonetheless, the government has recognized the socio-economic potential of biotechnology and specifically of the biopharmaceutical sector.[81] In this regard, it has expressed the goal of attracting biopharmaceutical investment, increasing local production to cover 70% of national demand by 2019,[82] and creating "the leading biopharmaceutical cluster of the MENA region by 2020" in Sidi Abellah.[83] Looking at a range of outputs Algeria has so far not achieved its stated goals and ambitions. On the contrary, the country underperforms many of its peers in terms of FDI and clinical activities. As is detailed below Section 4's Biotech Policy Performance Measure and accompanying Annex, Algeria has across the board the lowest biotechnology and biopharmaceutical outputs of all 44 countries included in this edition of *Building the Bioeconomy*. Why is this? There are substantial gaps in key policy areas and enabling factors. This includes: the regulatory space; commercial and market incentives (including biopharmaceutical pricing and reimbursement policies); and inadequate protection of IP. Localization and investment policies aimed at favoring local production – such as the long-standing 51% local ownership obligation and procurement preferences – act as a disincentive to foreign partnering and investment, especially for R&D.[84] Algeria prohibits imports of almost all biopharmaceutical products that compete with similar products that are manufactured domestically. To date, 357 products are listed as excluded from import, while annual import quotas are in place for products that are not locally manufactured.[85] Recurrent delays in approving such quotas also disrupt supplies to both patients and local manufacturers. Finally, given the current political unrest, there is a high level of uncertainty as to the policy environment and the future direction of Algerian biotechnology policy.

Of the five new lower-middle income countries included in this year's sample **Kenya** is the poorest with the lowest GDP per capita, at around USD1,500 in 2017. Yet despite this, more than many richer countries, Kenya has taken tangible steps to build a functioning STI institutional system. This includes: creating the National Commission for Science, Technology and Innovation;[86] the Kenya National Innovation Agency; and a National Research Fund. The government has also developed several national economic plans that attempt to integrate STI in the national production process to enable economic development. This includes the *Vision 2030*[87] and the more recent President's *Big 4 Agenda*.[88] Specific to biotechnologies, in 2006 Kenya developed a comprehensive national

policy to guide research, development and the commercialization of modern biotechnology products.[89] The strategy emphasized the medical application of biotechnology.[90] There are also plans for a dedicated *Biotechnology and Biosciences Programme* including the creation of biotechnology Centers of Excellence, and a national *Biotechnology Development Policy*.[91] For ag-bio, while there exists a structured policy framework, there is real uncertainty over the biotech crop policy environment; in 2012 there was a GE food import ban.

Nigeria is Africa's largest economy and most populous country. Like Algeria, the country is largely dependent on oil and gas, and has struggled to diversify its economy. Unlike Algeria, however, agriculture accounts for a large share of GDP and employment. Similar to Kenya, Nigeria has put in place a legal and institutional innovation policy framework to foster innovation. This includes a national STI Policy,[92] a National Science Technology and Innovation Roadmap (2017-2030),[93] a National Research and Innovation Council[94] and, since 2018, an Advisory Group on Technology and Creativity.[95] In 2001 the Federal Executive Council adopted a biotechnology policy and approved the establishment of the National Biotechnology Development Agency[96] to promote, coordinate and deploy cutting-edge biotechnology R&D, processes and products covering agricultural, medical and environmental biotech.[97] In 2015 Nigeria established the National Biosafety Management Agency to oversee the use and commercialization of ag-biotech products and strengthen Nigeria's food security. Yet, in spite of these initiatives, public support for biotechnology development and innovation remains low. In addition to low levels of investment in research, lack of infrastructure and skilled human capital, major policy roadblocks exist in the form of inadequate IP protection, government intervention in private licensing activities, and forced localization.[98]

In the **Philippines** there are also ongoing efforts to build a national innovation policy. The *Philippine Innovation Act* was passed in 2017 and provides for the establishment of a National Innovation Council and a National Innovation Fund.[99] There is a bill to encourage start-ups, the *Innovative Start-up Act*.[100] Looking at biotechnologies the policy environment is somewhat mixed depending on the sector and type of technology. For biopharmaceuticals the regulatory capacity remains limited, though the authorities have taken some steps to tackle the long approval backlog.[101] Other shortcomings include domestic procurement preferences, a lack of commercial and market incentives (including offset programs for medicines) and a generally limited national IP environment. In contrast, when it comes to ag-bio, the Philippines has a solid track record as regional biotechnology leader. Biotechnology programs were first started back in 1980 and have multiplied during the years.[102] In 1990 the Philippines was the first ASEAN country to initiate a biotechnology regulatory system based on strict scientific standards (Executive Order No. 430) and established the National Committee on Biosafety of the Philippines. In the same year, a Master Science Plan by the Department of Science and Technology identified biotechnology as a high priority sector.[103]

