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CHALLENGES AND OPPORTUNITIES – DEVELOPING THE BIOTECHNOLOGY SECTOR IN COLOMBIA

This report was supported by Amgen. The views represented here are those of the authors only.

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LIST OF ABBREVIATIONS

AFIDRO	Association of Pharmaceutical Laboratories for Research & Development (Colombia)
ANVISA	Brazilian National Health Surveillance Agency
Colciencias	*Departamento Administrativo de Ciencia, Tecnología e Innovación*
CLs	Compulsory Licenses
FDA	US Food and Drug Administration
FDI	Foreign direct investment
GCP	Good Clinical Practices
GMP	Good Manufacturing Practices
GM	Genetically Modified
IP	Intellectual Property
IPRs	Intellectual Property Rights
IRP	International Reference Pricing
NGO	Non-Governmental Organization
OECD	Organisation for Economic Co-operation and Development
PCT	Patent Cooperation Treaty
PRO	Public Research Organization
RDP	Regulatory Data Protection
R&D	Research and Development
SME	Small and Medium Enterprises
TRIPS	Trade-Related Aspects of Intellectual Property Rights
UPOV	Union for the Protection of New Varieties of Plants
VC	Venture Capital
WHO	World Health Organization
WIPO	World Intellectual Property Organization
WTO	World Trade Organization

EXECUTIVE SUMMARY

Growing numbers of economies around the world are looking to the biotechnology field as a future engine for economic growth and development. Indeed, several of the world's biggest and fastest growing economies, including the BRICs, have launched new or updated national plans or strategies to promote the growth of this sector.

And in the developed world building the bioeconomy remains at the core of economic and national policy making. This is most prominent in the US which has since the 1980s and the beginning of the biotechnology revolution embraced the use of biotechnologies across all major sectors – biopharmaceuticals, ag-bio and industrial biotechnology. Critically, the economic contribution of biotechnologies to American national output is high and growing. The most recent estimates from 2016 of the value of the three major biotechnologies (biopharmaceuticals, biotech crops and industrial biotechnology) place their contributions at about 2% of GDP in the US.

Colombia – A story of untapped potential?

Colombia has long recognized its biodiversity and the importance of biotechnology and the potential of this sector. A national biotechnology institute and specific national program was introduced as early as the 1980s and 1990s, respectively, and a national framework/strategic plan has been in place since the late 1990s. Yet unlike many other countries with high levels of biodiversity Colombia has not been able to fully translate this natural resource into a world-leading biotechnology sector. For example, Brazil – also having a high level of biodiversity – has for many years been a pioneer in using and developing biotech crops and biofuels.

Report overview

The purpose of this report is to, firstly, give a comparative overview of the biotechnology sector in Colombia and, secondly, provide an estimate of how an improvement to Colombia's policy environment can result in higher biotechnology outputs including rates of biomedical FDI and clinical trials. The report maps the current policy environment as it relates to biotechnology in Colombia and gives a detailed comparison on key major biotechnology and R&D related outputs between Colombia and other economies:

– Where does Colombia stand today with regards to its biotechnology capacity?

– And how does Colombia's current biotechnology capacity compare to other middle income economies, OECD economies and other economies in the Latin America region?

A key aspect of the report is the identification of policy areas where the existing legal framework is not in line with international best practices and are actually limiting the development of Colombia's biotechnology sectors. Through economic modelling the report quantifies the potential direct financial and R&D benefits Colombia could derive from introducing positive reforms aimed at stimulating international biotechnology investment and, in particular, greater levels of biopharmaceutical investment through clinical trials.

Within the context of Colombia seeking to improve its attractiveness to clinical research this report is accompanied by a separate "Clinical Trials Policy Annex". This Annex provides a detailed overview of the socio-economic benefits of conducting clinical trials to a host country. It seeks to explain the benefits clinical research has to local patients and the wider economy in a host country. The Annex also looks at some of the best practices and policy measures aimed at enhancing domestic attractiveness for clinical research as adopted by a sample of countries which are now considered leaders in the global clinical research arena.

Key findings

This report's findings can be grouped along three key findings.

Key finding 1: Colombia currently lags behind other middle-income, OECD economies and world leaders on biotechnology outputs

While biodiverse Colombia's capacity and level of innovation in the area of biotechnology is limited by international standards and compared to its regional and socio-economic peers. Rates of general and biotech-specific R&D and innovation inputs and outputs are often lower than expected and, in many cases, have remained flat for several years. Given the high level of biodiversity and socio-economic development in Colombia rates of biotech patenting, biofuels production, ag-bio crop cultivation and level of clinical trial activity are relatively low.

Key finding 2: Colombia has a potential pocket for growth and development in clinical research on biologic products and technologies

Analysis of clinical trial activity shows that within the realm of R&D of biologic medicines Colombia could be a regional leader, with the share of these clinical trials the highest in Latin America and rising. While on the one hand in absolute terms Colombia's rate of clinical trials in this area is low: the number of clinical trials on biologic drugs to date is slightly over 100, between 50% to 150% lower than the top 3 economies in Latin America – Brazil, Mexico and Argentina.

Yet, Colombia's share of biologic trials relative to the total number of trials is quite high. Biologic-related trials were 11.3% of total trials, while this share is closer to 5% in Brazil and 8% in Mexico and Chile.

Though clinical trials related to biologic drugs are mostly concentrated in Phase III trials, a generally upward trend in absolute number of Phase II (and Phase I to some extent) trials is visible since 2010. Moreover, the share of Phase I and II trials on biologics relative to the total number of trials on biologics has risen, from around 25% in 2011-12 to 33-40% in 2013-15.

Key finding 3:

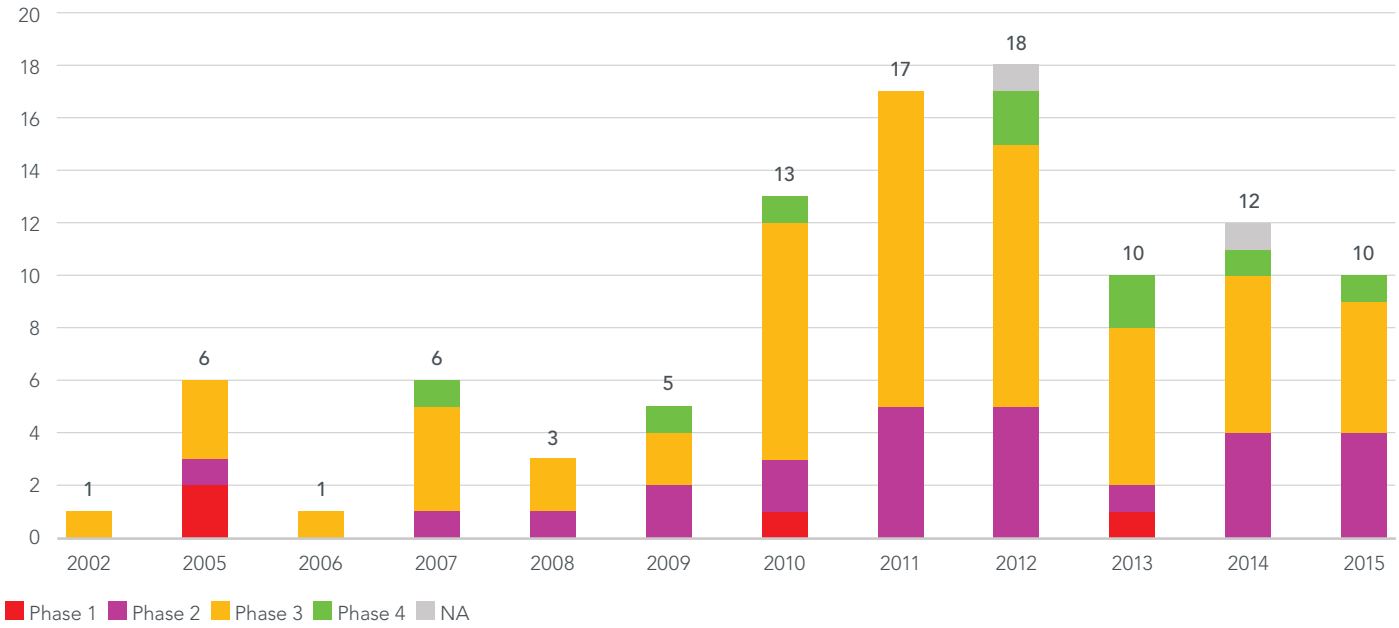
- Reforming Colombia's biopharmaceutical policy environment could almost double current levels of clinical research to over 100 additional clinical trials per year and close to USD200 million of direct economic gains.
- Equally a deterioration to the biopharmaceutical policy environment could result in a decrease of 30% or more from current levels of clinical research a year and total economic losses including externalities of over USD100 million.

Clinical trials of biologic drugs – A regional comparison

Country	Total number of CTs to date	Number of CTs on biologic drug	% share of total
Colombia	903	102	11.30%
Peru	801	87	10.86%
Argentina	2018	163	8.08%
Chile	1129	91	8.06%
Mexico	2513	198	7.88%
Brazil	4803	251	5.23%
Venezuela	154	3	1.95%
Ecuador	107	0	0.00%

Source: Clinicaltrials.gov, 2016; Pugatch Consilium analysis

Clinical trials on biologic drugs in Colombia by phases, 2002-2015



Source: Clinicaltrials.gov, 2016; Pugatch Consilium analysis

Using an econometric model which analyzes Colombia's clinical research policy environment in relation to international best practices and identifies which policy improvements might support greater clinical trial activity in the country, the report quantifies the resulting wider, positive economic effects of either improving this environment or seeing a deterioration. For example, the IP environment for biopharmaceuticals in Colombia is holding back biopharmaceutical investment and development. For biopharmaceutical as well as non-pharmaceutical biological products and technologies the evidence suggests that IPRs incentivise and support the research and development of new biological technologies and products. Unfortunately, the last few years have seen increased uncertainty with regards to the protection of IP and biopharmaceutical IPRs in particular in Colombia. An increased focus on the use of compulsory licensing and overriding of property rights as a cost-containment tool, lack of patentability for biopharmaceutical innovation and uncertainty over the application of RDP to biologics create an environment which is not the best for attracting investment and long-term biopharmaceutical R&D.

The model built provides three different scenarios of the impact potential biopharmaceutical policy reform could have in Colombia:

- **Scenario 1: Conservative:** a half-scale (i.e. a 30%) improvement of Colombia's biopharmaceutical policy environment to the levels of leading/ emerging clinical research hubs.

- **Scenario 2: Optimistic:** a full-scale improvement (i.e. a 60% improvement) of Colombia's biopharmaceutical policy environment to the levels of leading/emerging clinical research hubs.

- **Scenario 3: Pessimistic:** a negative scenario considers the expected losses from a deterioration of the biopharmaceutical policy environment.

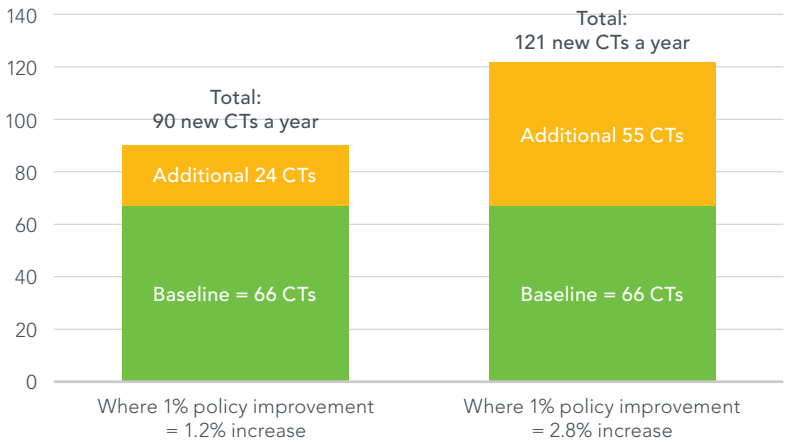
The conservative scenario

Under the more conservative scenario of improving Colombia's clinical research policy environment by 30%, the expected impact ranges from an increase of 36% in both clinical trial activity and associated monetary transfers (where 1% improvement results in an increase of 1.2%) to 84% (where 1% improvement results in an increase of 2.8%), as well as an additional 150% in indirect economic gains.

The below figure and table show, under a conservative scenario of a 30% improvement to the clinical research policy environment, Colombia could expect anywhere between 24 and 55 additional new clinical trials a year and up to USD312.8 million in total economic gains.

The table at the bottom provides an illustrative distribution of direct and indirect monetary flows accrued to key stakeholders under the conservative scenario. It shows how even a relatively conservative improvement to the biopharmaceutical policy environment could lead to considerable benefits across key stakeholders, including discounted access to new medicines, savings to hospitals and payers and additional funding towards infrastructure and clinicians and other personnel as well as revenue supporting the growth of the local CRO industry.

Gains to clinical trial activity in a given year under the conservative scenario



Expected economic gains in a given year under the conservative scenario

Estimated total monetary flows associated with clinical research resulting following policy reform	
Direct monetary gain where 1% improvement = 1.2% increase	Total economic gain (including externalities)
$92.4 Million	$231 Million
Direct monetary gain where 1% improvement = 2.8% increase	Total economic gain (including externalities)
$125.1 Million	$312.8 Million

Monetary and economic benefits associated with clinical trials accrued to key stakeholders under a conservative scenario of biopharmaceutical policy reform

Stakeholder	Bottom of range	Top of range
Hospitals and related services	$92.4 Million	$125.1 Million
CROs and related services	$104 Million	$140.7 Million

Stakeholder	Bottom of range	Top of range
Payers	$34.7 Million	$46.9 Million
Other (including patients)	$34.7 Million	$46.9 Million

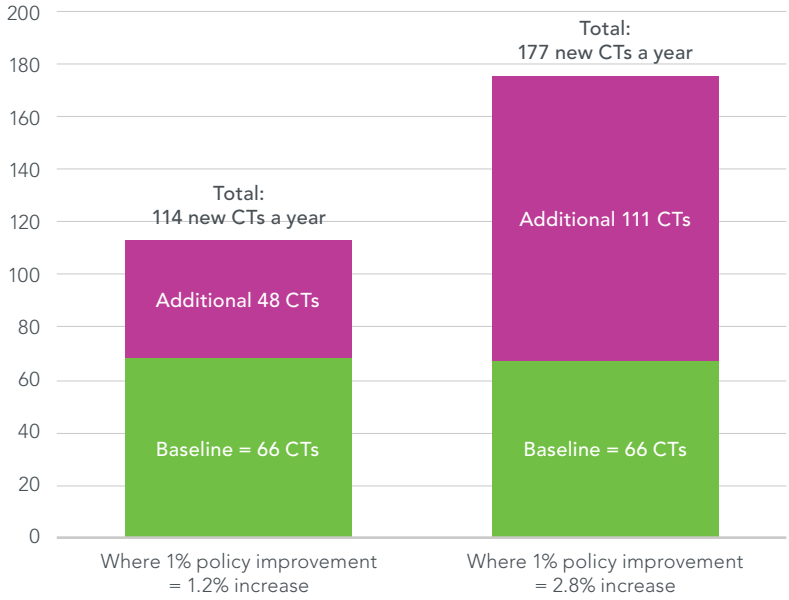
The optimistic scenario

Under the optimistic scenario of improving Colombia's biopharmaceutical policy environment to the entry level of current leading clinical research hubs, the expected impact ranges from an increase of 72% in both clinical trial activity and associated monetary transfers (where 1% improvement results in an increase of 1.2%) to 168% (where 1% improvement results in an increase of 2.8%), as well as an additional 150% in indirect economic gains.

As the below figure and table show, under the optimistic scenario of a 60% improvement to the biopharmaceutical policy environment, Colombia could expect an increase of anywhere between 48 and 111 additional new clinical trials a year and up to 455.5 million USD total economic gains.

Under the optimistic scenario, as the table at the bottom shows, an improvement to the biopharmaceutical policy environment to the entry level of current leading clinical research hubs could lead to a significant increase in gains to key stakeholders, with wider benefits for public health, cost containment and industrial development. To put these gains in perspective, the overall gains estimated in this scenario of around $455 million represent a significant portion of Colombia's total annual spending on medicines – around 14%.

Gains to clinical trial activity in a given year under the optimistic scenario



Expected economic gains in a given year under the optimistic scenario

Estimated total monetary flows associated with clinical research resulting following policy reform	
Direct monetary gain where 1% improvement = 1.2% increase	Total economic gain (including externalities)
$116.9 Million	$292.3 Million
Direct monetary gain where 1% improvement = 2.8% increase	Total economic gain (including externalities)
$182.2 Million	$455.5 Million

Monetary and economic benefits associated with clinical trials accrued to key stakeholders under an optimistic scenario of biopharmaceutical policy reform

Stakeholder	Bottom of range	Top of range
Hospitals and related services	$116.9 Million	$182.2 Million
CROs and related services	$131.5 Million	$205.5 Million

Stakeholder	Bottom of range	Top of range
Payers	$43.8 Million	$68.3 Million
Other (including patients)	$43.8 Million	$68.3 Million

Moving in the wrong direction – A pessimistic scenario

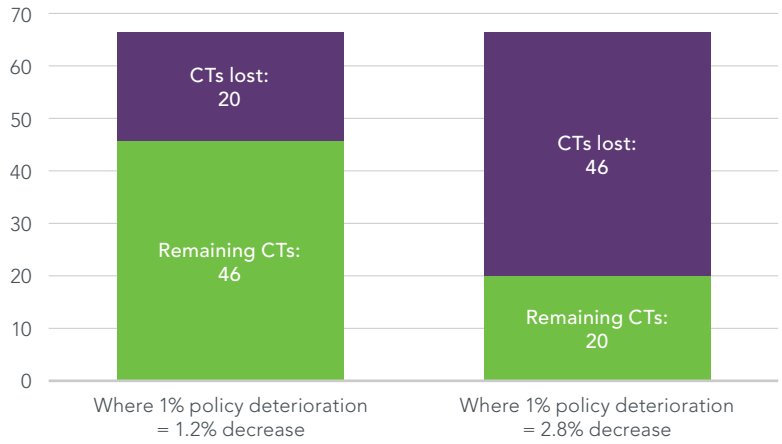
Just as an improvement to Colombia's biopharmaceutical policy environment is estimated to result in direct and indirect societal and economic gains, a deterioration of the environment would also result in direct and indirect losses.

For example, the failure to achieve INVIMA's new policy of a 60-day timeframe for the regulatory approval of clinical trials would mean that the current 225-days timeframe would remain or could even increase. Furthermore, continued uncertainty and deterioration of the IP environment for biopharmaceuticals (including the continued use of, or the threat to use, compulsory licensing or unilateral ad hoc price reductions through a notice of public interest) may deter clinical trials' sponsors and future investments in the biopharmaceutical sector.

Under this pessimistic scenario, where Colombia's biopharmaceutical policy environment deteriorates by at least 25%, Colombia could expect a decrease of anywhere between 20 and 46 clinical trials a year and total economic losses of up to 119 million USD, as shown in the figure and table below.

In a similar yet inverted manner to the other scenarios, the table below shows how the deterioration of Colombia's biopharmaceutical policy environment would lead not only to a lower amount of clinical trials (which consequentially means that fewer Colombian patients will benefit from early access to cutting-edge treatments) but also to substantial losses.

Expected losses to clinical trials activity in a given year under the pessimistic scenario



Expected economic losses in a given year under the pessimistic scenario

Estimated losses of monetary flows associated with clinical research resulting from a 25% deterioration of the clinical research policy environment

Direct monetary loss where 1% deterioration = 1.2% decrease	Total economic loss (including externalities)
$-20.4 Million	$-51 Million
Direct monetary loss where 1% deterioration = 2.8% decrease	Total economic loss (including externalities)
$-47.6 Million	$-119 Million

INTRODUCTION

Biotechnologies are today used in a wide variety of sectors and industries to produce everything from advanced biopharmaceutical medicines, genetically modified crops to household goods such as enzyme-based cleaning detergents. In the major fields of human socio-economic development from food production, to health to the development of clean energies, biological processes and biotechnologies are being utilized more and more and to greater effect.

For example, breakthroughs and the increased use of agricultural biotechnology over the past few decades have allowed farmers to produce increasing amounts of crops and foods to feed a growing proportion of the world's population. In 2015 the total acreage of biotechnology derived crops was just under 180million hectares of biotech crops under cultivation.[1] Over the past two decades the commercial cultivation of biotech crops has increased by a factor of over 100 growing from 1.7million hectares in 1996 to close to 180million in 2015. Significantly, most of this production was concentrated in developing and emerging markets in Latin America, Asia and Africa.[2] In fact in Brazil, Argentina, India, China and South Africa biotech crops make up a growing (if not the biggest) form of agricultural crops.

