pugatchconsilium

THE BIOPHARMACEUTICAL COMPETITIVENESS & INVESTMENT (BCI) SURVEY 2017

LatAm Special Report

This report was commissioned by the Federación Latinoamericana de la Industria Farmacéutica, FIFARMA (Latin American Federation of the Pharmaceutical Industry). The views represented here are those of the authors only.

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LIST OF ABBREVIATIONS

ANMAT	Argentinian Regulatory Agency
API	Active pharmaceutical ingredient
ANVISA	Brazilian Regulatory Agency
BCI	Biopharmaceutical Competitiveness & Investment Survey
CINDE	Costa Rica's agency in charge of attracting foreign investment
COFEPRIS	Mexican Regulatory Agency
CORFO	Chilean agency in charge of attracting foreign investment
CTs	Clinical trials
EMA	European Regulatory Agency
FDA	US Regulatory Agency
FDI	Foreign direct investment
FTA	Free trade agreement
HTA	Health Technology Assessment
ICH	International Conference on Harmonisation
ICT	Information and communication technology
INPI	Brazilian Patent Office
INVIMA	Colombian Regulatory Agency
IP	Intellectual property
LatAm	Latin America
OECD	Organisation for Economic Cooperation and Development
PDP	Productive Development Program
PTE	Patent term extension
RDP	Regulatory data protection
R&D	Research and development
USTR	U.S. Trade Representative

PREFACE

This Special Report on Latin America is derived from the main 2017 Biopharmaceutical Competitiveness & Investment (BCI) Survey, a global executive opinion survey and index that measures the relative attractiveness of economies to investment from biopharmaceutical research-based companies.

The BCI provides governments and other key stakeholders with a snapshot of major markets' global competitiveness. In 2017 the main BCI report covers 31 of the largest and most active biopharmaceutical markets worldwide, five of them in Latin America; in this Special Report we cover an additional five Latin American markets, bringing the total to 10.

The 2017 BCI Survey is split into two separate surveys, one targeting "mature" markets and the other, "newcomer" markets. This division is based on sophistication of the health and biopharmaceutical system as well as extent of historical biopharmaceutical R&D and manufacturing capabilities. The two surveys have been collected, scored and analyzed separately. The Latin American markets are all benchmarked using the newcomer market survey.

Now in its fourth edition, the BCI Report is a growing tool for gauging competitiveness across the world. This Special Report complements the wider 2017 BCI Survey with a deep dive analysis and important insight regarding the impact of biopharmaceutical policies on investment decisions in the challenging and evolving microcosm of Latin America. The report is aimed at supporting policy makers, business executives and other key stakeholders in identifying what economic and policy aspects are hindering the ability to meet today's healthcare challenges in the region and create a thriving biopharmaceutical sector there.


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EXECUTIVE SUMMARY

Latin America is a region in flux. With the fastest-growing smartphone market in the world[1] and extremely high social media participation[2], it is not surprising that a combined population of 626 million is turning as empowered and educated as those in more developed economies.

This is especially so when it comes to healthcare. Policymakers and government agencies, however, have been unable to keep pace with public demands for best-in-class healthcare.[3] Why has Latin America been unable to meet the evolving challenges in healthcare like other newcomers? Why is there no innovation clusters in the biopharma sector in an otherwise vibrant and highly creative region?

To help answer these fundamental questions, FIFARMA, the Latin American Federation of Pharmaceutical Industry commissioned Pugatch Consilum to develop a Special Report on Latin America (LatAm Special Report) as part of the 2017 Biopharmaceutical Competitiveness & Investment Survey. The Survey benchmarks performance and overall attractiveness of different economies for investment in the biopharmaceutical sector, as reported by executives on the ground. It examines the entire ecosystem in which biomedical innovation takes place from scientific capabilities and infrastructure; to state of the clinical environment; quality and efficiency of biomedical manufacturing and logistics operations; the biomedical regulatory framework (including the protection of intellectual property); healthcare financing; and overall market and business conditions.

The BCI adopts a "bottom-up" approach based on feedback from executives – country managers and their teams – to get a snapshot of the biomedical competitiveness of a given country. Their responses reflect a candid and often accurate understanding of the different aspects of their respective markets.

The LatAm Special Report is a regional version of the 2017 BCI Survey. It deep-dives in ten Latin American countries: Argentina, Brazil, Chile, Colombia, Costa Rica, Dominican Republic, Ecuador, Mexico, Panama and Peru. A statistical analysis ranked each country with a quantitative score (out of 100). The result benchmarks each country in relation to others in the region, revealing their relative attractiveness for biopharmaceutical investment. To provide further context, throughout the report, three countries benchmarked against the same survey (targeting "newcomer markets") and falling into the top group in the global BCI Survey are mentioned as points of reference of best practices:" Israel, Taiwan and Singapore.

Two fundamental findings of the 2017 BCI LatAm Special Report stand out: 1) Focusing on a handful of areas of reform does not lead to a thriving biopharmaceutical sector; instead a holistic comprehensive approach is required addressing variables of the entire biopharmaceutical ecosystem. 2) Achieving and maintaining a successful healthcare system is not guaranteed by brute economic force or market size. Instead, countries like Israel, Taiwan and Singapore have adopted a "work-in-progress" approach focusing on getting the policies right, and making themselves attractive and competitive. These are economies that resist tempestuous budget cuts and keep laser-focused on a long-term vision of becoming magnets of biopharmaceutical activity.

The 2017 BCI LatAm Special Report consists of four main sections. Part I describes the components of the BCI Survey and the methodology used. Part II discusses the overall findings of the BCI Survey for the ten LatAm markets. It seeks to answer the question of what the results of the BCI actually mean for countries. What can government officials and policymakers take from the results both in aggregate and on an individual category by category basis? What are the results of the BCI and what do they tell us about best practices for enabling biopharmaceutical innovation? What can the countries learn from the BCI results and what do they mean for other countries not included but aspiring to develop their biopharmaceutical capacity? Part III goes into greater granularity on specific findings in each of the key areas of the biopharmaceutical sector. Part IV presents the results on a country-by-country basis with a more detailed discussion of the particular challenges facing the country, and the opportunities to leverage.

1 DESCRIPTION OF THE 2017 BCI LATAM SPECIAL REPORT

Generally speaking, key measures of broad competitiveness and innovation in the biopharmaceutical policy ecosystem rely on a combination of hard data and surveys.

One aspect that, thus far, has been missing from the existing body of data is the on-the-ground perspective of the investment attractiveness of a given economy in Latin America specific to the biopharmaceutical sector – its biomedical "pulse". The BCI Survey, an executive opinion survey and index of economies' biopharmaceutical investment attractiveness, aims to fill this gap.

The answers from executives surveyed are statistically analyzed and translated into a quantitative score, which is used to benchmark the performance of their respective economies and overall attractiveness for investment. In doing so, the BCI LatAm Report captures a wealth of data and observations concerning major areas of the biopharmaceutical environment in the region, and provides new insights on policy strengths and challenges in the sampled markets. The insights generated by the BCI LatAm may be of value in several different ways and for different stakeholders. The BCI LatAm provides a common, numeric and regional measure of biopharmaceutical competitiveness that may be used by governments, biopharmaceutical companies and other organizations to understand and compare economies' performance on a like-for-like basis. As a quantitative measure of investment attractiveness, the BCI LatAm may also be used to analyze the relationship between various policy inputs and investment outputs.

In addition, on an individual economy basis the scores of the BCI LatAm Report shed light on the particular areas for improvement in a given economy in terms of the total biopharmaceutical ecosystem as well as specific areas/categories within the ecosystem. As such, the BCI is an evidence-based platform for supporting efforts to strengthen the biopharmaceutical policy environment at the national and regional levels.

1.1 What it takes to attract foreign investment?

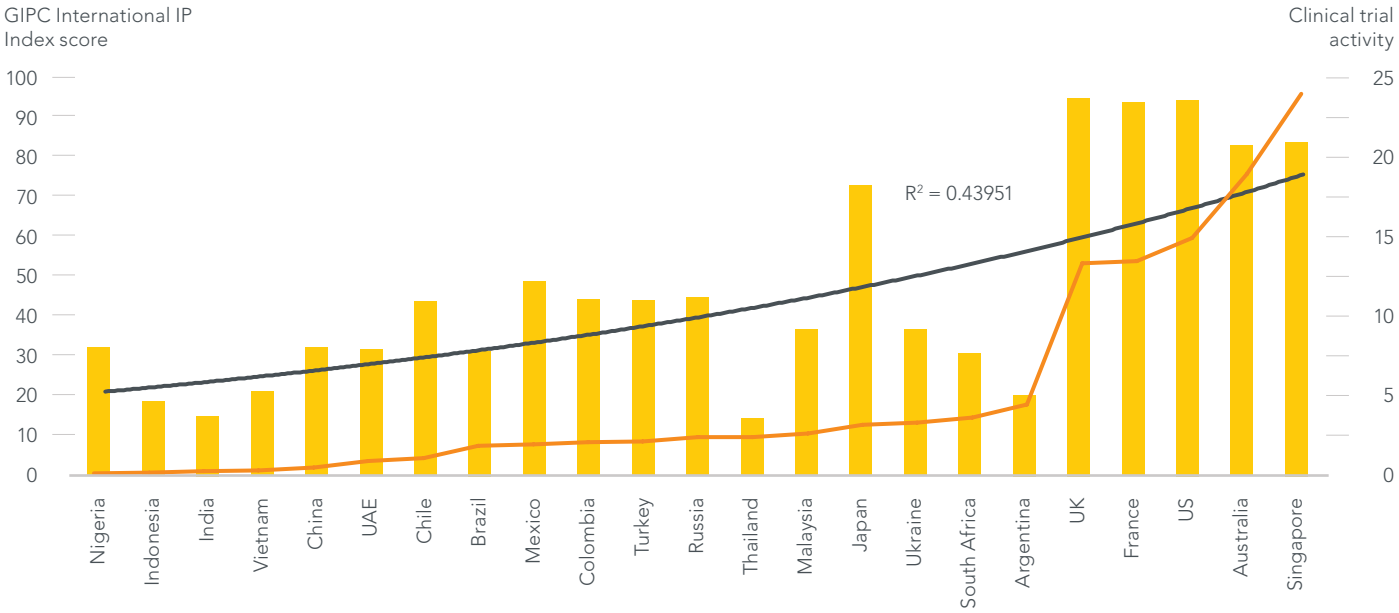
To secure a larger piece of global biopharmaceutical investment, a growing body of data suggests that market size, demand and costs, while of obvious importance, are not necessarily the only driving factors. Instead, support for basic research, strong life sciences-related IP rights, robust regulatory standards, transparency, streamlined processes and a fair pricing and reimbursement environment are all critical in shaping an environment that is attractive to biopharmaceutical investment. These are all deeply intertwined factors: alter one, and all others are inevitably affected.

To illustrate, one policy area demonstrating this link is IP protection and the effect of an economy's IP environment on the number of clinical trials hosted there (as a proxy for biopharmaceutical investment).[4] In fact, regression analysis suggests that strength of IP protection can explain over 40% of clinical trial intensity – which is significant given that a number of other factors are also typically considered important for attracting clinical trials (such as adequate technical capabilities, relevant patient pool and scientific resources).[5]

IP protection is just one element of a wide range of policies needed to create a biopharmaceutical innovation and investment "ecosystem," i.e., the total policy environment that defines how attractive an economy is for biopharmaceutical investment.[6]

Thus, for economies that have targeted biopharmaceutical investment as being of strategic importance to national economic development and growth, there is a pressing need to understand and map the state of the

FIGURE 1 IP Index vs. Clinical Trial Activity



GIPC International IP Index score as % of total score, life sciences-related indicators, 2014
Clinical trial activity (standardized per million population), average rate 2009-13
Expon. (GIPC International IP Index score, life sciences-related indicators, 2014)

Source: Pugatch Consilium, Clinicaltrials.gov, GIPC International IP Index (2014)

biopharmaceutical investment environment in a given economy. This includes identifying which policies are in place, which are not and how biopharmaceutical investment is affected.

1.2 What kinds of foreign investment does the BCI LatAm Report refer to?

When discussing foreign investment in the context of the biopharmaceutical sector, local executives refer to a wide range of activities undertaken by companies and other organizations that contribute economic value in a given economy.

In general, there are three different forms or phases of investment that are typically undertaken in the biopharmaceutical field:

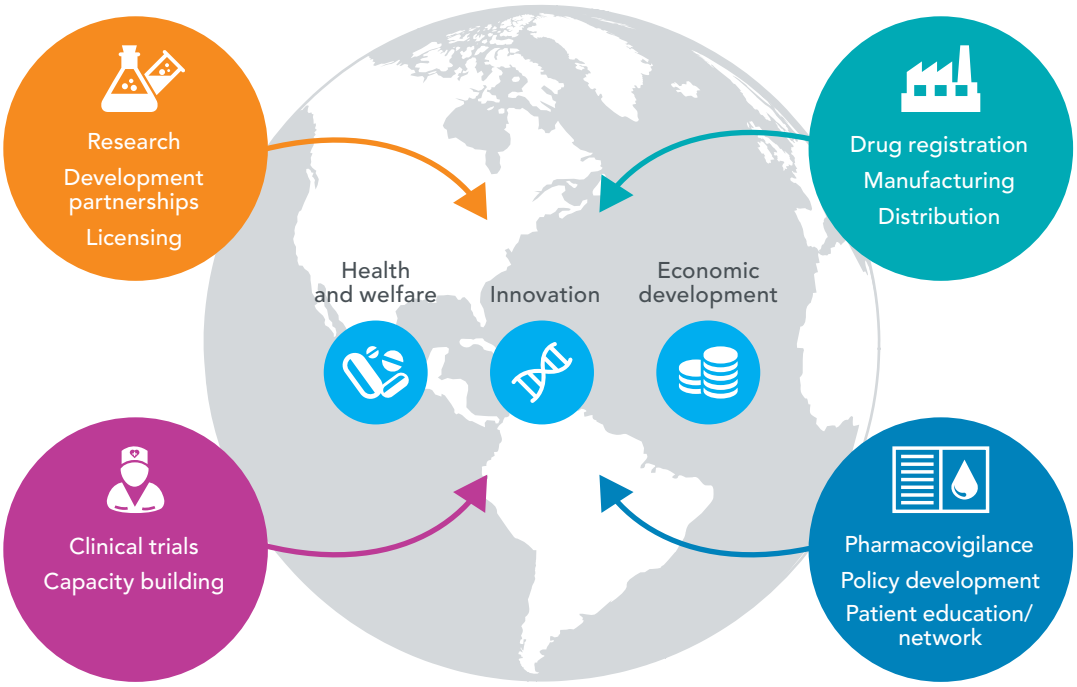
Research and Development

Most of the investment that drug innovators make is likely to take place in research and development, from basic research to translation of new discoveries into useful medicines and health technologies, as well as clinical testing of these new products. This phase includes research partnerships between academia, local firms, research institutes or clinical research organizations and large multinational research-based companies. It also involves technology transfer of assets and know-how, including licensing-in of new technologies and molecules by companies that are involved in later stages or "downstream" development of products.

Manufacturing

Companies are also likely to make investments in biopharmaceutical manufacturing operations, including bulk production, formulation, tableting and packaging. Specifically, manufacturing operations can range from secondary activities, such as packaging and labeling, to more advanced or primary activities, such as production of APIs or other product substances, and formulation of these ingredients into a product. Over the last few decades manufacturing – as a share of research-based companies investment activities – has been on the decline. Instead, the majority of non-capital investment is in R&D and specific clinical research.

FIGURE 2 Types of R&D Investment in the Biomedical Sector



Source: Pugatch Consilium

Commercial and market access operations

Finally, companies may undertake a range of commercial operations, including setting up an entity, sales and marketing, licensing and distribution and arrangements for regulatory approval. This phase may also involve a number of activities promoting safe and effective use of a drug, such as development of health policy, support for medical and community health, patient education, professional training and participation in pharmacovigilance activities.

Figure 2 illustrates the full range of investment activities that may take place in a given economy across the biopharmaceutical R&D process and product pipeline.

1.3 The sample of the BCI Survey

The 2017 BCI LatAm Report covers ten countries in Latin America selected on the basis of their contribution to the regional GDP and trade and relative size of the biopharmaceutical market. As such, the 10 markets included in the BCI LatAm in 2017 capture many of the largest and most active biopharmaceutical markets region-wide.

A statistical analysis ranked each country with a quantitative score in the scale of 100. The result benchmarks each country in relation to its neighbors in the region, revealing their relative attractiveness for biopharmaceutical investment.

As is discussed below, Argentina, Brazil, Colombia and Mexico have all previously been included in earlier BCI Surveys. Comparing their current results with previous scores reveals a number of important trends regarding the competitiveness of the respective economies. Has the environment improved or are executives on the ground in these countries still facing many of the same challenges they were three years ago?

TABLE 1 Economies covered in the 2017 BCI LatAm Special Report

Argentina*	Dominican Republic
Brazil*	Ecuador
Chile	Mexico*
Colombia*	Panama
Costa Rica	Peru

*Analyzed in previous BCIs

1.4 Factors measured by the Survey

Based on existing literature and experience, it is possible to piece together a set of principles and factors which - evidence suggests – are collectively enablers of biopharmaceutical innovation. These factors range from what might be termed "hardware" such as R&D infrastructure and human resources, and "software" such as public policies ranging from IPRs to regulatory capacity and standards to market and commercial incentives. These enabling factors are as follows:

Scientific Capabilities and Infrastructure

Biopharmaceutical innovation is driven by an adequate environment on which biomedical research can take place. This includes a sustained supply of modern infrastructure and specialized human resources available and utilized for biopharmaceutical innovation.[7] Specific elements that are often identified are:

- a sufficient quantity of highly-skilled biomedical professionals and researchers;
- updated scientific infrastructure;
- the presence of research clusters; and
- technology transfer frameworks and financial support for R&D, including both public and private investment.[8]

Notably, universities and public research institutions can play a key role in the process of fundamental biomedical research and discovery of new molecules and biologics.[9]

As such, questions in this category assess the quality of personnel, technologies and facilities in biopharmaceutical research forums in the economy; the extent of collaboration between public and private research partners; and the ability to leverage these to translate discoveries into products.

Clinical Research Conditions & Framework

Clinical trials are the most significant part of the research and development of new medicines. It determines whether a chemical compound or biologic is safe and effective for treating a medical condition. It helps determine optimum dosages and best ways of administration. It also can uncover new applications or tailor drugs to different populations. Furthermore, it provides a wide number of social and economic benefits to patients, health systems and national economies, including advance access to innovative drugs, opportunities for local participation in cutting-edge research and clinical standards and improvements to infrastructure.[10]

Investment in clinical research naturally flows where trials can be performed according to international scientific standards, by well trained professionals, in well-equipped facilities, and with the ability to accurately and efficiently collect the required data. Therefore, companies consider a wide range of factors when deciding to conduct clinical trials in a given economy. These factors include:

- the characteristics of the population related to the specific product to be tested;
- the availability and willingness of the population to participate throughout the duration of the trial;
- the infrastructure of local hospitals and research centers;
- the ability of physicians and supporting medical staff to carry out clinical trials and work with international organizations;
- the ease of the regulatory system, including approval of clinical trials; and
- the costs of performing the trials in the economy.[11]

FIGURE 3 Factors that Enable Biopharmaceutical Innovation

Source: Pugatch Consilium, based on the 2017 Biopharmaceutical Competitiveness & Investment (BCI) Survey (Pugatch Consilium, forthcoming)

Accordingly, questions in this category assess the ability of research institutions in the economy to conduct clinical research in a high quality and efficient manner.

The Regulatory System – Drug Approval, Quality Assurance and Pharmacovigilance

The regulatory environment in a given economy plays an important role in shaping incentives for investment and establishing adequate levels of quality and safety for biomedical products.

Inadequate approval standards may promote the presence of substandard drugs in the market, which could affect demand for high quality drugs and discourage investment in new products.[12] Conversely, a strong regulatory environment creates the conditions for the production and sale of high quality products and technologies.[13]

While complying with these standards may impose costs on manufacturers it also gives patients and health care providers confidence that new biomedical products are safe and effective. High regulatory standards tend to refer to those which assess the quality, safety and efficacy of products in line with ICH. These standards also require systems for monitoring products once they are in the market (known as pharmacovigilance).[14]

These standards vary depending on the type of product, whether it be a completely new drug application, a generic or a biosimilar, with generic approval requiring bioequivalence testing and biosimilar approval requiring clinical testing.[15]

Accordingly, questions in this category assess the ability of the regulatory system in the economy to ensure that only high quality, safe biopharmaceutical products enter the market, yet do so in a timely manner.

Market Access & Financing

Most health care systems today have either direct or indirect mechanisms in place for regulating the pricing and reimbursement of medicines. While some countries maintain the traditional transactional approach searching for the lowest cost, others have adopted systems of pharmacoeconomic and cost-effectiveness analysis and comparisons, and aiming to more sustainable value-based solutions.

The continued rise of health care costs has put more pressure on health authorities and payers to limit future increases in health spending through different pricing, reimbursement and procurement policies. The manner and extent to which these policies are put in place can have a

profound impact on the incentives for biomedical investment.[16]

Academic research and modeling suggests that for biomedical products restrictive pricing and reimbursement policies limit and delay investment in a market, including new product launches.[17]

Hence, the questions in this category assess the ability of new biopharmaceutical products to access the market via the pricing, reimbursement and procurement system in the economy in an efficient manner and at an acceptable price.

Effective Protection of Intellectual Property

A number of empirical studies published over the last decade have documented the positive and cumulative effect of IP protection on investment generally. For instance, one OECD study 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.[18]

In particular, patents and other forms of exclusivity for biomedical products, 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 biomedical products and technologies. Moreover, as will be discussed later in the report, protection of incremental innovation in the form of follow-on medicines have brought significant benefits to nascent bio-economies such as Taiwan.

In relation to the life sciences, IP rights play at least three major roles: 1) provide an incentive to prioritize the launch of new products in the country as soon as they are fully developed, 2) act as a platform for transferring technologies among R&D entities, and 3) encourage domestic innovation. Hence, a strong legal basis for IP protection as well as its enforcement in a given market assures biomedical companies and other investors that their IP assets will be protected from infringement as they develop, test and launch products in that market.

The research process for biomedical products is unique in its time, cost and high rate of failure. The market exclusivity period provided by IP rights gives 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 IP rights.[19] And no new drugs means no new generics upon patent expiry; a lose-lose proposition.

Equally important for biomedical products is the on-the-ground enforcement of IP protections. Key concerns for biomedical investors are the extent to which the production and availability of infringing products, including counterfeits, are limited and deterred in a meaningful way.

Accordingly, questions in this category assess the ability to fully realize required terms of intellectual property protections for biopharmaceutical products.

1.5 Benchmark methodology

Each category is designed to provide a comprehensive, relevant and accurate picture of an economy's performance at different segments of the biopharmaceutical "pipeline", and hence its attractiveness for investment.

The survey covers key policy issues prevalent in Latin America such as existence of and compliance with Good Manufacturing Practices and pharmacovigilance and presence of delays between market approval in a given market and approval by the FDA or EMA.

The full text of the survey can be viewed in the Appendix to this report. For each question, respondents rate an economy's performance in relation to a certain benchmark.

Figure 4 on the following page gives examples of the benchmarks used in two survey questions. In Question 10, an adequate independent capacity for review and approval of new biopharmaceutical products in line with international standards provides the benchmark. For Question 24, the benchmark is the existence of a regulatory mechanism that ensures timely and effective patent enforcement.

FIGURE 4 Sample Questions for the 2017 BCI Survey

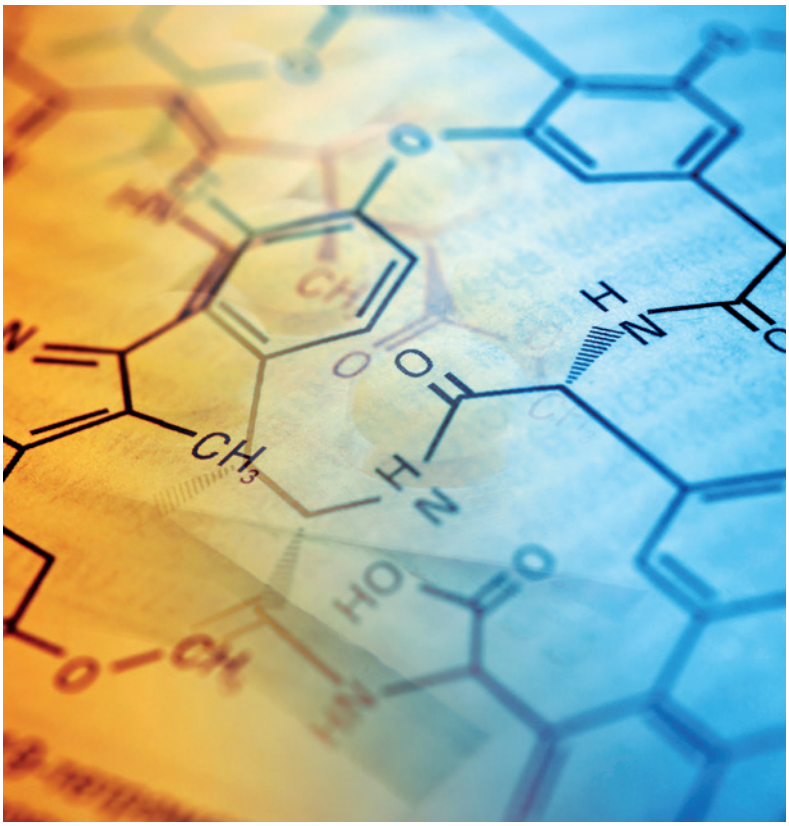
Question 10
How would you describe the capacity of the health regulator in your country to review the data submitted to it for the approval of new biopharmaceutical products?