Ecuador has been actively pursuing a national innovation agenda with the direct participation and engagement of its general population. In October 2016 Ecuador's National Assembly

passed the *Código Orgánico de Economía Social del Conocimiento, la Creatividad y la Innovación (Código Ingenios)*. The legislation touches on all facets of IP rights, research and development and innovation. While the law aims to encourage innovation, R&D and the development of new technologies, it contains a strong element of local preferencing and discrimination against foreign companies. The legislation also contains a number of negative provisions relating to existing patent laws and practices and trademarks. For example, articles 268 increases the number of non-patentable subject matter and article 274 eliminates any patentability of second use inventions. While the latter is part of Andean Decision 486 this had nevertheless not been codified previously in Ecuador's existing Intellectual Property Law. With regards to the protection of trademarks the term of protection has been amended with renewal periods under article 365 limited to 2 renewals. This markedly stands in contrast to TRIPS article 18 which states that "the registration of a trademark shall be renewable indefinitely". In addition, a series of policies have been initiated including the *Agendas of Productive Transformation (2013)*, the *Strategy of Change of the Productive Matrix (2015),*[104] the *2016-2025 Industrial Policy* and the *Buen Vivir National Plan (2017-2021)*.[105] Biotech, with an emphasis on industrial and environmental biotechnologies, has been identified as needed to develop the country's new productive matrix. The *Buen Vivir National Plan* states that Ecuador will "give space to researchers and entrepreneurs to open up the possibilities to bio-knowledge, the bio-economy and biotechnology". The plan also mentions the preparation of a *National Bio-knowledge and Biotechnology Strategy*. Yet, despite these ambitions, Ecuador has not been able to change the fundamentals of its economy. Overall the economy remains focused on low productive sectors and very limited, incremental innovation.[106] As is detailed below in Section 4's Biotech Policy Performance Measure and accompanying Annex, Ecuador has some of the lowest biotechnology and biopharmaceutical outputs of all 44 countries included in this edition of *Building the Bioeconomy*. In large measure this is due to a fundamentally negative policy environment. Indeed, the government continues to actively pursue an innovation policy that undermines or weakens IP protection including the use of compulsory license for biopharmaceutical products. Ecuador has since 2010 been an active user of compulsory licensing for biopharmaceutical products. Nine licenses have been granted since 2010 and more are being considered. These licenses have been issued on a basis of being a cost containment mechanism and policy of encouraging domestic innovation, import substitution and industrialization.

3.2 Reaching for biotech excellence: Canada, France, Germany, Lithuania, the Netherlands and Norway

The *Building the Bioeconomy 2019* also adds a group of six high-income OECD members: four EU members – **Lithuania**, **France**, **Germany**, **the Netherlands** – and **Canada** and **Norway**.

To varying degrees, all these countries have research structures in place and look at biotechnologies as a key enabler of future growth. Some, notably Lithuania and to a lesser extent Norway, have joined the race more recently, but are making strides to compete. In France, Germany and the Netherlands strategies to foster both medical and industrial/bio-based products have been put in place, but like most EU Member States agricultural biotechnologies have been marginalized or banned. In Norway the most promising applications of biotechnologies are in the area of industrial and environmental biotechnology. Only Canada has moved to reap the economic, health and environmental benefits of agricultural biotechnologies, with a well-established scientific approach in place since 1983[107] and a series of ag-biotech clusters,[108] including the most recent protein industrial supercluster.[109]

Country-by-country description

In **Lithuania** the life sciences are estimated to account for more than 1% of national wealth – six times the EU average.[110] The country aims to raise this share to 5% GDP by 2030.[111] More than 130 life sciences companies are currently operating in Lithuania,[112] and the biotech and pharmaceutical research and manufacturing sector is reported as growing at approximately 14% annually.[113]

This small country of 2.8 million inhabitants has developed relatively strong capacities with regard to skilled human capital. As reported by its Education Minister, Lithuania has one of the highest density of biomedicines and technology students in the EU[114] and has achieved several critical scientific breakthroughs. For instance, scientists from the Vilnius University Institute of Biotechnology were among the first to discover the gene-editing potential of the Cas9 proteins, and in 2017 were granted a US patent relating to CRISPR-Cas technology.[115] The country has also made strides to develop research infrastructure and its technology transfer capacities. The Vilnius University Life sciences Center provides a state-of-the-art facility for education, training and research in life sciences.[116] It also provides a bio-incubator. Vilnius University is also part of the Sunrise Valley Science and Technology park.[117] [118] Other integrated science, study, and business valleys have been established as part of the ministries of Economy and Education' efforts to promote innovation. The fruits of these positive policies can be seen in high levels of biotech outputs. For example, with respect to clinical research Lithuania is a global leader with more than 320 trials per million population to date. Similarly, Lithuania has high levels of trials on biologic medicines and early phase biologic research.