Similarly, in the health sector the importance of biotechnology cannot be overstated. Biologic medicines and technologies are increasingly being used in the treatment of patients with the most difficult conditions as well as in cutting-edge medical research. Biotechnologies are often part of the discovery, clinical and pre-marketing studies on traditional small molecule drugs. This includes biotech processes such as pharmacogenetics, gene sequencing and diagnostics through the identification of biomarkers. And the path to new types of clinical and therapeutic environments – based on the personalization of medicines and medical treatments – is in large measure based on advances in biotechnology. Here pharmacogenetics and gene sequencing play a crucial role. The centrality of biotechnologies and biologic processes to medical research can be seen in the number and type of biopharmaceutical products being approved today. In 2015 the US FDA approved a record 45 NME and BLA products; the highest rate over the last decade.[3] Significantly, a growing portion of these approvals were for biologic medicines and therapies.

Building the bioeconomy – A national strategic priority

Growing numbers of economies around the world are looking to the biotechnology field as a future engine for economic growth and development. Indeed, several of the world's biggest and fastest growing economies have launched new or updated national plans or strategies to promote the growth of this sector. India and South Africa have both outlined ambitious and detailed national biotechnology policy plans over the last two years. And in the publication of its 13th Five-year Plan in March 2016 China recommitted to the biotechnology sector by designating it as a 'strategic industry'.[4] In fact, many emerging markets are world-leaders in the development and use of biotechnologies. For instance, Brazil has for many years been a pioneer in using and developing GM crops. Equally, in the field of biofuels Brazil is a world leader having made a national commitment to using sugar-cane ethanol as a primary form of transport fuel since the 1970s.

And in the developed world building the bioeconomy remains at the core of economic and national policy making. This is most prominent in the US which has since the 1980s and the beginning of the biotechnology revolution embraced the use of biotechnologies across all major sectors – biopharmaceuticals, ag-bio and industrial biotechnology. Indeed, in 2012, in the *National Bioeconomy Blueprint*, the Obama administration and US Government argued that the bioeconomy would "allow Americans to live longer,

healthier lives, reduce our dependence on oil, address key environmental challenges, transform manufacturing processes, and increase the productivity and scope of the agricultural sector while growing new jobs and industries."[5] And the economic contribution of biotechnologies to American national output is high and growing. The most recent estimates from 2016 of the value of the three major biotechnologies (biopharmaceuticals, biotech crops and industrial biotechnology) place their contributions at about 2% of US GDP.[6]

Colombia – A story of untapped potential?

"Biodiversity is to Colombia what oil is to Saudi Arabia."
EO Wilson[7]

According to the UN Convention on Biological Diversity Colombia is home to one of the world's most biodiverse environments, hosting close to 10% of global biodiversity.[8] Colombia has high levels of biodiversity of plants, birds, orchid species, freshwater fishes and amphibians as well as butterflies and is home to over 300 ecosystems.[9] The importance of this biodiversity cannot be overstated as biodiversity is a natural resource and a source for scientific research, biotechnological innovation and commercialization of biotech products and processes.[10]

Colombia has long recognized its biodiversity and the importance of biotechnology and the potential of this sector. A national biotechnology institute and specific national program was introduced as early as the 1980s and 1990s, respectively, and a national framework and strategic plan has been in place since the late 1990s.[11]

More recently, a number of policies and Government-led initiatives have been introduced with the view of stimulating research and the growth and development of the biotech sector. Early in his first term current President Santos emphasized the need for developing an economic model based on innovation, science and high-tech sectors including biotechnology.[12] In 2011 a framework for the commercialization and development of biotechnologies was introduced.[13] And biotechnology figures heavy in current Government plans and strategies including the 2014-2024 *Programa Nacional de Biocomercio Sostenible* and latest National Development Plan (*Plan Nacional de Desarrollo 2014-2018*); all of which are detailed below in section 1.

Yet unlike many other countries with high levels of biodiversity Colombia has not been able to fully translate this natural resource into a world-leading biotechnology sector. For example, as mentioned, Brazil – also having a high level of biodiversity – has for many years been a pioneer in agricultural biotechnology. In 2015 Brazil had 44.2 million hectares of biotech crops under cultivation growing maize, soybeans and cotton; second only to the US.[14] And the Brazilian Government through EMBRAPA has for decades been closely involved in the R&D and commercialisation of agricultural biotechnologies. Equally, Brazil has since the 1970s had in place the National Alcohol Program (*Proalcool*). This program has contributed to the building of the Brazilian sugar-cane based ethanol industry. As recently as 2006 Brazil was the biggest producer of bioethanol in the world producing 16 billion litres or approximately 36% of global production.[15] Although no longer the top producer, 2014 figures show that Brazil is the second largest producer of biofuels in the world accounting for approximately a quarter of global production.[16] Still, there are limits as to how far natural resources can take a given economy. Despite significant efforts, Brazil has not been as successful in the realm of building an innovative, R&D driven biopharmaceutical capacity. Innovation in the life sciences remains behind other emerging and developed markets and clinical research levels are still relatively low given Brazil's market and population size.

In this sense one of the broader lessons for Colombia and other aspiring biotechnology countries from this study is that the policy environment is absolutely critical to ensuring success in stimulating innovation and building a biotech R&D capacity.

Report overview

The purpose of this report is to, firstly, give a comparative overview of the biotechnology sector in Colombia and, secondly, provide an estimate of how an improvement to Colombia's policy environment can result in higher biotechnology outputs including rates of biomedical FDI and clinical trials.

The report maps the current policy environment as it relates to biotechnology in Colombia and gives a detailed comparison on key major biotechnology and R&D related outputs between Colombia and other economies:

– Where does Colombia stand today with regards to its biotechnology capacity?

– And how does Colombia's current biotechnology capacity compare to other middle income economies, OECD economies and other economies in the Latin America region?

A key aspect of the report is the identification of policy areas where the existing legal and policy framework is not in line with international best practices and is actually limiting the development of Colombia's biotechnology sectors. Through economic modelling the report quantifies the potential direct financial and R&D benefits Colombia could derive from introducing positive reforms aimed at stimulating international biotechnology investment and, in particular, greater levels of biopharmaceutical investment through clinical trials.

The report consists of five main sections:

Section 1 provides an overview of the current national innovation and biotechnology policy environment in Colombia. What are the major policy tools in place aimed at spurring the general innovation and R&D environment, biotechnology, and policies aimed at specific sectors of biotechnology (e.g. biopharmaceuticals, energy, ag-bio and cosmetics)?

Section 2 compares Colombia's performance on a range of biotech indicators to a sample of other middle-income economies, the OECD and wider Latin America region. The section looks specifically at indicators ranging from general indicators of innovation and innovative output, to general biotechnology indicators, to key biotech sectors and performance indicators for the main biotechnology sectors i.e. ag-bio, biofuels, cosmetics and biopharmaceuticals. This section includes a deep-dive analysis of Colombia's clinical trials environment including R&D for biologics.

Section 3 focuses on some of the key challenges in Colombia's policy environment as they relate to the development of the biotechnology sectors. Building on the work carried out by the Colombian Government in 2013 through the chief investment and business development agency (INNPULSA) this section zooms in on key areas of policy reform where Colombia is currently lagging behind other major economies.

Section 4 provides modelled estimates of the tangible economic benefits a positive improvement in the policy environment for biotechnology would have in Colombia. Specifically, the economic model built estimates the amount of higher net inflows of biotech FDI and higher levels of clinical research an improvement in the policy environment could result in.

Section 5 provides an overview of the key findings of the report and concluding thoughts, tying together the policy review, comparative data analysis and modelling of the preceding sections.

1 FROM A – Z: MAPPING COLOMBIA'S BIOTECH ENVIRONMENT

What does Colombia's biotechnology policy framework look like? How has it developed over time?

1.1 Colombia: Macroeconomic and innovation policy overview

Macroeconomic development

Colombia is the third largest economy in Latin America with a 2014 total national output of 638.3 billion USD measured on a PPP basis.[17] Measured on a GDP per capita basis Colombia is an upper-middle income country with a per capita income of 6,209 USD for 2014 at current USD.[18] Colombia is the 61st most competitive economy in the world according to the World Economic Forum's 2015-16 Global Competitiveness rankings, a rise of 5 spots from the 2014-2015 rankings, and 8 spots from the 2013-2014 rankings.[19]

Since 2000 Colombia has changed rapidly. The economy has expanded and developed aided by relative political stability and a significant and sustained improvement to the security situation. GDP growth since 2000 has been robust, averaging 4.4% per year in the period 2000-2014.[20] During this time period the structure and composition of the Colombian economy has shifted from basic manufacturing to commodity exports and minerals (primarily oil) which is responsible for circa 7% of economic output per the OECD.[21] Colombia has successfully participated in international trade negotiations, including most notably with the US, and increased its overall participation in world trade.

The sustained levels of economic growth and political stability have moved Colombian government policy to focus on modernizing the economy, shifting to an innovation, knowledge-based socio-economic development model. Since 2013 Colombia has been in accession talks to the OECD.

Innovation framework

Colombia has a number of institutions and layers of government working towards promoting greater innovation and building R&D and innovative capacity within the economy. These range from specific governmental departments (such as *Colciencias*, the Administrative Department of Science, Technology and Innovation), to sector specific initiatives (discussed below with regards to biotechnology) to two major general policy levers/mechanisms for innovation policy which includes:

- Successive National Development Plans (2010-2014; 2014-2018) which both provide a sustained and significant focus on strengthening science and technology in Colombia and the economy's innovation capacity; and

- the General Royalties System which in 2011 introduced a 10% diversion of royalties from mineral income to science and technology development.[22]

In addition to providing the strategic roadmap for Colombia's economic development together these two general levers also provide much of the major policy framework and direction for Colombia's biotechnology specific policies. Indeed, biotechnology development figures heavily and in detail in both national development plans.

1.2 Biotechnology policy framework

From 2010-2018 – the National Development Plans

The concept of a national development plan is central to Colombian national economic and industrial policymaking. The plan provides a blueprint to policymakers, the political establishment and the country at large as to where

and how the Government and country is headed. The idea of a national plan and its specific contents is described in the Colombian constitution. Article 339 states that "There will be a National Development Plan…[which] will include long term national purposes and objectives, the goals and priorities of intermediate-term state activities, and the strategies and general orientation of economic, social, and environmental policy to be adopted by the government."[23]

Accordingly, the national plan is critical to the development of a specific sector or set of industries – including biotechnology.

Plan Nacional de Desarrollo 2010-2014 "Prosperidad para Todos

Colombia's first National Development Plan of 2010-2014 – *Plan Nacional de Desarrollo 2010-2014 "Prosperidad para Todos"* – placed a heavy emphasis on strengthening Colombia's science, technology and innovation capacity.[24] A major part of this plan was developing and building the biotechnology sector. More specifically, it included the "Policy for the commercial development of biotechnology from the sustainable use of biodiversity" (CONPES 3697), a framework for the commercialization and development of biotechnologies, released by the National Council for Economic and Social Policy and National Department of Planning.[25]

CONPES 3697 sought to improve the investment environment in the area of biotechnology in order to draw in greater private and public investment in commercial development within the sector, with a total public investment of 27 billion USD.[26] The framework targeted a wide range of biotech sectors including cosmetics, biopharmaceuticals, food and agriculture. It sought/seeks to strengthen support for biotech activities across public and private sectors. Specifically the framework boosted support for various government agencies (including the Ministry of Commerce and *Colciencias*); scientific capacity building and applied research in universities and research institutions; as well as support for industry-academic collaboration, technology transfer and biotech start-ups. Another key feature of the framework was to enable greater access to genetic and biological resources, adjusting the regulation on the production and marketing of biological drugs, and establishing venture capital funds.[27] A major part of this plan was the potential creation of a national bioprospecting company.[28] As of the time of research the establishment of such an entity was still being debated.

CONPES 3697 built on previous strategic biotechnology initiatives: the Policy to Promote Research and Innovation in Colombia from 2008, and the National Policy of Science, Technology and Innovation of 2009, both of which focused on biotechnology as a strategic sector. The framework was introduced as part of the administration's broader policy goals of improving the conditions for private sector investment as well as increasing public spending on science and technology.[29]

Plan Nacional de Desarrollo 2014-2018 Todos por un Nuevo País

The most recent national development plan covers the period 2014-2018. It focuses on three main pillars: peace, equity and education. These pillars are to be achieved with what is termed five "cross-cutting strategies.[30] These strategies cut across all segments of socio-economic development from general competitiveness and improvements to infrastructure (physical as well as technological); social mobility; security and reforms to the justice and legal system; and an emphasis on good governance. Improving the framework and culture of innovation, building human capital and improving scientific and technological capacities is a key part of the plan.

In addition to being a strategic vision and outline of Colombia's future development the 2014-2018 National Development Plan also includes legislation directly affecting the incentives for biotechnology innovation and R&D. Unfortunately, much of this legislation negatively affects Colombia's policy environment in areas where, as is discussed below in section 3, Colombia already faces a number of challenges including the protection of intellectual property.

For example, article 70 widens the basis for the issuing of compulsory licenses in a manner that goes beyond the TRIPS Agreement, Article 31

and the 2001 Doha Ministerial Declaration and subsequent General Council decision concerning Paragraph 6.[31] The provision allows Colombian authorities to define public health emergencies broadly and to actively seek out compulsory licenses, allowing for grounds outside extreme circumstances including industrial or commercial objectives, to play a role in the issuing of compulsory licenses. (On a separate track and an issue which is detailed below in section 3, the Ministry of Health and Social Services threatened to issues a compulsory license for a cancer treatment. The request for the license appears to be outside the scope of a public health emergency with, according to the patent holder, no reported shortages of the product and a reduction in the price already in place.[32] At the time of research no license had been issued. Instead a Declaration of Public Interest had been made allowing the health authorities to cut the price negotiated and paid to the manufacturer.)

In addition, both articles 70 and 72 link two distinct and independent processes with regulatory approval of biopharmaceuticals: patent examination and pricing decisions.[33] Article 70 allows the Ministry of Health and Social Services to participate in the patent review process by the Ministry of Industry. This potentially allows non-legal or factors outside of technical patent criteria to be factored into decisions on whether to grant a biopharmaceutical patent, rather than examination solely by patent specialists and officials based on established and accepted legal and technical criteria. Article 72 links approval of biopharmaceuticals with pricing decisions. Specifically pricing decisions must be made as part of the market approval process. This is outside international standards and the process used in developed markets. In most countries pricing and reimbursement decisions (whether they be by a public or private health payer) is a separate process from product registration and market approval. Decisions on registration and product approval are based solely on scientific and technical determinations examining the safety, quality and efficacy of a given product and technology.

Additional biotechnology policy frameworks

In addition to the national plans there are a number of biotech specific initiatives taking place at various levels of the Colombian Government. For instance, *El Programa Nacional de Biocomercio Sostenible de Colombia 2014 – 2024 (PNBS)* – is a 10-year program aimed at improving Colombia's position as a major competitor in the global trade of biotechnological products, or 'bio-trade'.[34] The program presents a revised framework which is based on an ecosystem conception, adaptive management, and the development of sustainable value chains from a shared management of natural resources.[35] Specifically, the plan sets to harmonize the legal, regulatory, institutional and political frameworks across Colombia, prioritize the potential of different value chains in order to identify and address the technological needs of each value chain, achieve international accreditation for locally-produced biotechnological products, and encourage investment from the private sector in R&D and bioprospecting as a strategy for conservation and sustainable economic development.[36] The funding for this plan comes from a national support system comprised of several national funds, designated governmental budgets (such as from *Colciencias*) as well as from general taxation and BANCOLDEX, the Colombian Business Development Bank.[37]

Colciencias has also laid out an ambitious plan to develop the country's biotechnology capacity. The plan includes targets of increasing innovation in the private sector, the development of commercial biotechnology products, increased levels of patenting and significantly increasing the contribution to national GDP from biotechnology.[38] The plan has focused on 4 strategic areas of development:

1. Science

   This includes investing in new research and mapping of new biological finds through increased exploration. There is also a target of increasing the number of doctoral students and scientific infrastructure.

2. Business/commercial development
   This includes creating incentives, partnerships and the right conditions for the commercial development of biotechnologies and concrete products for market in Colombia and internationally. A target has been set to increase rates of innovation and partnership with Colombian companies with 2,000-8,000 companies to partner with *Colciencias*.[39]

3. Institutional capacity building
   This area focuses on both developing new and using existing institutional and regulatory frameworks at the national and regional level to promote the biotechnology sector. An emphasis has been placed by *Colciencias* on improving existing regulatory capacity and capabilities.

2. Socio-cultural development
   The plan also seeks to encourage national participation and ownership as it relates to biotechnology. In particular the plan aims to encourage greater awareness of Colombian biodiversity and the sustainable use of existing biological resources.

1.3 Section summary

Developing Colombia's biotechnology capacity is a long-standing priority for the Colombian government. As this section has outlined a number of policies and strategic initiatives have been introduced to stimulate biotech R&D and grow this sector.

The next section will assess how Colombia performs on a broad range of biotech indicators (general and sub-sector specific) compared to other middle-income economies, OECD economies and the wider Latin America region

2 COMPARING PERFORMANCE: COLOMBIA'S BIOTECHNOLOGY CAPACITY COMPARED TO OTHER ECONOMIES

In light of the targeted and strategic effort by the Colombian government to develop the biotechnology sector in Colombia, where does Colombia stand today with regards to its biotechnology capacity? How does Colombia's current biotechnology capacity compare to other middle-income economies, OECD economies and other economies in the Latin America region?

This section will take stock of Colombia's current performance and estimate its domestic capacity in biotech innovation through benchmarking the country's biotech environment – both generally and in specific sectors. It will primarily do this through looking at how Colombia compares to other economies on key indicators for general innovation, biotechnology and specific biotech sub-sectors, including agricultural biotechnology, cosmetics, biofuels and biopharmaceuticals. A particular focus will be placed on biopharmaceuticals and biologic medicines and the relative level of R&D taking place in this area.

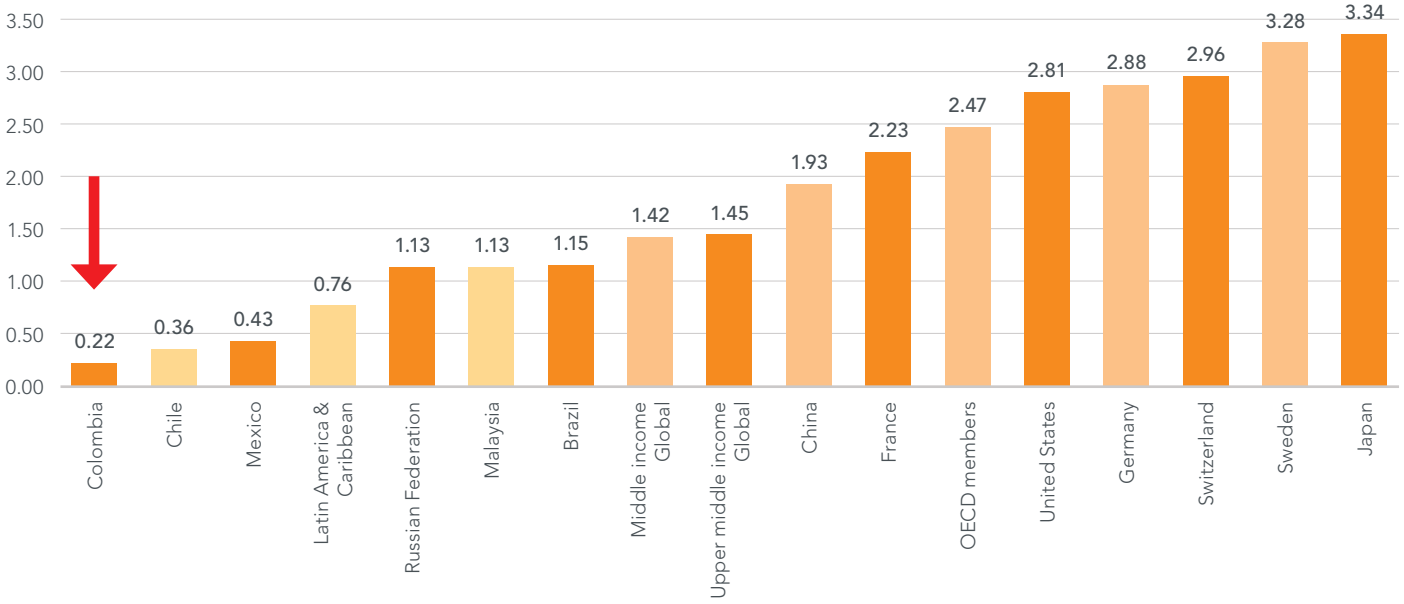
2.1 Colombia's overall R&D capacity

General levels of innovation, including spending on innovative activities and actual levels of innovative outputs, reflect the overall high-tech capacity and performance in a given country. Examining Colombia's performance in these areas provides a picture of the resources invested in innovation in the economy generally as well as how productive R&D entities are in terms of generating innovative outputs such as new technologies and know-how that then drive further innovation – which includes innovation resources and activity in the biotechnology sector. Indeed, given that biotechnology is a highly complex, technically demanding field, economies with strong biotech environments tend to have strong general levels of R&D capacity and spending. Overall, based on the below sample of standard measures of the R&D capacity and performance, Colombia falls behind its socio-economic peers.