Very low (low capacity for independent review) ☐	Basic (most reviews based on prior approval in other countries; lacks significant capacity for independent review) ☐	Good (review based on prior approval in other countries as well as on independent review) ☐	Excellent (full capacity to conduct independent review) ☐

Question 24
In your view, how effective are civil and criminal remedies for infringement of intellectual property rights and battling counterfeit medicines in your country?

Highly ineffective (framework for litigation and penalties does not exist) ☐	Fairly ineffective (framework exists but is generally not implemented or enforced) ☐	Fairly effective (framework is generally implemented and enforced but with key exceptions) ☐	Very effective (including compensation, injunctions, seizures and penalties; ability to challenge validity of a patent) ☐

Source: BCI Survey (2017)



In order to capture specific nuances of economy performance, respondents select from a scale of our answers for each question. This scale ranges from the lowest possible performance to the highest possible performance (i.e., the benchmark), but the exact scale varies for each question. This design gives respondents a framework for gauging their views, but in a way that minimizes constraining their answers as much as possible.

1.6 Validation of the 2017 BCI LatAm Report

The 2017 BCI LatAm Survey was distributed primarily to general managers and executive staffers of multinational research-based biopharmaceutical companies operating in the 10 sampled economies – in other words, experts in the field and on-the-ground practitioners with deep knowledge of the local biopharmaceutical investment environment in a given economy. Heads of local trade associations were also interviewed to discuss and validate the concerns and opinions expressed by the executives.

When asked about the utility and accuracy of the BCI, the overwhelming majority of survey respondents found the BCI to be a useful tool for assessing the biopharmaceutical ecosystem. In the view of over 90% of respondents, most, if not all, of the questions covered relevant elements of an economy's attractiveness for biopharmaceutical investment.

1.7 Calculation and classification of scores

Based on a statistical analysis of the responses, each market is assigned a quantitative score (out of 100). Since all sampled countries belong to the same Latin American region, economies are gauged in relation to other markets with similar levels of development, allowing for an even more fine-tuned snapshot of each market's attractiveness for biopharmaceutical investment.

To score the responses each question accounts for a total of 4 points. The four answer options for each question correspond to scores of 1, 2, 3 and 4 – ranging, in order, from the options reflecting the poorest to the highest performance. Based on the analysis of responses to all 25 questions, each economy receives a score for each category as well as an overall score, out of a maximum of 100.

Based on category and overall scores, economies are classified into levels of competitiveness for biopharmaceutical investment and innovation relative to the other sampled markets in each group, ranging from most likely to secure investment to those losing out on investment. LatAm markets are divided into three groups, with the upper and lower ends based on the distribution of the scores (which follows a typical bell curve pattern in which the scores are concentrated in a certain score range, in this case roughly between 50 and 70). The three newcomer markets included from the global BCI Survey – Israel, Singapore and Taiwan – constitute a fourth group, scoring above any of the LatAm markets in a range of approximately 75 to 90.

2 OVERALL FINDINGS OF THE 2017 BCI LATAM REPORT

While virtually all Latin American countries in some way or another have stated a commitment to improve their biopharmaceutical competitiveness, relatively few actually recognize and execute a plan of comprehensive and long-lasting reforms. Most often countries tend to target one area such as streamlining clinical trials, improving patent backlog, investing in R&D infrastructure or the like. As essential as those efforts are, this is a relatively limited approach.

The countries that have the best measurable performance are the ones that have the right policies simultaneously in place for all enabling factors. Interestingly, both CINDE in Costa Rica and CORFO in Chile, two entities in charge of turning their countries into innovation hubs, are credited for both countries leading the BCI LatAm. There is one thing which is abundantly clear from the results of this Survey: protectionist policies – regardless how narrow they may be – can taint the biopharmaceutical ecosystem and cancel out any progress towards building a bio-economy. All factors are intrinsically interdependent; you attain a positive multiplying effect by improving one factor, and a negative multiplying effect when inhibiting one.

For context, three markets from the global 2017 BCI Survey, Israel, Singapore and Taiwan are included as benchmarks. These countries - all newcomer economies on par in many respects with Latin American economies - are responding to the new realities of economic development by focusing heavily on continuous innovation, despite uncertainties.[20] These economies score in the top group of newcomer markets in the global BCI in 2017 and are seen as "pace-setters" among these markets globally. In other words, for them a strategic priority is the implementation of robust biopharmaceutical industrial policies focused more on R&D and less on manufacturing. Their ability to constantly adopt best practices and experiences, and shift to a collective forward-thinking mindset, have enabled these pace-setters to catch up to the top-performers and stay ahead of the competition for foreign investment.[21]

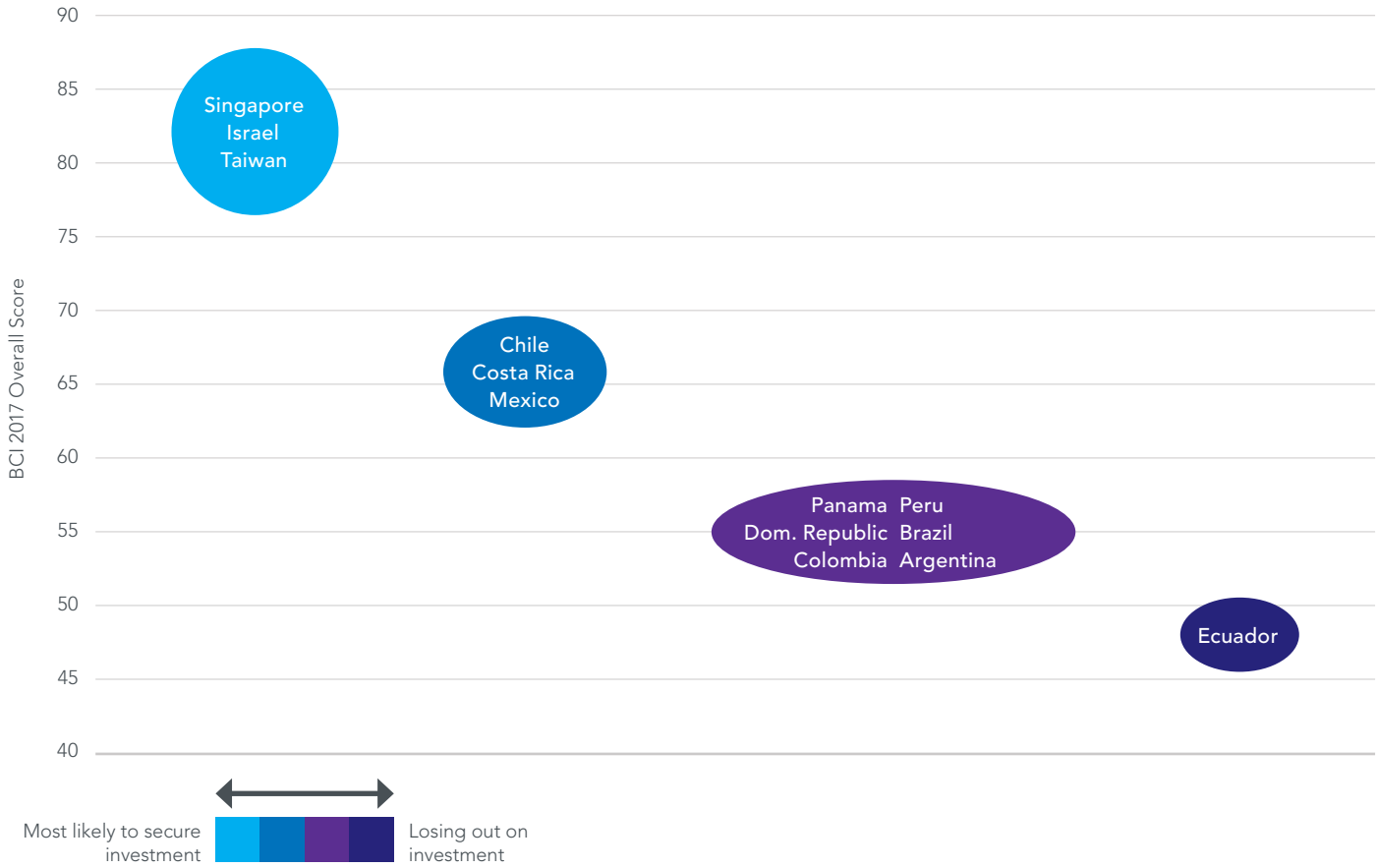
2.1 Regional Policy Trends: Why are there no "pace-setters"?

Latin American countries are either trailing or struggling to compete for foreign investment and to develop an active and thriving bio-economy – for the most part because of a lack of a comprehensive set of policies. The BCI results reveals a clear link between protectionism and a poor competitive standing. While seemingly embracing policies designed to enable their biopharmaceutical sector, many economies are still clinging to protectionist ideas that are actually contradictory and counter-productive; whether it be mandating the use of local content, manufacturing and hiring requirements or loosening standards for the protection of intellectual property. Innovation will simply go elsewhere when erecting barriers or mandatory requirements that make investment and R&D more, not less, difficult. And as discussed below, when it comes to achieving real world desired biopharmaceutical outputs, having a comprehensive set of policies that enable - rather than protect - local innovators is key to 21st century biopharmaceutical competitiveness.

Commitment to innovation is lackluster across the board

Notwithstanding widespread acknowledgment across the region that innovation should be a national priority, when the rubber meets the road Latin American governments seem unable to "walk the walk". There is no consistent long-term commitment to investment in their R&D

FIGURE 5 2017 BCI LatAm Overall Results Compared to Top Performing BCI Newcomer Markets



infrastructure, and to implement a comprehensive set of enabling policies with the clear vision of turning their country into a world-class bio-economy. Similarly, there is no apparent effort to implement international standards in the respective intellectual property legal frameworks. The only two exceptions to this rule appear to be Chile and Costa Rica, both with stated missions of becoming hubs of innovation, and implementing a coherent set of policies (with some setbacks from time to time).

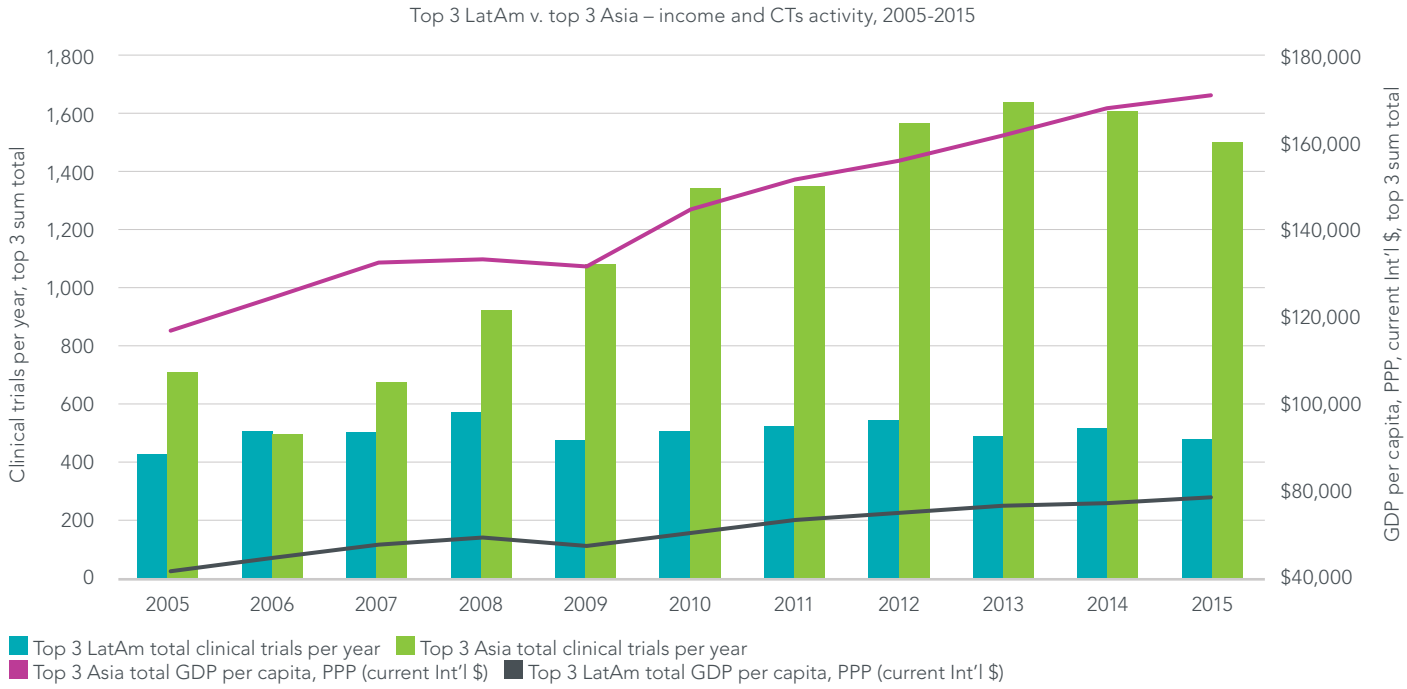
Lack of transparency and a race to the bottom on price and quality

Accessing Latin American markets is significantly challenging. Poor and inefficient management of healthcare budgets prevent health agencies from seeing beyond the pill; missing out on more efficient best practices of risk-sharing and evidence-based access models. In this purely transactional environment, the cheapest wins at the expense of the better. Substandard medicines win over more effective and safer alternatives – costing upwards of three times more on the long run in side effects, therapeutic inefficiency and loss of productivity.[22]

Inability of regulators to catch up with new technologies

Regulatory agencies across the region are struggling to catch up with the accelerating pace of scientific advancements in the field of biologics. WHO has set stringent approval standards for biosimilars. Nonetheless, Latin American countries often treat biologics and chemical entities interchangeably, when it comes to regulating them – ignoring WHO guidelines. Biosimilars are often approved by only submitting

FIGURE 6 Regional Comparison of CT Intensity: LatAm vs. Asia



Source: the International Committee of Medical Journal Editors (ICMJE); NB Top 3 LatAm: CL, AR, MX; Top 3 Asia: KR, SG, TW

bio-equivalence studies. Some even have a third category sometimes called "*similares*" (discussed in more detail below) requiring even less testing adding further confusion to the landscape. As such, there have been significant public health risk and commercial downside for companies.

The benefits of clinical trials is gaining traction, albeit slowly. LatAm is still missing out

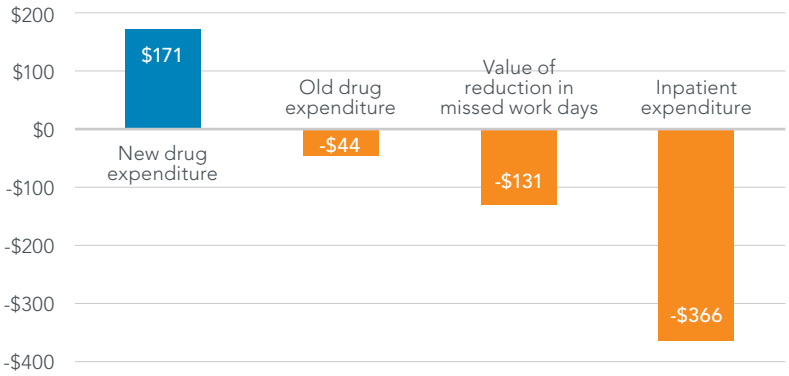
Countries in the region are acknowledging the benefits that clinical trials bring to patients, the local scientific and medical community, and the economy at large. As such, many are streamlining their approval process and investing in clinical infrastructure to attract clinical studies. The majority of the activity, however, remain in later stages of clinical R&D. Early stage Phase I or Phase II studies and clinical trials on biologics and new technologies such as immunotherapies are still not widespread. Overall, the region still has a long way to go to compete with other regions. Figure 6 contrasts the three top countries in clinical trial activity as reported by the International Committee of Medical Journal Editors in Asia and Latin America (South Korea, Singapore and Taiwan vs. Chile, Argentina and Mexico). The taking off since 2006 of these Asian markets teach the importance of embarking on long-term reforms – reforms that are comprehensive and coordinated towards building a world-leading biopharmaceutical research capacity.

Focus on price rather than value

Healthcare systems throughout the region do not place a premium on innovation, hence formularies are seldom updated with newer generation therapies. This appears to be a symptom of a broader stagnant mindset that hinders potential growth in the biopharmaceutical sector. Much has been published on more sustainable value-based and highly efficient best practices, and how they can be implemented in Latin America.[23] Even the value of innovative medicines has been estimated to cost three times less than keeping obsolete therapies and the resulting loss of productivity and hospital admissions as shown in Figure 7.[24]

There are similar outcomes with respect to longevity. Medical advances and biopharmaceutical innovation have long been recognized as major contributors to longevity.[25] In a recent study

FIGURE 7 Impact of Pharmaceutical Innovation on Per Capita Drug Expenditure, Loss of Productivity, and Inpatient Expense



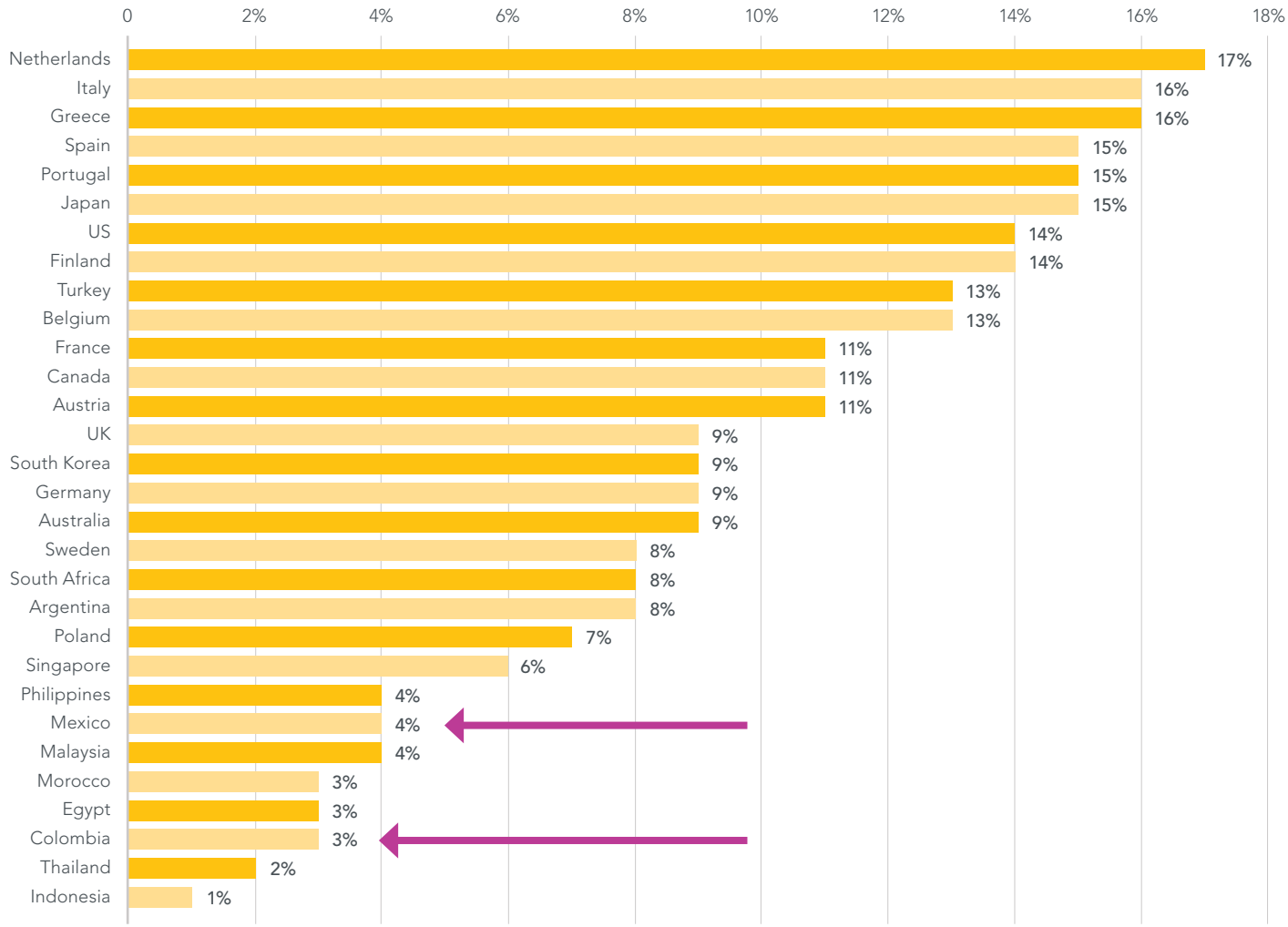
Source: Lichtenberg FR (2014), "The impact of pharmaceutical innovation on disability days and the use of medical services in the United States, 1997-2010," *Journal of Human Capital* 8(4): 432-480.

from 2012, Lichtenberg examined the impact of prescription drugs consumption on longevity in 30 developing and high-income countries during the period 2000-2009.[26] The study's first major finding is unequivocal: of the mean increase of 1.74 years in life expectancy in the 30 countries sampled, the increase in life expectancy at birth due to the increase in the consumption of biopharmaceutical drugs launched after 1990 was 1.27 years. In other words biopharmaceutical innovation can be attributed with 73% of the actual increase in life expectancy at birth.[27]

Furthermore, comparing longevity and biopharmaceutical data in the sample of 30 countries the study provides a second major finding: life expectancy and survival rates (for ages 25 and above) increased faster in countries with more and newer product launches.

This means that populations in countries with higher rates and access to biopharmaceutical innovation (measured in the share of post-1990 medicines consumed) had higher life expectancy than population in countries where biopharmaceutical innovation and new products were less abundant. The study finds that 37%, or 3.4 years of the difference in life expectancy between the top 5 and bottom 5 countries in the sample is attributed to the differences in their share of biopharmaceutical innovation and new products.

FIGURE 8 Share (%) of post-1990 drugs sold in 2009 in 30 countries



Source: Lichtenberg, F. R. (2012). "Pharmaceutical Innovation and Longevity Growth in 30 Developing and High-income Countries, 2000-2009", NBER Working Paper No. 18235.

As Figures 8 and 9 show, the two Latin American countries included in the study (Mexico and Colombia) both had lower levels of newer medicines on the market and had gained significantly less in longevity (or in the case of Mexico actually seen reduced rates of life expectancy) than countries with newer medicines on the market.

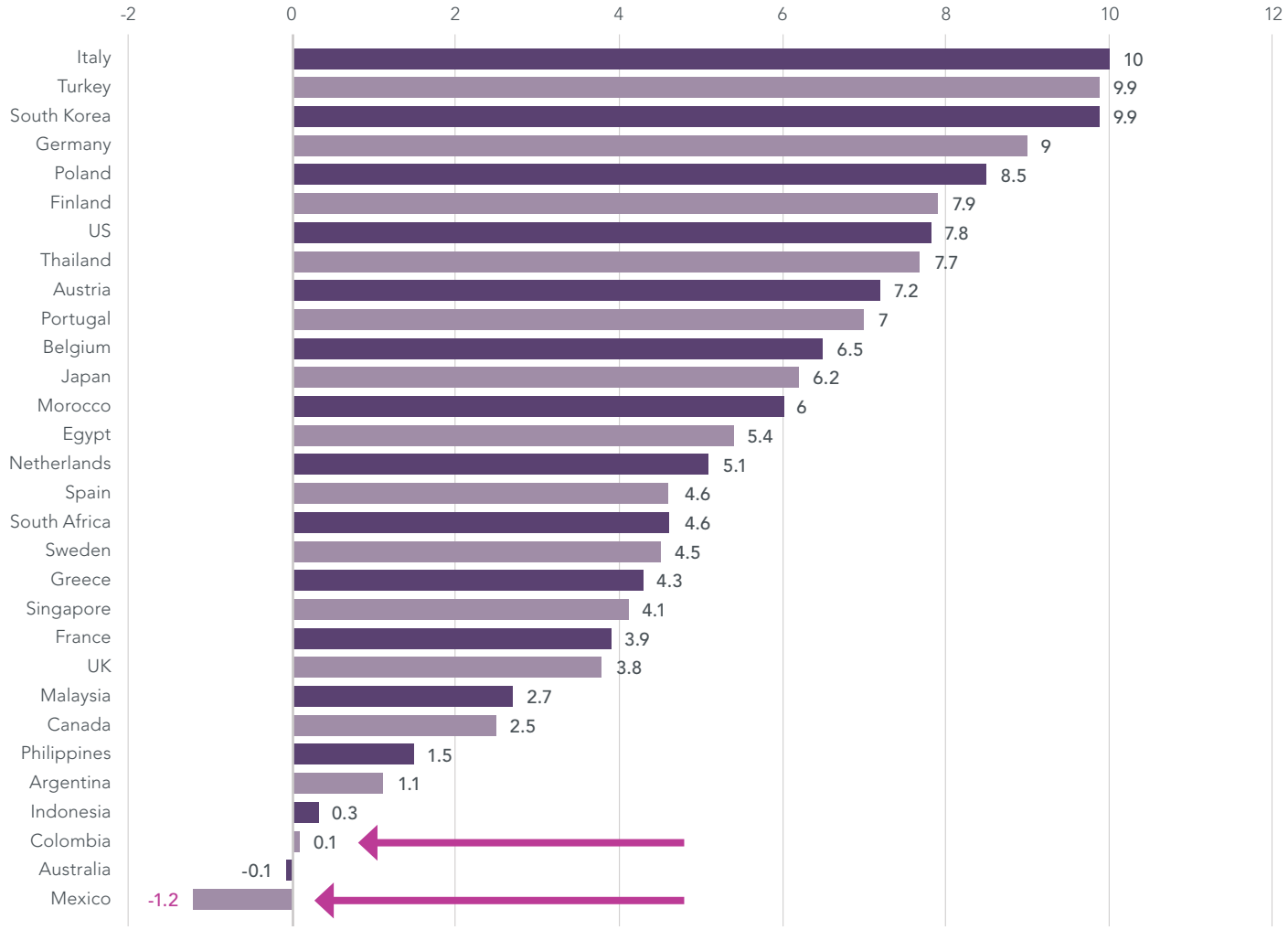
Yet, Latin American healthcare systems remain focused on strict cost containment, where the cheapest wins at the expense of the better.