In **Norway**, the government is striving to enhance the contribution of the research and innovation system to its economy.[119] Norway dedicates a high level of public spending in support of R&D, and has a history of high-tech innovation and technical skills in the oil and gas and aquaculture industries. The *National Strategy for Biotechnology 2011-2020* identifies four thematic areas in which biotechnology can play a role in addressing social challenges: industrial and environmental biotechnologies, health biotech, but also aquaculture and fisheries, and land-based food and biomass production.[120] A *National Bioeconomy Strategy* issued in 2017 focuses both on traditional bio-based industries such as agriculture, forestry, fisheries and aquaculture, and on newer applications related to energy, waste, chemicals, health, climate and the environment.[121] In 2018 Norway was the first country to ban palm oil for biodiesel[122] and to introduce a biofuel blending mandate for jet aviation.[123] At present, traditional bio-based industries (agriculture, forestry, fisheries and aquaculture) account for roughly 6% of the Norwegian economy.[124] Yet, biotechnologies are not used transversally in all these areas. Indeed, due to the Gene Technology Act, no GMOs are grown or sold in Norway.[125]

Like many OECD economies Canada has an advanced research and innovation agenda.[126] There is a high-skilled and highly-educated workforce, generous tax incentives and a relatively high level of R&D spending. Yet like many high-income OECD economies Canada has struggled to translate its technical skills, human capital and research infrastructure into IP assets and commercialized products. To help overcome these challenges, the government in 2017 launched *A nation of Innovators – Innovation and Skills Plan*.[127] The Plan identified six sectors where Canada could become a global leader, including biotechnology.[128] Yet, there are many fundamental challenges to Canada achieving these goals. For a high-income developed OECD economy Canada has one of the weakest national IP environments. Also, pricing methodology reforms for biopharmaceuticals proposed by the Patented Medicine Prices Review Board are likely to have a negative impact on incentives to innovate and R&D.[129] No specific life science strategy exists at the federal level to ensure a whole-of-government approach.[130] Instead some of the bigger provinces have forged ahead independently and developed their own strategies and policies. This includes for example Quebec, which in 2017 launched its own life sciences strategy. Ontario has also been active and has established a office dedicated to supporting a whole-of-government approach to health innovation, the Office of the Chief Health Innovation Strategist.[131] Finally, consultation is ongoing to develop a national strategy for the industrial bioeconomy and agricultural/forestry biomass utilization, stepping up efforts from province-level initiatives such as Ontario's BioProducts strategy[132] and BioFuture Alberta.[133]

France too has world-class research facilities and strengths in human capital and biotechnology. France has introduced a range of national innovation laws and policies over the last 20 years to encourage the development and commercialization of new technologies. These

include the 1999 Law on Innovation and Research (*Loi sur l'innovation et la recherche*), 2010 Investments for the Future Program *(Programme d'Investissements d'Avenir,* PIA) as well as the founding and regulations guiding the French National Research Agency (*l'Agence nationale de la recherche*). Traditionally, French research and technology creation has been concentrated in PROs. For the sixth year in a row the French Alternative Energies and Atomic Energy Commission (*Commissariat à l´énergie atomique et aux énergies alternative*, CEA) was the top PCT applicant in the government and public research organizations in WIPO's *Patent Cooperation Treaty Yearly Review 2017*, with 329 published applications. Out of top 10 PCT applicants among government and PROs three came from France. Looking at biotechnology, the 2017 *Medicine of the Future* initiative looks at medical biotechnologies alongside digital solutions and medical devices to modernize the French medical industry, as part of the larger *Industry of the Future* industrial transformation plans.[134] Other initiatives include *Genomic Medicine France 2025*,[135] the *Digital Health Plan 2020*[136] and the *National Health Strategy 2018-2022*. Like most EU Member States France has completely outlawed ag-bio cultivation, citing environmental risks, and restricts biotech crop research.[137] Within the context of agricultural production the Ministry of Agriculture and government have promoted increased use and production of 'bio-based' products (such as bio-gas) through a 2017 *Bioeconomy Strategy for France*, followed in 2018 by the *Bioeconomy Action plan*.[138]

Germany has a strong and well-established tradition of biotechnological manufacturing and product development. As of 2015, Germany had over 30 'bioregions' – regional biotech clusters each specializing in a particular area and working to further collaboration between universities, research entities and industry. In 2018 the Federal Cabinet's *Framework Program Health Research* outlined the medical areas considered to have a large unmet need and which should receive larger government funding over the next ten years.[139] The *National Decade of Cancer* was launched at the beginning of 2019 under the auspices of the Federal Ministry of Education and Research to advance research into the prevention, diagnosis and treatment of cancer.[140] The cross-departmental *From Biology to Innovation* agenda is set to start in 2019,[141] overseen by the Federal Ministry of Education and Research and the Federal Ministry for Economic Affairs and Energy in close partnership with business, academia and civil society.[142] There are long-standing bioeconomy strategies including the *National Bioeconomy Policy Strategy* of 2013[143] and the 2010 *National Research Strategy BioEconomy 2030*. Germany is focusing on strengthening the system approach in the bioeconomy, furthering public private alliances, efficiency in the use of biological resources, and public participation.

