WILL MEXICO BUILD ON ITS REFORMS TO BECOME A REGIONAL LEADER IN BIOPHARMACEUTICAL INNOVATION?

BIOPHARMACEUTICAL INNOVATION IN MEXICO: *AT THE CROSSROADS*

By Sandra Fuentes & Giulia Salieri

- *Mexico has the potential to become a leader in biopharmaceutical innovation.*
- *Policymakers must improve enforcement of intellectual property rules and speed up patient access to innovative drugs if the sector is to realize its true innovation potential.*

Almost a decade ago, IMS Health listed 21 countries it described as pharmerging - developing countries with increasingly important pharmaceutical industries, including Mexico.[1] Since then, Mexico has grown to become the second largest pharmaceutical market in Latin America after Brazil, and the eleventh largest globally.

Mexico offers distinctive competitive advantages in pharmaceuticals and other

1 Pharmerging countries are those having more than $1 billion in spending growth from 2012 to 2016 and a per capita GDP of less than $25,000: China, Brazil, Russia, India Turkey, Mexico, Poland, Venezuela, Argentina, Indonesia, South Africa, Thailand, Romania, Egypt, Ukraine, Pakistan and Vietnam.

manufacturing industries. Among them is a large population, low manufacturing costs, advanced legal frameworks, skilled scientists, and strategic position as a hub for US companies and a natural gateway to Latin American markets.

The Mexican government has prioritized growth and innovation in the sector. In particular, it has strengthened the legal and regulatory framework to provide greater certainty to investors, drug makers, care providers and patients. Biotech clusters are also emerging in several Mexican states as major drivers of the country's biotechnology innovation.

That being said, certain parts of the industry remain fragile and require policy attention for Mexico to realize its potential and become a leading biopharmaceutical innovator. Areas of weakness include enforcement of intellectual property laws, still a major concern among the research community, and a lengthy and overly complicated process for introducing innovative drugs into the local market.

If these issues are addressed, Mexico has the potential to become an emerging market leader in biopharmaceutical innovation.

BUILDING THE REGULATORY FRAMEWORK

As the Mexican economy opened in the 1990s, Mexico began to attract large flows of foreign direct investment and it established new commercial ties with the world's leading economies. Around this time, several multinational companies—including biopharmaceutical firms—set up on Mexican soil for the first time. Others expanded their existing operations.

Business-friendly reforms continued with 1994's North American Free Trade Agreement (NAFTA), which triggered regional integration and, in Mexico's case, introduced world-class standards for the protection for intellectual property.

NAFTA was the first free trade agreement to include intellectual property provisions, ranging widely from patents to trademarks. Of particular relevance for pharmaceuticals was the requirement for NAFTA members to grant 20-year patent terms, as well as five years of protection for data generated in biopharmaceutical clinical trials. [2]

Despite NAFTA's introduction of world-class IP standards to Mexico, government and private sector efforts to grow biotech and innovation remained fragmented over the following decade. The situation began to change with the creation of the Federal Commission for the Protection against Sanitary Risk (COFEPRIS) —the national drug regulatory authority—in 2001, which marked a regulatory milestone in pharmaceutical and biotechnology public policies and the first steps for Mexico's policy framework. The existence of this new body created policy and legal coherence that provided greater certainty to innovators and investors, setting the sector on the path to growth (See infographic opposite).