For example, this is visible in one measure of the high-tech capacity in a country – the level of spending on R&D. R&D investment supports innovative activities in different sectors, including biotechnology, and establishes a foundation for long-term economic growth. It also enables economies and governments to develop and enhance technologies. As Figure 1 shows, Colombia spends a very small percentage of its GDP on R&D – just around 0.2% of GDP.[40] This level is below several other Latin American economies and less than a third of the average level spent in the region. It is also below middle-income economy averages and average spending in the BRICS, and far below OECD economies (which spend on average around 2.5% of GDP on R&D). Private sector spending on R&D is particularly low in Colombia. For instance according to the World Economic Forum's Executive Opinion Survey companies in Colombia spend a limited amount on R&D, less than Brazil, Mexico and Chile, though on par with Argentina and Ecuador and more than Peru and Venezuela.[41]

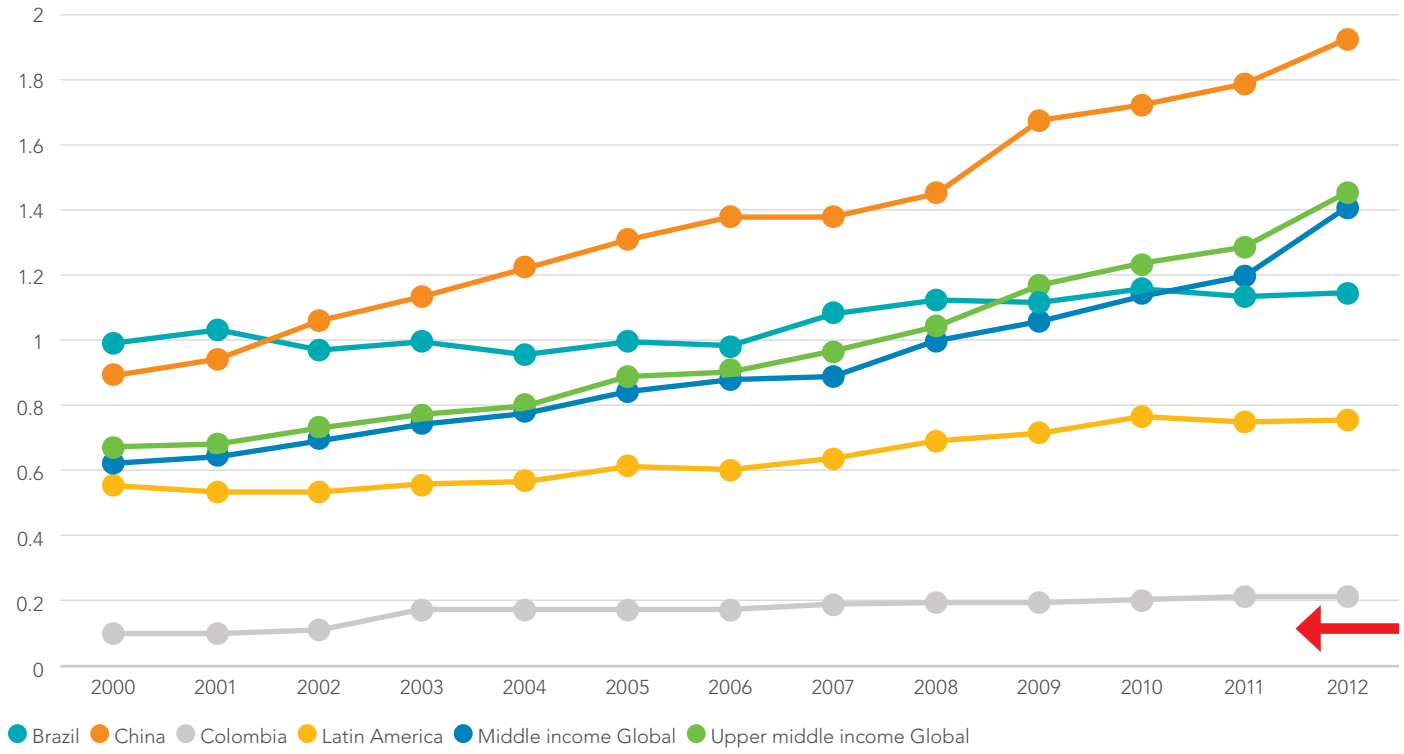
Perhaps the most critical observation, however, is that investment in R&D in Colombia has not grown over the past 15 years. Rather, as Figure 2 indicates the share of GDP spent on R&D has stayed flat since 2000.[42] While Latin American economies in general have not made a great deal of progress in increasing R&D investment, average rates of R&D spending in the region have still grown relative to Colombia's. In other regions middle-income economies have had much more success in this area: a dedicated effort among certain middle-income economies (such as China) to increase

FIGURE 1 R&D spending, % of GDP, 2012



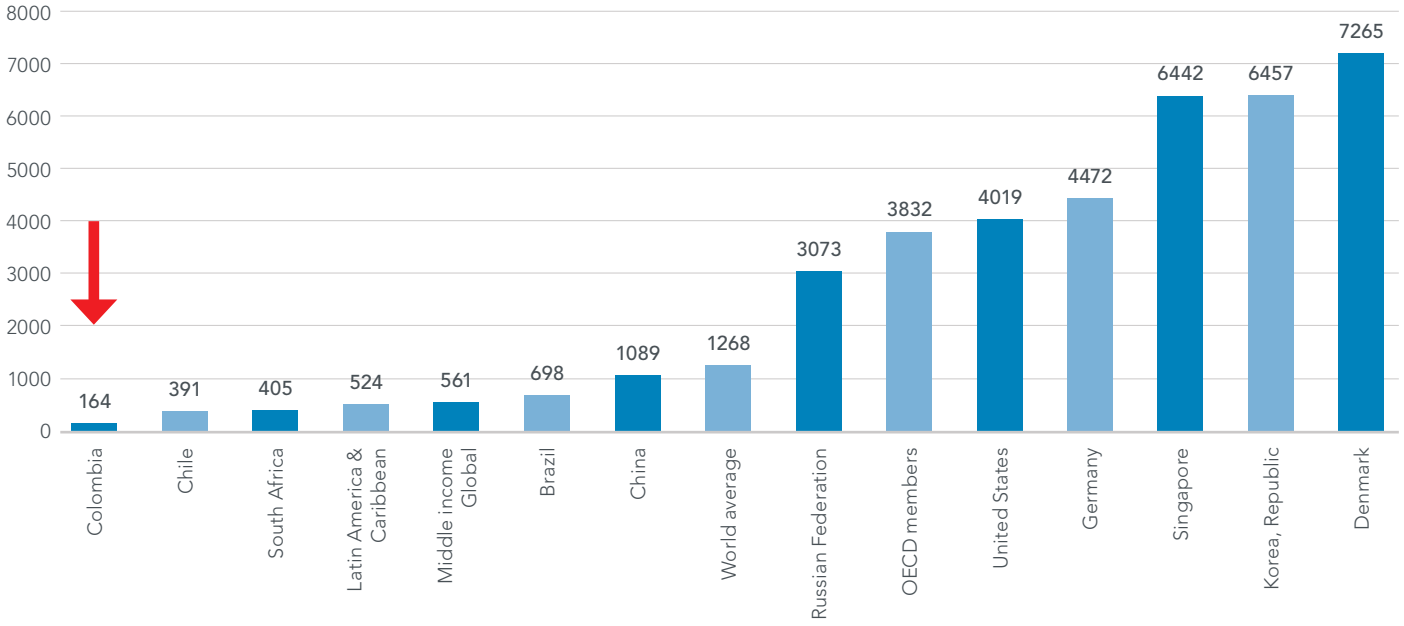
Source: World Bank (2016)

FIGURE 2 R&D spending, % of GDP, 2000-2012



Source: World Bank (2015)

FIGURE 3 Researchers in R&D (per million people), 2013 or nearest year



Source: World Bank (2016)

investment in R&D has resulted in a doubling of growth rates over the same period.

In addition to financial resources for R&D, Colombia also faces gaps in the availability of human capital. The number of researchers and scientists involved in R&D activities relative to the total population is very low, at just around 160 per million people.[43] As Figure 3 shows, this rate is less than a third of the average in Latin American economies as well as in middle-income economies globally. OECD members display an exponentially higher rate at an average of 3,800 researchers per million people.

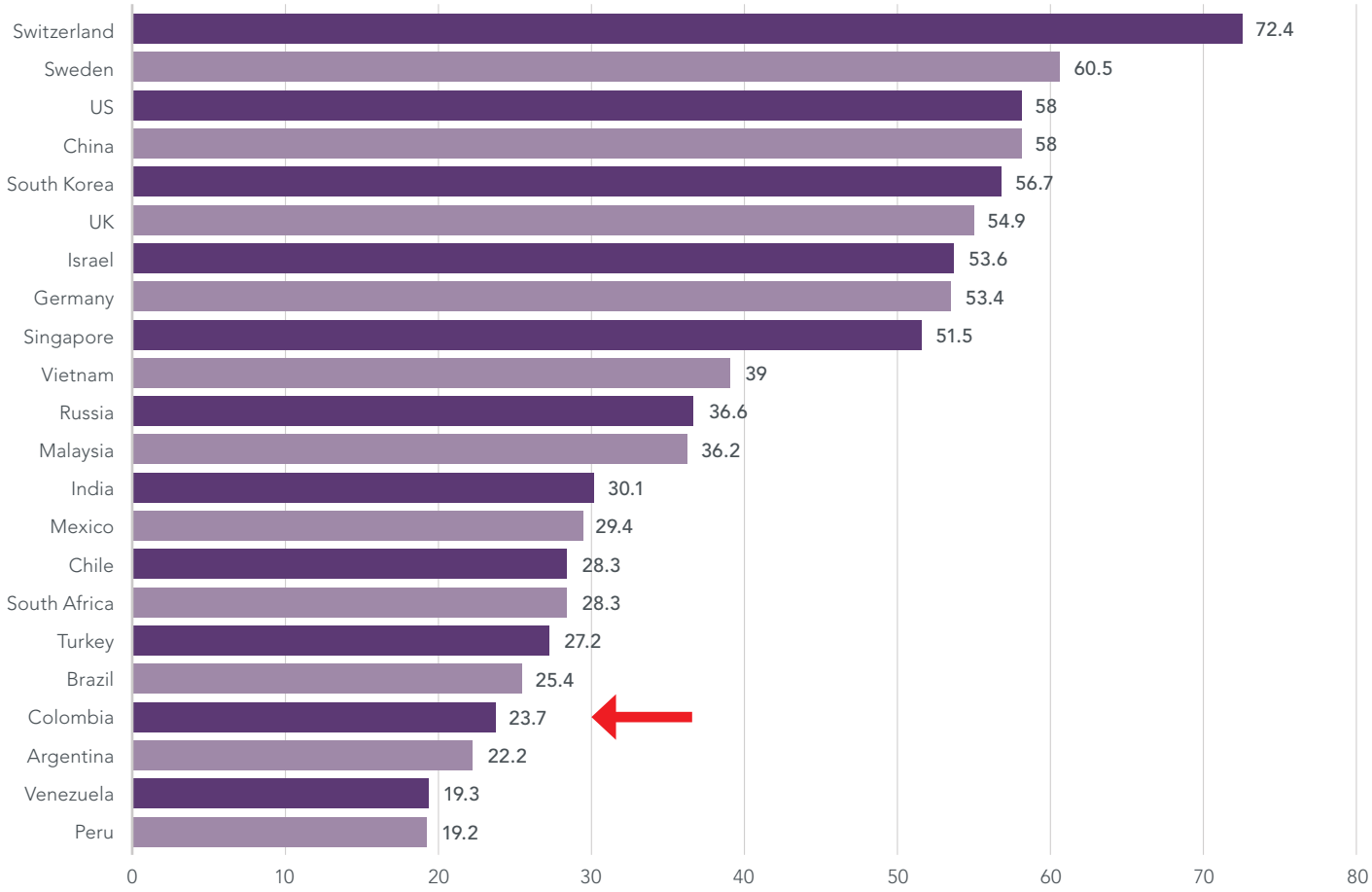
Looking at high-tech capacity from another angle – from the perspective of high-tech outputs, such as the creation, diffusion and use of technologies and knowledge-based services, Colombia also lags behind other economies. High-tech outputs are measured by the Global Innovation Index's Innovation Output Sub-index score. This Sub-index captures the creation of technologies, media, and knowledge-based services as well as their diffusion and use across the economy. As Figure 4 suggests, Colombia's score in this measure is closer to low-performing economies such as Venezuela than other middle-income economies such as Malaysia and Russia, and again, far below high-income OECD members such as Switzerland, Sweden and the US.

2.2 Colombia's biotechnology R&D capacity

Looking at the activity and performance in R&D of Colombia's biotech sector specifically, a similar picture emerges – Colombia still has a ways to go to match levels of biotech R&D compared to its peers and to advanced OECD economies. One measure of biotech activity is the rate of biotechnology patenting.

Generally speaking, patenting rates are a standard measure of the existing capabilities and activity of high-tech entities a in a given country. Specifically patenting rates provide an indication of an economy's high-tech innovation output and technical capacity. Patenting rates also reflect the propensity to seek commercialization of a product or technology, and as part of that the commercial and strategic value of the technologies being developed. As such the volume of patents

FIGURE 4 Global Innovation Index 2015, Knowledge and technology outputs, total score



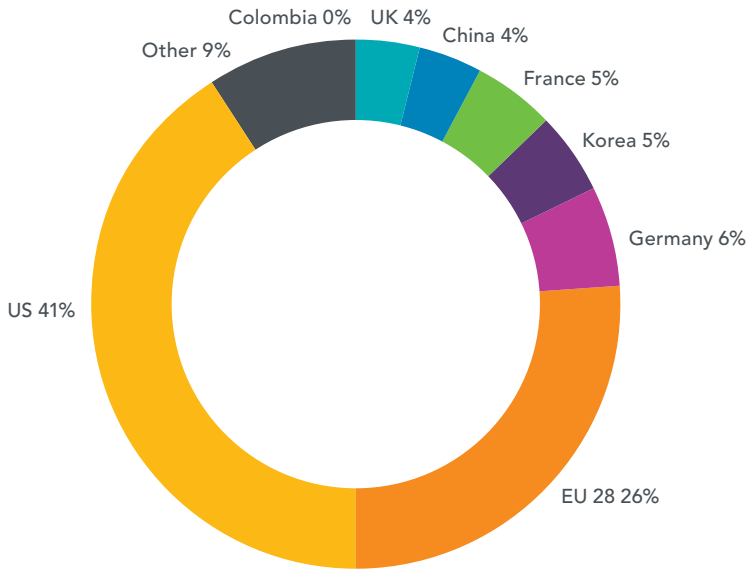
Source: GII (2015)

in a country indicates the level and scope of R&D capabilities among firms and research institutions in the country – particularly the ability to generate technologies that are strategic and commercially valuable enough to be patented.

Patenting statistics found in international databases, most prominently the WIPO database and OECDstat, provide measures of different types of patenting activity that together give a good picture of patenting activity in different countries, including Colombia. For example, OECDstat includes rates of applications filed under the international PCT system (providing protection internationally) and the WIPO database rates of national-level patents published by country. (Publication is a key stage in the patent application process, normally taking place after 1-2 years, and represents another measure of the level of patenting in a country.) Moreover, within these databases it is possible to isolate patents in different sectors and technology fields.

Looking granularly at patenting rates in the biotechnology sector shows that overall Colombia's biotech patenting activity is behind its regional and socio-economic peers, and far behind advanced OECD economies and world leaders. As a share of total PCT applications globally (seen in Figure 5), Colombia is responsible for a very small figure (4 of 10,217 in 2012, or close to 0%). World leaders in biotech patenting rates are dominated by large economies/economic regions – the US, EU, China and Korea.[44] Having said this as Figure 6 suggests, economic size is not necessarily a main factor behind biotech patenting rates. Colombia's biotech patenting is just a fraction of small economies such as Denmark, Switzerland

FIGURE 5 Biotechnology patent applications under PCT, share of total, 2012



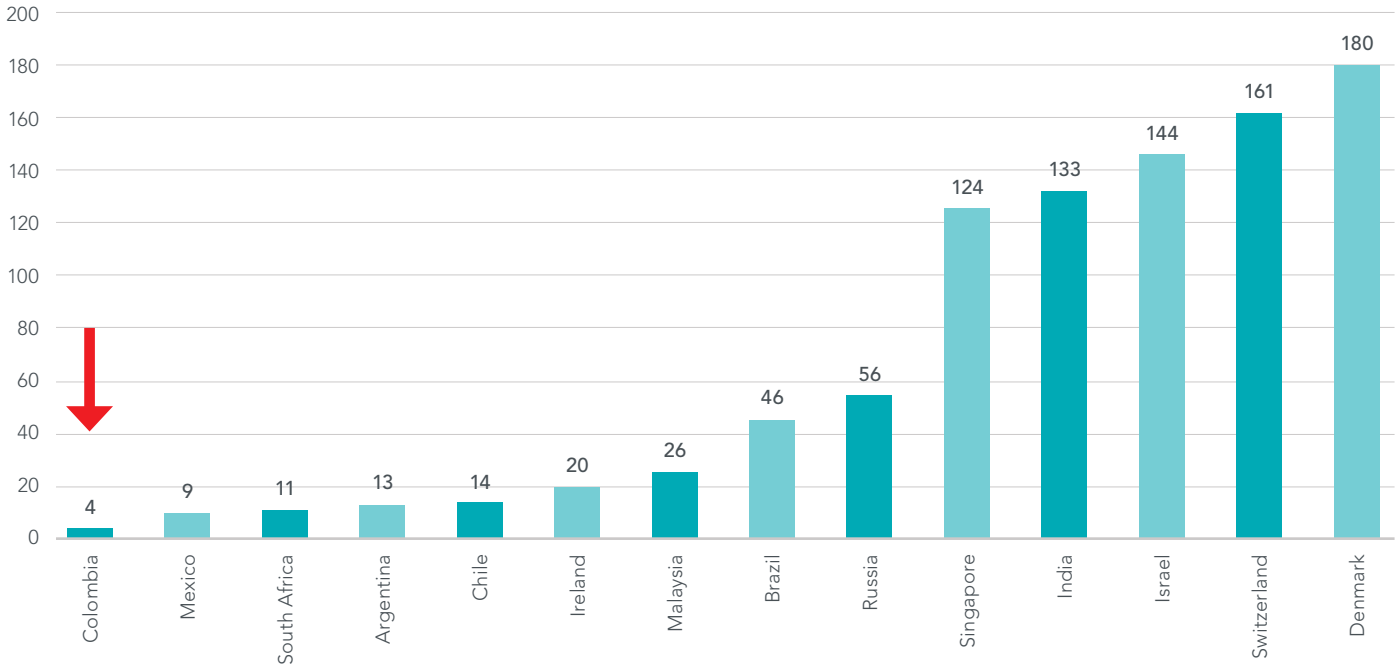
Source: OECDstat, 2016

and Israel. It is also behind other socio-economic peers such as the remaining BRICS economies and its Latin American neighbors, Chile, Argentina and Mexico.[45]

Colombia's level of biotech patenting has also remained relatively static for the past 10-15 years. Figure 7 indicates that between 1999 and 2012 Colombia's rate of PCT biotech applications stayed mostly flat compared to other Latin American economies and other middle income economies such as Malaysia. In contrast, in the same period many of these economies (Brazil, Chile, Mexico and Malaysia) experienced double digit growth.