The **Netherlands** has a well-established and high-quality innovation capacity. Rates of human capital and general R&D spending are relatively high at close to 5,000 researchers in R&D per million population and 2% of GDP, respectively. There are also high levels of life sciences specific graduates, comparable to Germany and Israel and higher than the US. In terms of policy frameworks the Netherlands has a well-developed national innovation policy including for knowledge transfer and 'valorization' activities. Universities are encouraged to engage in commercialization and actively work with industry to develop

new products and technologies. Most major Dutch universities have functioning technology transfer offices and well developed programs. The Netherlands has also introduced a small business specific technology transfer and commercialization venture, the *Small Business Innovation Research* program. Looking at biotechnologies the Netherlands has a relatively advanced biopharmaceutical capacity. The life science and health clusters account for more than 2,200 healthcare companies and research organizations.[144] The life sciences and health sector is one of nine "top sectors", designated by the Dutch Ministry of Economic Affairs.[145] A dedicated "Life Sciences & Health" national action program is expected to be launched in 2019.[146] As discussed below in the Annex, like many EU Member States Dutch health authorities have imposed drastic cuts in expenditure on mediciens and new medical technologies. The Dutch government stopped in 2015 to automatically reimburse new, expensive medicines used in hospitals to instead add centralized reimbursement negotiations with a capped negotiating time.[147] Drugs judged too expensive for immediate inclusion in the basic package are included in the "lock for expensive medicines" (Pakketsluis). Within the "lock period", the Ministry of Health negotiates price rebates from manufacturers; drugs are marketed but not reimbursed. Since May 2018 the system applies to all patented drugs with an annual cost of EUR50,000 or more per patient. In addition, past cost containment reforms have transferred high-cost in-patient medicines to hospital budgets and capped hospital budgets' growth to an annual rate increase of 1%. While like many other EU Member States the Dutch have largely outlawed the cultivation of biotech crops, as a global leader in plant breeding and seed technology the Netherlands has been pushing an exemption to existing EU GMO procedures for so-called "New Plant Breeding Techniques" which include the use of CRISPR technology in plant breeding. However, a decision of the European Court of Justice (ECJ) risks halting research in this field. On July 25, 2018, the ECJ issued its judgment that organisms created through genome editing techniques are to be regulated as GE organisms in the EU. The decision could also limit the ability of the EU agricultural sector to reduce its environmental impact and to fight future crop pests and diseases. The ECJ decision was widely criticized by Dutch plant breeders.[148]

4 MEASURING POLICY IMPACT AND REAL-WORLD BIOTECHNOLOGY RESULTS – THE BIOTECH POLICY PERFORMANCE MEASURE

First featured in 2015 the Biotech Policy Performance Measure (the "Measure") is an empirical tool that directly compares economies' policy inputs with real-life biotech outputs. At essence, this is a way of illustrating the negative impact of short-sighted and contradictory policy frameworks on real-world biotechnology outputs.

Originally the Measure was solely intended to provide readers a quick overview of a given economy's policy framework and performance in relation to the other economies included in the report. It consisted of some of the most important elements for each of the seven enabling factors delineated in the *Building the Bioeconomy* series. In 2016 the Measure was fundamentally revamped and significantly expanded to also take into account biotech outcomes. Indicators on biotechnology outputs measured 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.

This year the Measure examines a total of 30 indicators with two new indicators having been added to this edition of *Building the Bioeconomy*. These indicators are divided between 18 measures of policy inputs (as in previous editions related to the seven enabling factors) and 12 indicators of biotechnology outputs. Together they provide a rich and detailed measure of the biotechnology environment for a given economy. As with previous editions the purpose of the Biotech Policy Performance Measure is not to benchmark individual countries to a pre-determined set of criteria; this is not a computational index. Rather, the purpose 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 these policy inputs translate into.

4.1 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. These are indicators that provide a sense of a given economy's policies and direction under each of the enabling factors.

This year there are 18 policy input indicators measured; two more compared to last year's edition. Below Table 3 shows all 18 indicators for the 7 enabling factors.

TABLE 3 Biotech Policy Performance Measure, policy input indicators

Key enabling factors	Indicators
Human capital	• Number of researchers per million population • Life sciences graduates (PhD & Masters), per million population
Infrastructure for R&D	• R&D spending % of GDP • BERD spending as a % of total R&D spending • Total biotechnology R&D expenditure, millions USD PPP, per million population • Biotech R&D as a percentage of BERD
Intellectual property protection	• Availability of regulatory data protection for submitted clinical data during the regulatory approval process • Availability of Patent Term Restoration for biopharmaceuticals • US Chamber of Commerce International IP Index 2019 life sciences score, standardized to a %
Regulatory environment	• Regulatory framework for biopharmaceuticals • Regulatory framework for agricultural biotechnologies
Technology transfer	University/Industry technology transfer framework • Barriers to technology transfer of publicly funded and supported research (US Chamber of Commerce International IP Index 2019 indicator 26 score standardized to a %) • University/Industry Collaboration (World Competitiveness Index Indicator 12.04 score standardized to a %) Private to private licensing framework • Registration and disclosure requirements of licensing deals (US Chamber of Commerce International IP Index 2019 indicator 27 score standardized to a %) • Direct government intervention in setting licensing terms (US Chamber of Commerce International IP Index 2019 indicator 28 score standardized to a %)
Market and commercial incentives	• Biopharmaceutical pricing and reimbursement policies • Tax incentives for the creation of IP assets (US Chamber of Commerce International IP Index 2019 indicator 30 score standardized to a %)
Rule of law	• World Justice Project *Rule of Law Index 2019* country ranking