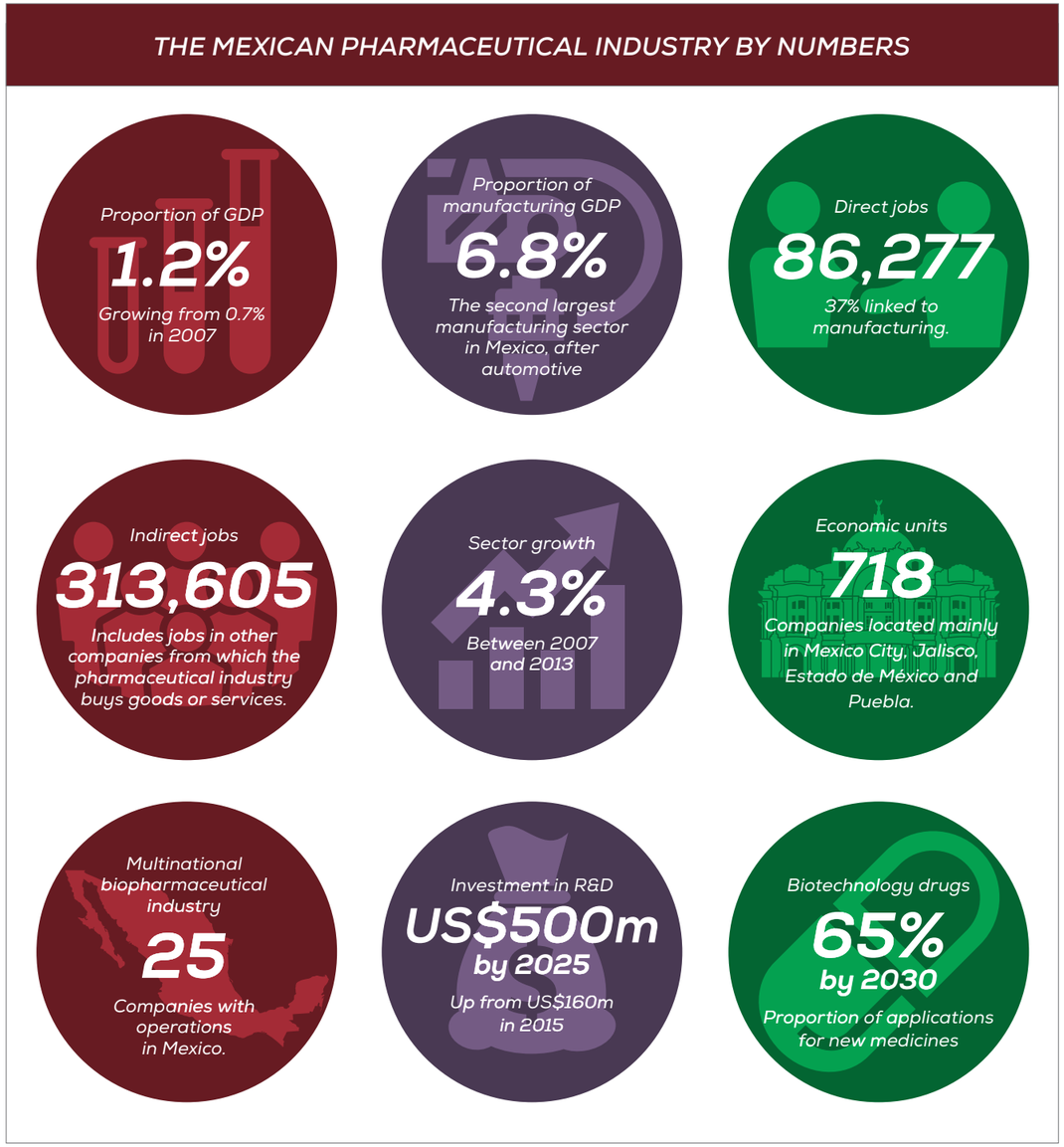
THE OPPORTUNITY FOR INNOVATION

With an estimated 123 million people, Mexico is the second most populous Latin American country and the 11th largest globally.

Like many emerging markets, the country is undergoing a demographic transition away from high birth and mortality rates, which means Mexico's population is ageing. This in turn presents significant social security and health challenges.

The other implication of this transition is an increasing burden of chronic, non-communicable diseases and a decline in deaths from infectious diseases. This means that more medicines and diagnostic tools must be developed for non-communicable, chronic diseases, tailored to the particular needs of the Mexican population. Researching and developing these new products represents a great opportunity for growth in the Mexican biopharmaceutical industry.

2 Dorothy Schrader, "Intellectual Property Provisions of the NAFTA", Congressional Research Service, American Law Division, 1994, p. 6, available in http://www.ipmall.info/hosted_resources/crs/94-59_940124.pdf



BARRIERS TO INNOVATION IN MEXICO

One of the main roadblocks to innovation in Mexico is the long and difficult road to getting a new medicine through regulatory approval for use in the Mexican market.

In order to gain regulatory approval, a new medication must pass four official checkpoints: COFEPRIS, General Health Council (CSG), a public health institutions evaluation and an evaluation of the patient's case (Figure 2).

COFEPRIS has improved accountability, transparency and the speed of the first phase of evaluation, but the rest of the approval path remains inefficient and arbitrary. According to Cristóbal Thompson, Executive Director of the Mexican Association of Industries of Pharmaceutical Research (AMIIF), only 10% of drugs approved by COFEPRIS and the CSG are actually made available for patients in public healthcare institutions.[3]

New drug approvals also take a long time.[4] On average, it takes 4.2 years for a drug to be available at Mexican public health institutions, twice as long as in Japan, France and the UK and comparable to developing countries like India. AMIIF says the process can last six years for biotechnology drugs.