Zooming out of LatAm: How does it fare compared to other regions?

Putting it all together, it is illustrative to contrast LatAm with two other regions of "newcomer" economies: Asia Pacific (AP) and Middle East and Africa (MEA).

So, how does Latin America compare to other "newcomer" regions? Not that much differently. Looking at average overall scores for markets included in LatAm, AP and MEA, all three regions still have a long way to go and collectively are at more or less the same level – around 60% of the

FIGURE 9 Increase (in number of years) in average launch year of RX drugs between 2000 and 2009, 30 countries



Source: Lichtenberg, F. R. (2012). "Pharmaceutical Innovation and Longevity Growth in 30 Developing and High-income Countries, 2000-2009", NBER Working Paper No. 18235.

total possible score. All three tend to face the most significant challenges (and lowest scores) in the areas of market access and regulatory systems (and in LatAm and MEA also in the effectiveness of IP protections). Among the three regions, on average the greatest strength among markets is in the area of clinical trials, suggesting that LatAm is not alone in building capacity and conditions for clinical research. At the same time, a distinct weakness of LatAm is in the area of scientific capabilities and research, where on average LatAm markets fall behind their peers in other regions, scoring on average nearly 10% lower in this category than the average score in AP.

What this means is that Latin America is not alone in the quest for attracting biopharmaceutical foreign investment. Improvement in any one of the regions (or a significant number of countries in the region) will likely divert investment away from the others. That seems to be the case for AP: while still scoring relatively low overall, in certain categories, such as IP, clinical research and scientific capabilities AP rises above the rest largely due to the relatively strong performance of Singapore and Taiwan (and with the exception of the market access category, Korea). The more LatAm markets strengthen key areas of their biopharmaceutical environment the more likely they are to have an advantage when competing for global investment.

FIGURE 10 BCI results among select newcomer markets by region

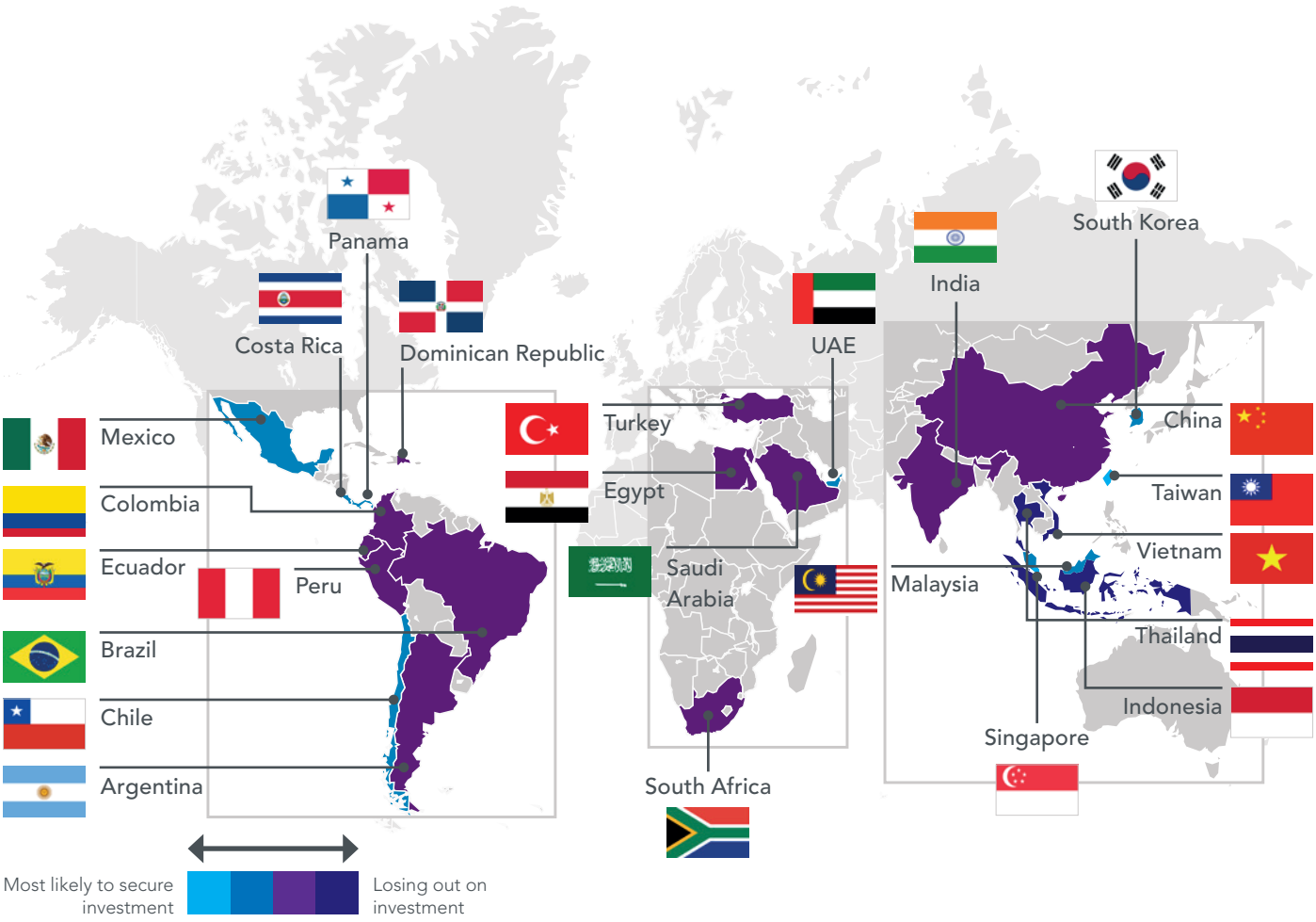


TABLE 2 Comparing average category scores in LatAm, Asia Pacific and Middle East & Africa

	Scientific Capabilities & Infrastructure	Clinical Research Conditions & Framework	The Regulatory System	Market Access & Financing	Effective Intellectual Property Protections	Overall scores
Middle East & Africa average	54%	61%	57%	53%	55%	**57%**
Latin America average	55%	62%	57%	58%	56%	**59%**
Asia Pacific average	62%	69%	59%	54%	63%	**61%**

2.2 The Swinging Pendulum

Political and economic uncertainty has characterized 2016 and 2017. In turn, the biopharmaceutical sector has been one of the proverbial "canaries in the coalmine," exposed to how governments react to health care challenges. The US withdrawal from TPP is a case on point. With the potential to truly set a new post-TRIPS standard of IP protection, the US was laying the foundation for international trade in a globalized economy.[28] Throughout the region, economies were generally trending -albeit reluctantly – towards implementing international IP standards in their respective legal frameworks.[29] Now, at least in the near term, the future of globalization remains uncertain and with it, the development of conditions that favor local biopharmaceutical investment and innovation.

Another example of looming uncertainty is the future of NAFTA and its impact on the biopharmaceutical sector - particularly in Mexico, but also broadly throughout Latin America. The USTR's official position is that "the Trump Administration is to use all possible sources of leverage to encourage other countries to open their markets to U.S. exports of goods and services, and provide adequate and effective protection and enforcement of U.S. intellectual property (IP) rights."[30] Yet the administration has also been clear that all options are on the table including the US leaving NAFTA altogether.[31] Current conditions point to NAFTA transitioning into a new bilateral framework likely to negatively impact the Mexican biopharmaceutical sector as a result of a potential new exchange rate (affecting top-line results), potential trade disruptions, and less foreign direct investment.[32] The issue of trade disruption is of particular concern given Mexico's leading position as the largest exporter of medicines throughout the Americas, to the tune of $1,578 million in 2016, with a compound annual growth rate of 19.3% since 1994.[33]

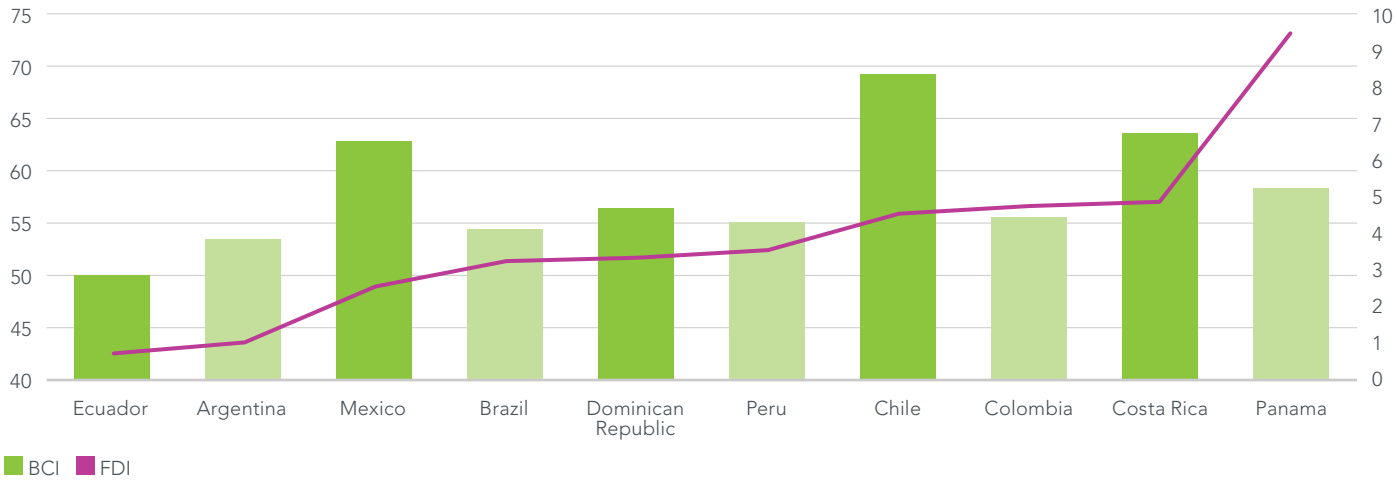
Notably, leaders like Israel, Singapore and Taiwan have accepted the universal principle that globalization plays a key enabling role for development and growth, particularly in the biopharmaceutical field. As such, these markets are in a strong position to weather the current anti-globalization trend, and likely to emerge with a robust biopharmaceutical sector when the pendulum swings back.

2.3 The FDI and BCI Landscapes in Latin America

Whether it is IP protection, market access policies, regulatory framework, capacity for clinical trials, or proper scientific infrastructure, the BCI Index reveals that key to a successful bio-economy is the adoption of an "ecosystem" approach. Investment gravitates around countries that provide supportive conditions actively and consistently – regardless of how large or developed their economies are. Figure 11 on the following page can be viewed as a "score card" of the countries' attractiveness for foreign investment across all sectors.

While Panama - the top performer in the chart - is heavily invested in banking and maritime traffic, much of its success in attracting FDI is credited to transparent regulatory frameworks and significant customs and tax advantages from the Colon Free Trade Zone.[34]

FIGURE 11 FDI per GDP vs. BCI Scoring



Source for FDI: Santandertrade.com
Source for GDP: World Bank

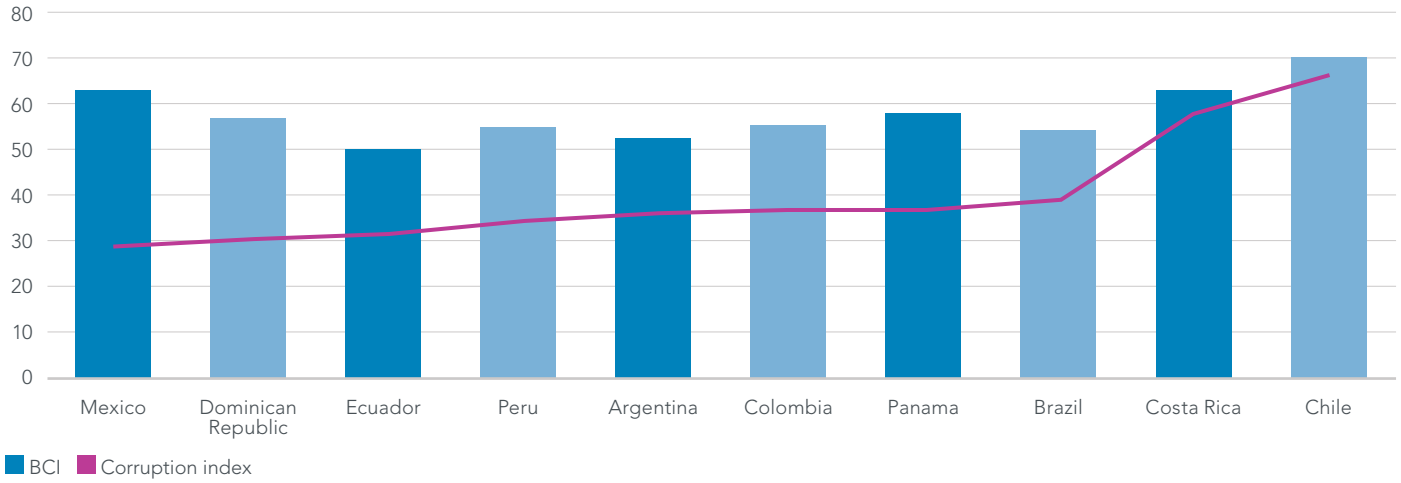
2.4 BCI and Corruption

Another link the Survey reveals is between the BCI scoring and the transparency (or lack thereof) of governments. Not surprisingly, corruption, inefficiency and the misuse of public power for private benefit can drag policies and efforts to attract biopharmaceutical investment. Latin American countries have always scored relatively high on perceived levels of corruption (the *Global Corruption Barometer* has been tracking this for many years). However, while the correlation is not perfect countries with lower levels of perceived corruption tend to do better on the BCI Survey. The main exception to this appears to be Mexico where public perceptions of the rate of corruption are very high, yet it's one of the more competitive economies in the region on the BCI.

2.5 Trends for economies previously analyzed in the 2015 and 2016 BCI Surveys: Argentina, Brazil, Colombia and Mexico

The results of the 2017 BCI LatAm Report when compared with the 2016 and 2015 global BCI Surveys for the four countries previously analyzed show a downward trend for Argentina and Brazil. The trend suggests policy challenges across the biopharmaceutical R&D eco-system, particularly at the market access, regulatory and IP levels that have remained unaddressed or have further

FIGURE 12 Corruption Index vs. BCI Scoring



Source: Transparency International, *Global Corruption Barometer*, inverted scale

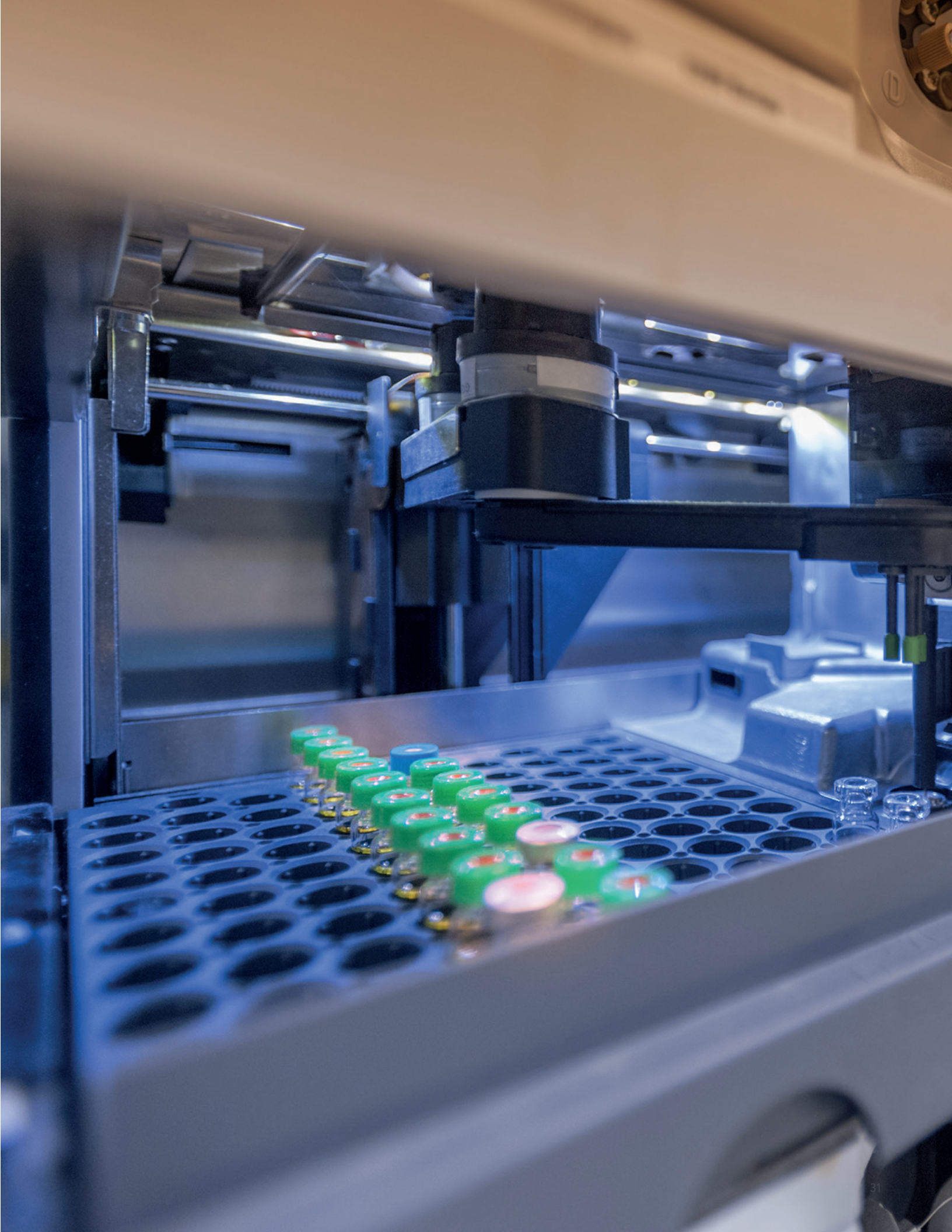
FIGURE 13 Overall scores for Argentina, Brazil, Colombia and Mexico: Three editions of BCI

2015-2017

deteriorated. It is worth noting, however, that the new set of policies of the Macri administration is placing Argentina on a path to sustained growth in foreign investment: from $5 billion in 2016 to a forecast of over $14 billion this year, and a reported $58.6 billion in investment announcements since Macri took office, many for projects that would take an average of four to five years.[36]

Scoring for Mexico on balance remained stable in 2017, both making improvements to its policy environments but also maintaining or introducing new barriers to investment in certain respects. Overall, Mexico stands out as being relatively more competitive than its major counterpart economies, Argentina and Brazil. One factor enhancing Mexico's competitiveness includes the introduction of a more integrated market authorization procedure with shorter timelines. Mexico has also implemented improvements to its national IP environment including availability of patents for biopharmaceuticals and RDP for new chemical entities. Areas that executives cite as still needing improvement include further strengthening of patent enforcement and RDP for biologics.

Colombia remains stalled as a trailing economy, unchanged for the most part from the 2016 BCI Survey. The implementation of contradictory policies can explain this: significant progress in the area of clinical trials is counterbalanced with weakening IP and market access environment.



3 FACTOR-SPECIFIC FINDINGS

Below is a more in-depth analysis of the BCI LatAm findings, divided along the five enabling factors and survey categories.

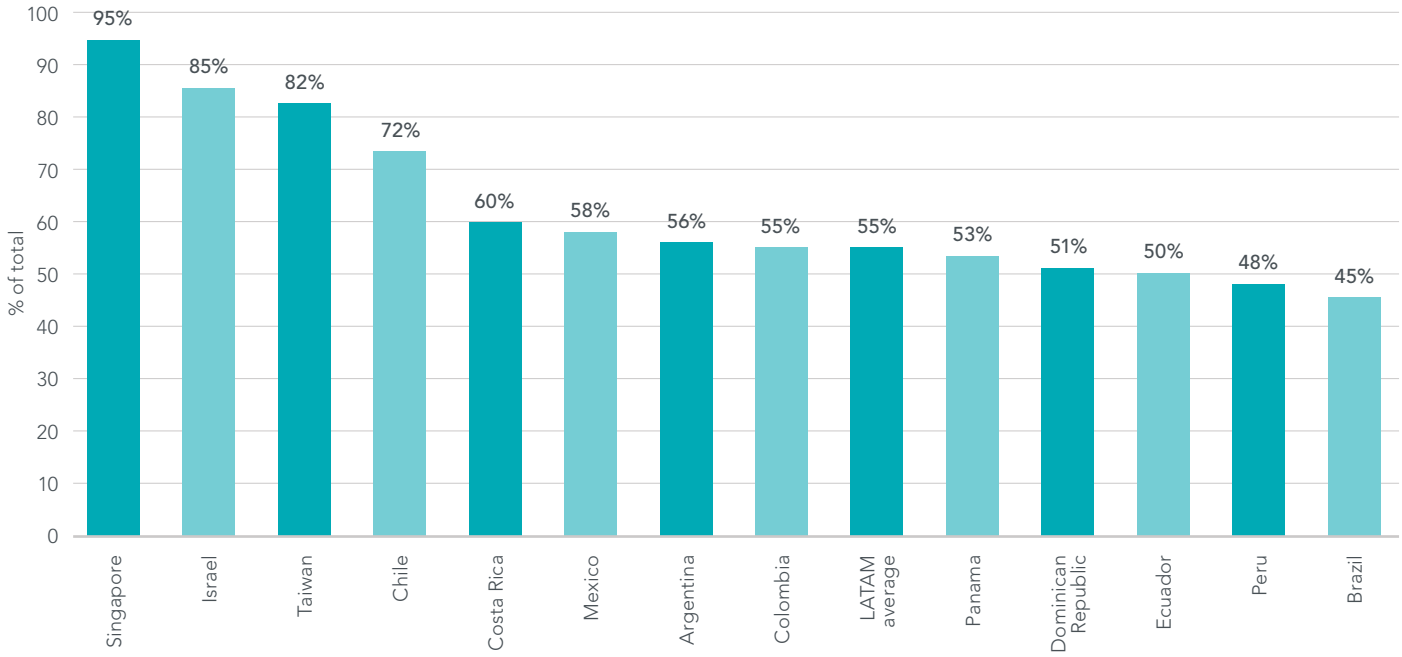
3.1 Scientific Capabilities and Infrastructure

Policymakers throughout the region agree that creating scientific capabilities and infrastructure should be a national priority. Realities on the ground, however, tell a different story. Collectively, the BCI ranks Latin America at just 55% of the total possible score, representing the lowest average score out of all five categories.

Mexico, for example, has a stated policy goal of increasing R&D spending to 1% of its GDP.[37] The latest data from the World Bank (2014), shows however, Mexican R&D expenditure at 0.54% of GDP; only marginally higher than the 0.4% spent a decade ago.[38] The "talk the talk" is not matched with a corresponding "walk the walk".

Chile is an exception to the rule. Chile is poised in the coming years to make significant progress attaining a world-class scientific infrastructure – some call it "Chilecon Valley".[39] Despite a relatively low percentage of GDP spending in R&D of 0.38%,[40] its BCI rank reveals such spending having a multiplying effect in the context of an overall strategy to create an enabling R&D infrastructure. Conversely, although Brazil spends 1.23%, three times as much on R&D as Chile; Brazil scores at the low end of the BCI spectrum. Thus, it is not a matter of how much you spend, but how well you spend it. Executives surveyed credited the Chilean Economic Development Agency CORFO (*Corporacion de Fomento de la Produccion de Chile*) for designing "Start-Up Chile", a set of concerted government policies dating back to 2010 aimed at making Chile a regional a hub of innovation and entrepreneurship.[41] The Brazil/Chile dichotomy also underscores the importance of a long-term holistic approach to creating an ecosystem with a focus on equally critical policy areas including the

FIGURE 14 BCI Results of Capabilities and Infrastructure (% of total)



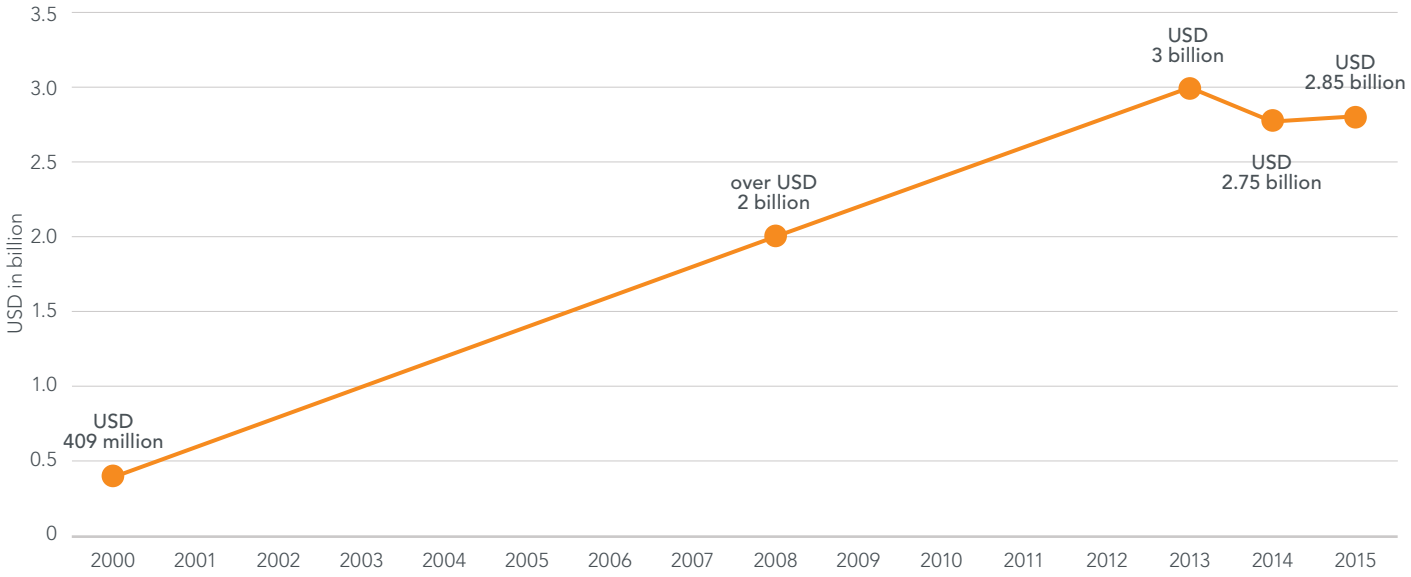
protection of intellectual property, the regulatory environment, technology transfer and market and commercial incentives.