Factor 1: Human capital

Number of researchers per million population

This indicator estimates the level of technical capacity and human resources available within a given country by measuring the number of researchers in R&D activities standardized per million population. This indicator is not biotechnology specific but covers all major forms of scientific and technical fields.[149] The data is collected by the World Bank and forms part of the Bank's World Development Indicators.

This data set includes all of the economies sampled in *Building the Bioeconomy 2019* except Peru and Saudi Arabia. Equivalent data for Taiwan was collected from the Ministry of Science and Technology's 2018 International Comparison of S&T Activities available on the Ministry's website.

Life sciences graduates (PhD & Masters), per million population

This indicator compares the number of post-graduate graduates in the life sciences for each of the sampled economies. This data provides an indication of a given economy's overall technical capacity for advanced R&D activities in the life sciences. This information is collected by the OECD and forms part of the OECD.Stat databank.

The number of life sciences graduates has been standardized for population to provide a more accurate reflection of intensity in a given economy regardless of population size.

This OECD dataset includes all of the economies sampled in *Building the Bioeconomy 2019* except Algeria, Argentina, Canada, China, Costa Rica, Ecuador, Egypt, Japan, Kenya, Malaysia, Nigeria, Peru, Philippines, Saudi Arabia, Singapore, South Africa, Taiwan, Thailand, the UAE and Vietnam. Data for Singapore was collected from the *Yearbook of Statistics Singapore 2018* published by the Department of Statistics Singapore. Data for Taiwan was collected from the Ministry of Science and Technology's 2018 International Comparison of S&T Activities available on the Ministry's website.

Factor 2: Infrastructure for R&D

R&D spending % of GDP

This indicator measures the investment into R&D taking place in each economy as a percentage of that economy's GDP. This indicator is not biotechnology specific but covers all major forms of scientific and technical fields.[150] The data is collected from the World Bank World Development Indicators and OECD.Stat for all countries covered in the report, except for Saudi Arabia and Peru for whom data is provided by the UNESCO Institute for Statistics (UNESCO-UIS).

This dataset includes all of the economies sampled in *Building the Bioeconomy 2019*.

BERD spending as a % of total R&D spending

This indicator measures the investment into R&D taking place by business and private sector enterprise in each economy as a percentage of the total expenditure on R&D. High levels of BERD suggests a higher propensity for private sector investment and commitment to innovation and creating new processes, products and technologies for commercialization. This indicator is not biotechnology specific but covers all major forms of scientific and technical fields. The data is collected from the OECD.Stat databank.

This data set includes all of the economies sampled in *Building the Bioeconomy 2019* except Algeria, Brazil, Colombia, Costa Rica, Ecuador, Egypt, India, Indonesia, Kenya, Malaysia, Nigeria, Peru, Philippines, Saudi Arabia, Thailand, the UAE and Vietnam.

Total biotechnology R&D expenditure in the business sector, millions USD PPP, per million population

This indicator measures R&D expenditure in the business sector that is specific to the biotechnology field. The amount of R&D investment has been standardized for population to provide a more accurate reflection of intensity in a given economy regardless of population size. The data is collected from the OECD.Stat databank and forms part of its "Key Biotech Indicators" measure.

This data set includes 15 of the economies sampled in *Building the Bioeconomy 2019*, namely Canada, Denmark, Finland, France, Germany, Ireland, Korea, Lithuania, Mexico, Norway, Russia, Sweden, Switzerland, Taiwan, and the US. Data for Taiwan was collected from the Ministry of Science and Technology's 2018 *International Comparison of S&T Activities* available on the Ministry's website.

Biotech R&D as a percentage of BERD

This indicator measures R&D expenditure specific to the biotechnology field as a percentage of overall business enterprise R&D spending. The data is collected from the OECD.Stat databank and forms part of its "Key Biotech Indicators" measure.

As for the previous indicator, this data set includes 15 of the economies sampled in *Building the Bioeconomy 2019*, namely Canada, Denmark, Finland, France, Germany, Ireland, Korea, Lithuania, Mexico, Norway, Russia, Sweden, Switzerland, Taiwan, and the US.

Factor 3: Intellectual property protection

Availability of regulatory data protection for submitted clinical data during the regulatory approval process

This indicator measures the availability of regulatory data protection for submitted clinical data during the regulatory approval process.