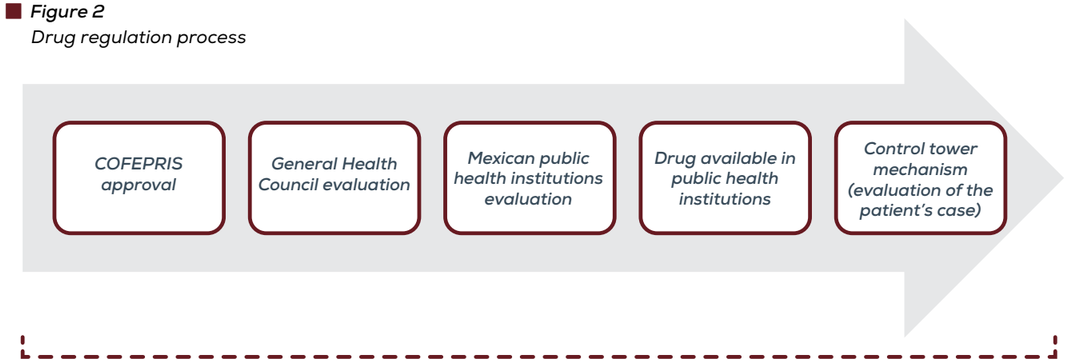
Since 2011, important steps have been taken to streamline this process. Among others, COFEPRIS recently adopted an equivalency agreement with five regulatory agencies (United States, Canada, Switzerland, Australia and EU), which aims to speed up the launch of new molecules.

This as well as other measures have accelerated the time required to register a new drug in Mexico, but the regulatory approval process still remains a significant roadblock to innovation by local companies.

NOT ENOUGH PUBLIC SPENDING ON HEALTH

Between 2004 and 2013, Mexico's public healthcare spending rose 127%, from MX$231bn to MX$524bn[5]. This is still some way short of international standards— Mexico invests around 6.2% of its GDP in health, well below the average 7.4% of

Figure 2
Drug regulation process

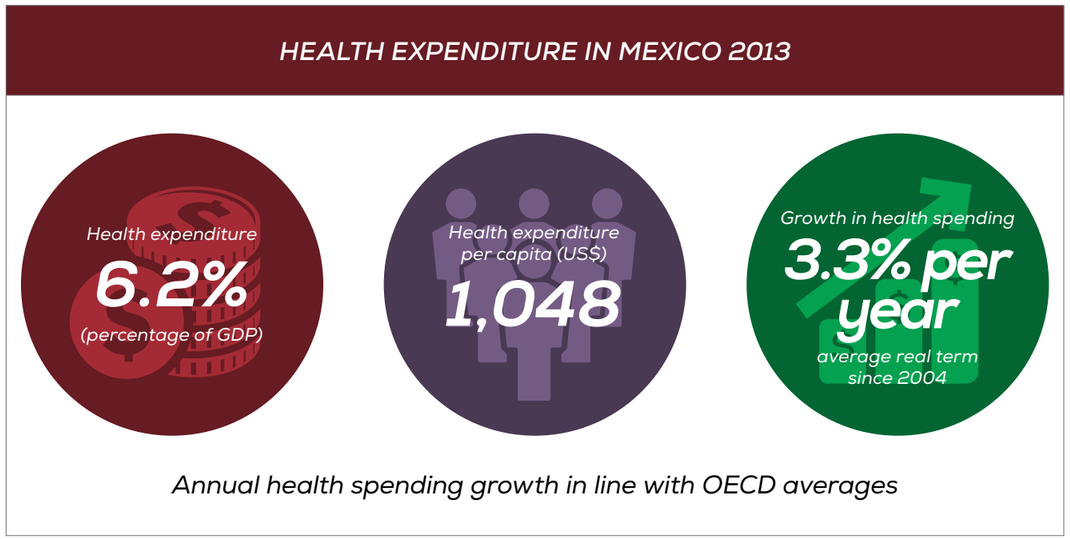


3 Interview with authors
4 Héctor Valle, "A changing health scenario", Review of the Second High-Level Innovation Forum for Policy Makers, Woodrow Wilson International Center for Scholars and Fundación IDEA, Washington, DC, November 2014, p. 20
5 Mexico Health Review 2015, p. 40
6 Ibid
7 Ibid