Looking at the rate of published patents in biotechnology as measured by WIPO (at the national level though not necessarily part of PCT applications), Colombia's performance is slightly better than under the PCT system.[46] As Figure 8 shows the rate of patents published is on par with Singapore and above Malaysia, though still well below key Latin American neighbors.[47] This data suggests that while biotech innovators in Colombia

FIGURE 6 Total biotechnology patent applications filed under the PCT, 2012



Source: OECDstat, 2016

are somewhat active in patenting under the national system, generally speaking they are not making use of the PCT system when filing patents – and this may indicate a lower level of estimated quality or value of the patents that are filed as they are not seeking international protection

2.3 Colombia's R&D capacity in agricultural biotechnology

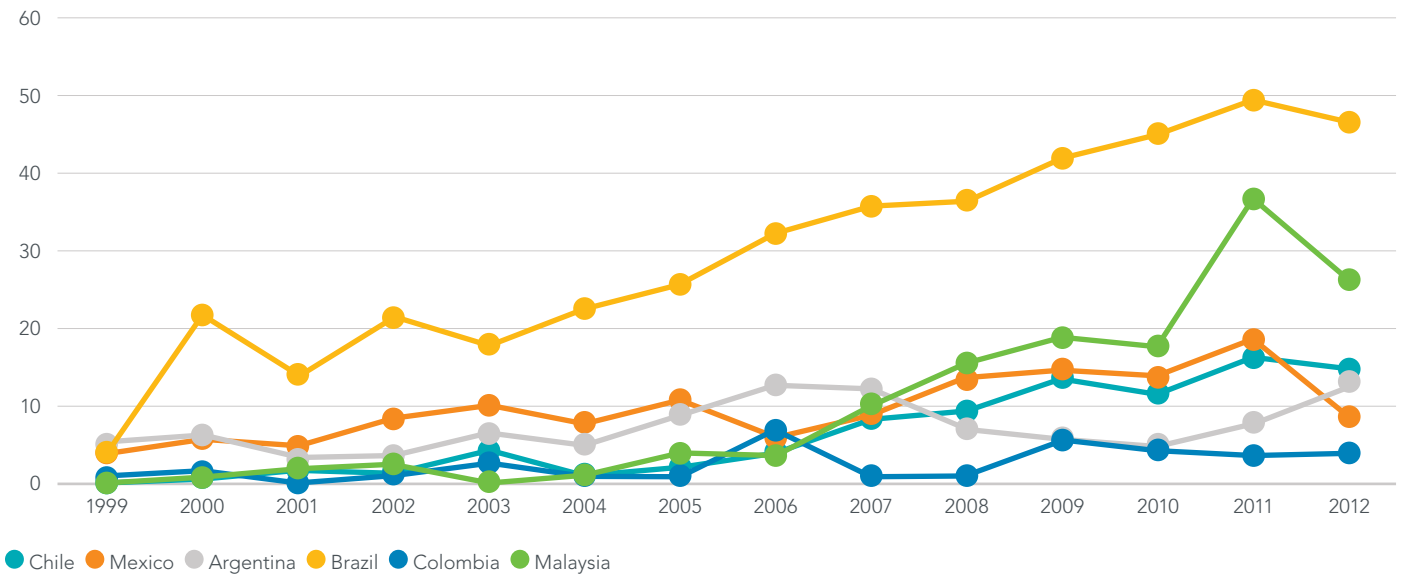
Agricultural biotechnology is currently the largest biotech sector in Colombia. Among biotech firms in the country the large majority are focused on agriculture and food (along with cosmetics). By some estimates, firms in the ag-bio sector represents around 40% of the total biotech sector in Colombia (with a related sector, food and alcoholic beverages, just under at around 30%).[48]

Within its wider development plan for the biotechnology sector, the Colombian government has made growth of the ag-bio sector a priority over the past 15+ years, among other factors in order to reduce reliance on food imports. Colombia has traditionally been a net importer of grains, particularly of corn (estimated at around 70% in 2010[49]). In this context, cultivation of biotech crops has taken place in Colombia since the early 2000s. As of 2015 the sector has grown exponentially (although a large portion is not yet dedicated to commercial cultivation), with genetically modified corn and cotton among the top crops produced. According to the Colombian Agriculture Institute the production of genetically modified corn has grown from around 7,000 hectares to close to 90,000 between 2007 and 2015.[50] Colombia has also approved GM seeds for certain plants, mainly limited to corn, cotton and flowers.

Nevertheless, within its national Cultivation Plan the government has set its sights on increasing GM crop cultivation by several times this current level – with targets for GM corn set at 790,000 hectares by the end of the decade in order to reduce imports by 50% within the period.[51]

By global comparison Colombia is notably an active country in terms of production of GM crops but still has substantial room for growth, including in the area of ag-bio innovation. In terms of R&D, available data on ag-bio R&D spending from the Inter-American Development Bank and the Food and Agriculture Association, though somewhat dated, suggests that Colombian R&D expenditure on ag-bio is very low. As a share of the total

FIGURE 7 Biotechnology patent applications filed under the PCT, 1999-2012



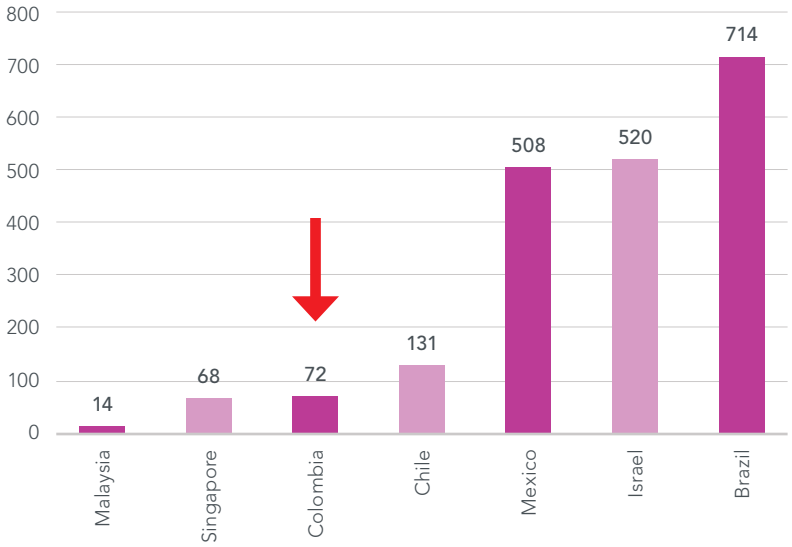
Source: OECDstat, 2016

spending in Latin America in 2006, Colombia spent just 3.3% with Brazil responsible for over 50% if total investments.[52]

While the amount of biotech crops under cultivation in Colombia has grown substantially over the past several years, this level is still small compared to other leading countries. Colombia's level of GM crops under cultivation – as Table 1 shows, at around 100,000 hectares in total – is in the top 20 globally but nevertheless near the bottom of the group and significantly lower than the leading countries, US, Brazil and Argentina.[53]

Another indicator of R&D activity in ag-bio is rates of plant variety protection. As seen in Figure 9, data from UPOV and WIPO indicate that between 2010 and 2014 Colombia saw 93-119 applications and 90-109 approvals for plant variety protection.[54] This represents a rate similar to Chile and higher than Germany and Denmark, but still lower than most other Latin American countries (including Brazil, Mexico and Argentina). However, it is important to note that the majority of the UPOV applications are submitted by non-residents, rather than domestic applicants. Complementing the above data on ag-bio R&D spending, this also suggests that domestic ago-bio innovation is limited.

FIGURE 8 Patent publications by technology, biotechnology, 2014



Source: WIPO database, 2016

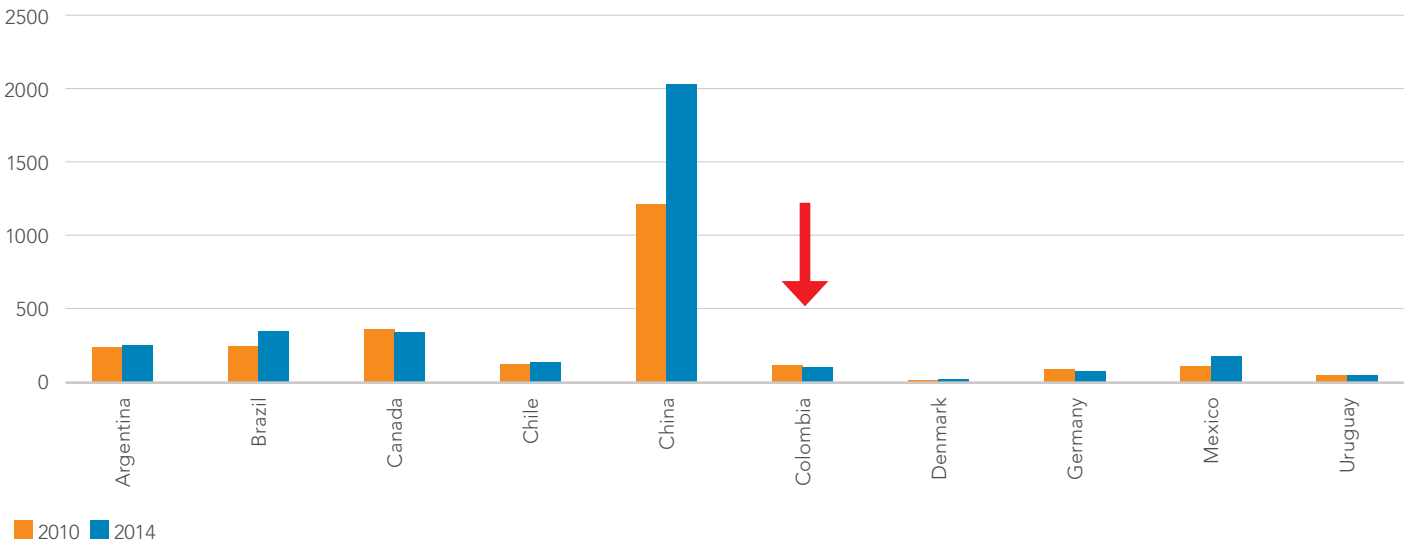
2.4 Colombia's capacity in bio-cosmetics

Bio-cosmetics, "cosmoceuticals" or natural cosmetics is a small but growing sector in Colombia in the area of biotech, with significant growth expected over the next 10-15 years. Worldwide, the use and development of biotechnologies in cosmetics is a growing trend and key future use for biotechnology. Global industry data suggest that the cosmeceuticals segment of the global cosmetics industry is set to grow substantially – by some estimates, projected to account for around USD30 billion in 2016 and to grow at around 15% annually – a faster rate than the cosmetics market generally.[55]

Drawing on Colombia's rich biodiversity, use of biotechnologies, medicinal plants, essential oils and unique natural extracts in cosmetics is targeted as having potential to make Colombia a regional hub and even global supplier of bio-cosmetics and personalized natural cosmetics. Indeed, some 6,000 plant species registered in Colombia are thought to have medicinal properties, many of which have been identified as having application in the natural or bio-cosmetics sector.[56]

Most if not all data on market size in Colombia do not distinguish bio-cosmetics from the general cosmetics market, but current market estimates suggest that the sector is growing substantially. Indeed, 2015 estimates by the National Business Association of Colombia (ANDI) value the Colombian cosmetics sector at around USD3.9 billion.[57] According to government data, sales in cosmetics have grown at an average rate of 8.5% since 2000 and are expected to continue growing at 4-6% through 2019.[58] Today Colombia is the fifth largest market in cosmetics in Latin America. Of this, existing estimates suggest that the bio-cosmetics sector remains fairly small, just a fraction of the total cosmetics market. For example, in 2009 Colombia exported just over USD7.5 million in medicinal plants and only around USD300,000 in essential oils, compared to over USD800 million worth of exports in the total cosmetics sector during the same period.[59] More recent analysis indicates that natural cosmetics remain a small but growing portion of the cosmetics sector in Colombia.[60]

FIGURE 9 Plant variety protection, applications, 2010-2014



Source: UPOV 2016

TABLE 1 Top-20 economies, biotech crops under cultivation

Country	Million hectares under cultivation	Country	Million hectares under cultivation
US	73.1	Bolivia	1
Brazil	42.2	Philippines	0.8
Argentina	24.3	Australia	0.5
India	11.6	Burkina Faso	0.5
Canada	11.6	Myanmar	0.3
China	3.9	Mexico	0.2
Paraguay	3.9	Spain	0.1
Pakistan	2.9	Colombia	0.1
South Africa	2.7	Sudan	0.1
Uruguay	1.6	Honduras	less than 0.05

Source: ISAAA 2015

R&D in the bio-cosmetics sector is also growing in Colombia. For example, one study found that between 2001 and 2007, publications on research in the field of natural cosmetics more than doubled to over 100 per year in Colombia.[61] Since 2008 Colombia has also experienced a jump in the number of patents related to bio-cosmetics. One analysis of the field of "phytotherapeutics", of which natural cosmetics is one of the largest segments, found that the number of patent applications in the field rose from under 10 per year to around 24 per year between 2008 and 2011, with a total of 181 patent applications in Colombia to date in the field.[62] However, it is worth noting that the majority of these applications were from non-residents, and there is substantial room for growth in local R&D capacity in the field of bio-cosmetics.

2.5 Colombia's capacity in biofuels

Since 2005 the Colombian government has targeted biofuels as a strategic sector, particularly in order to capitalize on rising global demand for renewable energy and to meet targets for reduced CO2 emissions in Colombia.[63]

As a result, the biofuels sector in Colombia has grown markedly over the past decade. The two largest segments within the sector are sugar cane-based ethanol and palm oil-based biodiesel. Colombia is one of the leading sugar cane producers globally, and a substantial portion of the sector is now devoted to ethanol production.[64] In addition, Colombia is considered to be the top producer of palm oil in Latin America and fifth largest in the world, producing more than 945,000 tons of palm oil and over 500,000 tons of palm oil-based biodiesel in 2014. Capacity for biodiesel production is reportedly already in excess of domestic demand, at around 800,000 tons per year (with demand in Colombia identified as around 520,000 tons per year).[65] In contrast, the ethanol segment in Colombia still has substantial room for growth to meet clean energy targets. For example, current estimates put daily ethanol production at about 1.65 million liters, representing about 8% of gasoline consumption in Colombia.[66] Moreover, today just about 8% of biotech firms in Colombia are focused on biofuels.[67]

Still, the Colombian biofuels sector is small compared to world leaders in the sector. Though reliable international data is difficult to find, energy giant BP provides an annual statistical breakdown of energy production globally, including renewables such as biofuels. The latest available data from BP suggest that Colombia is one of the top three producers of biofuels in Latin America, along with Brazil and Argentina.[68] As seen in Figure 10, prior to 2005 production of biofuels in the country was negligible, but since 2006 the sector has seen strong growth, with production increasing manifold by 2014.

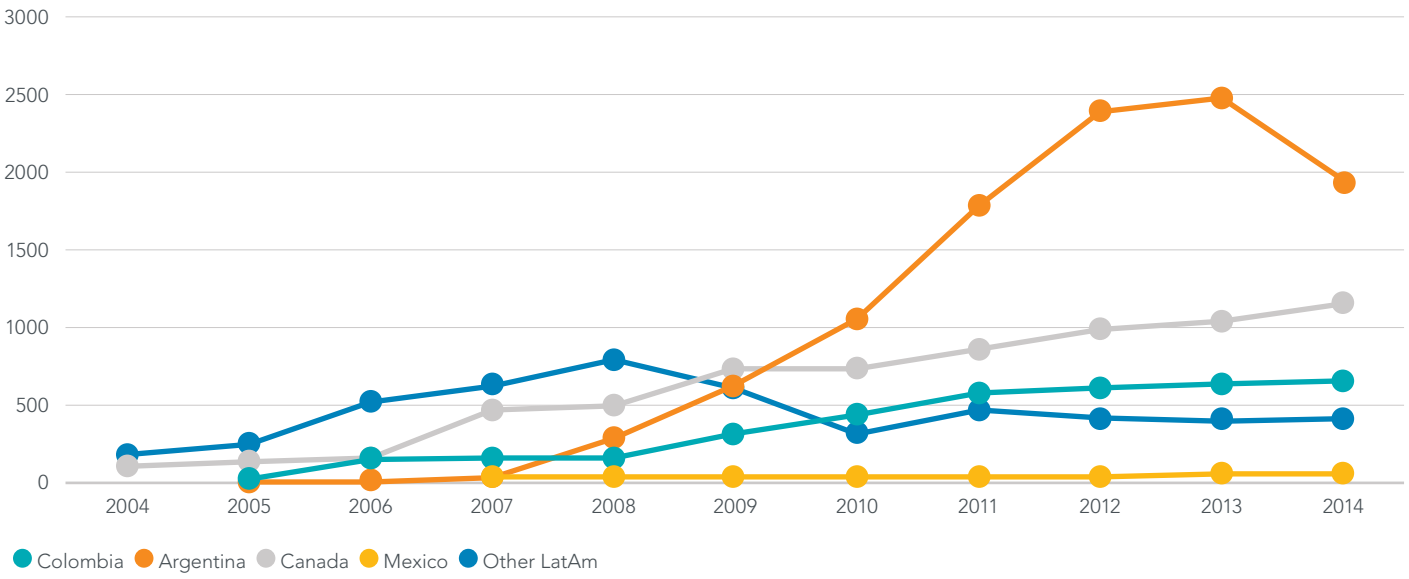
Still, as Figure 11 shows, as a share of the global total production of biofuels, Colombian production remains negligible compared to the top 2 producers worldwide – the US (at 42.5% of the global total) and Brazil (23.5%). Nevertheless, it is just slightly below Argentina and above Mexico, the second and fourth performers in Latin America.

2.6 Colombia's capacity in biopharmaceuticals – Zooming in on clinical research

What do levels of clinical research tell us?

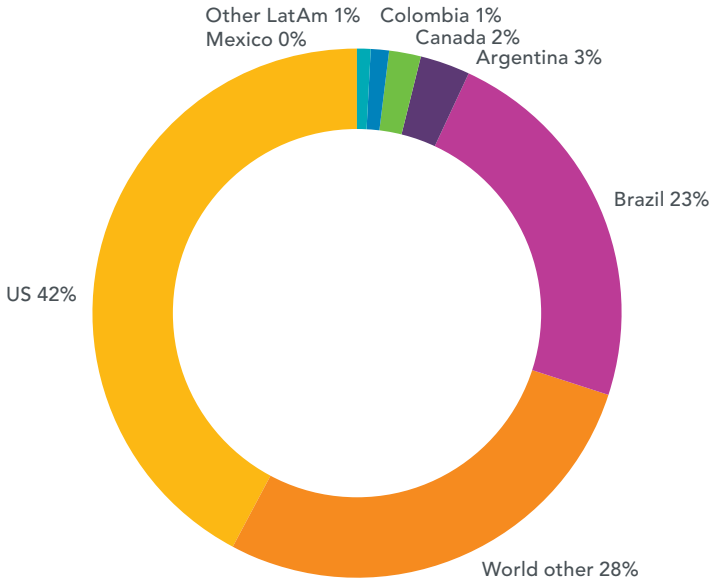
As a high-tech and high-value sector, biopharmaceutical development and R&D represents an important component of biotechnological capacity and structure in a given country. Indeed, developing, launching and accessing innovative medical technologies carry huge socio-economic benefits, including increased levels of economic activity, job creation, access to new medicines, creation of knowledge-intensive sectors and building of high-tech capacity. Many, if not all, emerging and developed economies view developing a competitive life sciences and biopharmaceutical sector as a national strategic priority. Not least, this is visible in numerous "vision" and strategy documents published by various governments over the past several years that lay out strategic targets and policies for building up domestic innovative biopharmaceutical sectors. As discussed in section 1 Colombia has identified biotechnology (including biopharmaceuticals) as a key sector for development, including through the National Plan 2014-2018.

FIGURE 10 Biofuels, Country Production, 2004-2014



Source: BP 2015

FIGURE 11 Biofuels, Global production, 2014



Source: BP 2015

Currently, the Colombian biopharmaceutical market is relatively small but growing at a fairly robust rate. Looking at the pharmaceutical market as a whole (without distinguishing biotech products), in 2009-11 the projected annual average growth rate was 6% and around 5% in 2012-15. Based on the most recent projections, the market is valued at around USD3.3 billion (COP9,101 billion) and is set to grow over 5% (in local currency terms) between 2015 and 2016 (though this represents a drop of 12% in US dollar terms).[69] Based on a 2013 survey from the national statistics agency DANE, the pharmaceutical sector represents just under 5% of the total value added. Among the manufacturing sectors it is the 6th largest contributor to value added out of 64 sectors.[70]

As such, the pharmaceutical market, particularly in the area of biopharmaceuticals and biologics, holds significant potential as a high value added sector to be developed in Colombia.