Availability of patent term restoration for biopharmaceuticals

This indicator measures the availability of a term of patent restoration for biopharmaceuticals due to delays caused during the sanitary regulatory review process.

US Chamber of Commerce International IP Index 2019 life sciences score, standardized to a %

This indicator measures the availability and enforcement of IPRs related to the life sciences sector. This is a composite measure based on an aggregation of relevant indicators included in the International IP Index 2019.

All three above indicators are drawn from the US Chamber of Commerce's International IP Index 2019.

The International IP Index includes all of the economies sampled in *Building the Bioeconomy 2019* except Denmark, Finland, Lithuania and Norway. For these countries, information for the first two indicators relating to RDP and PTE are drawn from public legal sources.

Factor 4: Regulatory environment

Regulatory framework for biopharmaceuticals

This indicator seeks to measure all aspects of the regulatory framework in place for biopharmaceuticals, from product approval and manufacturing standards to clinical standards. This incudes, for instance: the speed of market authorization; patent office backlogs; bioequivalence requirements for generic products; and the existence of a biosimilars pathway in line with international standards. Each economy sampled in *Building the Bioeconomy 2019* is evaluated individually on a qualitative basis.

Regulatory framework for agricultural biotechnologies

This indicator is based on the existence and efficiency of an ag-bio framework that spells out a clear, science-based pathway for the adoption and use of ag-bio products and technologies. This includes, for instance: rules for the trade, production, cultivation, trials and other research activities of GE crops, as well as labelling of GE products. Each economy sampled in *Building the Bioeconomy 2019* is evaluated individually on a qualitative basis.

Factor 5: Technology transfer

Barriers to technology transfer of publicly funded and supported research

This indicator looks at the existence and extent of technology transfer frameworks and operational arrangements in a given economy that aim to facilitate the development and commercialization of technologies developed within public sector entities. It also examines the extent to which laws and regulations but also *de facto* practices act as barriers to technology transfer and commercialization activities of publicly funded and supported research. This indicator is not biotechnology specific. The data is collected from "Indicator 26 Barriers to Technology Transfer" in the U.S. Chamber of Commerce's International IP Index 2019. The International IP Index includes all of the economies sampled in *Building the Bioeconomy 2019* except Denmark, Finland, Lithuania and Norway.

University/Industry research collaboration

This indicator examines the level of collaboration between business and universities on R&D, as measured by the World Economic Forum *Global Competitiveness Index 2017-2018*. The data is collected from indicator 12.04 "University Industry Research Collaboration in R&D", which is not biotechnology specific. This data set includes all of the economies sampled in *Building the Bioeconomy 2019* except Taiwan.

Registration and disclosure requirements of licensing deals

This indicator measures the existence of barriers to private entity licensing and commercialization activities in a given economy. In particular, it looks at the extent to which licensing agreements must be registered and/or disclosed with relevant authorities to carry legal effect. The data is collected from "Indicator 27 Registration and disclosure requirements of licensing deals" in

the U.S. Chamber of Commerce's International IP Index 2019. This indicator is not biotechnology specific. The International IP Index includes all of the economies sampled in *Building the Bioeconomy 2019* except Denmark, Finland, Lithuania and Norway.

Direct government intervention in setting licensing terms

This indicator measures the existence of barriers to private entity licensing and commercialization activities in a given economy. More specifically, it looks at the extent to which the relevant authorities directly intervene and set licensing terms between licensee and licensor. This can be done through, for example, governmental preapproval for any licensing agreement between two parties as well as government intervention in the setting of licensing terms, including royalty rates. The data is collected from "Indicator 28 Direct government intervention in setting licensing terms" in the U.S. Chamber of Commerce's International IP Index 2019. This indicator is not biotechnology specific. The International IP Index includes all of the economies sampled in *Building the Bioeconomy 2019* except Denmark, Finland, Lithuania and Norway.

Factor 6: Market and commercial incentives

Biopharmaceutical pricing and reimbursement policies

This indicator examines the commercial incentives provided through existing biopharmaceutical pricing and reimbursement policies. For the biopharmaceutical sector market and commercial incentives are primarily determined by the existing pricing and reimbursement systems for medicines and health technologies. The manner and extent to which these policies are put in place can have a profound impact on the commercial and market incentives for innovation more broadly in the health sector as well as for biotechnology R&D. Each economy sampled in *Building the Bioeconomy 2019* is evaluated individually on a qualitative basis.

Tax incentives for the creation of IP assets

This indicator examines the tax incentives available and provided in a given economy as a means of encouraging R&D. 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. Each economy sampled in *Building the Bioeconomy 2019* is evaluated individually on a qualitative basis.

The data is collected from "Indicator 30 Tax incentives for the creation of IP assets" in the U.S. Chamber of Commerce's International IP Index 2019. This indicator is not biotechnology specific. The International IP Index includes all of the economies sampled in *Building the Bioeconomy 2019* except Denmark, Finland, Lithuania and Norway.