Another example of strategic spending is Costa Rica, which manages to eke out of the pack being a somewhat distant second in the BCI LatAm rankings. Spending on R&D is also on the low end, 0.61% of Costa Rica's GDP, but it is invested in high-impact projects under a concerted National Plan for Science, Technology and Innovation. Critically, projects undertaken under this National Plan have coincided with a steady increase of FDI as shown in Figure 15.[42]

Costa Rica's accession process to the OECD dating back to 2015, further benefitted the investment climate through its broad review of government policy and actions and concrete proposals to improve perceived challenges.[44] More specifically, the Investment Promotion Agency (*Coalición Costarricense de Iniciativas de Desarrollo* - CINDE) develops and implements policies to attract foreign investment with remarkable results: 40 new investment projects started in 2016 in the multinational services, life sciences, advanced and light manufacturing and food industry sectors, and virtually all existing multinationals either maintained or expanded their business footprint in the country.[45] As one of the few Latin American countries with a ministry in charge of science, technology, and innovation (MICITT), together with CINDE Costa Rica is in a strong position to align innovation and FDI promotion policies.[46]

More broadly, Latin America can learn from the Taiwan experience. Their concerted effort to build a competitive scientific capability and infrastructure base for the life sciences started with passage of the Biotech and New Pharmaceutical Development Act of 2007 granting aggressive tax breaks, public funding for R&D, and other incentives to stimulate growth of the biomedical industry. Notably, the policy was focused towards the creation of follow-on technologies instead of pioneering ones. Taiwan created R&D clusters and strong links between public research institutions and the private sector and offered incentives like tax credits. Taiwan's National Development Plan 2017-2020 and plan for 2017 issued by the National Development Council (an inter-ministerial committee) in early 2017 aims to definitively shift the national economic model from high-tech manufacturing to R&D through promoting investment in innovation and carrying

FIGURE 15 FDI in Costa Rica 2000 to 2015[43]



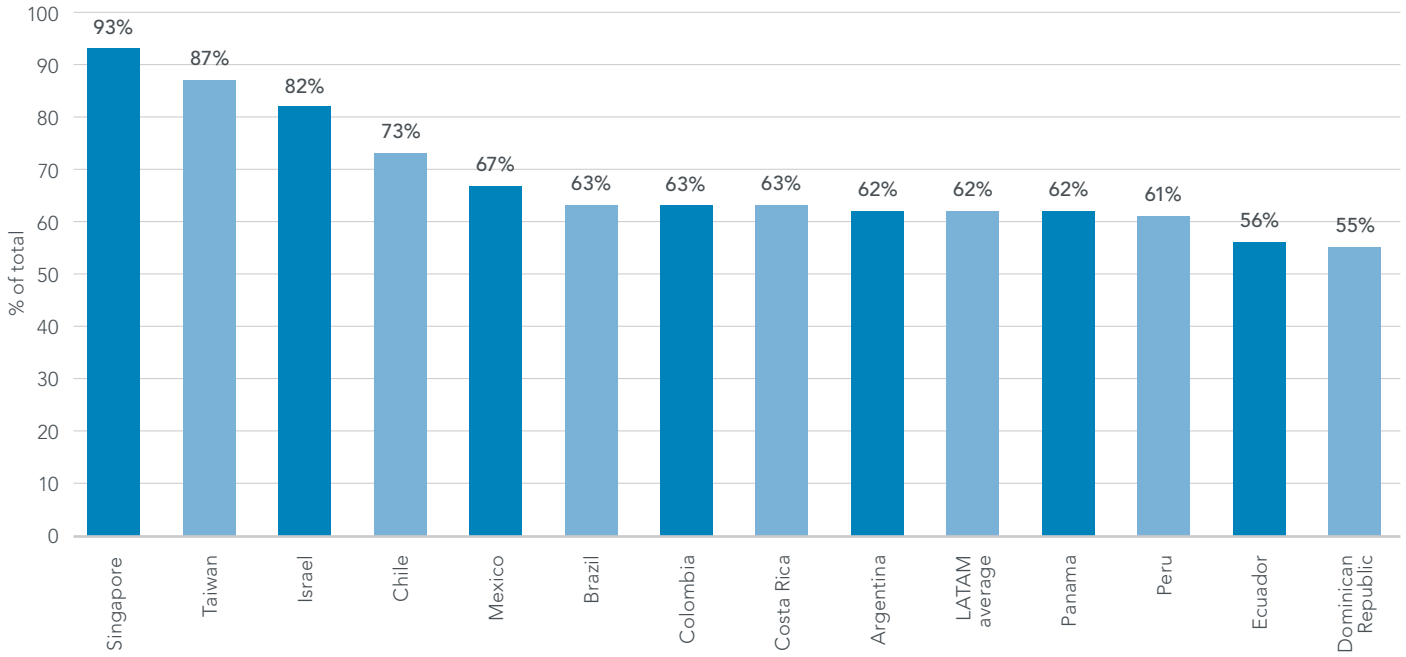
out structural reforms. Biotechnology is among the key sectors prioritized for investment in the plan. Despite having a relatively small biopharmaceutical sector, Taiwan has grown substantially over the past 15 years in part due to the government's emphasis on creating supportive framework conditions including introducing more robust IP protection for life sciences, an international-standard regulatory framework and various incentives and funding for R&D, as well as building on a traditionally strong science base. As of 2015 the biomedical sector was valued at $9,360 million (which was at least a tripling over the previous decade), with around 1,900 companies.[47] Efforts today have shifted towards cluster development and technology transfer support. For instance, a newly opened National Biotechnology Research Park focuses on R&D and product development, providing particular incentives and support for SMEs in pre-clinical and clinical development. New drug development is focused on a number of areas including biologics, cancer, rare diseases and other diseases thought to be incurable.[48] Biomedicine is one of the seven innovative industries targeted in the National Development Plan 2017-2020, with a view to becoming an "Asia-Pacific Biomedical R&D Industrial Center". The Plan identifies areas such as human and physical capital, FDI and growth of biomedical clusters as key areas for strengthening. In November 2016 Taiwan passed the Biomedical Industry Innovation Program, which includes a recently launched Center of Biomedical Industry Innovation focused on promoting FDI and integrating funding.[49]

3.2 Clinical Research Conditions and Framework

As a region, Latin America does slightly better in this category compared to other categories in the BCI. Chile again ranks the highest with Mexico as a close second.

Despite Chile's leading position in this area, local executives surveyed have expressed concern about the proposed Title V of the Ricarte Soto Law (governing high-cost medicines) currently being considered by the Chilean Chamber of Deputies. If enacted, Title V and subsequent regulations would change the clinical trial landscape in three significant ways: 1) Control and surveillance of clinical trials will be exclusively done by the Institute of Public Health – instead of the Clinical Research Review Boards of the entity performing the trial,

FIGURE 16 BCI Results of Clinical Research Conditions (% of total)

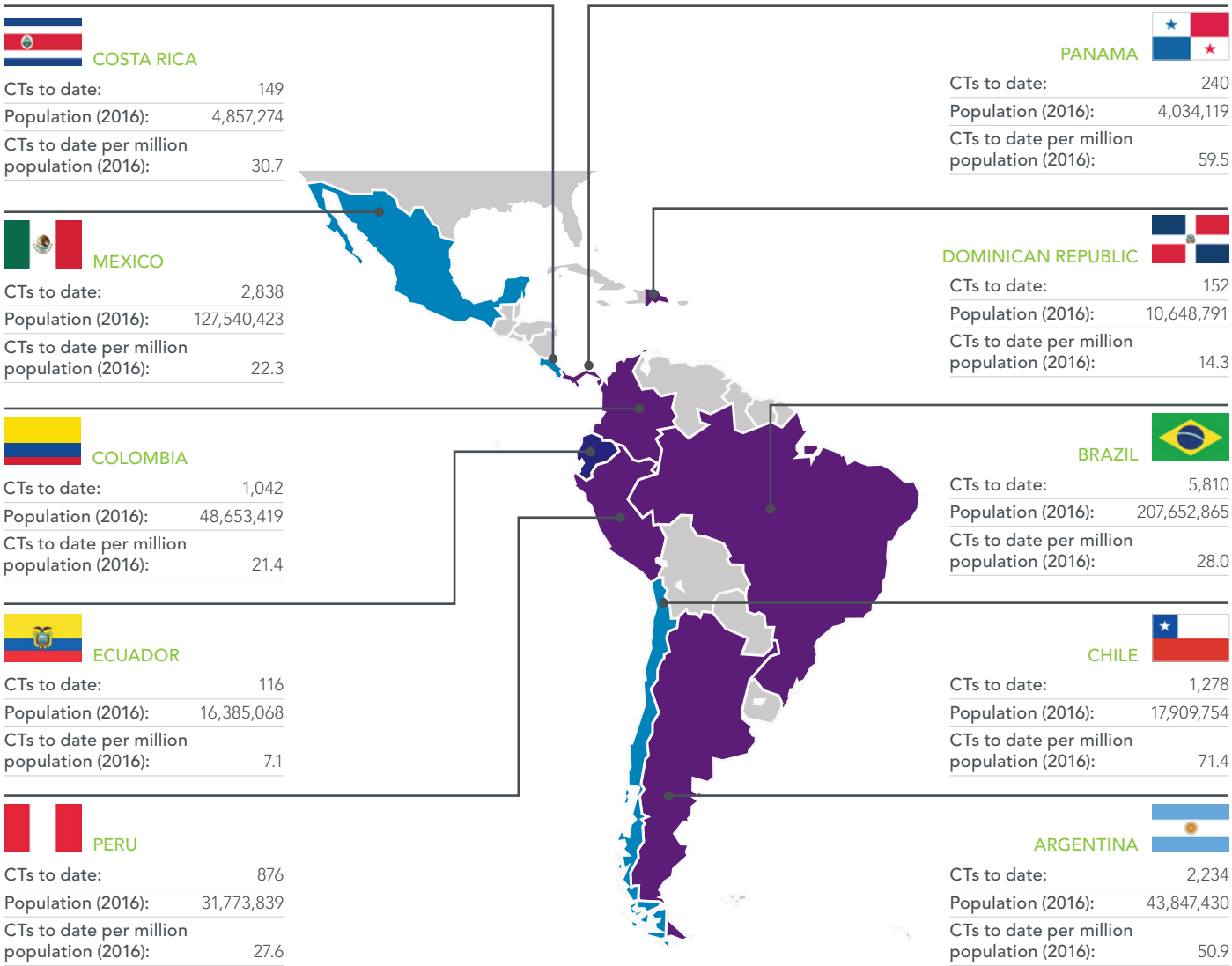


2) a 10-year rebuttable presumption that adverse effects are due to the drug under investigation, and 3) free post-trial access to the medicine by participants of the study. Key stakeholders such as the Chilean Academy of Medicine has expressed its concern that such regime will divert investment in clinical trials away from Chile.[50]

While the area of clinical trials fares somewhat better than other areas measured in the BCI, the region still falls short to effectively compete with biopharmaceutical leaders elsewhere in the world. Although the bulk of clinical research activity takes place in developed countries – which host on average around three times more clinical trials when compared to emerging markets[51] - some emerging markets manage to attract more clinical trials than others.

As discussed, as a region Latin America has not matched the pace of development of other regions such as Asia Pacific. Indeed, despite strong per capita income growth and investment levels over the last decade, clinical research levels for the top performers in Latin America are pretty much at the same level today as they were a decade ago. Conversely, Korea, Israel (another global leader outside the region) and Taiwan

FIGURE 17 Clinical trials to date per million population in ten Latin American countries



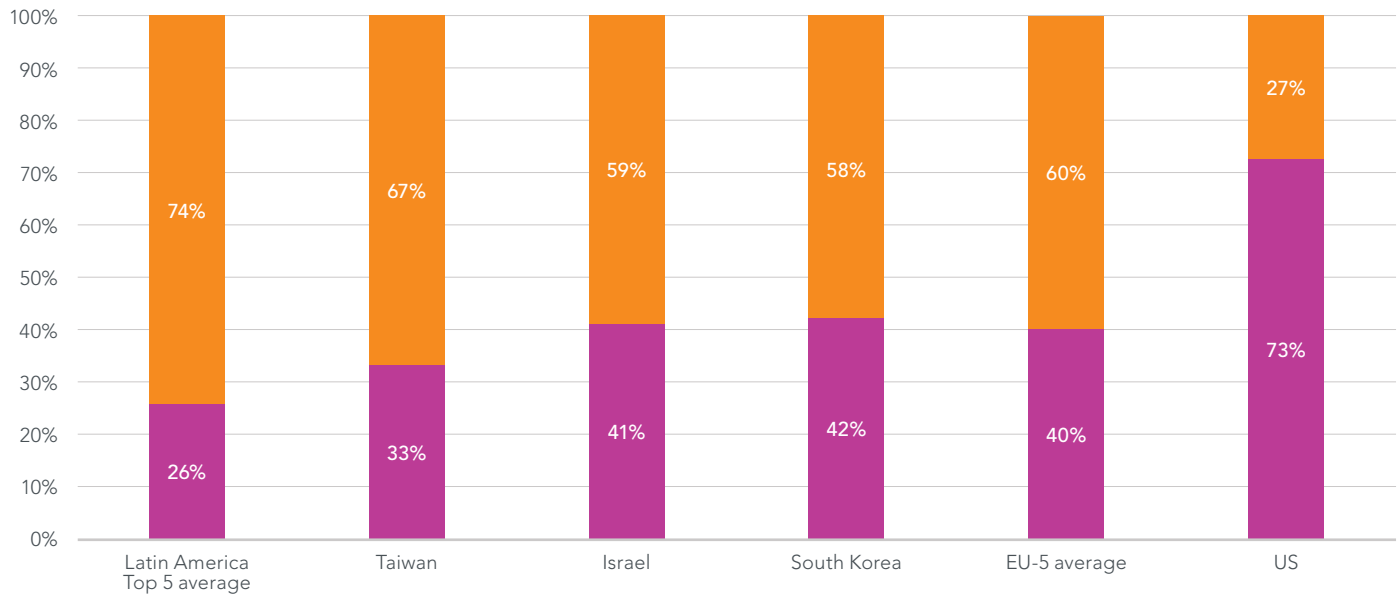
have become attractive hubs for global clinical research. When adjusting for population size, these countries are placed at the top of the list with 150-200 clinical trials per million population in Korea and Taiwan, and up to 770 clinical trials per million population in Israel. By contrast, countries like Brazil and Mexico list with only 1 to 20 clinical trials per million population.[52]

Clearly, Latin America – both as a region and by individual countries – is failing to meet its potential in terms of general clinical trials activity, and is missing out on the numerous advantages that clinical trials can bring to patients, the local scientific sector, and the economy at large. Yet, Latin America is recognizing advantages that can be leveraged to attract clinical research: some countries provide adequate universal healthcare, high-quality healthcare institutions with research-oriented physicians, ease of recruiting patients and relatively low costs of conducting clinical trials.[53]

Critically, leaders among newcomer markets like Israel, Taiwan and Singapore also attract a larger share of the riskier, early-phase trials which represent the cutting-edge research in therapeutic areas such as oncology or of biologic drugs, as is shown in the below Figure 18. Latin America still has not caught up yet.

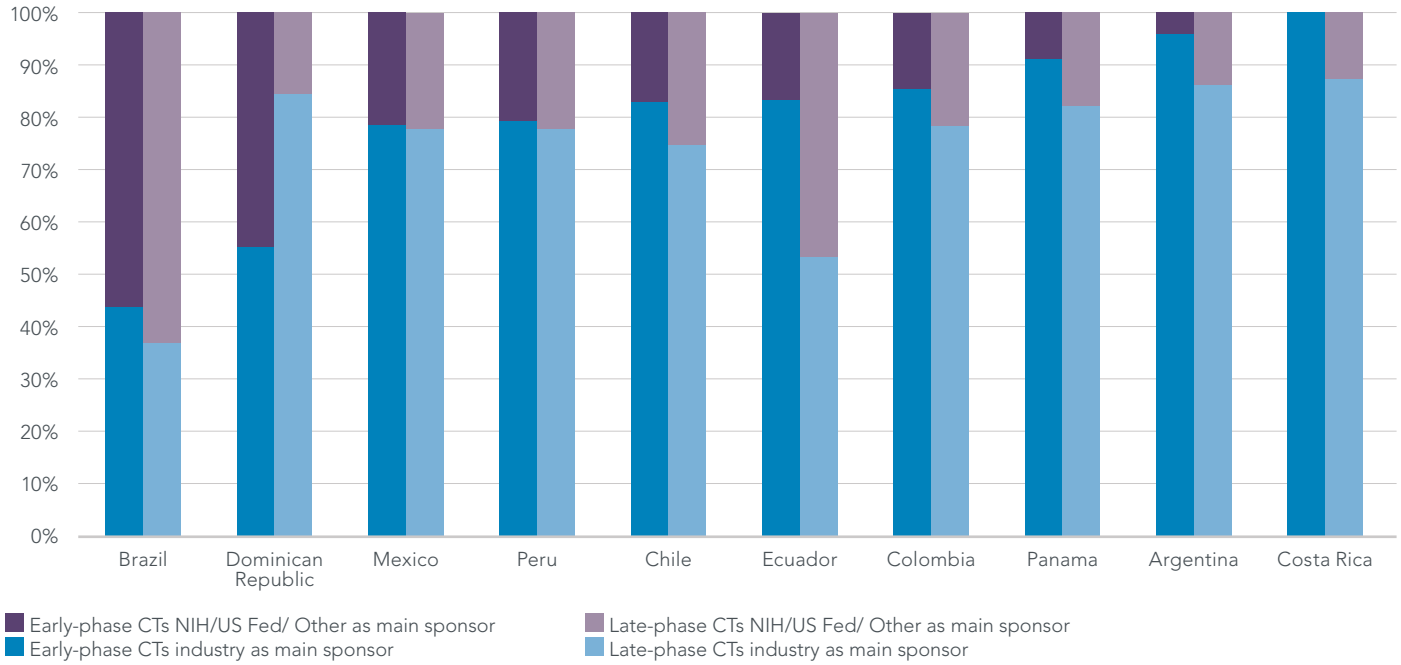
Most of the clinical trials in Latin America are sponsored by the biopharmaceutical industry. In eight of the ten countries examined, 90% of clinical research on average is privately-funded. Brazil is an outlier for both early and late-phase trials, with only 40% involvement of private funds. While on the one hand this may suggest a strong research base including public universities and medical research centers supported by public funds,[55] on the other hand it shows the existence of barriers for industry-sponsored clinical research, including a burden of red tape and long timeframes for approval.[56] Executives surveyed point to the proposed new regulatory framework PL 200 as a significant initiative to lower the barriers for private funds.

FIGURE 18 Early-phase v. late-phase clinical trials on biologic drugs in regional leaders[54]



Source: Clinicaltrials.gov, 2017; analysis: Pugatch Consilium

FIGURE 19 Private/Public Mix in Sponsorship: Early-phase v. Late-phase CTs in LatAm[57]

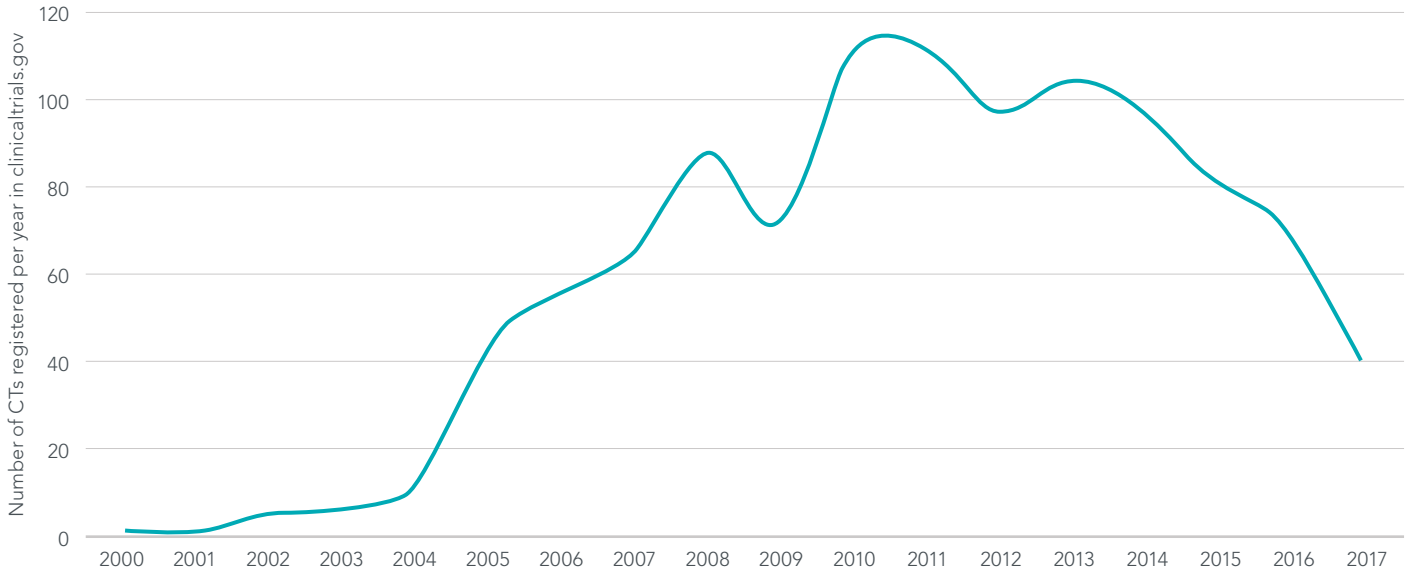


Source: clinicaltrials.gov, 2017; analysis: Pugatch Consilium

Colombia is worth mentioning as a case study of how aggressive improvement in one area can be cancelled out by counterproductive measures elsewhere in the biopharmaceutical sector. Enacted in 2008, Resolution 2,378 brought the then Colombian regulatory framework to ICH standards.[58] More recently, in March 2016 the Colombian DRA INVIMA introduced new timeframes for approval with a target of 60 days.[59] Clinical trial approval is streamlined through simultaneous review of research protocol with quality control evaluations of the drug being tested.[60] Moreover, since February 2017 a specialized entity, the *Sala Especializada de Medicamentos y Productos Biológicos al Grupo de Investigación Clínica de la Dirección de Medicamentos y Productos Biológicos* reviews applications relating to large molecules. Today there are 63 GCP-certified institutional ethics committees and over 120 medical facilities approved by INVIMA for clinical research. Colombia ranks relatively highly in several BCI questions in the Clinical Trial category. A number of global and local CROs operate in Colombia and maintain an open communication with INVIMA, and a US-based clinical development company entered into an agreement with the Government of Colombia to position Colombia as a preferred destination for conducting clinical trials by US-based sponsors.[61] Yet as discussed throughout this report, while these are positive steps to improve the attractiveness of Colombia in one enabling area, the lack of certainty in the IP space and strict pricing regulations crowd-out these positive reforms, as seen in Figure 20 indicating a sharp drop in clinical trial activity.

In contrast, Singapore is a shining example of a country committing to a set of comprehensive, coordinated and long-term reforms and becoming a global leader in clinical trials, and a magnet for biopharmaceutical investment. A key turning point in Singapore's development and a critical part of its overall reform efforts was the US-FTA in the late 1990s which ushered in the modernization of Singapore's IP environment, including the introduction of regulatory data protection and patent term restoration. Similarly, Singapore over the past decade has reformed its clinical trials regulatory infrastructure to make itself more attractive for clinical research. Indeed, clinical trial applications are usually processed within a

FIGURE 20 CT Activity in Colombia 2000-2017[62]



Source: clinicaltrials.gov, 2017; analysis: Pugatch Consilium

timeframe of 30 days, and small-scale clinical trials (such as for the assessment of bioequivalence or food-drug/drug-drug interactions) are processed within a timeframe of only 15 days.[63] Manufacturing today alone is estimated at SGD23 billion, a value close to 5 times higher than in 2000.[64] In relation to FDI, Singapore has made huge strides in attracting investment in both R&D and advanced manufacturing over the past 10-15 years. Around USD500 million in R&D spending (close to half of the total amount spent on biomedical R&D) was provided by foreign biomedical companies in 2013, more than a tenfold increase compared to their R&D investment in 2003.[65] Nearly half of clinical trials in Singapore are for the more complex and cutting edge Phase I and II trials.[66] Indeed, many of the top global research-based companies have also established their regional clinical trial center in there.[67] Moreover, of the top ten research-based biopharmaceutical companies worldwide, seven manufacture a portion of their products in Singapore and eight have regional headquarters in Singapore.[68] Some of them have chosen Singapore as a global manufacturing base.[69] In turn, Singapore now sees a very high presence of innovative drugs in the market; the innovative segment is substantial, at around 60% of the market, while generics represent just a fraction of that figure.[70] Some of these products are ones developed in Singapore itself.[71] Singapore also increasingly supplies international markets. It was the third fastest growing nation globally in the export of pharmaceutical goods from 2000 to 2010,[72] with a growth rate of 503% over the decade.[73] Exports in 2014 were worth USD1.39 billion per million population, i.e. around USD7.5 billion.[74] This is nine times more than the size of its internal market.[75]

3.3 The Regulatory System – Drug Approval, Quality Assurance and Pharmacovigilance

The regulatory landscape in LatAm looks uneven, with Chile, Costa Rica and Mexico performing better than the rest. These regulatory gaps and challenges are negatively affecting the biopharmaceutical ecosystem of these low-scoring countries, and in turn, discouraging foreign investment.