Estimates vary but on average around 30% of the total biopharmaceutical market today is composed of biotech products (including biologics and biosimilars).[71] But just around 5% of biotech firms in Colombia are reportedly focused on biopharmaceuticals.[72]

In terms of R&D capacity one indicator of the level and complexity of biopharmaceutical R&D being conducted in Colombia is the level of clinical research taking place. Global clinical trial registries provide a picture of the number, type and phase of clinical trials in a given country individually as well as in international comparison. One such resource is the US National Institutes of Health's Clinicaltrials.gov database, which provides comprehensive, in-depth data on global clinical research, including in Colombia.[73]

Analyzing clinical trial data can reveal key attributes of a country's biopharmaceutical R&D environment. Specifically, clinical research registries can provide the following picture of different countries' clinical research capacity and performance:

- **Clinical trial activity:** Absolute number of trials suggests a country is an attractive host for biopharmaceutical R&D (although numbers can be misleading, since large countries tend to attract more trials; standardizing for population ("research intensity") is one good solution;

- **Research intensity:** Number of clinical trials divided by population shows a country's research intensity relative to population; crucially, small countries can be competitive without hosting a large market (for instance, Singapore, Denmark and Israel)

- **R&D capacity:** the types of trials taking place and disease areas suggest the technical R&D capacity in a given country (for example, trials in areas such as oncology and rare diseases tend to require a higher level of R&D capacity);

- **Innovativeness:** In what types of phases are trials concentrated? Similar to a focus on certain disease areas, early phase (phase I and II) suggests cutting edge, innovative research is taking place, in the sense that these represent initial human testing of drug candidates' safety and efficacy, and therefore typically require very controlled environments and high quality human resources and infrastructure that can ensure such an environment; and

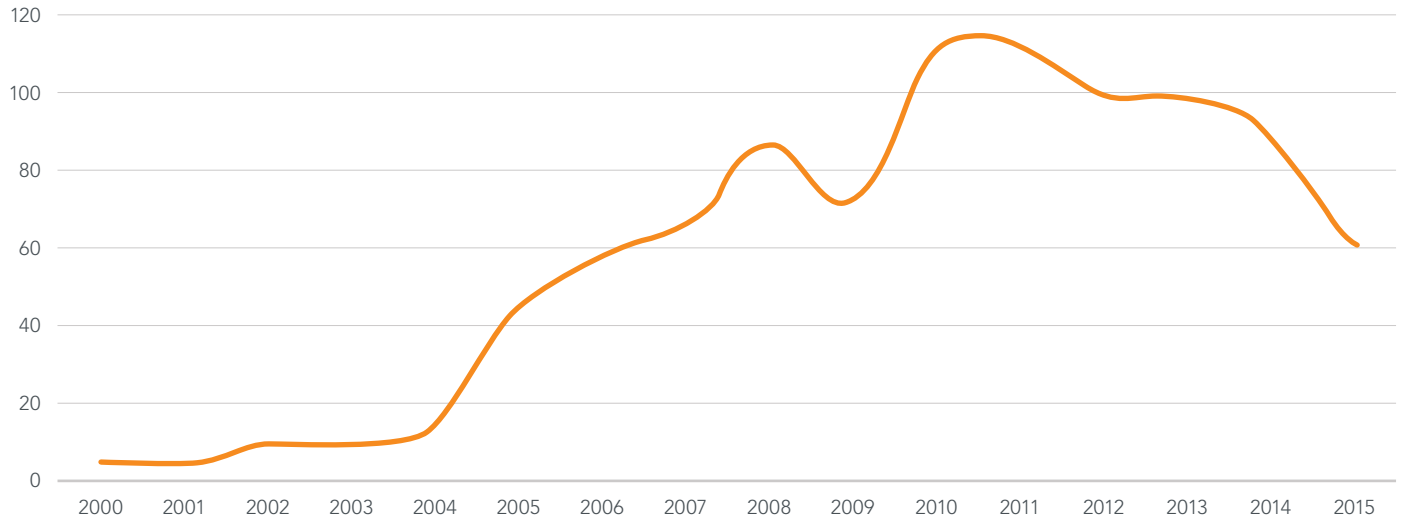
- **Biotechnology capacity:** How many trials are taking place that focus on biologics as opposed to NCEs? These provide an indication of the extent to which R&D capacity and performance, where relevant, is in line with government strategic priorities for sectoral development as well as how advanced the country's R&D capacity is; biologics research generally requires a relatively high level of complexity in terms of skills and resources.

Lagging behind: Colombia's share of global clinical research

Looking specifically at the available data on clinical trials conducted in Colombia and registered on Clinicaltrials.gov, Colombia performs below its potential. Looking at rates of clinical trials in Colombia over time suggests that in the ten-year period 2000-2010 there was significant growth in clinical research. During this time the number of trials increased from essentially single digits per year to over 100 trials in 2010-2011. However, in the following five-year period 2010-2015 the number of trials taking place decrease sharply dropping by close to 50%. Below Figure 12 shows this development.

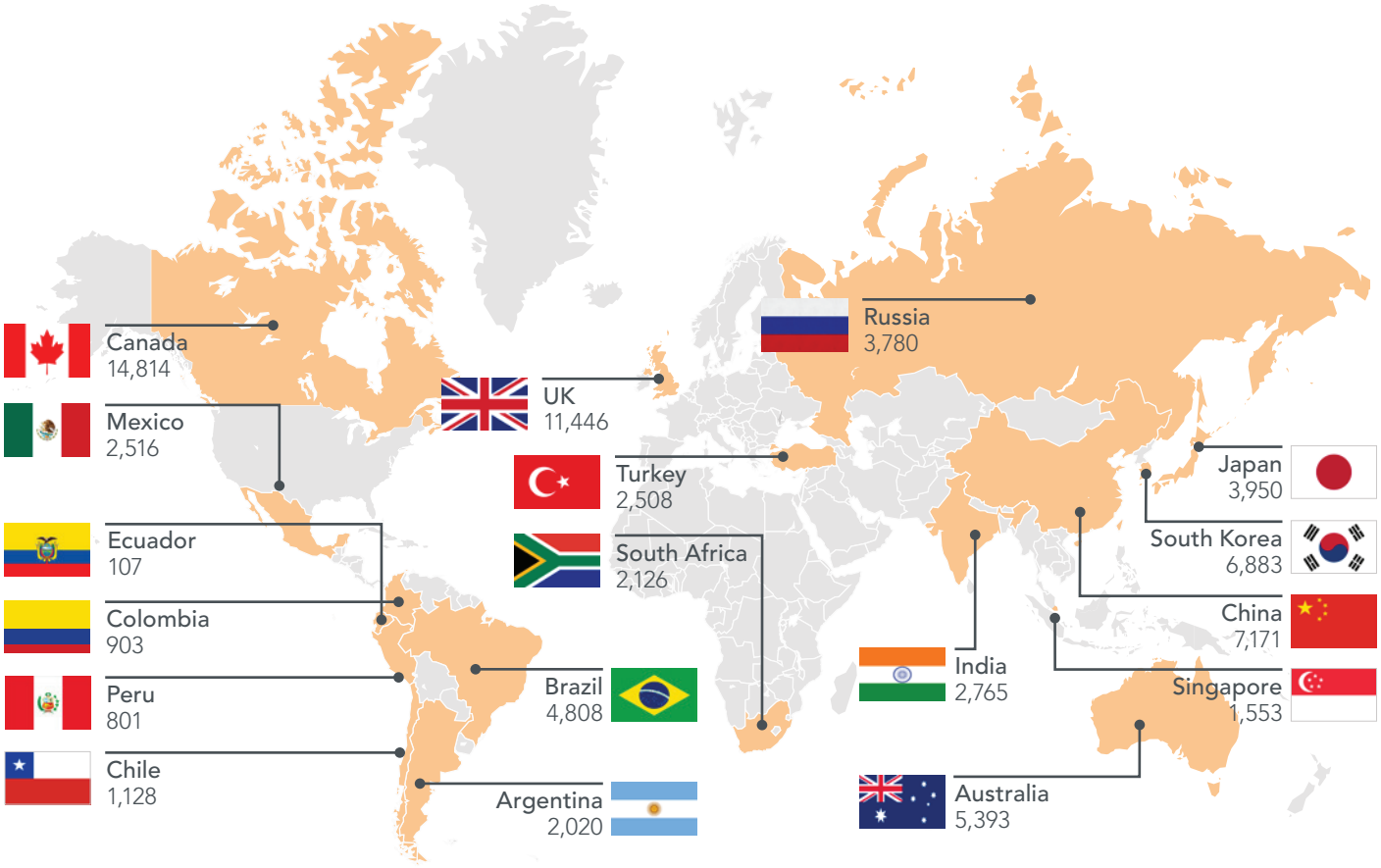
As Figure 13 shows the total number of clinical trials hosted in Colombia to date (registered in *Clinicaltrials.gov* in January 2016) is just around 900, compared to over 1,100 in Chile, 2,000 in Argentina, 2,500 in Mexico and 4,800 in Brazil. Adjusted for population, as Figure 14 shows, at around 18.56 clinical trials per million population Colombia is behind Chile and Argentina as well as certain other middle-income economies such as South Africa and global leaders like Singapore, Denmark, the US and Israel. Still Figure 15 shows that from the perspective of clinical trial intensity Colombia performs marginally better or at least is on par with the average among key emerging markets, including the BRIC economies and Turkey.

FIGURE 12 Clinical trial intensity in Colombia: annual number of new clinical trials in Colombia, 2000-2015[74]



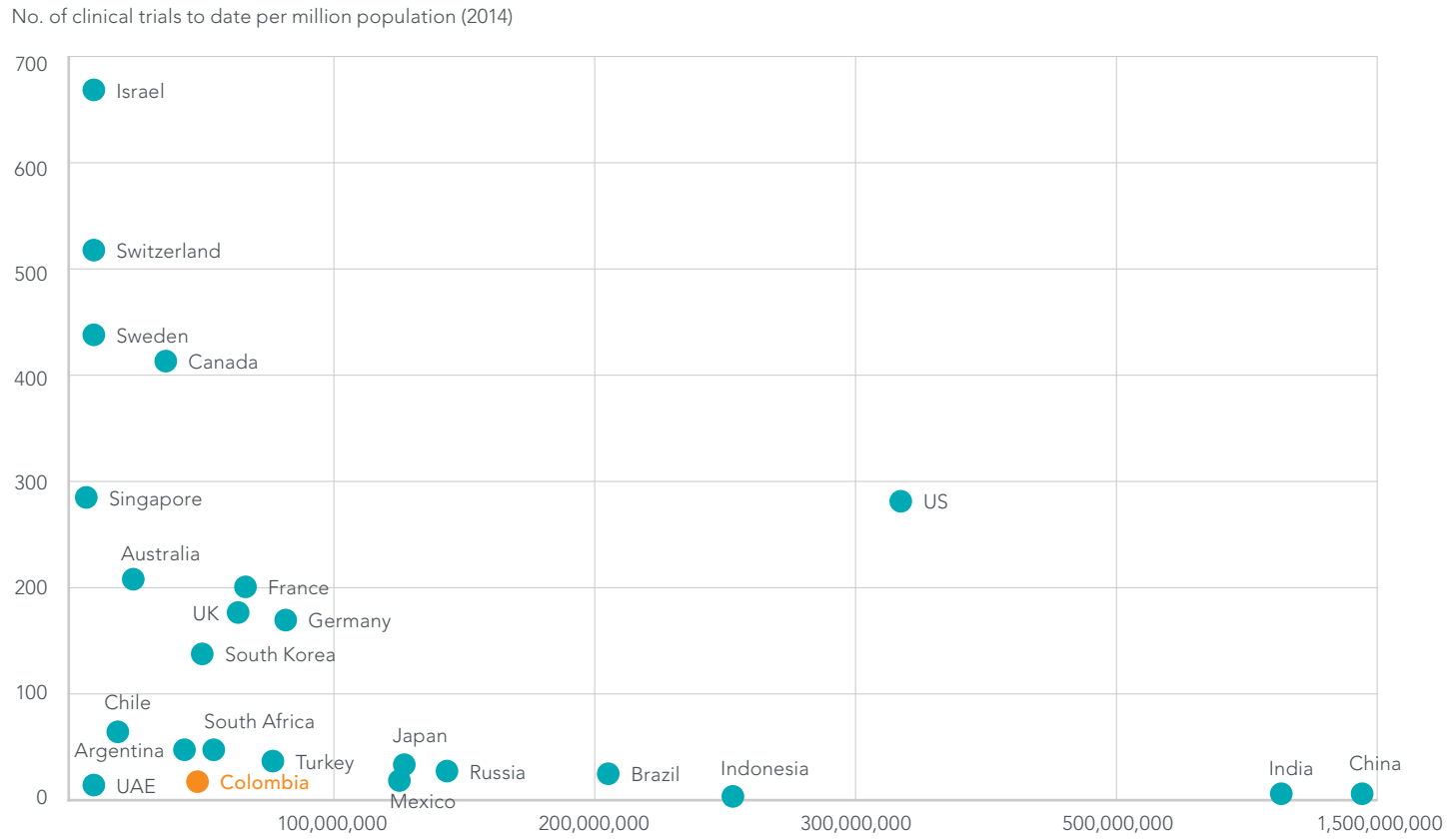
Source: Clinicaltrials.gov (2016)

FIGURE 13 Absolute number of clinical trials to date – Global comparison



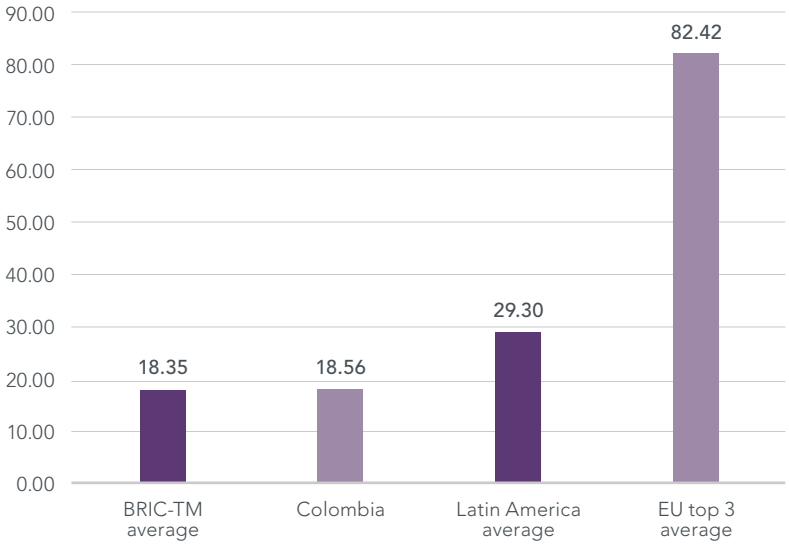
Source: Clinicaltrials.gov, 2016 (Note: data is based on number of clinical trials registered in the database in January 2016)

FIGURE 14 Number of clinical trials per million population in selected countries



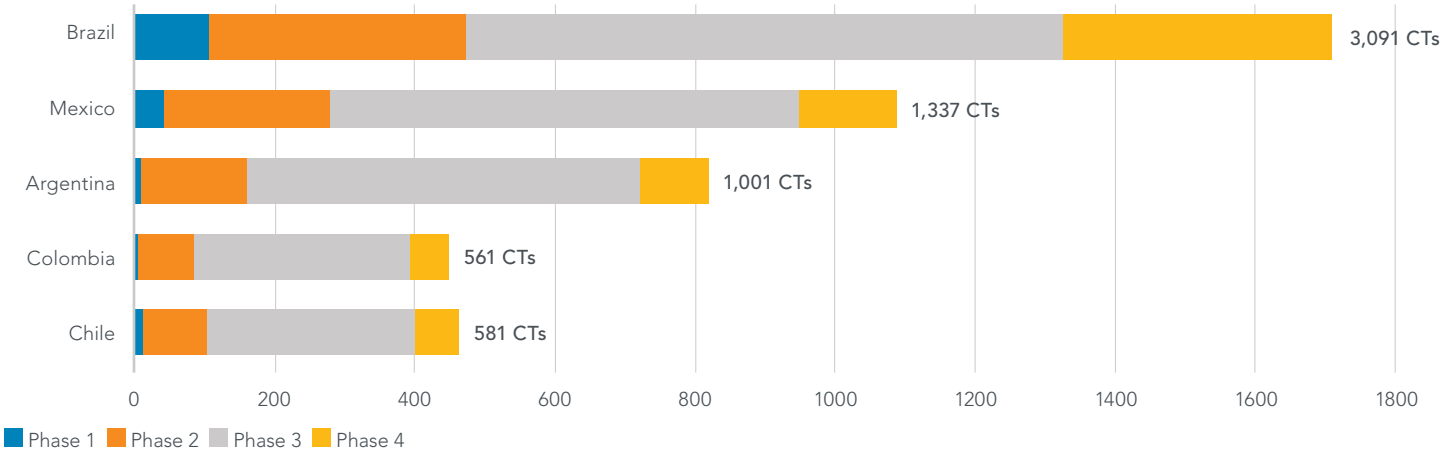
Source: Clinicaltrials.gov, 2016; World Bank, 2016

FIGURE 15 Number of clinical trials to date per million population – Colombia versus select regions



Source: Clinicaltrials.gov, 2016; World Bank, 2016

FIGURE 16 Gauging clinical trial activity by phase, regional leaders, 2010-2015



Source: Clinicaltrials.gov, 2016 (Note: data based on "first received" date)

TABLE 2 Gauging clinical trial activity by phase, regional leaders, 2010-2015

	Colombia	% of total	Argentina	% of total	Brazil	% of total	Chile	% of total	Mexico	% of total
Phase 1	8	1%	13	1%	111	4%	16	3%	52	4%
Phase 2	83	15%	145	14%	364	12%	91	16%	234	18%
Phase 3	304	54%	571	57%	847	27%	298	51%	666	50%
Phase 4	54	10%	92	9%	383	12%	61	10%	134	10%
Phase 0 / NA	112	20%	180	18%	1386	45%	115	20%	251	20%
Total	561		1001		3091		581		1337	

Source: Clinicaltrials.gov, 2016 (Note: data based on "first received" date); Pugatch Consilium analysis

Clinical research intensity = R&D capacity

Looking at clinical trial intensity by phase of trials conducted suggests that biopharmaceutical R&D capacity and ability to conduct cutting edge trials in Colombia is limited. Seen in Figure 16 and Table 2, two-thirds of all clinical trials conducted in Colombia to date have been later-phase and post-marketing trials. Moreover, compared to regional leaders during the period 2010-present, Colombia has had a low level of total level of Phase I trials and a relatively small portion of Phase II trials (around 83). In contrast Mexico and Brazil both have experienced considerably higher rates of Phase I and II trials during the same period (though the proportion of Phase I and II trials to total trials is relatively similar to Colombia's). Argentina also demonstrates much higher rates of Phase II trials compared to Colombia (though not Phase I). Chile and Colombia perform relatively on par in this area.

Similarly, when this analysis is expanded to include more countries – including global leaders and OECD averages for 2015 – Colombia is even further behind. On the following page Table 3 shows the total number of clinical trials for 2015 broken down by phase.

Compared to global leaders – US, EU countries, Singapore, South Korea etc. – Colombia in 2015

TABLE 3 Clinical trials in selected countries, distributed by phase of trial, 2015[75]

	Number of CTs in 2015	Phase 1 trials (%)	Phase 2 trials (%)	Phase 3 trials (%)	Phase 4 trials (%)
US	7734	13%	21%	11%	6%
EU-5 (total)	5892	9%	16%	22%	7%
France	1705	4%	13%	19%	5%
China	1337	8%	21%	17%	13%
Canada	1311	6%	18%	21%	7%
UK	1256	15%	15%	17%	5%
Germany	1254	10%	18%	22%	6%
South Korea	846	10%	18%	22%	13%
OECD average	655.9	11%	18%	20%	8%
Netherlands	586	9%	19%	19%	8%
Switzerland	472	4%	11%	16%	9%
Brazil	472	2%	10%	21%	14%
Australia	409	14%	24%	38%	7%
Sweden	369	5%	16%	22%	6%
Egypt	277	5%	18%	19%	16%
Turkey	275	2%	8%	23%	19%
Russia	251	4%	24%	52%	6%
Mexico	194	2%	17%	47%	9%
India	179	4%	7%	17%	17%
Thailand	161	7%	12%	25%	16%
South Africa	138	6%	28%	45%	4%
Singapore	120	17%	23%	25%	5%
Argentina	110	3%	15%	60%	9%
Chile	81	1%	12%	46%	12%
Colombia	67	0%	13%	60%	6%
Peru	43	2%	9%	58%	7%

Source: Clinicaltrials.gov, 2016; analysis: Pugatch Consilium

had significantly lower levels of clinical research and, from an R&D capacity stand-point, a low percentage of these trials were early phase.

Who sponsors clinical trials in Colombia?

Examining clinical trial sponsorship and disease area suggests that the private sector is the most active in terms of clinical research in Colombia and that clinical trials in the country are increasingly focused on cutting edge research areas such as oncology. In most countries the biopharmaceutical industry typically carries out the largest portion of trials, particularly in the more advanced disease areas. In this respect, over 80% of clinical trials to date in Colombia have been sponsored by biopharmaceutical companies, with the public sector relatively limited in its participation in clinical trials. As Table 4 shows, in 2015 all but one of the top 10 sponsors of clinical trials were multinational biopharmaceutical companies, although in 2014 the number of non-industry sponsors (including academic and public research institutions) rose to 4 of the top 10 sponsors overall. In terms of disease areas, Table 5 indicates that oncology research occupies a growing share of clinical trials in Colombia, with the number of trials related to oncology products more than doubling over the past decade. Moreover, the number of early phase cancer research trials has increased substantially as a share of total cancer-related trials between 2010 and 2014 to between 10 and 20% of total trials. This suggests that advanced disease areas such as oncology represent ripe areas for growth in terms of developing and leveraging cutting edge R&D capacity in Colombia.

An area of potential growth? Clinical research on biologic drugs

Finally, examining clinical research on biologic drugs, the picture is mixed but suggests that biologics could be an area for potential growth in Colombia.