Factor 7: Rule of law

World Justice Project Rule of Law Index country ranking

This indicator examines the legal certainty in a given economy as measured by the World Justice Project's *Rule of Law Index 2019*. This indicator is not biotechnology specific. The *Rule of Law Index 2019* includes all of the economies sampled in *Building the Bioeconomy 2019* except for Ireland, Israel, Lithuania and Switzerland.

4.2 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.

This half of the Measure includes 12 indicators in total described in table 4 below.

TABLE 4 Biotech Policy Performance Measure, biotech outputs

- Scientific publications per million population
- Quality of academic publications
- Clinical trials per million population to date
- Clinical trials for biologics per million population to date
- Early phase (Phase I and II) clinical trials for biologics, per million population to date
- Biotechnology triadic patenting, share of global total average 1999-2013
- 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, 2017
- Biotechnology crops, hectares under cultivation, % of total 2017
- Biopharmaceutical Competitiveness Index (BCI) Survey 2017 Ranking
- Venture Capital & Private Equity Country Attractiveness Index, Economy Ranking, 2018
- Biofuels production, % of global total, 2017

As can be seen 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 12 indicators is described below together with its source and the number of *Building the Bioeconomy* countries that 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.[151] 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.[152] 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. The data has also been aggregated and a calculated average has been used for the period 2003-2016.

This data set includes all of the economies sampled in Building the Bioeconomy 2019 except Taiwan. Equivalent data for Taiwan was collected from the Ministry of Science and Technology's 2018 *International Comparison of S&T Activities* available on the Ministry's website. This data measures annual papers and rank by nationality in the SCI ranking.

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 in 2015.[153]

This data set includes all of the economies sampled in *Building the Bioeconomy 2019* except Algeria, Argentina, Colombia, Costa Rica, Ecuador, Egypt, Kenya, Malaysia, Nigeria, Peru, Philippines, Saudi Arabia, Singapore, Taiwan, Thailand, UAE and Vietnam.

Indicator 3: Clinical trials per million population to date

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 of April 2019 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 2019*.

Indicator 4: Clinical trials for biologics per million population to date

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 of April 2019 as collated and registered on the website ClinicalTrials.gov to date. 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 2019*.

Indicator 5: Early phase (Phase I and II) clinical trials for biologics, per million population to date

This indicator focuses on early phase clinical research on biologic medicines to date (April 2019). Early phase trials are the most scientifically advanced and represent the most innovative and riskiest phases of the clinical development process. As with other indicators the total number of trials has been standardised to population to provide a more accurate reflection of levels of early phase biologics clinical research intensity in a given economy regardless of population size.

This dataset includes all of the economies sampled in *Building the Bioeconomy 2019*.

Indicator 6: Biotechnology triadic patenting, share of global total average 1999-2013

This indicator examines levels of triadic patenting and an economy's share of the global number of biotechnology patents between 1999-2013. 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.[154] This dataset includes all of the economies sampled in *Building the Bioeconomy 2019* except Vietnam.

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 2019* except Algeria, China, Kenya, Lithuania, Nigeria and Vietnam.[155]

Indicator 8: National % share total number of patents from top 50 PCT applicants: universities, 2017

This indicator examines rates of university PCT patenting as collected and published by WIPO.[156] 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 2019* 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 2017 by all 50 universities.

The underlying data includes all of the economies sampled in *Building the Bioeconomy 2019*.

Indicator 9: Biotechnology crops, hectares under cultivation, % of total 2017

This indicator compares levels of biotechnology-derived crops in the sampled economies.[157] Data on hectares of biotechnology crops under cultivation are collected by the International Service for the Acquisition of Agri-biotech Applications. 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 2019*.

Indicator 10: Biopharmaceutical Competitiveness Index (BCI) Survey, 2017 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.[158] 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 2019* except Algeria, Costa Rica, Denmark, Ecuador, Finland, France, Kenya, Lithuania, Netherlands, Nigeria, Norway, Peru, Philippines, and Sweden.

Indicator 11: Venture Capital & Private Equity Country Attractiveness Index 2018, Economy Ranking

This indicator compares economies relative attractiveness to venture capital and private equity.[159] 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.

This dataset includes all of the economies sampled in *Building the Bioeconomy 2019* except for Costa Rica.

Indicator 12: Biofuels production, % of global total, 2017

This indicator measures each country's percentage share of the total amount of biofuels produced globally in 2017. This data is collected from BP's *Statistical Review of World Energy*.

This data set includes all of the economies sampled in *Building the Bioeconomy 2019*.

4.3 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, higher levels of the measured indicators (for instance, R&D spending) translate 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 is viewed as attractive.

4.4 The Biotech Policy Performance Measure – Overall results

Below Figure 2 shows the overall results for the Biotech Policy Performance Measure. Economies move from top to bottom in the figure from those economies that have the most attractive policy environments and accompanying high levels of biotechnology outputs to those economies that have the most challenging environments for both policy inputs and biotech outputs. (A full set of tables with results for each indicator and inputs and outputs for each economy is provided in the accompanying Annex.)