Perhaps one of the most voiced concerns in the global investment community in this regard is Colombia's "third pathway" for "non-comparable" biosimilars as provided in decree 1782 of 2014.[76] This abbreviated pathway for registration of biosimilars allows for the expedited approval of non-comparable products without adequate controls or any clarity regarding the safety or efficacy of the product, and can use the same non-proprietary name as the innovator; when in fact they are not the "same" biologic product.[77] This departure from WHO guidelines heavily influences executives' perception of the Colombian bio-economy, as reflected by the particularly depressed values in the relevant survey questions.

Argentina is another example of how regulatory standards inconsistent with WHO and ICH guidelines can inhibit its bio-economy. More specifically, there are three separate regulatory drug classifications: innovative/original, generic and *similares*.[78] Generics require bioequivalence testing, while *similares* do not; they only need to contain the same active ingredient, concentration, pharmaceutical form and dosage, but can differ in size, shape, packaging and period of activity.[79] Only recently some *similares* in the "high health risk" category now need bioequivalence testing, but the large majority of biopharmaceuticals on the Argentine market are not bioequivalence tested and generics and similares are still used interchangeably.[80] Consequently, there is a great risk for substandard medicines penetrating the supply chain.

Long delays and excessive amounts of red tape is another concern raised by many executives surveyed and reflected in the BCI scores. Notably, Brazil is facing challenges in timely reviewing registrations of new drugs already approved by

FIGURE 21 BCI Results of Regulatory System (% of total)

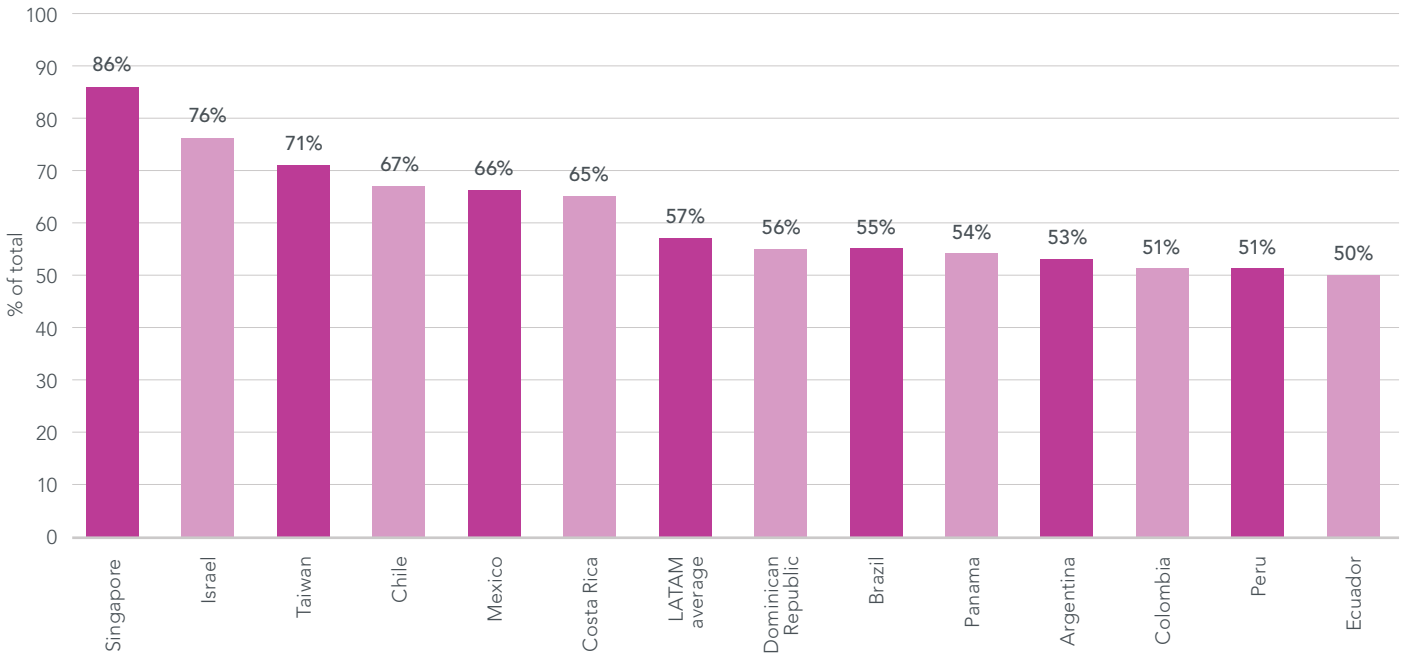


TABLE 3 WHO Guidelines for Biologics

Topic	WHO
Operative legal documents and guidelines	WHO, guidelines on Evaluation of similar Biotherapeutic Products (SBPs)
Market authorisation	
Reference product	Should be authorised in jurisdiction in question (or, where lacks and authorised reference product, in one with well-established framework)
Paradigm to demonstrate biosimilarity	Full (analytical, preclinical and clinical) characterisation and comparison
Preclinical and clinical data requirements	Required, amount and type depends on the product
Post-market asafety and access	
Pharmacovigilance plan	Recommended that a plan be submitted as part of approval dossier that follows the principles of relevant guidelines such as ICH E2E
Naming & labelling	Recommends that abiosimilars be clearly identifiable by a unique brand name
Interchangeability	Must be defined by national authorities; recommends determination be made by physicians
Automatic substitution	Must be defined by national authorities
Regulatory data protection	Not addressed

regulators in mature markets such as FDA or EMA. Unlike other regulatory agencies in the region, ANVISA audits the manufacturing facilities of the applicants, and requires local batch testing of imported medicines – adding to the delay in the approval process.[81]

Conversely, in an effort to attract more biopharmaceutical R&D investment, in 2012 Mexico introduced a fast-track system, which among other elements recognizes existing approvals from leading drug regulatory agencies, including the FDA and EMA. Approval for such new medicines have been reduced from 2+ years to 4.5 months.[82] As such, executives view the Mexican regulatory system as relatively better performing as reflected in the respective BCI scoring.

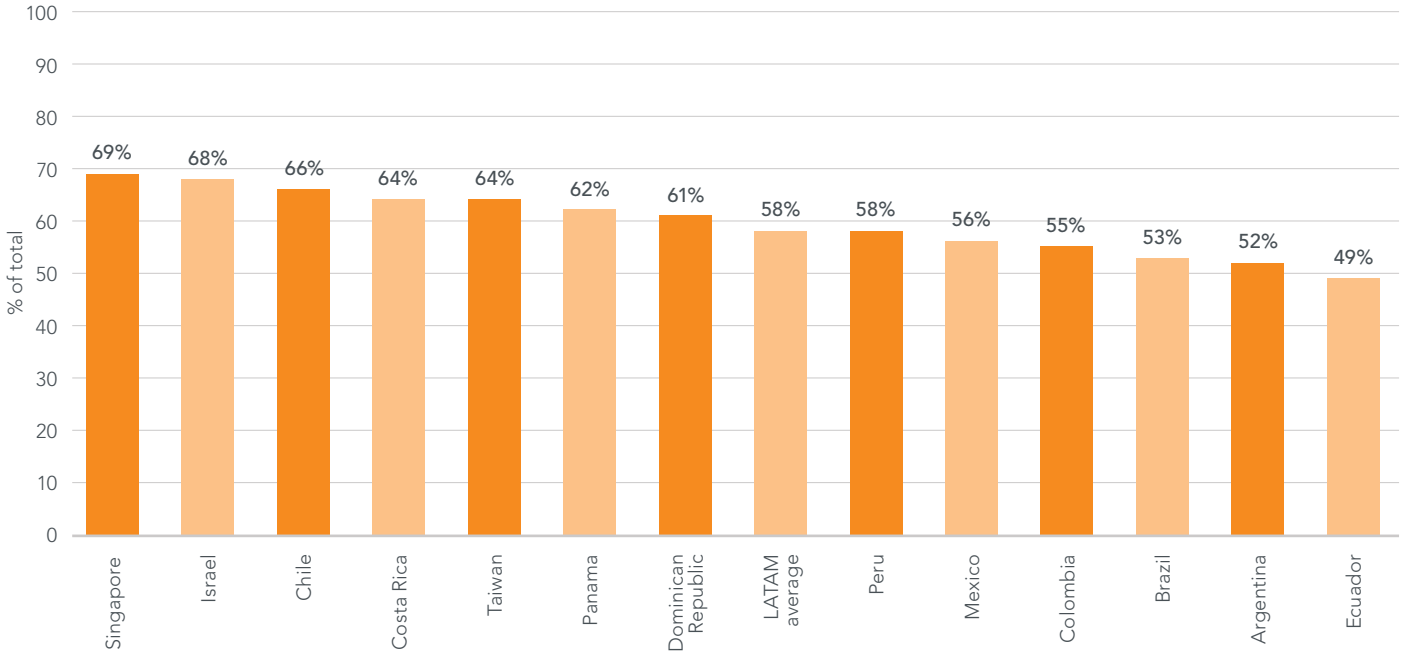
3.4 Market Access and Financing

Like the regulatory landscape, market access and financing also has leaders and laggards but the spread is smaller. Chile and Costa Rica again take leadership, while the majority is trailing. Brazil scored notably low – indeed, together with Ecuador and Argentina, Brazil is struggling to compete in this arena. Price controls is one of the driving factors inhibiting the Brazilian bio-economy, as reflected in the lowest score registered in the survey.

As a region, Latin America is still heavily focused on the traditional transactional approach of lowest bid and price controls. There are no meaningful efforts to look beyond the pill in value-based models. A key enabler for this approach is PAHO's initiative to use its Strategic Fund to purchase medicines on behalf of its 27 member states.[83] The pooled procurement process is aimed to achieving economies of scale and offer products at competitive prices – at the expense of suppliers' ability to negotiate with other entities elsewhere in the world in light of PAHO's on-line data bank of reference prices for everyone to see.[84]

Back to Brazil, its publicly funded healthcare system, SUS, dispenses medicines free of charge.[85] SUS procures medicines according to federal regulations that are notably bureaucratic, opaque, and inefficient.[86] The Medicines Market Regulatory Chamber (CMED) sets three price ceilings for each medicines: factory prices, maximum consumer

FIGURE 22 BCI Results of Market Access and Financing (% of total)



prices, and a discounted (about 25%) public sector prices.[87] All government purchases are done through an open bid, but the basis for the selection of the supplier is usually unclear. [88] Events postdating this survey are likely to depress even more Brazil's BCI scoring. In an effort to further control prices, on July 2017 SUS started to post on-line all prices of medicines negotiated with suppliers. While good for transparency, the move undermines suppliers' ability to negotiate prices elsewhere in the world – giving them pause to fully commit to larger investment plans in the country.

Another example is Mexico's pricing and reimbursement policies for biopharmaceuticals, which while meant to contain raising healthcare spending, instead limit and slow down access to new medicines and technologies. The National Formulary (*Cuadro Basico y Catalogo de Medicamentos*) determines what medicines are reimbursed by public institutions and insurance companies and at what price. The list is rarely updated, and for the most part lists generic medicines. Indeed, data published by IMS Health in 2014 comparing the availability of new molecules in a sample of markets found that Mexico had one of the lowest rates of inclusion of the economies sampled.[89] Out of a total of 154 new NMEs introduced between 2008-12, only 45 were on the Mexican market by 2013.[90] This in comparison to 104 in the US. Additional pressures to further depress drug prices come from recent consolidated national tenders from different government payors, including the Institute for Social Security and Services for State Workers ISSSTE (*Instituto de Seguridad y Servicios Sociales de los Trabajadores del Estado*) and the Mexican Institute of the Social Security IMS (*Instituto Mexicano del Seguro Social*), although the local pharmaceutical trade association AMIIF is gaining traction promoting managed entry agreements and other value-based models among several public institutions.[91]

Colombia also poses a set of challenges in this area. First, approval of biopharmaceuticals is conditioned on pricing requirements.[92] Specifically, pricing decisions must be made as part of the market approval process; elsewhere in the world this is based exclusively on scientific and technical determinations, independent of

pharmacoeconomic or political considerations.

Second, prices in Colombia are typically set from a basket of 17 reference countries, some more developed some less so.[93] On November 22, 2016, however, the National Commission of Prices of Medicines and Medical Devices (*Comisión Nacional de Precios de Medicamentos y Dispositivos Médicos*) issued Circular 03 of 2016, which defines the general pricing methodology applicable to all drugs under a public interest declaration (akin to "public interest" used for compulsory licenses); the lowest price in the basket of reference prices.[94] Subsequently, on December 2016 the National Pricing Commission issued Circular No. 4 of 2016 which sets the price of the oncology drug Glivec at ~44% of its former price.[95] Glivec was already under consideration for a compulsory license on pricing grounds even though no patient access concerns were cited. On the contrary, generics are widely available and the price of Glivec was set and reduced multiple times by the Colombian government under the existing price control regime in Colombia.[96] Following pressures from different stakeholders the Colombian Government on April 2017 issued Decree No. 670, which regulates the use of the public interest measure. This requires that any declaration of public interest will be issued by an inter-institutional technical committee composed of representatives from the Ministry of Commerce, Industry and Tourism and from the National Planning Department in addition to representatives from the Ministry of Health.[97] To date, the Colombian government has not yet issued a compulsory license for the drug.

Such display of hostile policies on price controls have severely hampered incentives to invest in the Colombian bio-economy, as is reflected in the previously reported diminishing activity in the clinical trials. Like in Brazil, the BCI score for Colombia in this category is remarkably low.

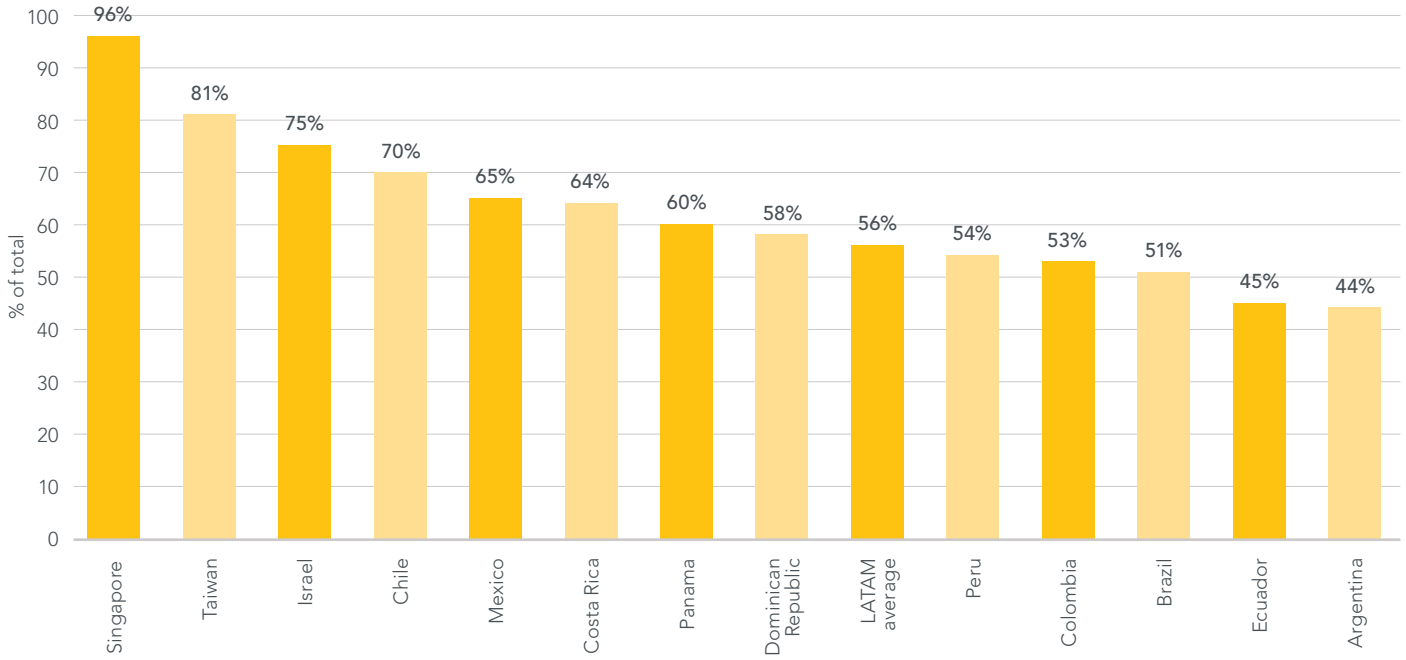
Localization barriers can also inhibit a bio-economy. For example, in an effort to foster a domestic biopharmaceutical sector and protect against supply shortages, Brazil has since 2008 implemented mechanisms whereby foreign access to the local market is tied to the entry of a "Productive Development Program" (PDP).[98] In effect, the Brazilian health agency buys medicines exclusively from a foreign supplier for a period of time -typically 5 to 10 years - provided that the supplier enters into a technology transfer agreement with a local partner.[99] Additionally, the Brazilian regulatory agency (ANVISA) grants "priority review" status to the medicine under PDP, significantly accelerating market entry.[100] Over time, the local partner presumably learns how to produce the medicine, and eventually replaces the originator.[101] While foreign suppliers obtain short-term gains, in the long run PDPs effectively act as semi-compulsory licenses. Whether foreign innovators are comfortable trading away their crown jewels for temporary exclusive market access depends on several factors, but many executives surveyed prefer a market-based approach.

Conversely, Singapore has been, and continues to be, at the forefront of seeking to stimulate public-private partnerships between higher education institutions and industry, particularly in the biopharmaceutical space. Singapore has created a specific body to liaise between universities, public research institutes and industry needs, called the Biomedical Sciences Industry Partnership Office. This body seeks to catalyze and promote partnerships between industry and public-sector research, linking upstream public-sector research with downstream commercialization partners.[102] Building up a high quality biomedical research base has allowed Singapore to attract a number of multinational pharmaceutical companies, which are now supporting the further development of a domestic biomedical industry, particularly in fields of biologics and translational and clinical research.[103]

3.5 Effective IP Protections

Evidence suggests the harder it is to get patent protection in a given country, the less attractive the country becomes for foreign investment. Historically, intellectual property protection in Latin America for biopharmaceutical innovations has been lukewarm at best, and non-existent at worse. Implementation of international intellectual property standards have been notoriously slow, patent examination backlogs are unreasonably long, enforcement actions can languish for years

FIGURE 23 BCI Results of IP Environment (% of total)



mired in excessive formalities, and infringers do not receive proper deterrent judgments. Indeed, virtually all countries sampled in the 2017 BCI LatAm are listed in the Watch List of the USTR's 2017 Special 301 Report, except Argentina and Chile which are in the Priority Watch list.[104] The BCI ranking confirms it by showing the region collectively as falling squarely below half of the total possible score. Again, the exceptions are Chile and Costa Rica, along with Mexico – all three performing relatively better.

Some countries are starting to recognize the importance of effective IP protections for their economy. For example, the Argentinian patent office, INPI has recently created expedited procedures for patent applications already issued elsewhere, is hiring more patent examiners to cut patent backlog, and is finally going digital.[105] In March 2017 INPI and the USPTO started a Patent Prosecution Highway (PPH) pilot program, and a bilateral US-Argentina commission is reporting progress in developing programs to enhance the local IP environment.[106] Yet, Argentina continues to summarily reject pharmaceutical and biologic patent applications, and there is no regulatory data protection, among other shortcomings.[107] In fact, 2016 saw a sharp increase in the refusal rate for pharmaceutical patents, with less than 5% accepted by INPI.[108] As such, executives surveyed scored Argentina at the very bottom of the scale despite progress made so far. The resulting low BCI scoring highlights the importance of a comprehensive approach to enabling a biopharmaceutical sector.

Although Brazil has taken steps last year to reduce its patent backlog averaging 11 years with its PPH with the US and Japan, the effort notably excludes pharmaceutical applications.[109] Moreover, the Brazilian Congress is still considering a pre-grant opposition system in a proposed amendment to the IP Law (PL5402/2013) which would significantly add delay to an already burdened patent examination process.[110] But the most notable drag to the IP environment is Brazil's policy of "prior consent" giving its regulatory agency ANVISA the right to examine – and potentially reject – pharmaceutical patent applications concurrently with the Brazilian patent office INPI.[111] This dual examination approach has been hotly contested in the courts, eventually leading to the publication

on April 2017 of Interagency Ordinance 1.[112] A close look at the Ordinance reveals a further deterioration of Brazil's biopharmaceutical IP environment in many respects. First, Article 2 moves ANVISA's examination to earlier stages in the application, well before the notice of allowance statutorily provided by Article 229-C of the Brazilian Patent Statute. Next, Article 5 specifically mentions drugs "of interest to the drug policies and pharmaceutical assistance of the Public Healthcare System (SUS);" essentially giving ANVISA significant veto power over a broad spectrum of types of medicines. Finally, Article 9 of the Ordinance calls for the establishment of an "Interagency Policy Group" between ANVISA and the INPI for the "harmonization of understandings between the agencies".[113] In effect the Ordinance imposes ANVISA's notably restrictive approach to patentability of pharmaceuticals over INPI's standard operating practices. Local legal analysis sees the Ordinance as a step backwards towards aligning Brazil to international IP standards.[114] Policies like prior consent, designed to impede rather than promote intellectual property standards severely inhibits aspirations to become competitive in the biopharmaceutical sector. Unsurprisingly, executives ranked Brazil quite low in this category.

Patent prosecution is a problem common to the region. Significant backlogs, understaffed and/or undertrained patent examiners, and excessive red tape put the region at a significant disadvantage when competing for international biopharmaceutical investment. Several countries provide for pre-grant opposition, further adding to delays.[115] In the Dominican Republic, for example, pharmaceutical patent applications remain

FIGURE 24 Patent Prosecution in Latin America

Tier	Country Patent Index	
Tier 1	Chile, Costa Rica, Mexico	• Easy prosecution • Less strict examiners: rely mainly on foreign prosecution • Reduced backlog • Patent Prosecution Highway (PPH)
Tier 2	Colombia, Dominican Republic, Panama, Peru	• Strict examiners (difficulties for proving inventiveness) • Reduced to Mid backlog • PPH
Tier 3	Argentina, Brazil, Ecuador	• Strict examiners (difficulties for proving inventiveness) • High Official Fees for exceeding claims, specially Brazil • Restrictions for protection of pharmaceutical inventions • Substantial backlog • Argentina is a Non-PCT country • PPH

Source: Rafael Freire, Clarke, Modet & C°, Brazil (2017)

pending for over a decade, yet there is no patent term adjustment.[116] Enforcement of intellectual property rights is also ineffective.[117] In an effort to address the backlog problem, the Brazilian patent office launched on July of this year its own Patent Prosecution Highway Project together with countries of ProSur, including Argentina, Chile, Colombia, Costa Rica, Ecuador and Peru.[118] This, in addition to PHHs the United States has with Argentina, Chile, Colombia, Mexico and Peru, should help reduce the patent backlog in many countries in the region – provided they include the biopharmaceutical field in the effort.

Breaking with a longstanding tradition of being the regional leader on Intellectual Property protection, the BCI Index ranks Colombia as trailing in the Intellectual Property environment for a number of reasons. First, while Decree 2085 has put Colombia as a pioneer in regulatory data protection since 2002, INVIMA has reportedly ignored the rights of certain innovators and it is unclear whether it applies to biologics.[119] Also, Colombia is taking a closer look at the Brazilian practice of dual examination. Specifically, Article 71 of the National Development Plan 2014-2018 allows the Ministry of Health to weigh in the patent review process. The plan widens the basis for issuing compulsory licenses, including the "risk" of a medicine shortage (Article 70).[120] Together with the potential for a compulsory license for the oncology drug Glivec based on price considerations as previously mentioned, the weakening of the IP environment is hampering Colombia's aspiration of becoming an OECD member.[121] Indeed, prior approval of 23 Committees is necessary before the OECD Council grants accession. To date, two Committees are still evaluating Colombia's policies, one of which is the Trade Committee which on April 2017 raised concerns about the deterioration of the IP environment and access to innovative medicines (Article 72 linking sanitary registration to pricing decisions).[122] Continuing along this policy route can delay or even threaten Colombia's accession to the OECD, and hurt its aspiration to become a biotechnology nation.[123]

The IP environment in Chile represents a drag in an otherwise relatively promising biopharmaceutical ecosystem. Enforcement of patent rights is relatively lax and hindered by gaps in the legal framework and expertise in IP law among judges.[124] Chile also continues to protract implementation of regulatory data protection provided in the US-Chile FTA.[125] More recently, the Chilean Chamber of Deputies passed on January, 2017 a bill directing the Ministries of Economy and Health to use compulsory licenses based on price considerations and to import less expensive generic versions.[126] The government is currently considering compulsory licenses for the prostate cancer drug Xtandi and hepatitis C drug Sovaldi.[127] This sudden deterioration in the Chilean IP environment post-dates the BCI Survey. Future BCI Surveys will measure the impact of these developments on the potential that Chile has towards becoming a regional innovation hub.