PROBIOMED

- Much of the Mexican biopharmaceutical industry consists of subsidiaries of foreign companies, which only conduct parts of the research or production processes in Mexico. PROMBIOMED is the only national (Mexican) innovative biopharmaceutical company that conducts all its R&D within the country, and it has become an important global player in vaccine development. The company started over 40 years ago as a manufacturer of active ingredients, and today researches, develops and manufactures both its own innovative biotech products and generic medicines.
- Its first biotechnology product, launched in 2007, was initially greeted with scepticism: "No-one could believe that this technology could come from Mexico. People thought it could only be done in Europe or the US," according to Jaime Uribe, the company's CEO. In addition to its vaccines, PROBIOMED also produces nine recombinant proteins, from gene to biomedication.[6]
- Today, its products are sold in 10 countries: Guatemala, El Salvador, Honduras, Panama, the Dominican Republic, Peru, Bolivia, Paraguay, Uruguay, Thailand, PROBIOMED's Hepatitis B vaccine – produced 100% in Mexico - currently meets 80% of global demand. The company provides over 1.000 direct jobs in Mexico.[7]

Figure 3



Source: Mexican Health Review 2015, Marketline, INEGI and CANIFARMA

other Latin American countries, and the average 9.3% of other OECD countries.[8] Public sector expenditure as a proportion of total health expenditure is also low, constituting only 51.7% of total health spending. 91.5% of private expenditure is out-of-pocket spending. [9]

Given the high levels of health expenditure born directly by patients, it is not surprising that rates of access to innovative drugs are so low.

The situation is likely to worsen in the near future. In 2016, the Mexican Healthcare system will face a budgetary cut of US$650 million, due to the austerity measures taken by the current administration.[10]

RIPE FOR RESEARCH

Despite the abovementioned problems, industry leaders say that Mexico is an attractive environment to develop, test, and commercialize a wide range of medications. According to José Luis Paz, Director of Government Relations at biotech firm Amgen, Mexico's large and diverse population and its well-developed research infrastructure make it an ideal place to recruit volunteers for clinical trials. At the same time its location makes it the perfect gateway to the Latin American market.

According to Mr. Paz, two main issues continue to hold the country back. Lengthy and complicated clinical protocols hamper its international competitiveness. For example, national rules require researchers to re-start the process if any modification occurs (including a change in the research team). According to the US Chamber 2016 International IP Index, Mexico's IP regime is undermined by weak enforcement and ambiguity around patent extension and regulatory data protection rules. [11]

8 Manuela D´Andrea, op. cit., p. 5.
9 Mexico Health Review 2015, p. 6.
10 Fernando Fon, op. cit.

COMPETITIVE MANUFACTURING COSTS

Competitive manufacturing costs have drawn 20 of the 25 largest biopharmaceutical companies to Mexico. According to KPMG, manufacturing costs in Mexico are approximately 14.4% lower than in the US. "Having manufacturing located here in Mexico gives us flexibility and it pays off. We have one of the most competitive manufacturing costs worldwide," according to Pedro Galvís, General Director of Merck.[12] Another major biopharmaceutical firm, Boehringer Ingelheim, is poised to move the manufacture of 80% of its diabetes care products to Mexico.[13]

AMGEN IN MEXICO

- *Established its first Latin American affiliate in Mexico in 2006.*
- *Has invested more than US$19 million in clinical trials in Mexico over the past eight years.*
- *10 products available in Mexico, eight are available at Mexican public health institutions.*
- *18 ongoing clinical trials in national health institutions.*

HUMAN CAPITAL

Mexico has the right conditions to build a strong and skilled scientific base from its undergraduate and graduate student population.

Figure 4 -Savings related to competitive costs

Source: ProMexico

11 US Chamber 2016 International IP Index, available at http://www.theglobalipcenter.com/gipc-index-map-detail/?country=mx
12 Manuela D´Andrea, op. cit., p. 16.
13 Mexico Health Review 2015, p. 99.

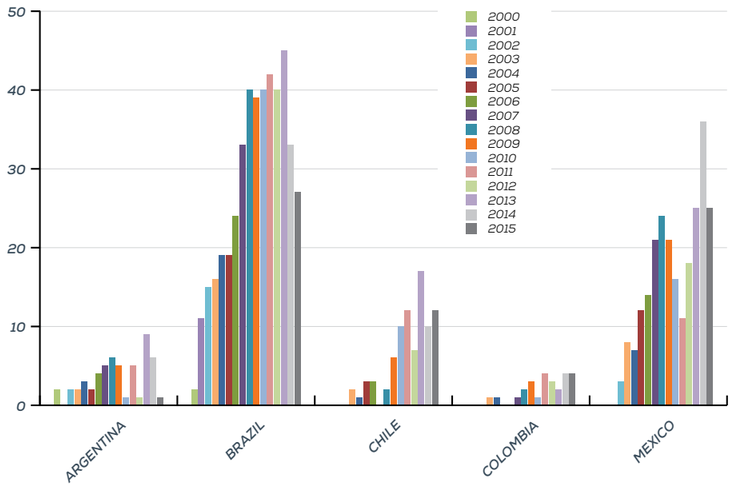


Figure 5 - Pharmaceutical patents filed through the Patent Cooperation Treaty
Source: WIPO