As mentioned, biologic medicines and technologies are increasingly being used in the treatment of some of the most difficult medical conditions today as well as in cutting edge medical research. Given the size, complexity and inherent instability of a biologic, the R&D process requires a considerable level of stability and technical capacity. Testing of a biologic drug candidate's safety and efficacy within a clinical trial necessitates a highly-controlled environment in which transportation and storage of the drug are

TABLE 4 Clinical trial sponsorship in Colombia: Top 10 sponsors in 2014 and 2015

Top 10 sponsors in 2015		Top 10 sponsors in 2014	
Bayer	6	Boehringer Ingelheim	5
Novartis Pharmaceuticals	5	Novartis Pharmaceuticals	4
Hoffmann-La Roche	4	AstraZeneca	3
MSD	4	Bayer	3
Bristol-Myers Squibb	3	Econometría Consultores / Inter-American Development Bank	3
Boehringer Ingelheim	2	Sanofi	3
Bristol-Myers Squibb / One Pharmaceutical Co. Ltd	2	Universidad de Antioquia	3
Fundación Santa Fe de Bogota	2	Universidad Nacional de Colombia	3
GlaxoSmithKline	2	Hoffmann-La Roche	2
Sanofi Pasteur, a Sanofi Company	2	Instituto Nacional de Cancerologia, Colombia	2

Source: Clinicaltrials.gov, 2016; Pugatch Consilium analysis

TABLE 5 Total and cancer-related clinical trials in Colombia

Year	Total number of CTs	Number of cancer-related CTs	% of early-phase cancer-related CTs	% of late-phase cancer-related CTs	% funded by industry
2015	58	14	14.29%	85.71%	93%
2014	88	11	18.18%	54.55%	73%
2013	97	7	14.29%	57.14%	86%
2012	97	9	11.11%	77.78%	89%
2011	111	10	10.00%	90.00%	80%
2010	110	8	0.00%	87.50%	100%
2009	71	11	0.00%	90.91%	91%
2008	84	11	9.09%	72.73%	91%
2007	64	11	9.09%	81.82%	100%
2006	55	3	0.00%	100.00%	100%
2005	42	5	20.00%	40.00%	60%

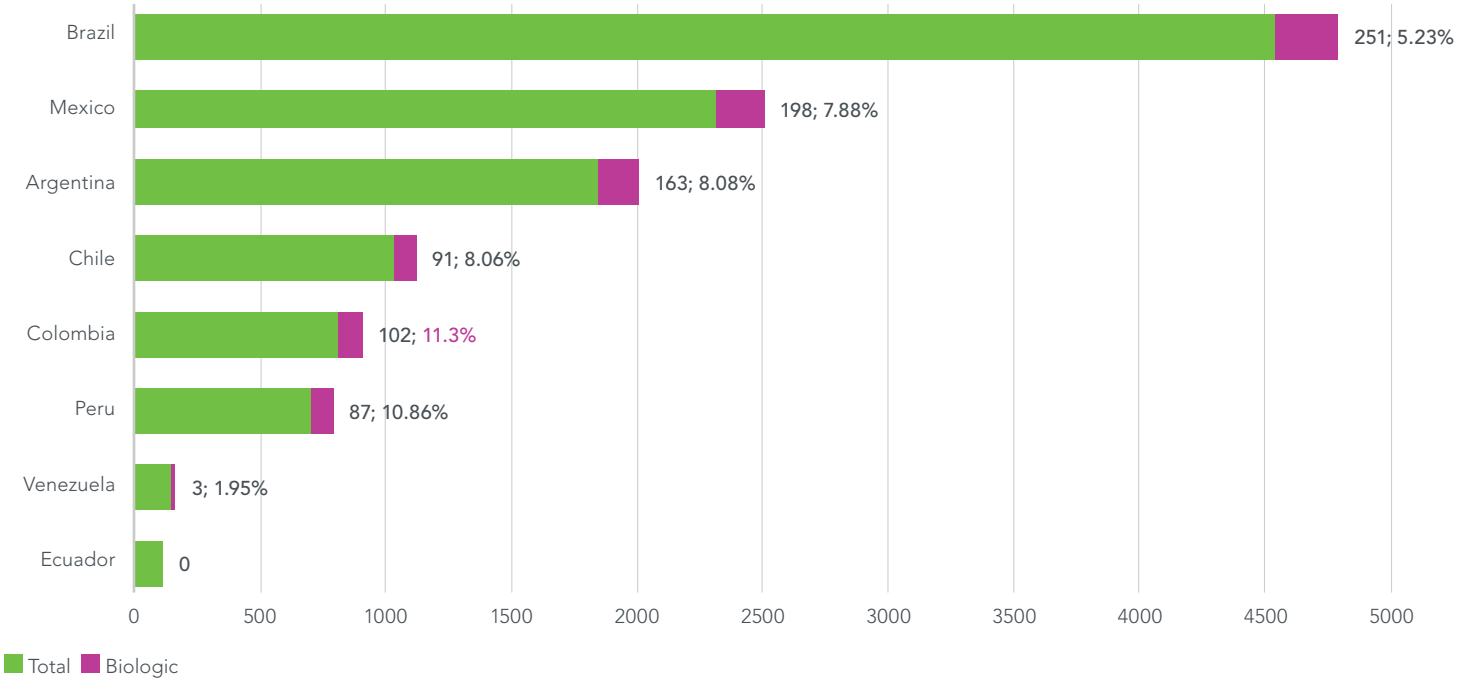
Source: Clinicaltrials.gov, 2016; Pugatch Consilium analysis

TABLE 6 Clinical trials of biologic drugs – A regional comparison

Country	Total number of CTs to date	Number of CTs on biologic drug	% share of total
Colombia	903	102	11.30%
Peru	801	87	10.86%
Argentina	2018	163	8.08%
Chile	1129	91	8.06%
Mexico	2513	198	7.88%
Brazil	4803	251	5.23%
Venezuela	154	3	1.95%
Ecuador	107	0	0.00%

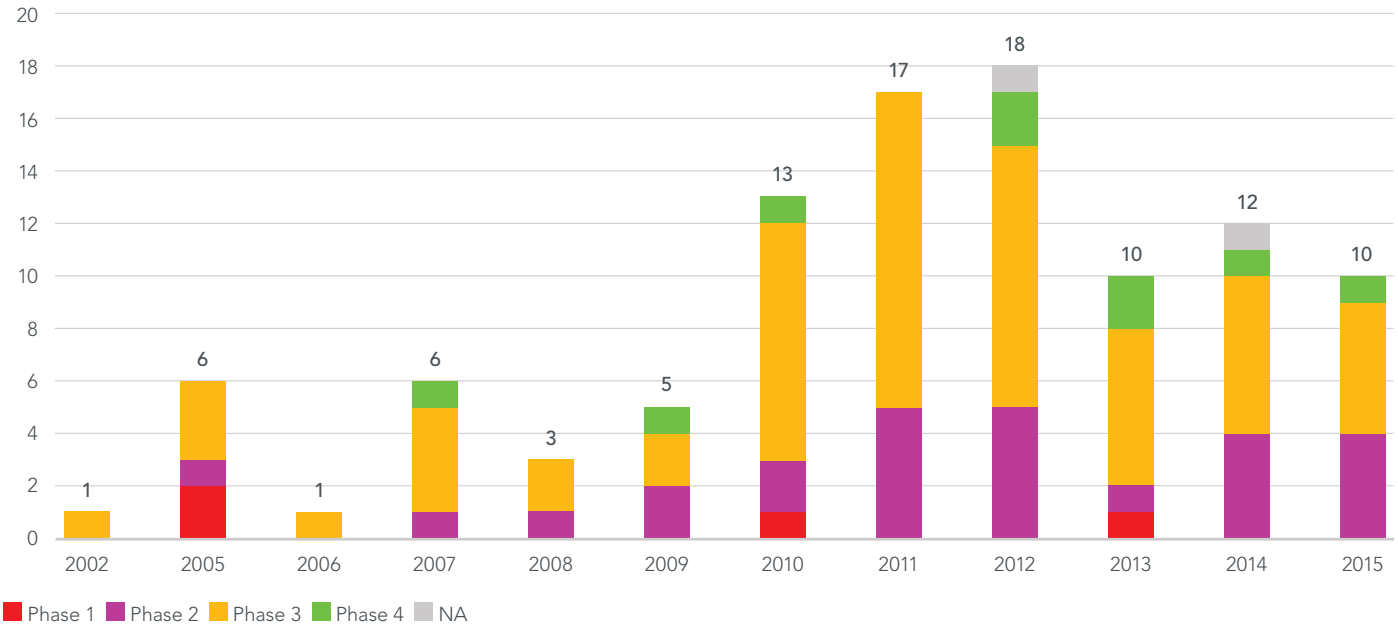
Source: Clinicaltrials.gov, 2016; Pugatch Consilium analysis

FIGURE 17 GClinical trials of biologic drugs – A regional comparison



Source: Clinicaltrials.gov, 2016; Pugatch Consilium analysis

FIGURE 18 Clinical trials on biologic drugs in Colombia by phases, 2002-2015



Source: Clinicaltrials.gov, 2016; Pugatch Consilium analysis

controlled, the trial protocols are strictly adhered to and patients are monitored carefully.

In absolute terms Colombia's rate of clinical trials on biologics is low. Table 6 indicates that the number of clinical trials on biologic drugs to date is slightly over 100, between 50-150% lower than the top 3 economies in Latin America – Brazil, Mexico and Argentina.

Yet, as both Table 6 and Figure 17 suggest, Colombia's share of biologic trials relative to total trials is quite high compared to that share in other Latin American economies. Biologic-related trials make up 11.3% of total trials, while this share is closer to 5% in Brazil and 8% in Mexico and Chile.

Similarly, although (as Figure 18 shows) clinical trials related to biologic drugs are mostly concentrated in Phase III trials, a generally upward trend in the absolute number of Phase II (and Phase I to some extent) trials is visible from 2010. Moreover, the share of Phase I and II trials on biologics relative to the total number of trials on biologics has risen, from around 25% in 2011-12 to 33-40% in 2013-15.

2.6 Section summary – Big picture trends in Colombia's biotech capacity and performance

As this section has discussed, Colombia's actual capacity and level of innovation in the area of biotechnology is limited by international standards and compared to its regional and socio-economic peers. Rates of general and biotech-specific R&D and innovation inputs and outputs are often lower than expected and, in many cases, have remained flat for several years. Given the high level of biodiversity and socio-economic development in Colombia rates of biotech patenting, biofuels production, ag-bio crop cultivation and level of clinical trial activity are relatively low. Still, pockets of growth and potential are visible, not least in the area of biopharmaceuticals and biologics. Analysis of clinical trial activity shows that within the realm of R&D on biologic products Colombia is a regional leader, with the share of these clinical trials the highest in Latin America and rising.

The following section shifts the focus onto the policy space and looks at what Colombia can do to develop this nascent biopharmaceutical capacity.

3 ENABLING BIOTECH INNOVATION

The preceding section has outlined how Colombia currently is lagging behind many other middle-income economies and developed OECD countries on biotechnology outputs. From general biotechnology indicators such as rates of triadic patenting to more sector specific indicators such as levels of clinical trials, Colombia has lower biotech outputs than its biodiversity and long-standing biotech policy emphasis would suggest.

3.1 The context – Building the Bioeconomy and seven enabling factors for biotech innovation

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

The analysis and policy mapping of *Building the Bioeconomy* is built around seven enabling factors for biotechnology development that together create an environment conducive to biotech innovation. The factors range from the institutional and eco-system level (such as levels of tertiary education and IP environment) to the more biotech specific (such as what type of biomedical and biotech R&D infrastructure does a country have

TABLE 7 Seven enabling factors for biotechnology innovation[76]

Key enabling factors	Explanation
Human capital	A basic and fundamental building block for the biotech sector is the availability of high skilled and technically trained human capital. Without the right human capital it is virtually impossible to create the conditions in which biotech innovation can take place.
Infrastructure for R&D	Combined with having adequate, educated and technically proficient levels of human capital, R&D infrastructure and capacity is critical to successfully fostering innovation and activity in high tech sectors including biotechnology. Without the necessary laboratories and clinical research facilities biotechnology R&D would be next to impossible.
Intellectual property protection	IPRs (including patents and regulatory data protection) are historically of real importance to the biotech and biopharmaceutical innovation process. For biopharmaceutical as well as non-pharmaceutical biological products and technologies the evidence suggests that IPRs incentivise and support the research and development of new biological technologies and products.
Regulatory environment	The regulatory and clinical environment in a given country or region plays an important role in shaping incentives for innovation and establishing adequate levels of quality and safety for biotech products, particularly biopharmaceuticals. A strong regulatory environment creates the conditions for the production and sale of high quality products and technologies.
Technology transfer	Technology transfer is a critical mechanism for commercialising and transferring research from public and governmental bodies to private entities and private to private entities for the purpose of developing usable and commercially available technologies.
Market and commercial incentives	Market and commercial incentives range from general R&D incentives to specific policies aimed at biotech sectors such as pricing and reimbursement policies for biopharmaceuticals. For the biopharmaceutical sector incentives determined by pricing and reimbursement systems for medicines and health technologies can have a profound impact on commercial and market incentives for innovation in health and biotech R&D.
Legal certainty (including the rule of law)	The general legal environment including as it relates to the rule of law and the rule of law within a business context is crucial to commercialization and business activities.

in place and availability of technology transfer laws and mechanisms). Together these factors create the conditions that through international experience have over the years given countries and policymakers the best chance of having success in developing their biotech capacity and promoting biotech innovation. The seven enabling factors are described in Table 7.

3.2 Intellectual property protection – a critical driver of biopharmaceutical innovation

A key finding of the *Building the Bioeconomy Examining* series is that economies that have the most sustained success in encouraging biotechnology R&D and innovation are those that introduce the right policies across all seven enabling factors. And while this also holds true for Colombia this section will focus on one of these enabling factors – protection of intellectual property – where Colombia is currently facing significant challenges.

Always a controversial field (particularly in relation to biopharmaceutical innovation) yet the economic and empirical evidence built up over the last few decades suggests strongly that overall IPRs tend to have a positive impact on economic activity, especially for high-tech industries and on rates of FDI.[77] Over the last decade a number of empirical studies have been published on the positive and cumulative economic effects of IPRs. In particular, there is a growing body of evidence suggesting a positive link between the strengthening of IPRs and economic growth and development, job creation, technology transfer, and increased rates of investment and innovation. For example, comparing WTO members (that is, signatories to the TRIPS Agreement) with non-members, a 2003 OECD study found that overall IPRs tend to have a positive impact on FDI with WTO members generally enjoying higher levels of FDI than non-members.[78] The authors found that with the exception of least developed countries, which may not yet have implemented the TRIPS Agreement due to transition period allowances, WTO members have higher levels of FDI than non-members. Léger used regression analysis to determine that IP protection is one of the most influential factors on innovation in both developing and industrialized countries.[79] Similarly, the OECD's Cavazos et al looked at R&D expenditure and technology transfer as well as FDI and found that a 1% change in the strength of a national IP environment (based on a statistical index) is associated with a 2.8% increase in FDI in-flows, a 2% increase in service imports and a 0.7% increase in domestic R&D.[80] Finally, looking at the US Pham found that IP-intensive industries generated one-third of total US economic output.[81]

IPRs are historically of real importance to the biotech and biopharmaceutical innovation process. For biopharmaceutical as well as non-pharmaceutical biological products and technologies the evidence suggests that IPRs incentivise and support the research and development of new technologies and products.[82] Patents and other forms of exclusivity for biopharmaceuticals such as regulatory data protection and special exclusivity incentives for the protection and production of orphan drugs provide research-based companies with an incentive to invest vast sums in R&D and the discovery of new biotech drugs, products and therapies. The research process for biopharmaceuticals (and many other biotech products) is unique in its time, cost and high rate of failure. The market exclusivity period provided by IPRs give firms the protection and incentive needed to recoup R&D investments made. Evidence suggests that many drugs and therapies would not have been discovered had it not been for the incentive and protection provided by these IPRs. For instance, analysis of market exclusivity periods and legislation finds that the combination of market exclusivity and income from patent protection drives private investment in innovation, which contributes to new drug development.[83] Older studies have estimated that between 60-65% of pharmaceutical products would not have been introduced or developed in the absence of patent protection.[84]

For biologics exclusivity periods under RDP are of particular importance as there may be a so-called 'gap' in patent protection between a biosimilar and the innovator, reference product. Because of the inherent characteristics of large molecule biologics a biosimilar can be approved for marketing – based on a comparison to a reference product – yet not directly infringe any existing, in force patents for the reference product due to differences in structure, administration, or mechanism of action.

Under this scenario the exclusivity provided by a RDP term is critical to a biotech innovator.

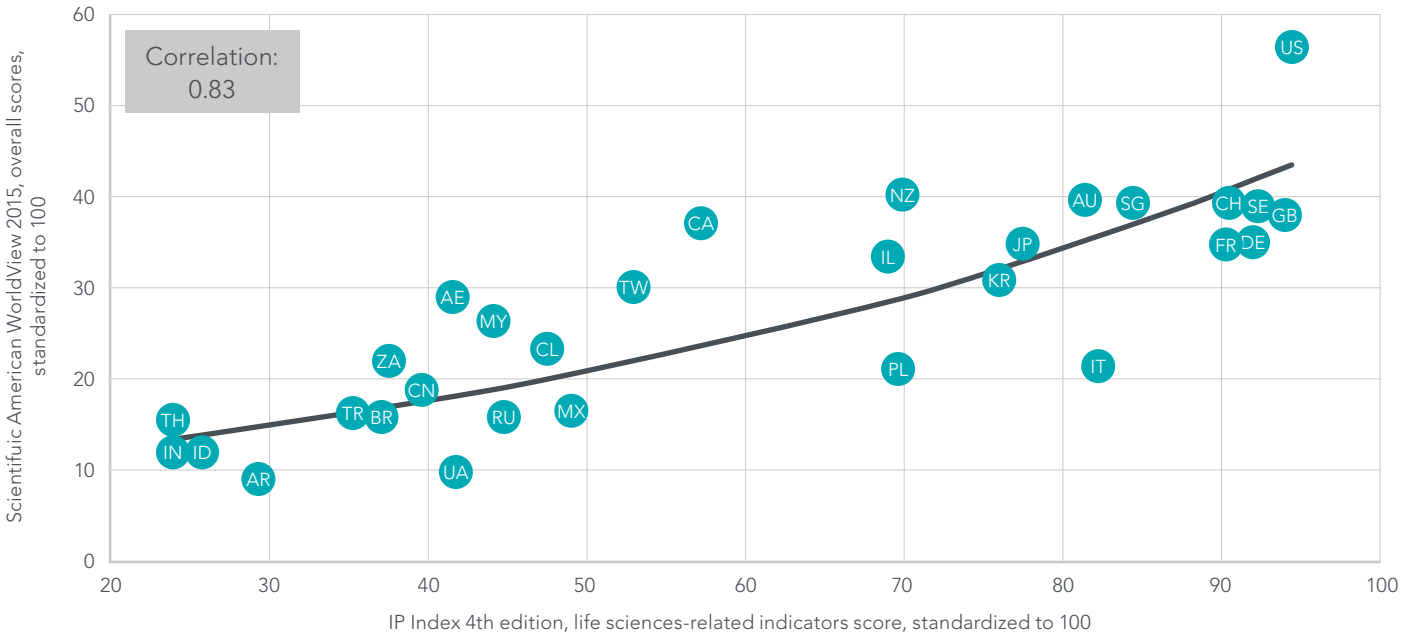
Looking at the direct link between biotechnology innovation and the strength of IP protection for life sciences, the 2016 edition of the US Chamber of Commerce's International IP Index correlates this relationship finding overall a strong positive relationship between the protection of IP and levels of biotechnology innovation. Below Figure 19 displays this association between the IP Index life sciences-related indicators' scores and biotech innovation as captured by the Scientific American *WorldView* scores.

As Figure 19 illustrates protecting IP rights related to the life sciences – such as patents, regulatory data protection, and patent term restoration – has a very clear and direct correlation with an environment in which biotechnology innovation can thrive. The IP Index life sciences-related indicators' scores correlate strongly – at 0.83 – with rates of biotech innovation as measured by the Scientific American *WorldView* overall scores.[85]

3.3 Heading in the wrong direction? Colombia and life sciences related IPRs

Colombia has in place a number of important mechanisms for the protection and enforcement of biotechnology specific IP rights. For example, a TRIPS standard 20 year term of patent protection is available, with some important exceptions discussed below, for most biotechnology and biopharmaceutical innovations. Unlike many countries in the region (including Brazil) Colombia has since 2002 through decree 2085 provided a five-year period of regulatory data protection for both pharmaceuticals and agrochemicals. Furthermore, Colombia has through the 2006 US FTA (in effect since 2012) committed to providing an effective patent enforcement mechanism linking and conditioning market registration for follow-on products with existing exclusivity periods for innovative products. And up until 2014-2015 Colombia did not have a history of invoking compulsory licensing or the threat of issuing such licenses outside of public emergencies.