Together with Argentina, Ecuador struggles to compete in the IP area for many reasons. First, Ecuador has actively embarked - although recently to a lesser degree- in an effort to weaken its IP environment through the overt manipulation, and frequent expropriation, of intellectual property.[128] Also, in 2012 patent filing fees spiked upwards of 3600% rendering Ecuador a virtually impossible destination for patent applicants – although in 2016 fees have decreased to more international levels, albeit still at the high end.[129] Finally, the Asamblea Nacional adopted on December 2016 the new *Código Orgánico de Economía Social del Conocimiento, la Creatividad y la Innovación* (*Código Ingenios*) which significantly erodes Intellectual property rights. For example, Article 268 increases the number of non-patentable subject matter to include a wide range of biopharmaceutical innovation, Article 273 excludes biopharmaceutical innovations not researched in Ecuador, Article 274 eliminates any patentability of second use inventions, and Article 310 requires local manufacturing. [130] Notably, Article 509 provides for a 5-year regulatory data protection; a promising stride in an otherwise opposing current.[131]

On compulsory licensing, nearly all respondents indicated how a mere consideration of compulsory license for medicines can severely undermine future expansion plans or direct investment in a given country. The threat -or worse, the actual issuance of a compulsory license- can set a

pervasive and long-lasting precedent tainting the biopharmaceutical environment. For instance, executives in Brazil noted how the compulsory license issued a decade ago for a patent covering an HIV drug still remains a consideration weighing against investment decisions. To be sure, the threat does not need to be directed at the company in question; the issue taints investment considerations of **everyone** in the sector. Today the competitor may be facing the challenge, but nothing stops a country from issuing a compulsory license to somebody else tomorrow.

A note on second use patents. Despite TRIPS Article 27.1., Andean Community members (Colombia, Ecuador, Peru and Bolivia) continue to refuse to recognize patents for second uses citing several legal opinions from the Andean Court of Justice (ACJ).[132] (89-AI-2000, 01-AI-2001 and 34-AI-2001). This has adversely affected local efforts to evaluate additional therapeutic benefits of known molecules in order to provide more effective solutions for unsatisfied medical needs.[133]

The Israeli experience protecting intellectual property is illustrative for Latin America. Since the mid-2000s Israel strengthened key components of its biopharmaceutical policy environment (including root and branch reform of its IP framework). Following a 2010 Memorandum of Understanding with the US, Israel carried out significant improvements in key areas of biopharmaceutical IP protection, including in relation to regulatory data protection, patent term restoration and legal remedies for infringement. And the positive results can be seen today. Two decades ago the biopharmaceutical sector consisted mainly of research organizations and early stage companies focused on licensing out technologies, with little development and commercialization of biopharmaceuticals and biomedical technologies in Israel. But today according to the Office of the Chief Scientist's 2015 Innovation Report, the number of life sciences companies in Israel has increased by more than five times in the past 15 years (from 200 in the late 1990s to around 1,100 in 2015) and the sector represents around 18% of total exports.[134] Today at least 40% of the total biopharmaceutical sector includes companies involved in biopharmaceutical discovery, development and delivery (with 22% engaged in drug discovery).[135] Despite a small domestic market, Israel hosts 19 local subsidiaries of research-based multinational biopharmaceutical companies. Besides being traditionally involved in importing and marketing of their products, multinational research-based companies are active in R&D activities and play a critical role in cooperating with local firms and creating a vibrant innovation start-up platform. Israel attracts a high level of R&D investment from PhRMA member companies; they invested USD8.8 million per million population in 2012 – a level comparable with Japan and leading EU markets. The Israeli innovative sector not only continues to play a role in many new biopharmaceuticals (with contributions from Israeli-developed technologies to a number of recent "blockbuster" biopharmaceuticals estimated at around 25%), but is also leading the development and marketing of cutting edge treatments, such as the Israeli company Protalix's BioTherapeutics plant cellbased enzyme replacement therapy for Gaucher disease.[136]

TABLE 4 Summary of Policy Developments at Country Level

	R&D/Clinical Research	Regulatory Framework	Market Access & Financing	Effective IP Protection
Chile BCI Score: 69.3%	CORFO credited for strategic spending, but still low at 0.38% Concern about proposed Title V of Ricarte Soto Law; otherwise reported as excellent for CTs	Some concerns over standards for approval of similares Room for improvement, leverage reference agencies (FDA, EMA)	Innovation Fund is limited in practice; additional discounts applied to tenders Formularies need update	Threat of CL, limited patent Linkage PPH in place Priority Watch List in 2017 in part for failing to implement RDP
Costa Rica BCI Score: 63.6%	CINDE and MICITT credited for coordinating set of coordinated policies enabling R&D Room for improvement in collaboration agreements	Extensive delays in regulatory approvals	No direct price controls but lacking transparency in reimbursement and procurement	Patent backlogs but country provides term restoration if delay exceeds 5 years Watch List in 2017 in part for failing to implement RDP, room for significant improvement in enforcement
Mexico BCI Score: 63.1%	Low R&D spending, uneven collaboration (IMSS low, SSA high) Largest HC entity (50 million insureds) opened broadly to run CTs	Pharmacovigilance done by industry. Opportunity to partner with stakeholders New policies at COFEPRI to streamline and speed up CTs and drug approvals yielding positive results Fast track for drugs previously approved by FDA or EMA	Still out-of-pocket in many areas – still room for improvement While no price controls, reimbursement in pesos do not catch up with inflation and devaluation vs dollars Outdated formularies, lowest rate of inclusion of new drugs	PPH in place RDP and Linkage for chemical entities. Unclear for biologics Uncertainty on impact of future NAFTA and TPP Watch List in 2017 in part for across-the-board budget cuts impacting IP enforcement
Panama BCI Score: 58.6%	Substandard R&D and clinical capabilities, excessive delays in CT approvals, lack of CROs Good pockets of compliance with GCPs	Slow drug approval even if FDA and EMA previously approved Lack of skills to handle approval of biosimilars	Enabling policies on pricing Preferential treatment to local competitors, procurement heavily generic focused	ProSur PPH RDP policies in place Neither Watch List nor Priority Watch List in 2017
Dominican Republic BCI Score: 56.6%	Substandard R&D and CRM capabilities Excessive delays in CT approvals Low cost to run CTs	Some regulatory improvements reported Still reported gaps in NDA, biosimilar approval and GMP compliance	Enabling policies in pricing and reimbursement Comprehensive formularies Local preference in bidding, lack of transparency	New commitment for priority review of long-pending applications, hiring new examiners. Watch List in 2017 in part for lack of patent term adjustment and poor implementation of RDP

TABLE 4 Summary of Policy Developments at Country Level (continued)

	R&D/Clinical Research	Regulatory Framework	Market Access & Financing	Effective IP Protection
Colombia BCI Score: 55.6%	Significant improvements in CT regulations and compliance, but needs better R&D capabilities Still reported excessive delays in isolated CT approvals	Conditioning drug approval to pricing and Third Pathway for biosimilars is deteriorating environment Regulators ill-equipped to handle review of biologics	Detrimental international price referencing and "public interest" pricing policies Formularies ranked as comprehensive	ProSur and US PPH RDP in place, unclear for biologics Detrimental threat of CL on pricing grounds and risk of shortages. Implementation of prior approval practices Watch List in 2017 with an OOC Review in part for detrimental IP policies in its NDP
Peru BCI Score: 58.6%	Poor collaboration with national R&D entities with sub-standard capabilities Excessive delays in CT approval. Patient population eager to participate in CTs	Excessive delays in approval, even if previously approved by FDA or EMA Gaps in BE requirements, red tape/ duplicative testing	Competitive pricing and reimbursement policies, but lack of transparency in implementation Pro-generic formulary	ProSur and Pac Alliance PPH RDP in place, unclear for biologics Ineffective remedies for infringement Watch List in 2017 in part for not fully implementing RDP
Brazil BCI Score: 54.5%	Excessive delays in CT approval Poor collaboration with research institutions Despite increased investment, R&D infrastructure remains outdated	Excessive delays in approval, ANVISA inspects manufacturing facilities All imports need local batch testing	Excessively stringent price control and reimbursement policies Access conditioned to tech transfer to locals (PDP). New regs increase transparency and accountability of PDPs	ProSur and US PPH No RDP available Satisfactory IP protection available New policies strengthening prior consent Watch List in 2017 in part for excessive patent backlog
Argentina BCI Score: 53.4%	Excessive delays in CT approval Poor collaboration with research institutions Outdated R&D infrastructure, but skilled human capital.	Substandard review of generics and biosilimars (similares). Poor quality control	Preferential treatment to local competitors Lack of transparency and restrictive pricing and reimbursement policies	ProSur and US PPH No RDP available Initial bilateral discussions with US on IP matters Priority Watch List in 2017 in part for ineffective enforcement, patent backlog, summary rejection of pharma patent applications and lack of RDP
Ecuador BCI Score: 50.1%	Substandard R&D and CRO capabilities Excessive delays in CT approvals	Slow drug approval even if FDA and EMA previously approved Lack of skills to handle approval of biosimilars and GMP compliance	Lack of transparency and restrictive pricing and reimbursement policies	ProSur PPH New RDP for 5 years, but may be ineffective if regulators bypass BE requirements New local working requirements Watch List in 2017 in part for Ingenuity Code banning pharma patents and poor IP enforcement

4 ECONOMY-SPECIFIC FINDINGS AND PROFILES

Introduction

The section presents a summary and analysis of each individual economy's overall and category scores.

Each profile first displays the overall BCI score in relation to the top scoring economy as well as the average score in Latin America. Where possible, the overall score is also presented in comparison to a market's score in the previous two editions of the BCI Survey (markets added in 2017 are presented with their respective investment attractiveness classification).

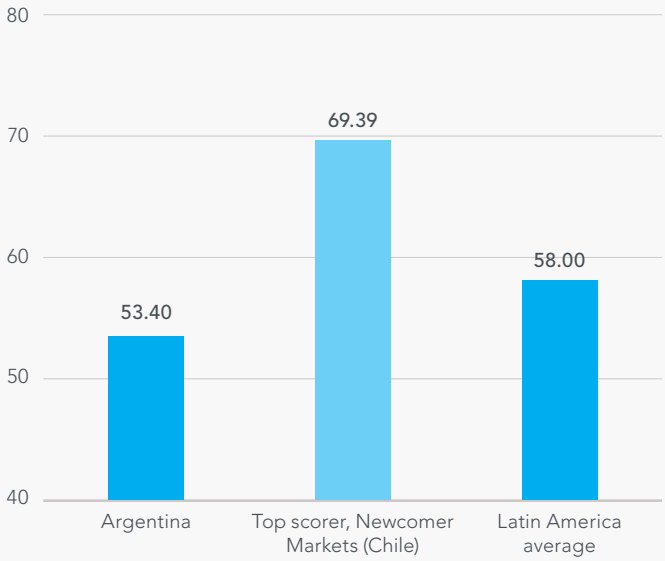
The profiles also provide a comparative analysis of the economy's score and performance by category (in terms of share of the total possible score), both in relation to the top scoring economy as well as how economies' scores are changing over time. In this respect, year-on-year trends in an economy's category scores are examined in terms of which scores rose, fell or stayed the same and which categories represent the driving factors behind a given economy's performance (based on the top and bottom scoring categories relative to the other categories). For economies added in 2017 instead of year-on-year trends, this section presents economies' category scores in light of whether they support or undermine biopharmaceutical competitiveness.

Finally, drawing on BCI responses and comments, a more in-depth analysis and explanation of the economy's BCI scores is provided. This section includes the key strengths, weaknesses, and trends identified by executives.

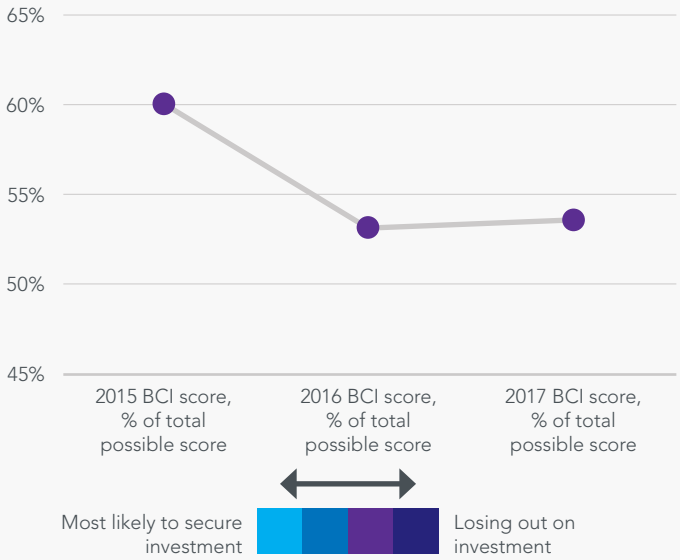
ARGENTINA

BCI Survey 2017 – Overall Scores

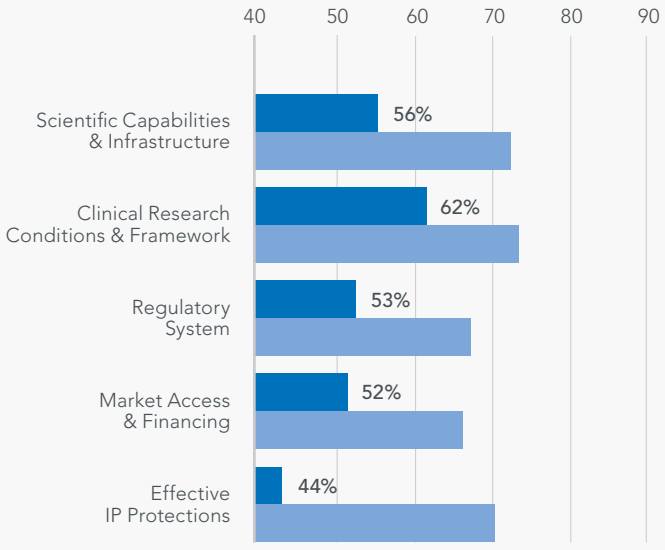
Comparison to Newcomer Markets



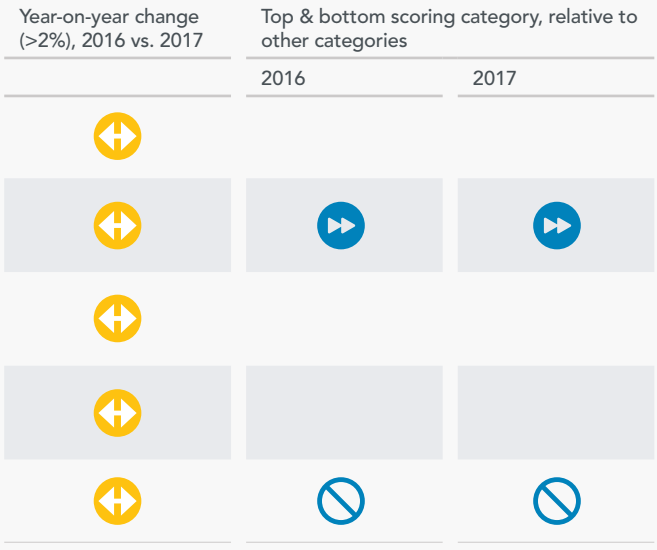
2015-2017



BCI Survey 2017 – Category Scores



Argentina, % of total possible score
Top scorer, Newcomer Markets (Chile), % of total possible score



Score rose · Score remained the same (<2% change in score) · Score fell
Top scoring category (SLOW indicates a top scoring category <60% or where significant challenges remain) · Bottom scoring category

BCI Results In Depth: What helps and what hinders Argentina's biopharmaceutical competitiveness?

Scientific Capabilities & Infrastructure

✘ Though academic and research entities are viewed as sophisticated and executives welcome recent efforts to strengthen innovation (such as establishment of the Innovation and Creativity Forum under the TIFA with the US), focus is mainly on other sectors and capabilities remain basic in relation to biopharmaceutical R&D.

✘ Executives regard opportunities for collaborative R&D and technology transfer in biopharmaceuticals as not properly leveraged.

Clinical Research Conditions & Framework

✔ Private clinical research capabilities (especially among CROs), including generally high compliance with global clinical standards (GCP), are seen as a relative strength, though not used to their full potential.

✘ Long clinical trial approval delays, red tape and gaps in technical capacity at ANMAT remain an impediment, though ANMAT recently committed to shorten timelines.

The Regulatory System

✘ Executives expressed concern that scrutiny of *similares* remains limited and capabilities and standards for review of biosimilars inadequate and out of sync with WHO guidelines.

✔ Capacity for review of new biopharmaceutical products is considered more developed and up to international standards.

Market Access & Financing

✘ Executives report that pricing and reimbursement models continue to be focused on the lowest price, and formularies do not factor in pharmacoeconomic data and quality.

✘ Stricter requirements applied to foreign companies and low rate of inclusion of new treatments in public reimbursement and procurement impact negatively on business plans.

Effective Intellectual Property Protections

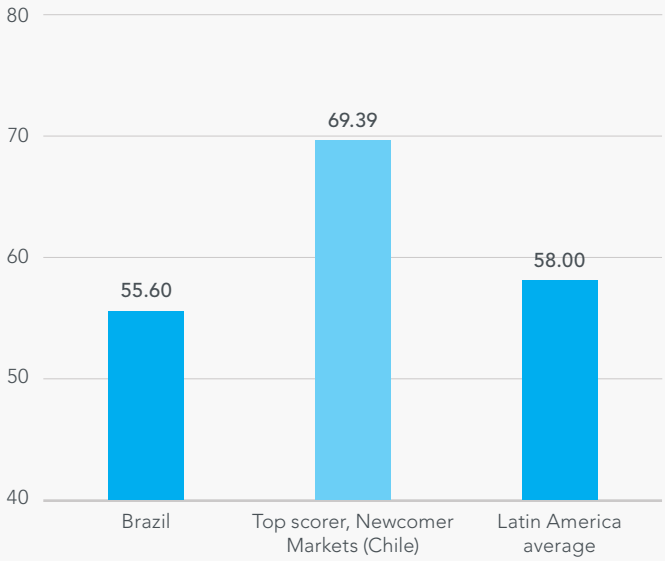
✘ Summary rejections of biopharmaceutical patents and lack of effective patent enforcement and RDP continue to weigh against greater investment.

✔ Consensus exists that efforts to modernize the patent office and speed up pendencies (such as through hiring of additional examiners and creation of Patent Prosecution Highways with the US and ProSur) are positive steps.

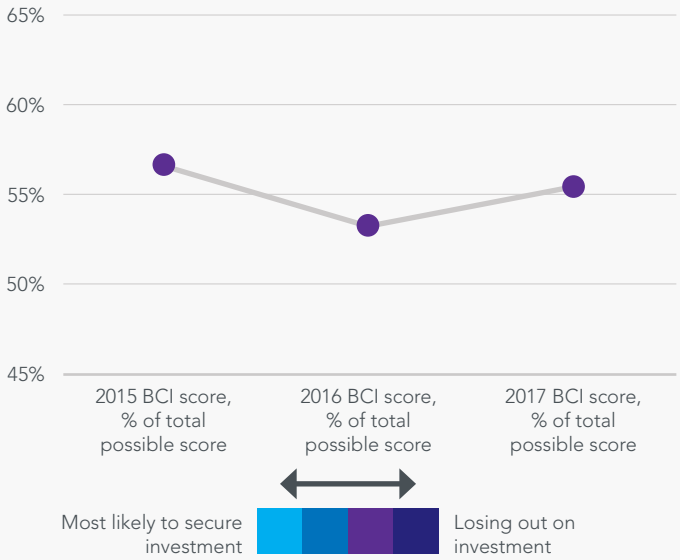
BRAZIL

BCI Survey 2017 – Overall Scores

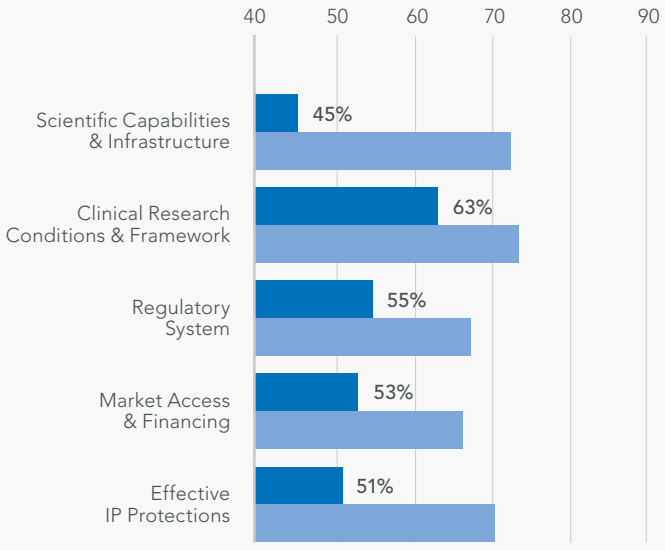
Comparison to Newcomer Markets



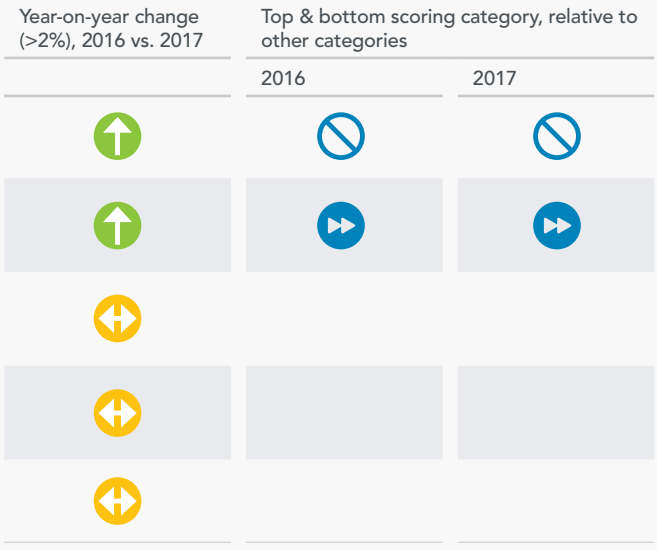
2015-2017



BCI Survey 2017 – Category Scores



Brazil, % of total possible score
Top scorer, Newcomer Markets (Chile), % of total possible score



Score rose · Score remained the same (<2% change in score) · Score fell
Top scoring category (indicates a top scoring category <60% or where significant challenges remain) Bottom scoring category

BCI Results In Depth: What helps and what hinders Brazil's biopharmaceutical competitiveness?

Scientific Capabilities & Infrastructure

- ✘ Though they view the level of funding for R&D more positively in 2017, executives see no comprehensive, long-term national policy or cohesive set of strategies to help modernize Brazil's scientific infrastructure and boost the volume of R&D professionals.
- ✘ Respondents note that the Brazilian PDP model has not led to a measurable increase in biopharmaceutical R&D capabilities, with PDPs often requiring extension due to inability to produce the medicine locally.

Clinical Research Conditions & Framework

- ✘ Executives cite excessive approval times for clinical trials – particularly for biologics – but welcome Law 200, which if implemented is expected to improve the accreditation of ethics committees and allow for fast track approval of clinical trial protocols.
- ✔ Clinical research capabilities among hospitals and CROs are viewed as fairly developed, with some room for improvement.

The Regulatory System

- ✘ Executives view drug approval as remaining excessively slow, unpredictable, and lacking in transparency.
- ✔ While respondents are encouraged by ANVISA's practice to routinely require more stringent evaluation of biosimilars (including clinical testing), some concerns exist about the possibility of using a less strict pathway.

Market Access & Financing

- ✘ Executives report a poor environment: very few innovative medicines are included in the national formulary, reimbursement is increasingly convoluted and cost-based, and ANVISA gives preferential treatment to local companies in the public procurement system.
- ✘ High taxes on imports are also mentioned as an additional barrier to accessing the market.

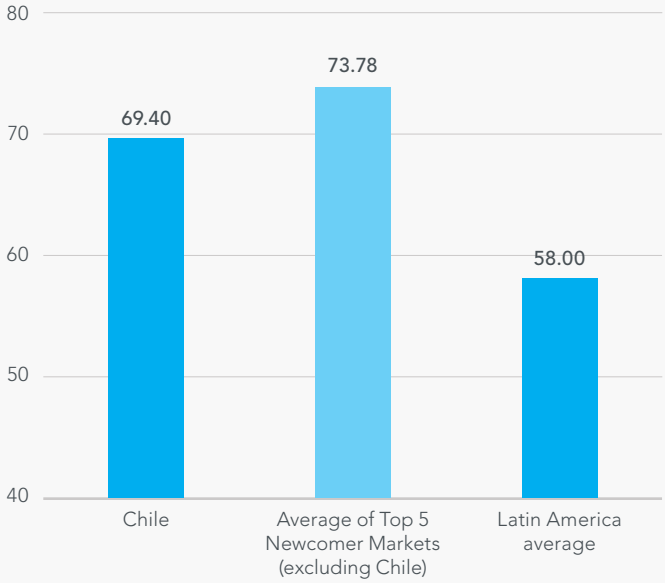
Effective Intellectual Property Protections

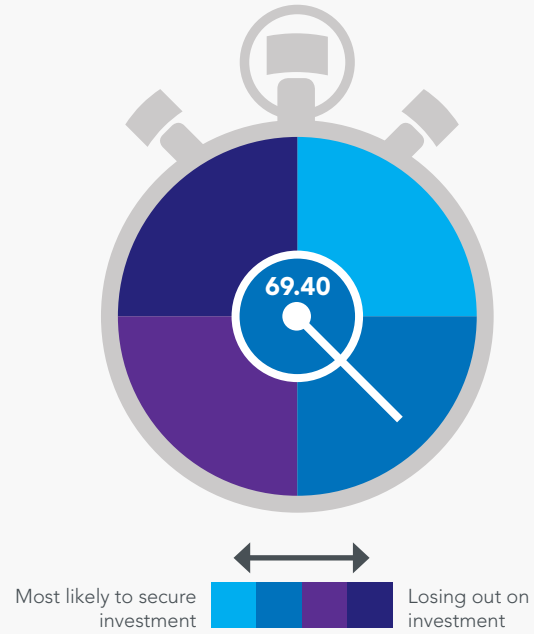
- ✘ Executives note that creation of the PPHs do not necessarily include pharmaceutical patent applications and may therefore not address the 10 year+ backlog.
- ✘ Concern remains regarding the policy of dual examination by ANVISA and INPI (including that it may have been reinforced through the two agencies' recent agreement) and continued denial of RDP to biopharmaceuticals.