FIGURE 2 The Biotech Policy Performance Measure – Overall results

4.5 The Biotech Policy Performance Measure – Discussion

As in previous editions of the Measure, data is only partially available for the non-OECD countries added in 2019. Countries for which data is incomplete include Algeria, Kenya, Nigeria, Vietnam and to a lesser extent Costa Rica and Lithuania; the latter of which only recently joined the OECD. Reliable, standardized data is a pre-condition for successful biotech policy-making. It allows researchers and policymakers to get as accurate and in-depth understanding of the strengths and weaknesses of the national biotech system, assessing the effectiveness of different policies in achieving stated objectives. In this sense, data shortages resonate both as an indicator and a consequence of a low-prioritized innovation system.

Looking at the available indicators, the addition of 11 new economies (a growth of 33% in the sample size) strengthens the overall message of previous editions of the Measure: Inputs equal outputs. There is a link between creating a positive enabling environment with real-world biotech outcomes.

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. Adopting a pragmatic, long-term approach focused on getting the policy environment right is key to reaping the economic and social benefit of biotechnologies.

Another important take-away from the Measure is that there is no shortcut to building a conducive biotech policy environment. Each economy has its own strengths, which it can leverage to enhance its attractiveness vis-à-vis other markets. Some – such as many Latin American countries – are blessed with rich and varied ecosystems that provide a strong starting point for biotechnological innovation and R&D. Others – such as Algeria, Nigeria and Norway – have benefitted from the inflow of revenues from natural resources. Relying only on the strengths cannot – alone – deliver the expected economic and social benefits of biotechnologies. Small economies with limited natural resources such as Israel, Denmark, Ireland and Singapore have to rely more on ingenuity, creativity and getting the incentives right to create an enabling environment.

Most countries have recognized the need of moving to or further strengthening the knowledge economy as a basis for long-term growth and development. To achieve this, many have set the objective of increasing R&D spending and research capacities. Human capital and an appropriate quality of R&D infrastructure are key to innovate or even take advantage of technological advances abroad. They are also a pre-requisite to effective knowledge transfer. As mentioned above, many countries are asserting their biotech ambition through a biotech hub, techno park or even a designated city as a flagship project. Yet, while the stated ambitions are there, only 14 out of the 44 countries sampled spend more than 2% of their GDP on R&D. As noted in last year's edition, while there is a link between the level of GDP (and economic structure) and R&D spending, there are also important variations based on individual countries' policy choices. For instance, Norway and China both basically spend between 2.1% of GDP on R&D activities, although Norway has a GDP per capita almost four times higher than China measured on a PPP basis.

5 FINAL THOUGHTS AND RECOMMENDATIONS

As discussed in Section 1 biotechnology has emerged as one of the main technological solutions for today's health, food and environmental needs. But to a greater or lesser degree all biotechnologies need policy support and depend on government actions.

Health biotechnology is a highly regulated sector that strongly depends on governments as its main buyer and on government policies for market access.

Similarly, government's policy decisions have closed off entire markets to agricultural biotechnologies.

And in the case of industrial biotechnologies, incentives and government support are often crucial to developing and enabling the commercial distribution and mass consumption of these products.

For six years, this report has reflected on how the right policies can help build thriving biotech sectors. This edition of *Building the Bioeconomy* again makes it clear that the countries that stand the best chance of enjoying the fruits of biotechnology innovation are the ones where forward-looking regulations act to encourage, and not hinder, innovation.

Based on the analysis and mapping of the national innovation systems and biotechnology policies and enabling factors in place in the 44 countries sampled it is possible to piece together five universal recommendations. They are:

1. **Create a national blueprint or plan of action** – The existence and creation of a blueprint or national biotechnology strategy can be a powerful tool in creating a vision and setting a goal for national aspirations. There are many ways in which governments can provide leadership and direction for the building of a biotechnology capacity. By and large most countries studied in this paper have directly or indirectly targeted biotechnology as a technology and industry of strategic importance to national economic development and growth. But not all 44 of the sampled countries had developed national blueprints or pans for developing the sector.

2. **Execute** – A national blue print or plan of action is a necessary starting point for all aspiring biotech nations, but it is only the first step. Once it has been formulated and drawn up it must be implemented. Building a bioeconomy is not a short-term proposition. It takes long term planning, patience and commitment. But where many countries fall short is in their ability and efforts to move from a planning phase to actually implementing and applying the necessary policies. This is where the hard work begins.

3. **Measure performance** – The measuring of performance and the creation of key performance indicators is critical. Without an understanding of whether or not implemented policies are actually working it is impossible to properly evaluate whether any progress is being made.

4. **Recognize and use existing best practices** – Although no two countries are the same and all face different circumstances, countries can learn from the experiences of each other.

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

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