FIGURE 19 Association between the IP Index biopharmaceutical-related indicators' scores and the Scientific American WorldView scores



Legend: AE – UAE, AR – Argentina, AU – Australia, BR – Brazil, CA – Canada, CH – Switzerland, CL – Chile, CN – China, DE – Germany, FR – France, GB – United Kingdom, ID – Indonesia, IL – Israel, IN – India, IT – Italy, JP – Japan, KR – South Korea, MX – Mexico, MY – Malaysia, NZ – New Zealand, PL – Poland, RU – Russia, SE – Sweden, SG, Singapore, TH – Thailand, TR – Turkey, TW – Taiwan, UA – Ukraine, US – United States, ZA – South Africa

Source: Clinicaltrials.gov, 2016; Pugatch Consilium analysis

Unfortunately, many of these critical IP rights and mechanisms are limited in their effective availability. And the IP environment in general for biopharmaceutical IPRs has worsened.

3.4 Patentability

To begin with there are significant restrictions on the patentability of new biotechnologies and biopharmaceutical innovation. Generally speaking inventions will be granted patent protection in Colombia provided they are new, involve an inventive step, and have industrial application. Yet the Andean Court of Justice (whose decisions Colombia must adhere to as a member of the Andean Community customs union) has issued several legal opinions denying patents on new pharmaceutical indications and biologics that are capable of being isolated.[86] Patents are also not typically granted for therapeutic methods.

Crucially these limits on patentability have been recognized as a significant barrier to biotechnology innovation by the Colombian authorities. For example, a 2013 in-depth study of Colombia's biotechnology capacity and regulatory framework by INNPULSA (a government investment promotion and business development agency) found that Colombia's IP environment was overly restrictive, impeding incentives for the licensing and commercialization of publicly generated knowledge. In their study INNPULSA stated that: **"la normativa de propiedad industrial en Colombia es muy restrictiva, impidiendo por ejemplo patentes de segundo uso, situando al país, a su tejido productivo y a investigadores en una clara inferioridad frente a otros países líderes en biotecnología."**[87]

3.5 Regulatory data protection

Similarly the availability of RDP for submitted biopharmaceutical test data in Colombia is questionable. As mentioned while in a positive step Colombia has in place a clear regulatory mechanism providing this exclusivity and a term of protection of five years for new chemical entities, it is not clear that RDP is available for biologic products. Decree 1782, signed in September 2014, which modifies the registration process for biological medicines, does not discuss regulatory data protection for biologics. As a result, in regard to RDP the legislation introduces ambiguity as to whether five years of protection are in fact afforded to biologics under the new regime.

As discussed, for biologics exclusivity periods under RDP are of particular importance as there may be a so-called 'gap' in patent protection between a biosimilar and the innovator, reference product. Under this scenario the exclusivity provided by a RDP term is critical to a biotech innovator. International best standards for the protection of submitted clinical test data for biologics range from a term of protection of ten years in the EU to twelves years in the US.

3.6 Compulsory licensing

TRIPS Article 31, including the amendments introduced in the 2001 Doha Ministerial Declaration, and subsequent General Council decision allowing the export of medicines produced under a compulsory license (outlined in Paragraph 6), form the international legal grounds for compulsory licensing for medicines. The main requirement is that developing countries must first seek to engage with patent owners to access a given medicine at a lower price, for instance through price negotiations or voluntary license agreements.[88] Failing this, they may issue a compulsory license to produce the drug in generic form. It is also possible to issue a compulsory license without first seeking a voluntary license in certain limited circumstances: national emergencies, other urgent circumstances and where the drug will not be commercialized but rather provided at no charge by the government. However, the Chairman's statement accompanying the General Council decision (concerning Paragraph 6 of the Doha Declaration) underscores that these provisions are not in any way intended for industrial or commercial objectives, and if used, it is expected that they would solely be aimed at protecting public health.[89]

A key issue in the global debate on compulsory licensing deals with what an adequate effort at a voluntary agreement should look like as well as how to define the appropriate circumstances for issuing a compulsory license without first seeking a voluntary license. The debate is not black and white, with various rationale, such as "public health emergencies" and "anti-competitive behavior", being defined differently by different parties and in different countries.[90]

To the extent that TRIPS permits the use of compulsory licensing in cases of national emergencies, it is clear that the **spirit** of Article 31 and of the Doha Declaration is that compulsory licensing represents a "measure of last resort", particularly due to its extreme effect on the market for the targeted drug and negotiating relationships. Specifically, in line with game theory and the classic prisoner's dilemma, the repeated use of compulsory licensing tells patent owners that the country is not interested in cooperation and collaboration, and will lead them to also be less collaborative. Under these circumstances, compulsory licensing will be less effective and related objectives, such as lowering prices, enabling supply in areas of unmet need and facilitating sharing of know-how and technology, will be less achievable. Accordingly, compulsory licensing is intended primarily for public health and humanitarian emergencies, and not for commercial or political objectives, and to be used only after all other options for negotiating pricing and supply have been exhausted.

Compulsory licensing has been employed in relation to medicines on a very limited basis and mainly for pandemics such as HIV/AIDS and the flu. However, in the manner that it is sometimes applied (or discussed), compulsory licensing can be discriminatory towards the life sciences field; for all intents and purposes an alternative pathway for excluding (or attempting to exclude) certain biopharmaceutical inventions from patentability, and often in support of domestic generic sectors.

Up until recently the imposition and discussion of compulsory licensing for biopharmaceuticals had not been a recurring issue in Colombia. However, as discussed above, article 70 of the latest National Development Plan widens the basis for the issuing of compulsory licenses in a manner that goes beyond the TRIPS Agreement.[91] The provision allows Colombian authorities to define public health emergencies broadly and to actively seek out compulsory licenses, allowing for grounds outside extreme circumstances including industrial or commercial objectives, to play a role in the issuing of compulsory licenses.

Echoing this legislative development the Ministry of Health and Colombian Government has recently been actively considering (on the basis of a recommendation of an internal committee) the issuing of a compulsory license for a drug on grounds of high prices.[92] In a number of interviews the Minister of Health made clear that the driving reason for the potential over-riding of the existing drug's patent was the issue of cost. In May 2016 the Minister was quoted in the Wall Street Journal as saying that: "Technological pressure and high drug prices have brought the health-care system to a financial crisis…Colombia is a paradigmatic case of a middle-income country, with a growing health system and with rising expectations from its middle class, which cannot pay high prices for new drugs."[93] At the time of research the Colombian Government had issued a "public interest declaration" which would allow the authorities the right to reduce the price.[94]

3.7 Section summary

For many years Colombia was one of the few Latin American countries heading in a positive direction with regards to biopharmaceutical IPRs. The 2006 US-FTA contained a number of important mechanisms of protection that together promised to strengthen IP protection in Colombia and provide biopharmaceutical innovators – domestic and foreign – the right incentives to invest and commercialize their products.

Unfortunately the last few years have seen increased uncertainty with regards to the protection of IP and biopharmaceutical IPRs in particular. An increased focus on the use of compulsory licensing and overriding of property rights as a cost-containment tool, lack of patentability for biopharmaceutical innovation and uncertainty over the application of RDP to biologics create an environment which is not the best for attracting investment and long-term biopharmaceutical R&D.

The following section will attempt to put a price on this uncertainty by through economic modelling provide an estimate of the direct financial gains and clinical trial investment Colombia could receive if it improved its policy environment, including the protection of IP.

4 QUANTIFYING THE ECONOMIC GAINS OF STRENGTHENING COLOMBIA'S CLINICAL RESEARCH POLICY ENVIRONMENT

Building on the preceding analysis of Colombia's low levels of biotech outputs (in particular clinical trials) and of the current gaps in the policy environment, this section provides a modelled estimates of the tangible economic benefits a positive improvement in the policy environment for biotechnology and in particular the biopharmaceutical environment would have in Colombia.

4.1 Punching below its weight: Global distribution of biopharmaceutical R&D and Colombia

As detailed in section 2, Colombia has by international comparisons relatively low levels of clinical research. This low clinical trial activity directly affects its share in the global distribution of R&D-directed FDI. In 2014 Colombia's share of global R&D spending by PhRMA member companies was only 0.1%, as seen in Table 8 – with roughly 60% of that thought to be attributed to clinical research.[95]

Considering the importance of the biopharmaceutical policy environment to clinical trial activity the following sub-sections will outline how the existing gaps in Colombia's policy environment (not least with regards to the protection of IP discussed in the preceding section) can be quantified and translated into an economic model of potential benefits.

4.2 Step 1: Measuring the biopharmaceutical policy environment

The first step in building an economic model that estimates the potential benefits Colombia stands to gain in improving its policy environment is to quantify the existing policy environment. What are some of the existing measures and indicators of Colombia's policy environment as it relates to biopharmaceuticals and the clinical environment?

With regards to clinical trials activity, a sizeable body of literature discusses which factors are most important for stimulating growth of investment in clinical trials in a given country including clinical capacity and infrastructure, access to health care, and various market conditions, quality of regulatory frameworks including approval times for trials applications.[96] Previous work done by Pugatch Consilium suggests that the strength of intellectual property protection can explain around 40% of clinical trial activity.[97]

The economic model used in this paper will rely on three indicators as a measure of the biopharmaceutical policy environment in Colombia. These indicators are:

1. The Biopharmaceutical Competitiveness & Investment (BCI) Survey:
   The BCI Survey is a global executive opinion survey and index of economies' biopharmaceutical investment-attractiveness. The BCI Survey examines the entire ecosystem in which biopharmaceutical innovation takes place from the R&D environment, to the regulatory framework, market access, to overall attractiveness of a given market. By taking a "bottom-up" approach the BCI enables a unique and highly relevant snapshot of economies' biopharmaceutical competitiveness. Indeed, the respondents to the BCI Survey – country managers and their teams – often have a candid and accurate understanding of how different aspects of the local policy environment affect the attractiveness of the market in which they operate.[98]

TABLE 8 Global distribution of R&D spending by PhRMA-member companies in selected countries, 2014[99]

Country	R&D spending by PhRMA-member companies, 2014 (in million USD)	% of total R&D spending by PhRMA-member companies in 2014
US	$40,737.3	76.5%
UK	$2,532.1	4.8%
Japan	$899.7	1.7%
Germany	$797.4	1.5%
China	$505.9	1.0%
Canada	$498.7	0.9%
France	$386.4	0.7%
Spain	$257.6	0.5%
Australia and New Zealand	$254.5	0.5%
Italy	$219.8	0.4%
Brazil	$138.3	0.3%
Russia	$100.1	0.2%
Mexico	$92.4	0.2%
Argentina	$83.4	0.2%
South Korea	$63.9	0.1%
Turkey	$51.8	0.1%
Colombia	$42.2	0.1%
South Africa	$35.5	0.1%
India	$25.8	0.0%
Chile	$20.1	0.0%
Egypt	$17.7	0.0%
Peru	$11.5	0.0%

Source: PhRMA Annual Membership Survey 2016

2. The U.S. Chamber of Commerce's International IP Index

The IP Index provides an in-depth assessment of economies' national IP frameworks and level of actual enforcement on the ground. Significantly, the Index can be isolated at the sector specific level with biopharmaceutical IPRs isolated and the biopharmaceutical IP environment in a given economy mapped.

3. The timeframe of the regulatory approval process for clinical trials

Evidence suggest that countries which have shortened the clinical trial approval timeframe have experienced a notable increase in clinical research intensity, as opposed to countries in which the approval times are lengthy and/or marred by significant delays.[100] Consequently, the time-frame for regulatory approval of clinical trial applications is a critical factor in incentivizing research activity.

Comparing Colombia's performance with other leading markets in these major indicators and benchmarks shows that, firstly, there is considerable room to improve Colombia's policy environment across all three indicators. Second, it is clear that it is possible to quantify the improvement needed and thus translate Colombia's current policy environment and where it could be heading into a tangible number.

Below is a discussion of each of the above three indicators and where and how Colombia currently performs.

Indicator 1: The Biopharmaceutical Competitiveness & Investment Survey

As mentioned, the results of the BCI Survey provide a strong indication of a given economy's absolute and relative biopharmaceutical competitiveness to other economies as seen from executives and managers on the ground. The survey examines the entire ecosystem in which biomedical innovation takes place by examining the following major areas:

- ability to leverage scientific capabilities and infrastructure;
- state of the clinical environment, from test tube to patient;
- quality and efficiency of biomedical manufacturing and logistics operations;
- soundness and effectiveness of the biomedical regulatory framework;
- healthcare financing; and
- overall market and business conditions.

FIGURE 20 The Biopharmaceutical Competitiveness & Investment Survey 2016, overall results, newcomer markets

Source: Pugatch Consilium, 2016

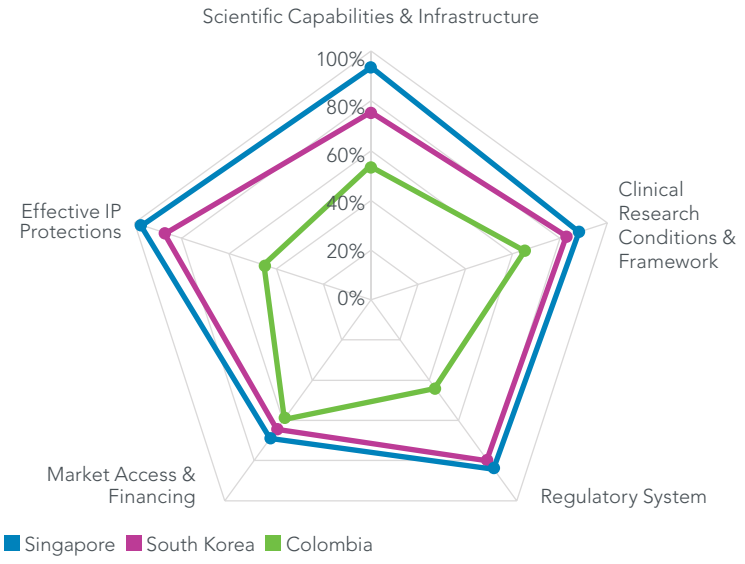
The results from the second edition of the BCI published in 2016 suggest that Colombia is lagging behind other middle-income and regional competitors and is in the 3rd tier of countries with an overall score of 53.6 out of 100.

Zooming in on the individual scores within the five categories composing the biopharmaceutical environment, Figure 21 suggests that Colombia lags substantially behind competitive biopharmaceutical research hubs in nearly all of the necessary conditions required for developing an attractive environment for conducting biopharmaceutical research and clinical trials.

Indicator 2: The IPRs environment for biopharmaceuticals in Colombia

As detailed in section 3 the effective provision of biopharmaceutical IPRs in Colombia is still relatively limited and there is scope for improvement in the IP environment. As Figure 22 shows, looking specifically at the 21 indicators in the International IP Index that relate to biopharmaceuticals,[101] for 2016 Colombia ranks below the median score in of a sample of 38 economies, scoring 10.45 or 49.76% of the total possible score of 21.[102] Looking at emerging markets in terms of clinical trials intensity, such as Singapore, Israel and South Korea, their average score on the same indicators is 16.05 or 76.4% out of the total possible score of 21.[103] Thus, reaching the entry level of emerging clinical research hubs would require Colombia to improve its biopharmaceutical related IP framework by at least 53%.

FIGURE 21 The Biopharmaceutical Competitiveness & Investment Survey 2016, scores by category, Colombia and selected countries



Source: Pugatch Consilium, 2016

Indicator 3: The timeframe for regulatory approval of clinical trials

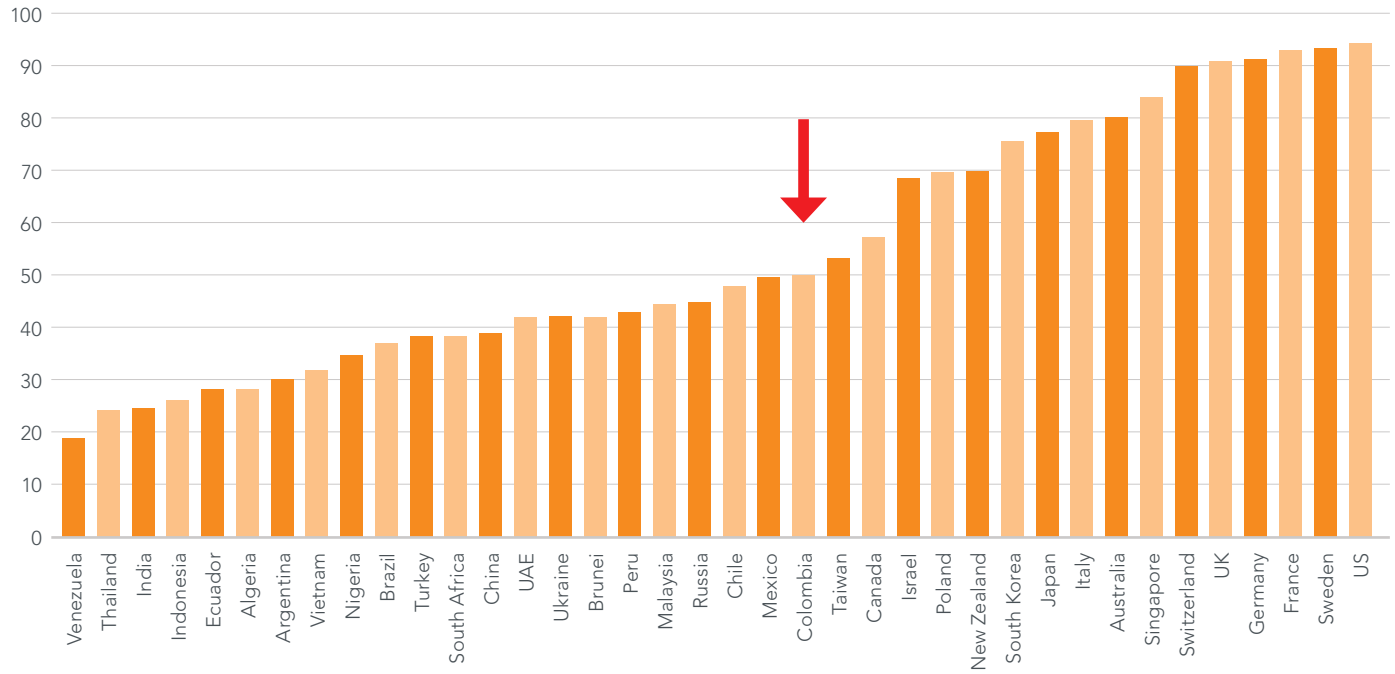
As noted, the timeframe for the regulatory approval of clinical trials is an essential component in sponsors' decision-making process on conducting clinical trials, and, as such, an important contributing factor in making a given country more or less attractive in the global clinical research arena.

Trial approval times-frames in Colombia are currently very long. According to recent research conducted by the local biopharmaceutical trade association AFIDRO the regulatory approval of a clinical trial in Colombia takes no less than 225 days: some 50-60 days for an approval by the Ethics Committee, and an additional 165 days for the approval by the regulatory agency.[104] As Table 9 below suggests, this is among the longest timeframes for approving clinical trials, both regionally and globally.

In April 2016 Colombia's DRA INVIMA announced significant changes to the regulatory approval process of clinical trials.[105] First, the timeframe for approval would be reduced to only 2 calendar months, or 60 days. This would be achieved by two significant administrative changes:

- enabling parallel submissions of clinical trials applications; and
- transferring the trial protocol evaluation of clinical trials on biologic drugs, which require particular expertise, to a designated group within INVIMA (*Sala Especializada de Medicamentos y Productos Biológicos al Grupo de Investigación Clínica de la Dirección de Medicamentos y Productos Biológicos*).[106]

FIGURE 22 The IP Index, 4th edition, biopharmaceutical related scores (standardized to 100)



Source: US Chamber of Commerce, 2016

TABLE 9 Timeframe for regulatory approval of clinical trials in selected countries

	Regulatory Agency approval time	Ethics Committee approval time	Application submission hierarchy	Total timeframe for approval
Singapore	30 days	30 days	Parallel submission	30 days
Australia	50 days	10-50 days	Parallel submission	50 days
South Korea	60 days	8 weeks	Parallel submission	60 days
India	90 days	60 days	Parallel submission	90 days
Russia	55 days	60 days	Ethics Committee approval first	115 days
Canada	30 days	120 days	Parallel submission	120 days
South Africa	120 days	45 days	Regulator's approval first	165 days
Argentina	150 days	30 days	Ethics Committee approval first	180 days
Brazil	120 days	60 days	Ethics Committee approval first	180 days
Colombia	165 days	50/60 days	Ethics Committee approval first	225 days
Peru	195 days	42 days	Ethics Committee approval first	237 days

Source: EFPIA, 2013; AFIDRO, 2015; analysis: Pugatch Consilium

A reduction from the current 225 days for approving a clinical trial to 60 days would significantly improve Colombia's attractiveness in the global clinical research arena. In itself, this will constitute an improvement of no less than 73% to the clinical research policy environment.