CHILE

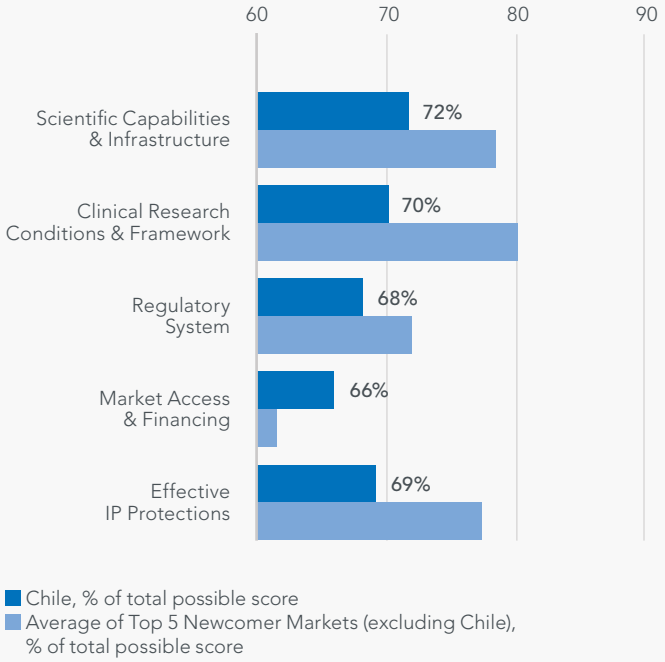
BCI Survey 2017 – Overall Scores

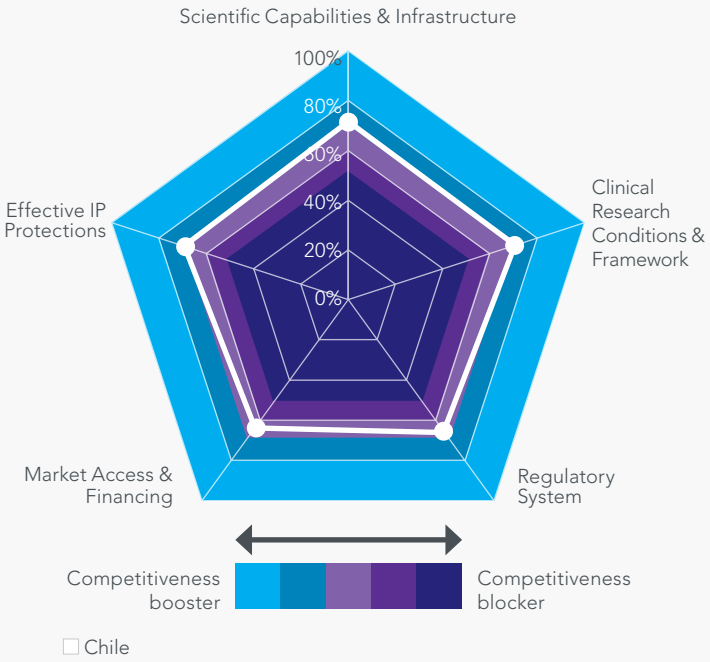
Comparison to Newcomer Markets





BCI Survey 2017 – Category Scores





BCI Results In Depth: What helps and what hinders Chile's biopharmaceutical competitiveness?

Scientific Capabilities & Infrastructure

✔ Despite a per capita R&D spending below the OECD average, executives see resources being invested strategically and consistent with an overall plan to turn Chile into a regional R&D hub.

✔ While biopharmaceutical R&D partnerships and infrastructure are considered nascent, they are seen as developing steadily.

Clinical Research Conditions & Framework

✔ Respondents rate the clinical trial environment fairly highly, with good CRO infrastructure and streamlined approval process, though the main hospitals and clinics are seen as lacking clinical research centers.

✘ Some aspects of the recent "Ricarte Soto" law (including lengthy sponsor liability) have created significant uncertainty, with executives voicing concern that it may hamper investment in clinical research.

The Regulatory System

✔ Executives rate positively the regulatory environment, noting high regulatory standards relating to biopharmaceuticals, and welcome the fact that Chile is seeking to become a Level 4 PAHO/WHO accredited regional authority.

✘ Concerns remain, however, over what are considered to be low approval standards for biosimilars.

Market Access & Financing

✘ Respondents report that heavy discounts negotiated in public tenders by CENABAST weigh down investment attractiveness.

✔ Executives are optimistic about efforts to increase the level and scope of funding for high-cost treatments under the Ricarte Soto Law, as well as what they consider an openness to value-based models by the health regulator.

Effective Intellectual Property Protections

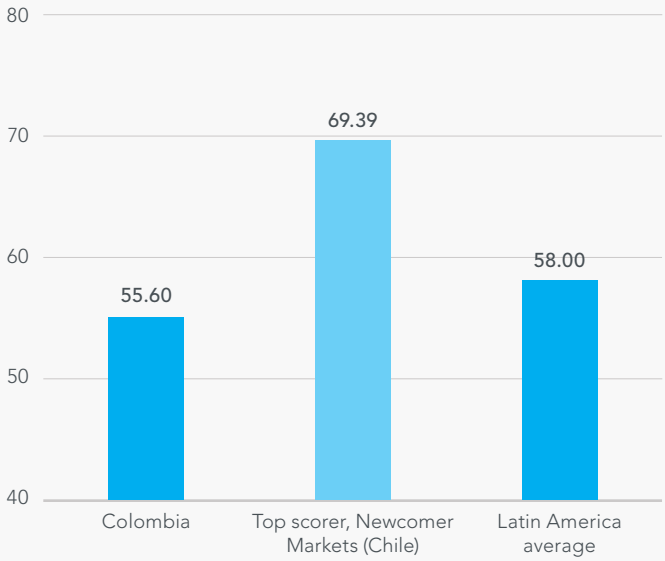
✘ Respondents view slow implementation of RDP and the recent threat of compulsory licensing based on pricing considerations as hindering an otherwise promising national efforts to turn Chile into a hub of innovation.

✔ The patenting process is viewed fairly strongly, with executives welcoming the Patent Prosecution Highway with ProSur and hiring of additional skilled examiners.

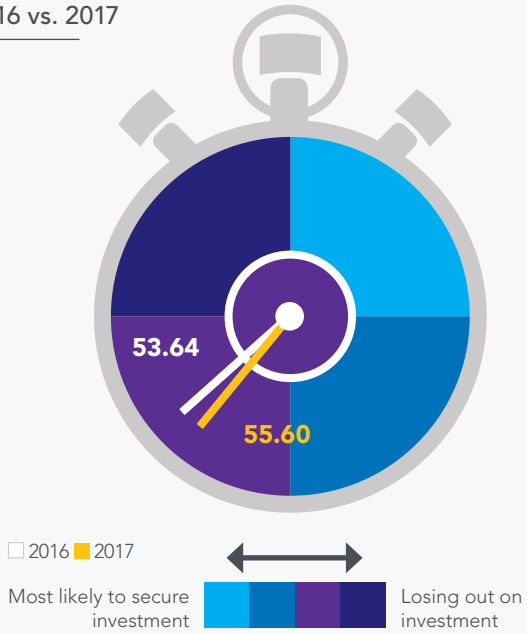
COLOMBIA

BCI Survey 2017 – Overall Scores

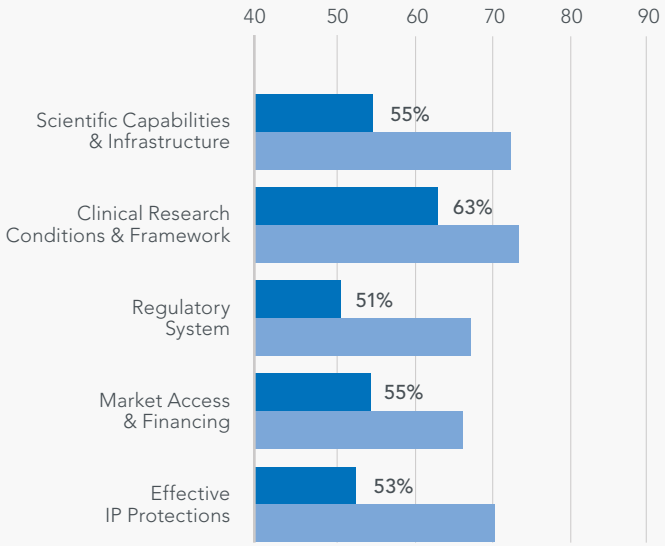
Comparison to Newcomer Markets



2016 vs. 2017



BCI Survey 2017 – Category Scores



Colombia, % of total possible score
Top scorer, Newcomer Markets (Chile), % of total possible score

Year-on-year change (>2%), 2016 vs. 2017	Top & bottom scoring category, relative to other categories	
	2016	2017
↔		
↔	⏩	⏩
↑	⊘	⊘
↓		
↑	⊘	

Score rose · Score remained the same (<2% change in score) · Score fell
⏩ Top scoring category (◈ indicates a top scoring category <60% or where significant challenges remain) ⊘ Bottom scoring category

BCI Results In Depth: What helps and what hinders Colombia's biopharmaceutical competitiveness?

Scientific Capabilities & Infrastructure

- ✘ Current scientific research infrastructure is still considered sub-standard, though the government's commitment to training highly-skilled professionals in its National Development Plan 2014-2018 is viewed positively.
- ✘ Executives indicate that while some collaboration with industry takes place between high level educational and research institution, very few have tangible results.

Clinical Research Conditions & Framework

- ✔ Respondents report a growing level of clinical research capabilities among hospitals and CROs.
- ✔ Executives note that recent adherence to ICH standards and streamlined timeframes for clinical trial approval has already attracted several global CROs, though deterioration in other aspects of the biopharmaceutical environment could detract from this growth.

The Regulatory System

- ✘ While executives cite a slight improvement in regulatory timelines, they largely still view INVIMA as bureaucratic and under-staffed and the regulatory process as lacking transparency.
- ✘ Consensus exists among executives that the abbreviated "third pathway" for follow-on biologics is creating uncertainty with regards to the quality, safety and efficacy of medicines.

Market Access & Financing

- ✘ Respondents view as counterproductive current policies attempting to achieve significant price cuts and reimbursement limits.
- ✘ Executives also warn that more extreme price control measures, including the threat of using compulsory licensing and the public interest declaration route outlined in 2016/17, can in the long-run crowd out any headway achieved in other areas.

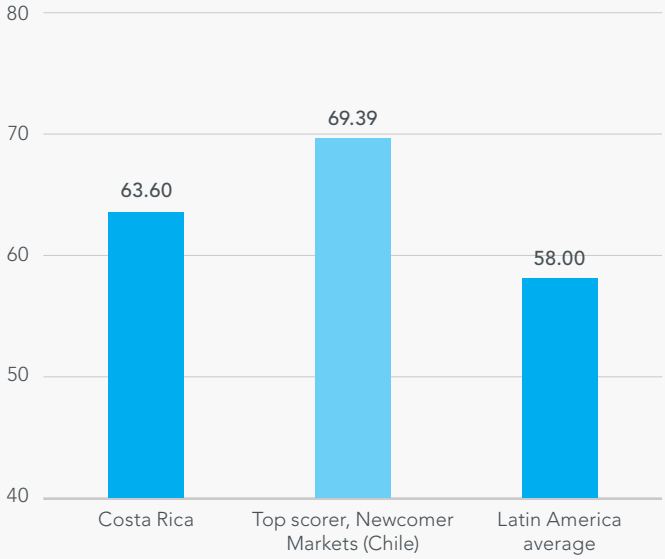
Effective Intellectual Property Protections

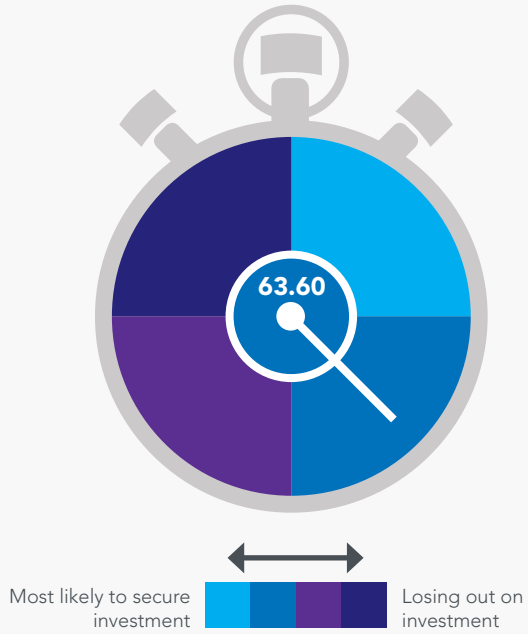
- ✘ Though executives' views of the biopharmaceutical IP environment improved slightly in 2017 (mainly in relation to the availability of RDP, at least for new chemical entities), overall they still note that significant improvements are needed.
- ✘ Lack of effective patent enforcement and INVIMA's potential role in patent examination are seen as greatly weakening the biopharmaceutical ecosystem.

COSTA RICA

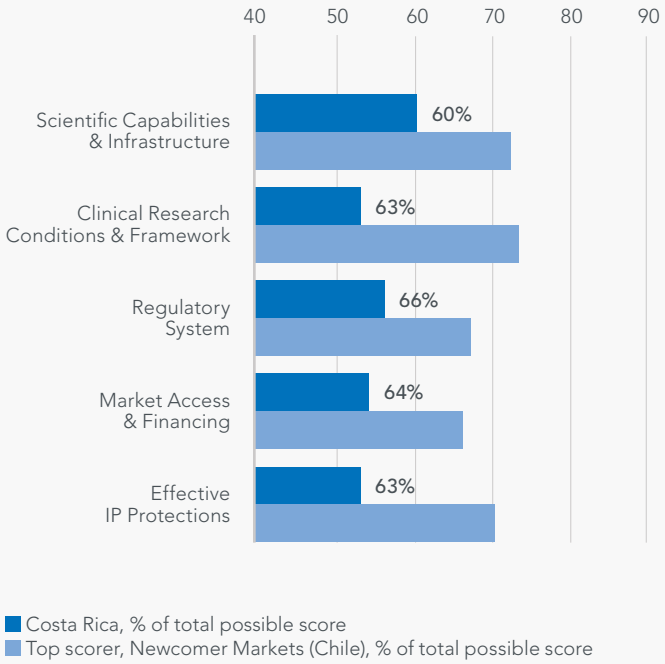
BCI Survey 2017 – Overall Scores

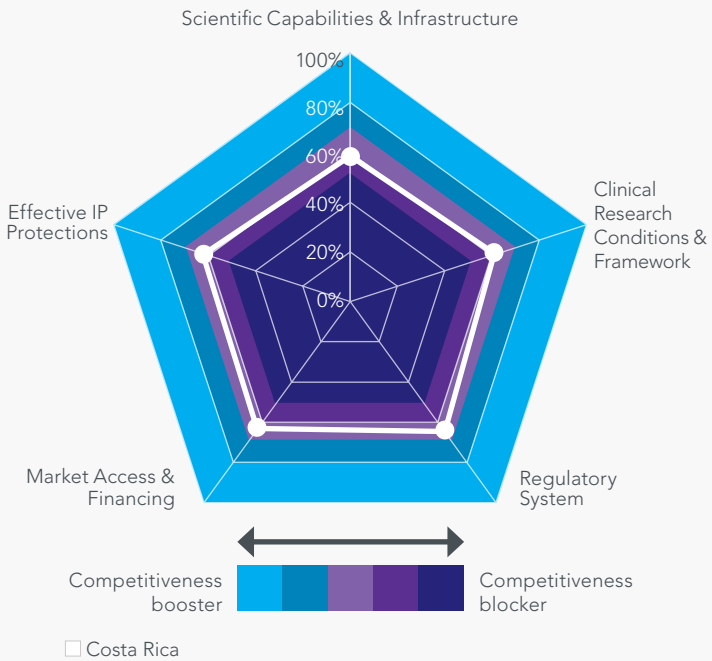
Comparison to Newcomer Markets





BCI Survey 2017 – Category Scores





BCI Results In Depth: What helps and what hinders Costa Rica's biopharmaceutical competitiveness?

Scientific Capabilities & Infrastructure

✔ While the scientific infrastructure is considered nascent, it is developing considerably and good human capital is properly leveraged.

✔ Executes are encouraged by the country's comprehensive plan to elevate Costa Rica's R&D capabilities, although there remains room for improvement in collaboration opportunities with public institutions.

Clinical Research Conditions & Framework

✔ Clinical research capabilities among hospitals and CROs are reportedly improving, although executives note that there are significant gaps in CT regulatory approval with extensive delays and unnecessary red tape.

The Regulatory System

✘ Identified as a key area for improvement to avoid derailing of concerted efforts to turn Costa Rica in a hub for biopharmaceutical R&D.

Market Access & Financing

✘ Still viewed as "work in progress." While policies are pointing in the right direction, there remains lack of transparency in pricing and reimbursement decisions.

Effective Intellectual Property Protections

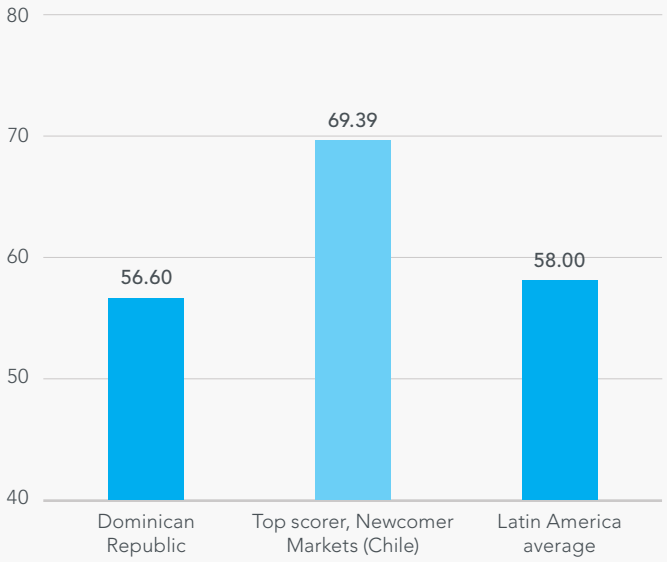
✔ Area considered as key to success in the country's efforts to elevate its sector. Improvement in this area could have a multiplying effect. For example, executives note that Costa Rica should accelerate implementation of RDP.

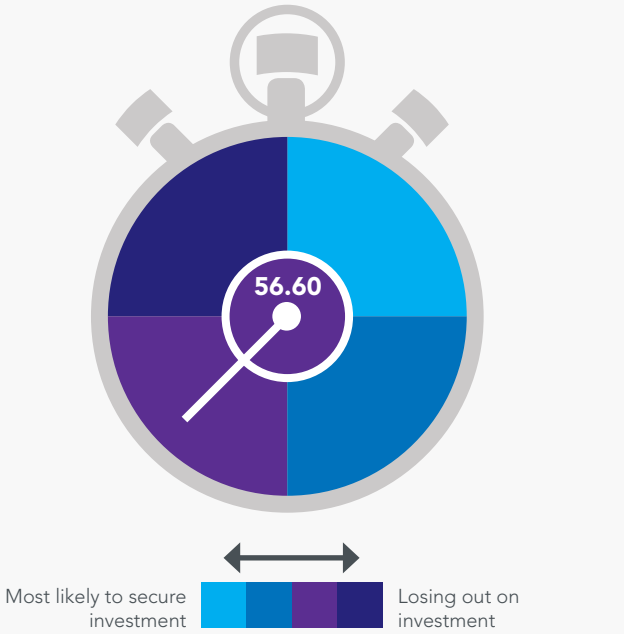
✔ While patent backlog is considered moderate, executives note that there is patent term restoration available to address administrative delays in issuance.

DOMINICAN REPUBLIC

BCI Survey 2017 – Overall Scores

Comparison to Newcomer Markets





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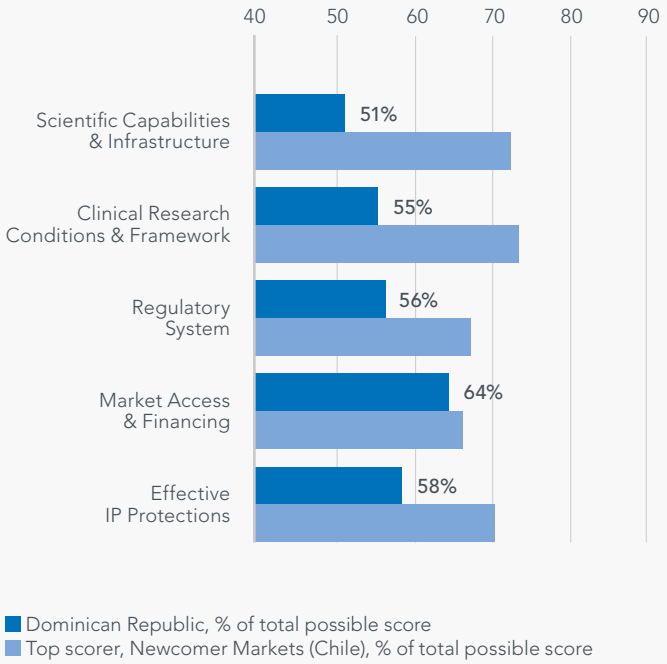
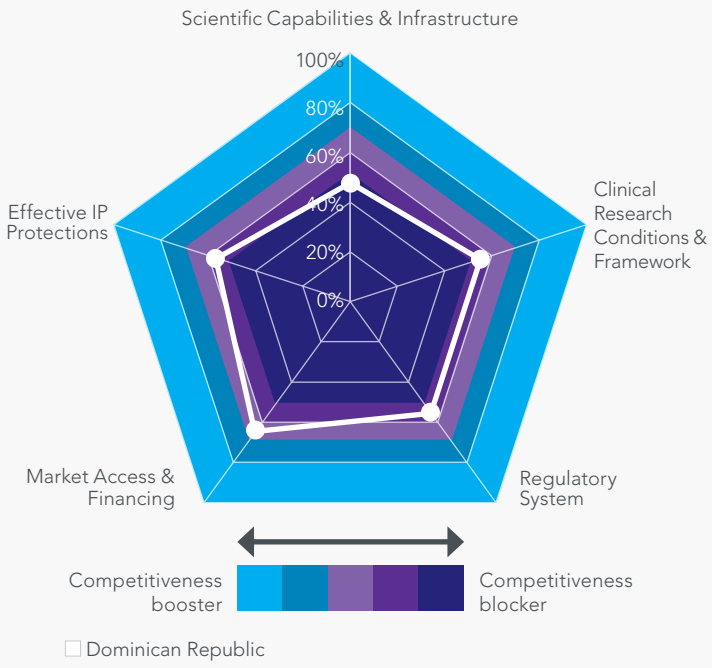




BCI Results In Depth: What helps and what hinders the Dominican Republic's biopharmaceutical competitiveness?

Scientific Capabilities & Infrastructure

✘ Executives rate poorly the country's research infrastructure, and see no existing national plans to invest in R&D. They also note that collaboration between industry and research institutions is almost non-existent.

Clinical Research Conditions & Framework

✔ Clinical research in the country has mixed reviews: capabilities among hospitals and CROs continue to improve, and CTs are inexpensive to run.

✘ Conversely, though, significant gaps remain in CT regulatory approval due to excessive delays and unnecessary red tape.

The Regulatory System

✘ Consensus around significant gaps in the regulatory system: while the regulatory agency is committing resources to elevate its technical capabilities, approval of substandard medicines is pervasive, and the country remains unable to evaluate quality, safety and efficacy of biosimilars.

Market Access & Financing

✘ Although lack of transparency in pricing and reimbursement decisions and widespread preferential treatment to local companies exist, executives note that pricing and reimbursement policies are less hostile than elsewhere in the region, and inclusion rates of new therapies are also above the regional average. There is consensus that the country can make strategic improvements to increase its competitiveness.

Effective Intellectual Property Protections

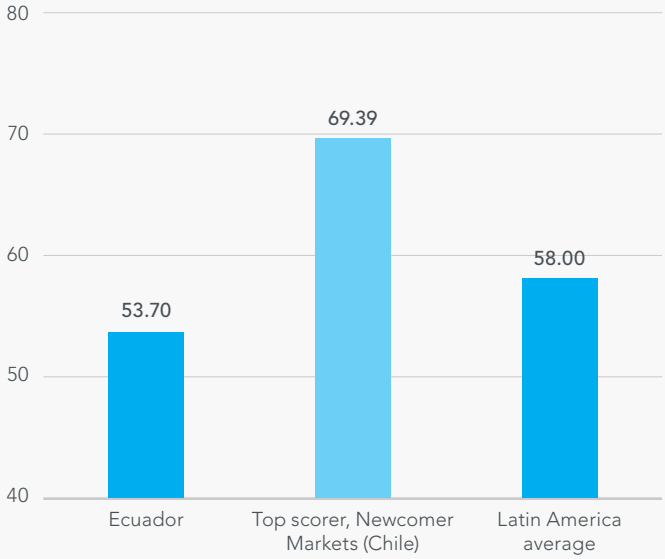
✔ While the country has been slowly implementing RDP, executives are encouraged by a renewed commitment to expedite long-pending patent applications.

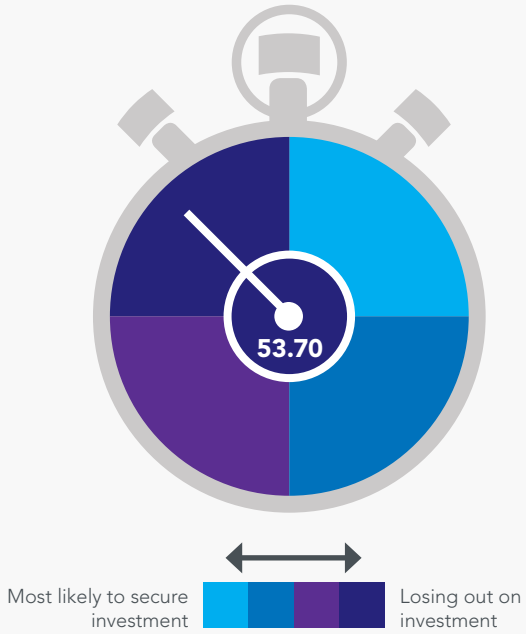
✘ Executives express concern that patent term extension is not available.

ECUADOR

BCI Survey 2017 – Overall Scores

Comparison to Newcomer Markets





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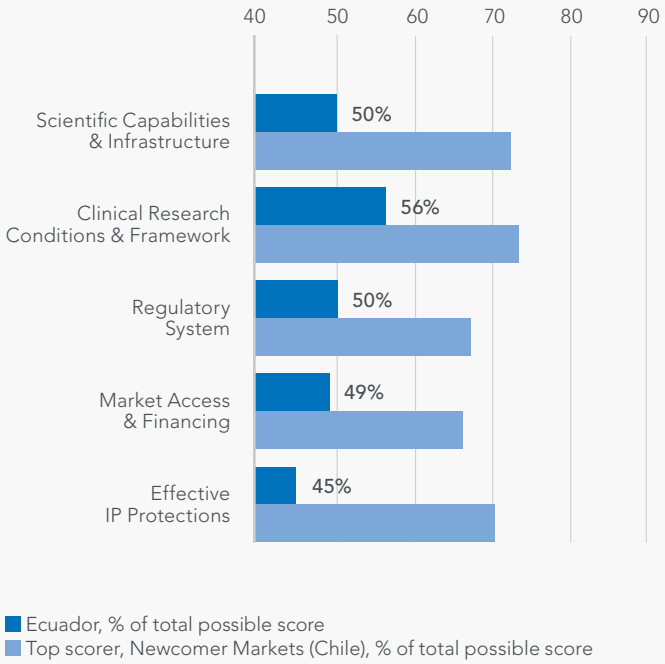
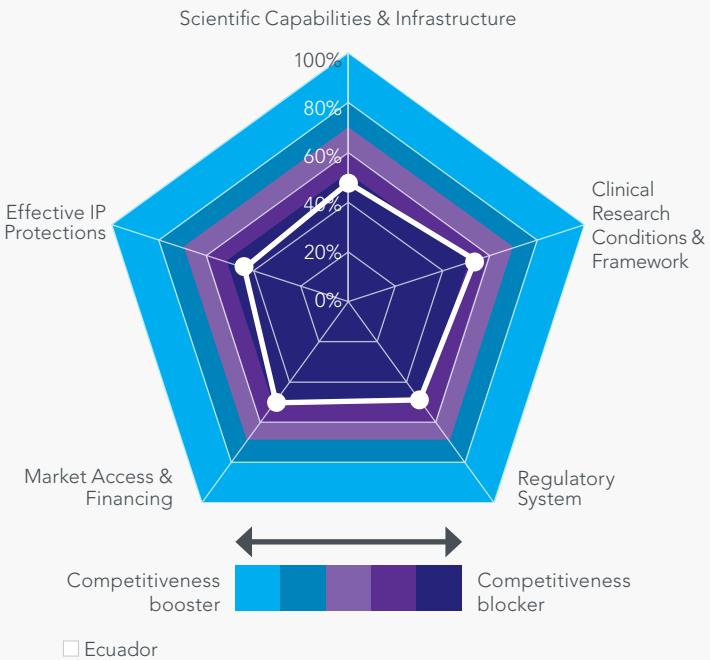




BCI Results In Depth: What helps and what hinders Ecuador's biopharmaceutical competitiveness?

Scientific Capabilities & Infrastructure

- ✘ Executives rate poorly the country's research infrastructure, and see no existing national plans to invest in R&D.
- ✘ They also note that collaboration between industry and research institutions is almost non-existent.

Clinical Research Conditions & Framework

- ✘ Clinical research and CRO platforms are rated as substandard.
- ✘ Executives note extensive delays in CT regulatory approval.

The Regulatory System

- ✘ Consensus around the regulatory system being below par: approval of substandard medicines is pervasive, and the country remains unable to evaluate quality, safety and efficacy of biosimilars.

Market Access & Financing

- ✘ Widespread concern reported on lack of transparency in pricing and reimbursement decisions.
- ✘ Respondents noted how excessive price controls and restrictive reimbursement policies are significantly counterproductive and hurt the biopharmaceutical sector.

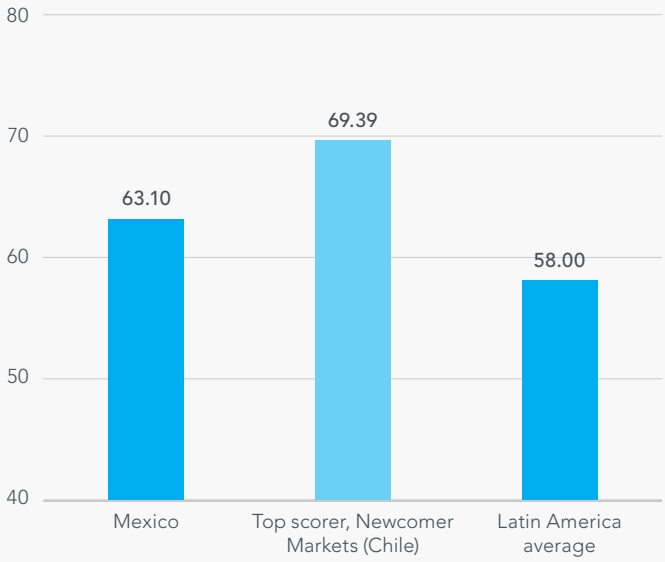
Effective Intellectual Property Protections

- ✘ While the New Ingenuity Code adopts an RDP regime of 5 years, concerns remain about how the regulatory agency will apply the provision or whether it will simply bypass it by not requiring bioequivalence dossiers from generics.
- ✘ Executives are also discouraged that the Code bans patentability of biopharmaceutical subject matter, and imposes new local working requirements that exclude importation.

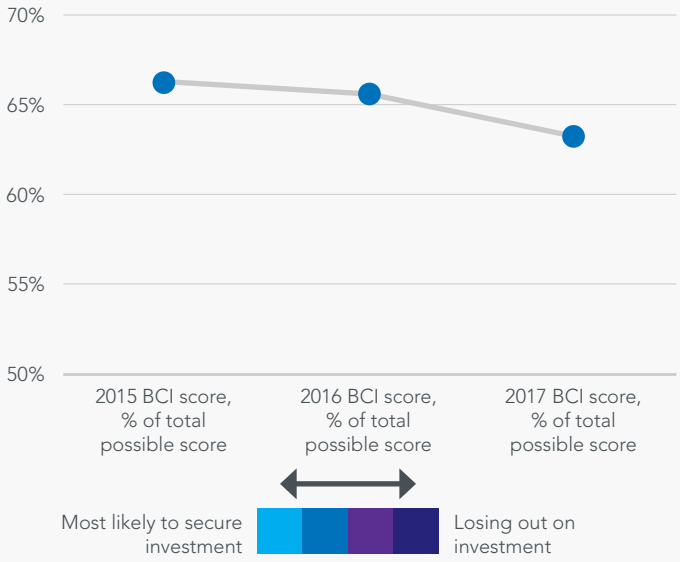
MEXICO

BCI Survey 2017 – Overall Scores

Comparison to Newcomer Markets



2015-2017



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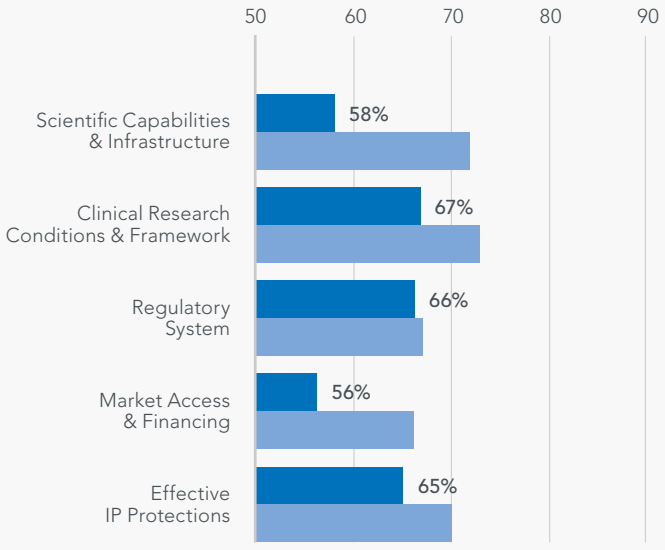
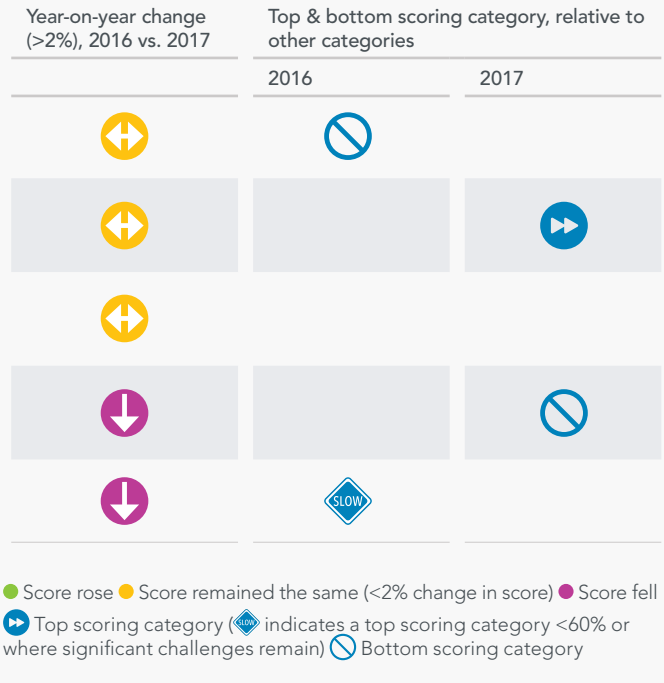




BCI Results In Depth: What helps and what hinders Mexico's biopharmaceutical competitiveness?

Scientific Capabilities & Infrastructure

✔ Research infrastructure continues to be substandard, although respondents are encouraged by Mexico's stated commitment to develop world-class scientific capabilities, which has translated into concrete and significant public R&D spending.

✘ Collaboration between industry and research institutions remains uneven, and is based largely on the policies in place at the institution receiving the public funding.

Clinical Research Conditions & Framework

✔ Respondents are largely optimistic about Mexico's efforts to attract clinical trial activity, noting that several healthcare systems (with millions of subscribers) are opening for clinical trial activity. Clinical trials in Mexico are seen as cost-efficient and in line with international standards, despite gaps in capacity for clinical research.

✔ Streamlining the clinical trial approval process is reportedly yielding positive results (displaying a drop of 2 months), although respondents note there is still room for improvement.

The Regulatory System

✔ Executives are encouraged by COFEPRIS' new policies to significantly cut delays in drug approvals, from 360 days to 60 days and what are considered to be relatively strong approval standards for biologics.

✔ A grass-roots pharmacovigilance mindset is considered as an opportunity for collaboration between industry, COFEPRIS and other stakeholders.

Market Access & Financing

✘ Respondents call worrisome a perceived lack of transparency in decision-making and preferential treatment of local companies in public tenders.

✘ Executives mention that public pricing and reimbursement is primarily focused on cost and drug formularies under the major public schemes all contain relatively low levels of innovative drugs.

Effective Intellectual Property Protections

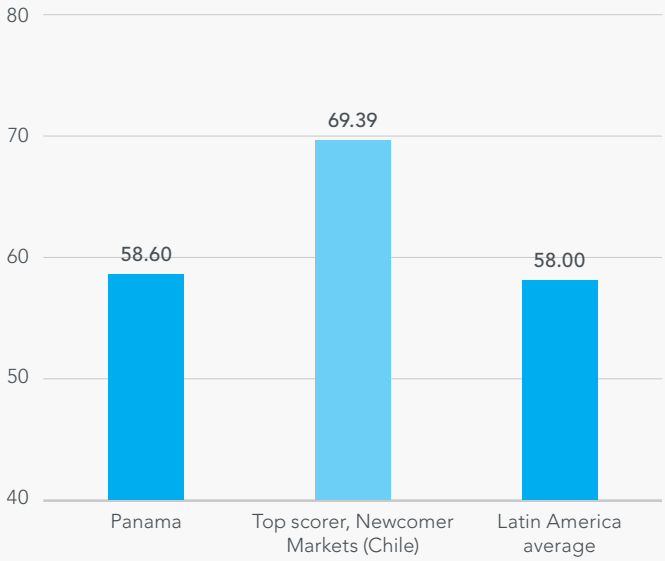
✔ Respondents are generally encouraged by Mexico's efforts to improve its IP environment, though they note the uneven application of RDP and patent linkage to biologics and certain types of biopharmaceutical innovations.

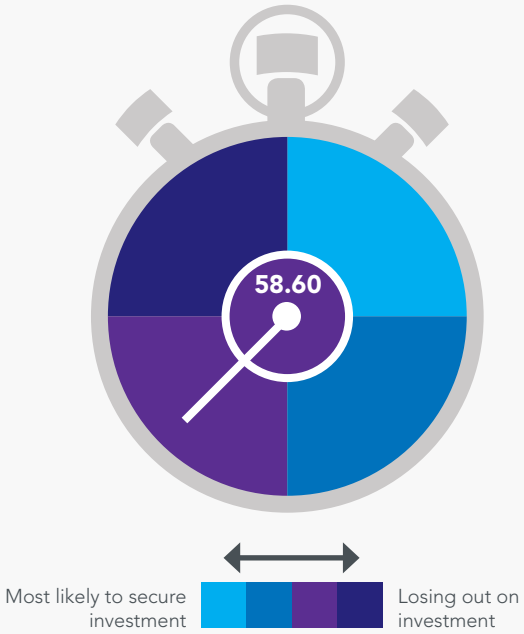
✘ Uncertainty over the future of biopharmaceutical IP protection under re-negotiated trade agreements and deep budgetary cuts to IP courts is one concern of executives.

PANAMA

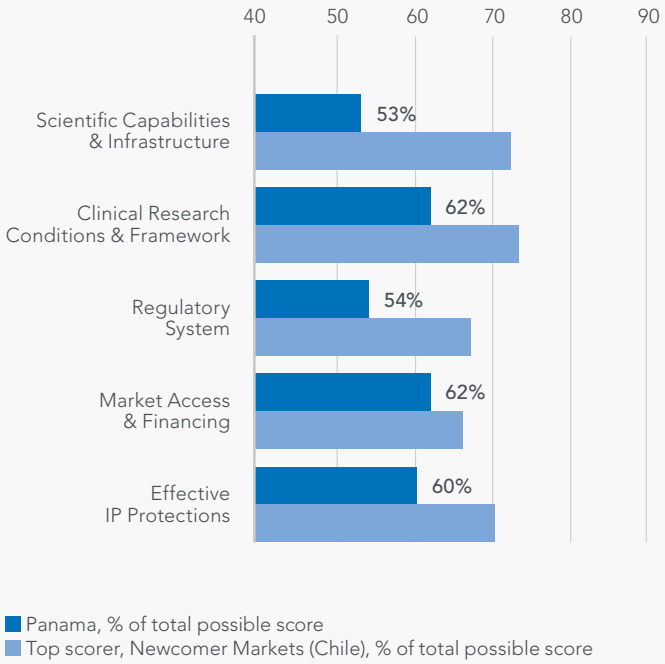
BCI Survey 2017 – Overall Scores

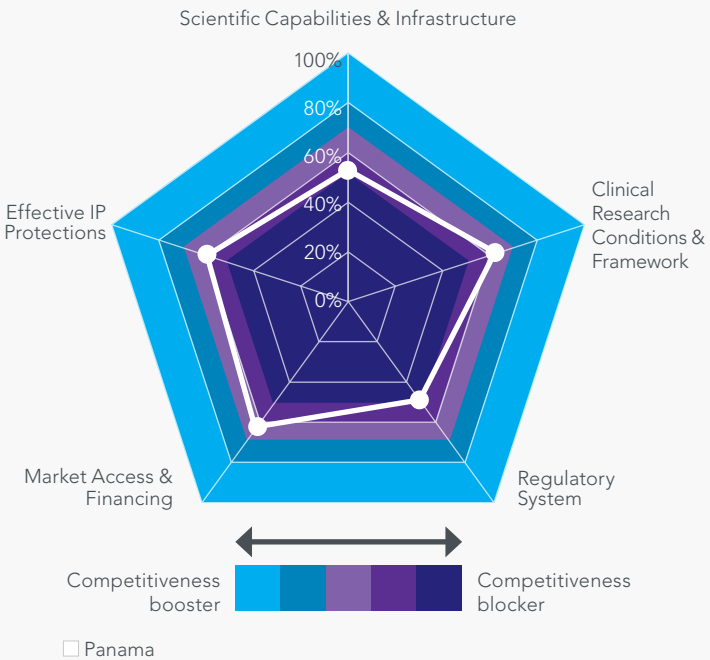
Comparison to Newcomer Markets





BCI Survey 2017 – Category Scores





BCI Results In Depth: What helps and what hinders Panama's biopharmaceutical competitiveness?

Scientific Capabilities & Infrastructure

- ✘ Executives rate poorly the country's research infrastructure, and see no existing national plans to invest in R&D.
- ✘ They also note that collaboration between industry and research institutions is almost non-existent.

Clinical Research Conditions & Framework

- ✘ Clinical research and CRO platforms are found to be substandard (though there are good pockets of compliance with GCPs).
- ✘ Executives cite extensive delays in CT regulatory approval.

The Regulatory System

- ✘ Consensus around the regulatory system being below par: approval of substandard medicines is seen as pervasive.
- ✘ Executives believe that the country remains unable to evaluate quality, safety and efficacy of biosimilars.

Market Access & Financing

- ✔ Although lack of transparency in pricing and reimbursement decisions and widespread preferential treatment to local companies exist, executives note that pricing and reimbursement policies are less hostile than elsewhere in the region, and inclusion rates of new therapies are also above the regional average, although still heavily weighted towards generics.

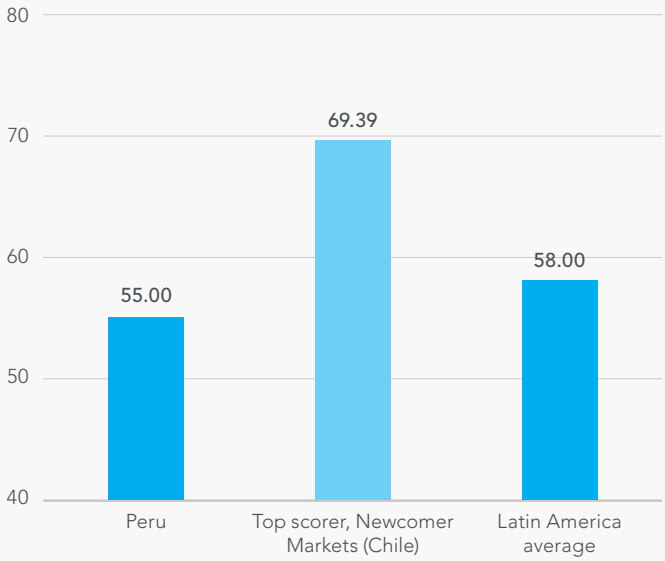
Effective Intellectual Property Protections

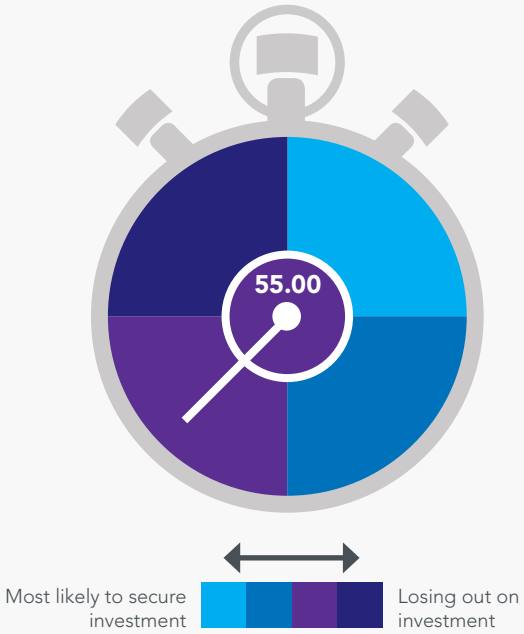
- ✘ Executives note that the country has been slowly and unevenly implementing RDP (unclear if biologics are included)
- ✔ Executives mention that patent backlog is moderate and patent term extension is available.

PERU

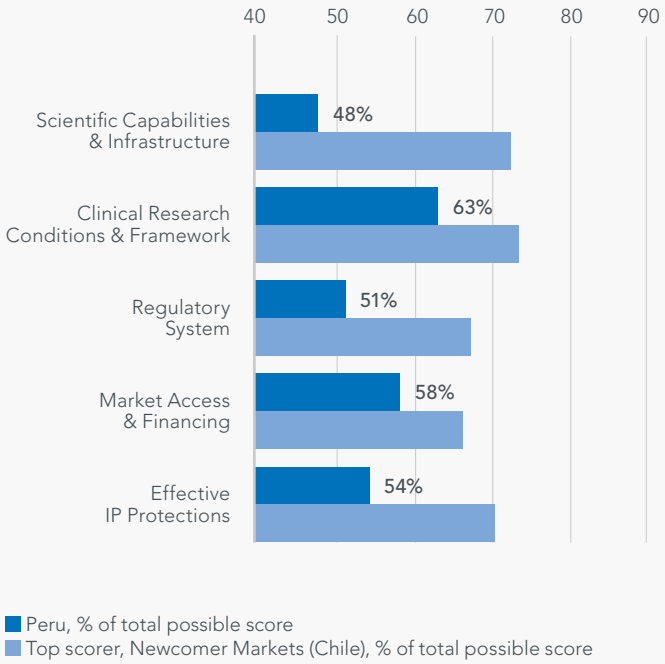
BCI Survey 2017 – Overall Scores

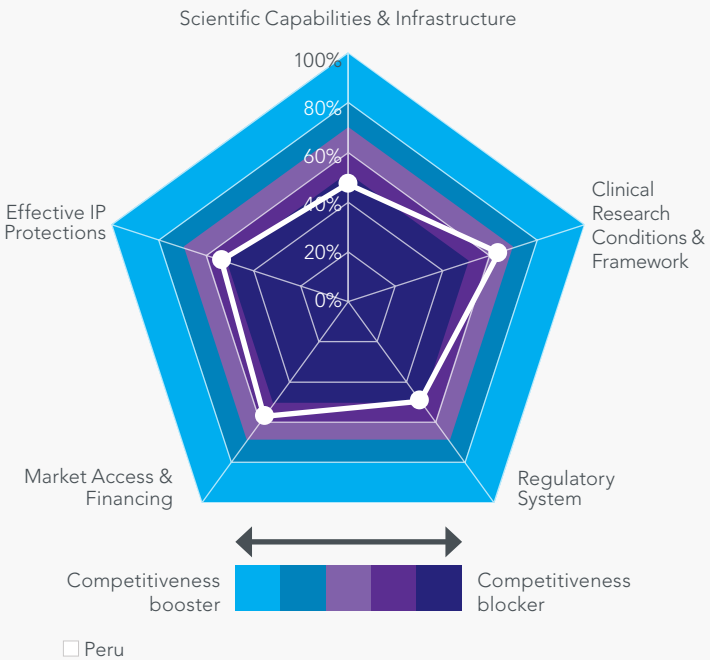
Comparison to Newcomer Markets





BCI Survey 2017 – Category Scores





BCI Results In Depth: What helps and what hinders Peru's biopharmaceutical competitiveness?

Scientific Capabilities & Infrastructure

✘ Executives rate poorly the country's research infrastructure, and see no existing national plans to invest in R&D.

✘ They also note that collaboration between industry and research institutions is almost non-existent.

Clinical Research Conditions & Framework

✔ Clinical research in the country has mixed reviews: capabilities among hospitals and CROs are seen as improving, patient populations are eager to participate, and CTs are inexpensive to run.

✘ Conversely, though, significant gaps remain in CT regulatory approval are noted due to excessive delays and unnecessary red tape.

The Regulatory System

✘ Consensus around the regulatory system being below par: approval of substandard medicines is seen as pervasive.

✘ Executives believe the country remains unable to evaluate quality, safety and efficacy of biosimilars.

Market Access & Financing

✘ Executives report lack of transparency in pricing and reimbursement decisions, widespread preferential treatment to local companies, and formularies heavily weighted towards generics.

Effective Intellectual Property Protections

✘ Respondents view the IP environment as an area that needs significant improvement: Slow implementation of RDP excluding biologics, significant patent backlog and no patent term extension available, and a prolonged and ineffective enforcement.

✔ Executives welcome the PPH with ProSur but remain uncertain whether biopharmaceutical patents will be included in the effort.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NOTES

1 www.cnbc.com/2015/02/17/latin-america-is-the-fastest-growing-smartphone-market.html

2 Deborah Weinswig (2016), Social Media in Latin America, Fung Global Retail & Technology.

3 Latin America is the regions with the greatest inequality in terms of access to healthcare. www.opendemocracy.net/democraciaabierta/isglobal-democraciaabierta/healthcare-in-latin-america-and-caribbean-democratic-ch.

4 Pugatch Consilium (2014), Scaling Up Clinical Trial Activity; Note: Strength of the IP environment is measured using the U.S. Chamber's GIPC International IP Index (GIPC Index) and clinical trials using the NIH's Clinicaltrials.gov database.

5 Ibid.

6 Pugatch, M.P. & Torstensson, D. (2014), Building the Bio-Economy: Examining National Biotechnology Industry Development Strategies, commissioned by BIO

7 OECD (2006), p.171; Léger, A. (2006), "Intellectual Property Rights and Innovation in Developing Countries: Evidence from Panel Data", Proceedings of the German Development Economics Conference, Berlin

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