Summing up the three indicators: How much would Colombia need to improve its policy environment to reach the top global performers?

The following Table 10 summarizes Colombia's place in the key global benchmarks and measures discussed in this section.

As Table 10 shows, a considerable room for improvement (~60% on average) is needed for Colombia to establish an attractive clinical research policy environment and place itself as a leading emerging clinical research hub in the world. Such an improvement would go a long way to supporting an increase in the level of clinical trial activity and the wider associated benefits across Colombia.

What would such an improvement in the policy environment translate to in direct and indirect economic benefits?

4.3 Step 2: Translating a change in the biopharmaceutical environment into an economic effect

In order to quantify the FDI and economic gains that Colombia might expect to result from improvements to its biopharmaceutical policy environment, this study utilizes existing statistical models of how changes (positive and negative) in a given economy's policy environment impacts foreign direct investment and associated economic gains.[107]

The level of existing FDI is captured by two measures.

First, clinical trial activity is measured by the number of clinical trials taking place in Colombia in a given year as recorded by Clinicaltrials.gov.[108] In 2015 only 66 new and ongoing clinical trials were registered as conducted in Colombia.[109] On this basis, the baseline level of clinical trial activity employed in the study's model is 66. It is important to note that while this figure reflects Colombia's clinical trials activity as accurately as possible, it only serves as a baseline to calculate the potential gains to Colombia's clinical trials activity.

TABLE 10 Colombia's biopharmaceutical policy environment: How Colombia performs

	Colombia's performance	Leading/emerging clinical research hubs	Percentage of improvement needed
The IP framework in the life-sciences sector	49.76 out of 100	76.4 out of 100	54% improvement
BCI Survey 2016 Results	53.6 out of 100	79.53 out of 100	49% improvement
Timeframe for regulatory approval of clinical trials	225 days	60 days	73% improvement

The second aspect of FDI captured is the direct economic gains derived from clinical trial activity, measured by monetary flows arising from clinical research. The existing and resulting monetary flows are calculated based on spending by research-based biopharmaceutical companies on R&D per year. Estimating the level of spending on R&D within the biopharmaceutical field, and specifically clinical research can be challenging, since most global measures tend to reflect a broader level of spending than just biopharmaceutical R&D, or do not sufficiently capture foreign investment.[110]

On this basis, the approach taken in this study is to extrapolate total R&D spending in Colombia by the biopharmaceutical industry by a) identifying the share of industry R&D spending in Colombia on a micro level (i.e. representative companies); and b) applying this share to the global figure on biopharmaceutical R&D spending.

As such, the baseline level of R&D spending in Colombia is derived from industry data as reported by PhRMA and IFPMA member companies. Specifically, the share of global R&D spending by PhRMA member companies (conducted by U.S.-owned companies and by the U.S. divisions of foreign-owned companies) – which, as mentioned above, is approximately 0.08% based on the latest available data (from 2014). Because this figure does not include R&D performed in Colombia by foreign divisions of foreign-owned companies, the baseline figure seeks to compensate for this as much as possible by extrapolating this share (0.08%) to the latest available global estimates on R&D spending by the biopharmaceutical research-based industry as published by IFPMA –141.6 billion USD in 2014.[111]

Thus, by this estimate, Colombia's share of global R&D spending can be approximated at around 113.28 million USD.

Different estimates exist as to the portion of R&D spending in the biopharmaceutical sector that is typically devoted to clinical research. However, average estimates place this figure at around 60% of annual R&D spending.[112]

Hence, the baseline figure for the existing level of spending or monetary transfers derived from clinical research is 67.97 million USD.

These monetary flows typically benefit or affect a wide range of stakeholders, such as hospitals (including physicians), CROs, patients, payers and others.

In addition, the model takes into account that direct investments in clinical research activities are accompanied by externalities: related monetary flows which circulate through and enhance the local economy. Examples of indirect economic gains include flow of funds to vendors/suppliers, jobs in sectors supporting clinical research, etc. The economic impact of externalities is estimated by several studies at around 150-175% of the direct investments in research activities.[113] On this basis, the model measures indirect economic gains – monetary transfers associated with clinical trials – as 150% of the direct increase in monetary flows. These externalities are captured in the model as additional economic gains on top of the direct monetary flows associated with clinical trials.

As mentioned above, the effect of policy changes on clinical trial activity and monetary transfers as types of FDI in the field of clinical research is based on existing modelling of the effect of policy change on FDI more generally. Several studies have examined the effect of improvements to national policy environments, including key areas relevant to the clinical research environment such as the regulatory system and level of IP protection, on in-flows of FDI. For example, a 2010 study by the OECD found that a 1% increase in IP protection is linked to a 2.8% increase in R&D-directed FDI.[114] In addition, Nicoletti et al (2003) tested the effect of improvements to economies' regulatory environments on FDI;[115] this study estimated that a 1% change in the regulatory environment is linked to, on average, a 1.2% increase in in-flows of investment.

Given the importance of the overall biopharmaceutical environment and specifically the IP and regulatory frameworks to clinical research activity (as described above in the three indicators used for measuring Colombia's policy environment), the model in the present study assumes that every 1% improvement to the clinical research policy environment can lead to between a 1.2% to a 2.8% direct increase in clinical trials and monetary transfers. Conversely

this study also assumes that a deterioration in the policy environment can lead to a similar 1.2% to a 2.8% direct decrease in clinical trials and monetary transfers.

4.4 Step 3: Constructing three scenarios applicable to Colombia

On the basis of what clinical trial and economic gains would be secured if Colombia improved its clinical research policy environment, the above model is tested, both positively and negatively, on three scenarios:

Scenario 1: Conservative

A half-scale improvement to the biopharmaceutical policy environment (requiring on average a 30% improvement and achieving a direct FDI impact of 36%-84%);

Scenario 2: Optimistic

A full-scale improvement to the biopharmaceutical policy environment (requiring on average a 60% improvement and achieving a direct FDI impact of 72%-168%); and

Scenario 3: Pessimistic

A deterioration of 25% to the biopharmaceutical environment, which could include the following factors: an inability to reduce the approval time for clinical trial applications from 225 days to 60 days; the continued use, or threats to use, compulsory licenses as a cost-containment tool for public health expenditure; and a general worsening of the biopharmaceutical policy environment with regards to market access and/or investment conditions.

Table 11 provides a stepwise overview of the structure of the computational model employed in this study to quantify the effect of improvement to Colombia's clinical research policy environment on its clinical trials activity and the expected economic gains.

4.5 Results 1: The economic gains of improving Colombia's biopharmaceutical policy environment

Applying the model described above to two positive scenarios (improving the biopharmaceutical policy environment by 30% and 60%, respectively) strongly suggests that Colombia stands to benefit considerably from even a conservative 30% improvement to its policy environment.

TABLE 11 Constructing a model for quantifying the effect of improving Colombia's clinical research policy environment on direct investments and economic gains

	Step	Model component	
1	Identifying proxies for FDI and associated economic gains	FDI =	Increase in annual clinical trials activity
			Associated monetary transfers to key stakeholders (= 60% of R&D-directed investment)
		Additional 150% indirect economic gains (externalities)	
2	Quantifying the increase in clinical trial activity and associated monetary transfers resulting from policy reform	Every 1% improvement leads to a 1.2% to 2.8% direct increase in clinical trials activity and monetary transfers plus additional 150% in externalities	
3	Constructing 3 scenarios for improvement / deterioration	A conservative scenario (30% improvement to the biopharmaceutical policy environment)	
		An optimistic scenario (60% improvement to the biopharmaceutical policy environment)	
		A pessimistic scenario (a 25% deterioration to the biopharmaceutical policy environment)	

The conservative scenario

Under the more conservative scenario of improving Colombia's clinical research policy environment by 30%, the expected impact ranges from an increase of 36% in both clinical trial activity and associated monetary transfers (where 1% improvement results in an increase of 1.2%) to 84% (where 1% improvement results in an increase of 2.8%), as well as an additional 150% in indirect economic gains.

As Figure 23 and Table 12 show, under a conservative scenario of a 30% improvement to the clinical research policy environment, Colombia could expect anywhere between 24 and 55 additional new clinical trials a year and up to USD312.8 million in total economic gains.

Table 13 provides an illustrative distribution of direct and indirect monetary flows accrued to key stakeholders under the conservative scenario. It shows how even a relatively conservative improvement to the biopharmaceutical policy environment could lead to considerable benefits across key stakeholders, including discounted access to new medicines, savings to hospitals and payers and additional funding towards infrastructure and clinicians and other personnel as well as revenue supporting the growth of the local CRO industry.

FIGURE 23 Gains to clinical trial activity in a given year under the conservative scenario

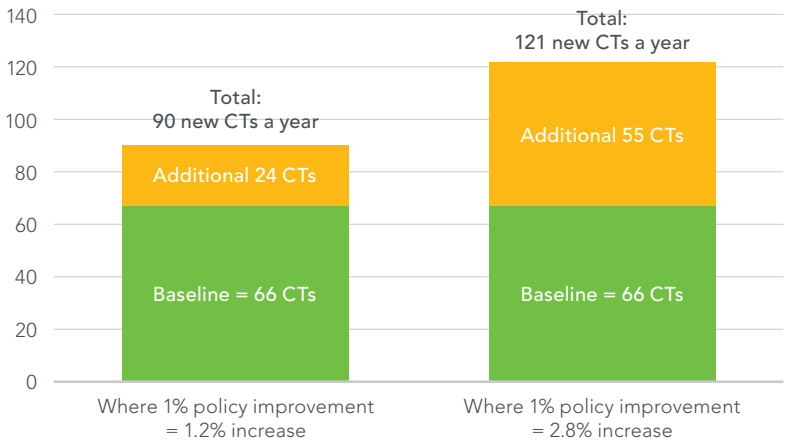


TABLE 12 Expected economic gains in a given year under the conservative scenario

Estimated total monetary flows associated with clinical research resulting following policy reform	
Direct monetary gain where 1% improvement = 1.2% increase	Total economic gain (including externalities)
$92.4 Million	$231 Million
Direct monetary gain where 1% improvement = 2.8% increase	Total economic gain (including externalities)
$125.1 Million	$312.8 Million

TABLE 13 Monetary and economic benefits associated with clinical trials accrued to key stakeholders under a conservative scenario of biopharmaceutical policy reform

Stakeholder	Bottom of range	Top of range	Stakeholder	Bottom of range	Top of range
Hospitals and related services	$92.4 Million	$125.1 Million	Payers	$34.7 Million	$46.9 Million
CROs and related services	$104 Million	$140.7 Million	Other (including patients)	$34.7 Million	$46.9 Million

The optimistic scenario

Under the optimistic scenario of improving Colombia's biopharmaceutical policy environment to the entry level of current leading clinical research hubs, the expected impact ranges from an increase of 72% in both clinical trial activity and associated monetary transfers (where 1% improvement results in an increase of 1.2%) to 168% (where 1% improvement results in an increase of 2.8%), as well as an additional 150% in indirect economic gains.

As Figure 24 and Table 14 show, under the optimistic scenario of a 60% improvement to the biopharmaceutical policy environment, Colombia could expect an increase of anywhere between 48 and 111 additional new clinical trials a year and up to 455.5 million USD total economic gains.

Under the optimistic scenario, as Table 14 shows, an improvement to the biopharmaceutical policy environment to the entry level of current leading clinical research hubs could lead to a significant increase in gains to key stakeholders, with wider benefits for public health, cost containment and industrial development. To put these gains in perspective, the overall gains estimated in this scenario of around $455 million represent a significant portion of Colombia's total annual spending on medicines – around 14%.[116]

FIGURE 24 Gains to clinical trial activity in a given year under the optimistic scenario

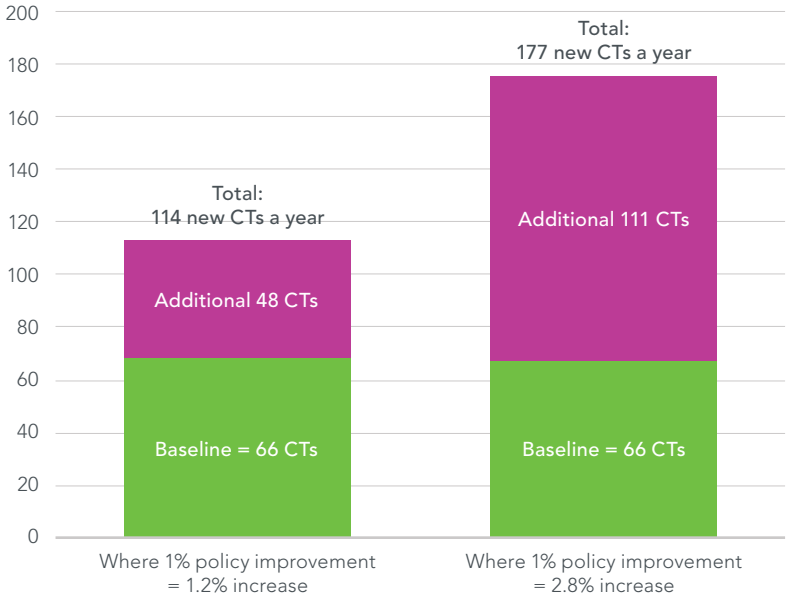


TABLE 14 Expected economic gains in a given year under the optimistic scenario

Estimated total monetary flows associated with clinical research resulting following policy reform	
Direct monetary gain where 1% improvement = 1.2% increase	Total economic gain (including externalities)
$116.9 Million	$292.3 Million
Direct monetary gain where 1% improvement = 2.8% increase	Total economic gain (including externalities)
$182.2 Million	$455.5 Million

TABLE 15 Monetary and economic benefits associated with clinical trials accrued to key stakeholders under an optimistic scenario of biopharmaceutical policy reform

Stakeholder	Bottom of range	Top of range	Stakeholder	Bottom of range	Top of range
Hospitals and related services	$116.9 Million	$182.2 Million	Payers	$43.8 Million	$68.3 Million
CROs and related services	$131.5 Million	$205.5 Million	Other (including patients)	$43.8 Million	$68.3 Million

4.6 Results 2: Moving in the wrong direction – A pessimistic scenario

Just as an improvement to Colombia's biopharmaceutical policy environment is estimated to result in direct and indirect societal and economic gains, a deterioration of the environment would also result in direct and indirect losses.

For example, the failure to achieve INVIMA's new policy of a 60-day timeframe for the regulatory approval of clinical trials would mean that the current 225-days timeframe would remain or could even increase.[117] Furthermore, continued uncertainty and deterioration of the IP environment for biopharmaceuticals (including the continued use of, or the threat to use, compulsory licensing or unilateral ad hoc price reductions through a notice of public interest) may deter clinical trials' sponsors and future investments in the biopharmaceutical sector.

Under this pessimistic scenario, where Colombia's biopharmaceutical policy environment deteriorates by at least 25%, Colombia could expect a decrease of anywhere between 20 and 46 clinical trials a year and total economic losses of up to 119 million USD, as shown in Figure 25 and Table 16 below.

In a similar yet inverted manner to the other scenarios, the below Table 16 shows how the deterioration of Colombia's biopharmaceutical policy environment would lead not only to a lower amount of clinical trials (which consequentially means that fewer Colombian patients will benefit from early access to cutting-edge treatments) but also to substantial economic losses.

FIGURE 25 Expected losses to clinical trials activity in a given year under the pessimistic scenario

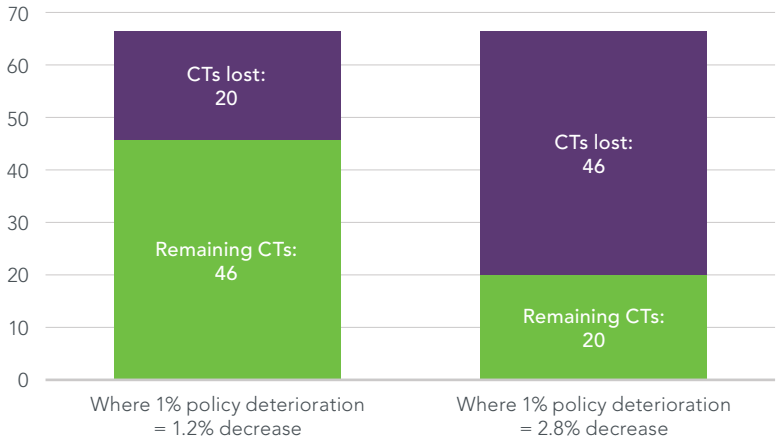


TABLE 16 Expected economic losses in a given year under the pessimistic scenario

Estimated losses of monetary flows associated with clinical research resulting from a 25% deterioration of the clinical research policy environment	
Direct monetary loss where 1% deterioration = 1.2% decrease	Total economic loss (including externalities)
$-20.4 Million	$-51 Million
Direct monetary loss where 1% deterioration = 2.8% decrease	Total economic loss (including externalities)
$-47.6 Million	$-119 Million

5 CONCLUSION AND FINAL THOUGHTS

The purpose of this report has been to, firstly, give a comparative overview of the biotechnology sector in Colombia and, secondly, provide an estimate of how an improvement to Colombia's policy environment can result in higher biotechnology outputs including rates of biomedical FDI and clinical trials.

The report identifies key policy areas where the existing legal framework is not in line with international best practices and are actually limiting the development of Colombia's biotechnology sectors. The report's findings can be grouped along three key findings.

Key finding 1: Colombia currently lags behind other middle-income, OECD economies and world leaders on biotechnology outputs

While biodiverse Colombia's capacity and level of innovation in the area of biotechnology is limited by international standards and compared to its regional and socio-economic peers. Rates of general and biotech-specific R&D and innovation inputs and outputs are often lower than expected and, in many cases, have remained flat for several years. Given the high level of biodiversity and socio-economic development in Colombia rates of biotech patenting, biofuels production, ag-bio crop cultivation and level of clinical trial activity are relatively low.

Key finding 2: Colombia has a potential pocket for growth and development in clinical research on biologic products and technologies

Analysis of clinical trial activity shows that within the realm of R&D of biologic medicines Colombia could be a regional leader, with the share of these clinical trials the highest in Latin America and rising. While on the one hand in absolute terms Colombia's rate of clinical trials in this area is low: the number of clinical trials on biologic drugs to date is slightly over 100, between 50% to 150% lower than the top 3 economies in Latin America – Brazil, Mexico and Argentina.

Yet, Colombia's share of biologic trials relative to the total number of trials is quite high. Biologic-related trials were 11.3% of total trials, while this share is closer to 5% in Brazil and 8% in Mexico and Chile.

Key finding 3:

- Reforming Colombia's biopharmaceutical policy environment could almost double current levels of clinical research to over 100 additional clinical trials per year and close to USD200 million of direct economic gains.

- Equally a deterioration to the biopharmaceutical policy environment could result in a decrease of 30% or more from current levels of clinical research a year and total economic losses including externalities of over USD100 million.

Using an econometric model which analyzes Colombia's clinical research policy environment in relation to international best practices and identifies which policy improvements might support greater clinical trial activity in the country, the report quantifies the resulting wider, positive economic effects of either improving this environment or seeing a deterioration. For example, the IP environment for biopharmaceuticals in Colombia is holding back biopharmaceutical investment and development. For biopharmaceutical as well as non-pharmaceutical biological products and technologies the evidence suggests that IPRs incentivise and support the research and development of new biological technologies and products. Unfortunately, the last few years have seen increased uncertainty with regards to the protection of IP and biopharmaceutical IPRs in particular. An increased focus on the use of compulsory licensing and overriding of property rights as a cost-containment tool, lack of patentability for biopharmaceutical innovation and uncertainty over the application of RDP to biologics create an environment which is not the

best for attracting investment and long-term biopharmaceutical R&D.

Concluding thoughts

Developing a world-leading biotechnology capacity is not easy. Whether it be in the ag-bio field, biofuels or biopharmaceuticals, the technological, human capital and R&D challenges are enormous. And the competition around the world and in Latin America is fierce. Colombia has many advantages – its biodiversity, growing population, stable government and recent record of strong governance – but the challenges are still very real. If there is one main lesson from this report and the international work that it builds on it is that putting in place the right policies is of critical importance. While it is possible for countries to succeed without the right policy framework in place, there are more examples of countries that have failed for a lack of the right policy framework than those who have succeeded without it. Indeed, a key finding of much of the international policy literature is the centrality of the policy environment in a given country to incentivizing innovation and investment in high tech sectors including biotechnology.[118] With the right policies in place countries can give themselves the best chance of achieving success. For biotechnology and the biopharmaceutical sector creating this enabling environment is of critical importance.

As this report shows Colombia over the last fifteen years has taken many key steps: committing to an innovation-based economic model, investing more in science and technology and developing a high-tech human capital capacity. Some improvements have or are being made to the regulatory framework. But to achieve a greater level of success and more substantial biotechnology outputs, Colombia needs to improve its policy environment particularly with regards to the protection of IP and biopharmaceuticals. As the above findings and economic model suggests, strengthening the policy environment is likely to have a significant and sustained positive economic impact.

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