More than 12,000 institutions offer programs linked to biotechnology research program, half of them in states with biotech clusters.[14] There are around 600 pure biotechnology programs in 130 universities and biotech graduate programs in 80 higher education institutions.[15]

But Mexico's brain drain is substantial; it sends more undergraduate and graduate students to US universities than any other Latin American country.[16] A lack of opportunities means most do not return. In 2010, around 20,000 of the 73,000 Mexicans with a PhD were living in the US.[17] A vibrant, well-paying industry would likely see that talent return.

A FRAGMENTED INNOVATION ECOSYSTEM

Mexico's innovation ecosystem remains disjointed. While in Western Europe and the United States there is regular collaboration between academia and the private sector, such collaboration is rare in Mexico - although the public sector is taking steps to change this.

A recent reform, passed in December 2015, removed previously existing legal barriers preventing researchers receiving public funding (i.e. personnel of public universities) to link up with the private sector to develop commercial patents. In addition, in 2012 the Ministry of Economy and the National Council for Science and Technology (CONACyT) combined to create and run Technology Transfer Offices. These offices help license new technologies and promote commercial innovation by acting as intermediaries between knowledge-generating institutions, such as research centers and universities, and the private sector.

STRONGER IP BUT ENFORCEMENT ISSUES REMAIN

Innovative biopharmaceutical industries depend on robust and enforceable intellectual property rights, whether they are located in the United States, Europe or in middle-income countries like Mexico.

Mexico's biopharmaceutical industry has benefited from NAFTA, ratified in 1994. This modernised the Mexican IP regime, bringing it in line with international standards.

Since the early 2000s, Mexican inventors have filed an increasing number of pharmaceutical patents through the Patent Cooperation Treaty, and rates of patent filing within this sector compare favorably to other Latin American countries (Figure 5).

In spite of this, the industry still faces regulatory gaps. Amgen's Jose Luis Paz is among those calling for clarifications of the ownership rules surrounding the clinical trials data submitted to the national drug regulatory authority. NAFTA rules require this data to be withheld from generic competitors for a period of five years, but this rule is not always enforced.

In fact, enforcement of existing intellectual property rules is one of the main problems faced by innovators in Mexico. Pirated products are still easily found in the country, despite greater government effort to stop them. Poor training of enforcement officials, corruption, and a lack of criminal prosecution are to blame.

A large and influential informal sector in Mexico's economy compounds the issue. Patent infringement of pharmaceutical drugs is a damaging reality, particularly close to Mexico's northern border with the US. Americans go to Mexico's border cities, Tijuana for example, in order to buy cheaper drugs without a prescription. Chemical analysis have found that an important proportion of drugs sold in border cities are counterfeit or substandard.

AT THE INNOVATION CROSSROADS

Mexico has created most of the conditions to develop a strong pharmaceutical industry driven by biotechnology. It is well placed to consolidate itself as a biopharmaceutical manufacturing power in the next five years.

Natural advantages such as geographic position and a large population have combined with improved regulatory frameworks and infrastructure to attract a large number of international companies as investors and collaborators.

Some of the conditions are in place to put Mexico on the path towards greater biopharmaceutical innovation. But more is needed to strengthen the innovation ecosystem, including incentivizing collaboration between academic and private sectors, and enforcing existing intellectual property laws. It is encouraging that Mexican policymakers are recognizing and acting towards solving those problems, so we expect improvements in the longer term.

A major roadblock to the emergence of an innovative domestic biopharmaceutical industry is the lengthy and complicated approval process for innovative drugs. Cuts to the public healthcare budget are likely to slow the penetration of innovative medications even further.

Mexico has the choice to remain as a low-value manufacturer of medicines, or develop as an innovator in its own right. The latter path will lead to faster and more sustainable economic growth, high-skilled jobs and new medicines tailored for the specific needs of Mexicans. Most of the parts of the puzzle are in place--it is up to the current generation of policymakers to complete it.

14 Minerva Valdés and Francisco Quezada, "Commercial Biotechnology in Mexico", Journal of Commercial Biotechnology, 2013, 19 (2), p.6.
15 Negocios ProMexico, "Biotechnology, medical devices, medical tourism and pharmaceutics: the four pillars of the Mexican Health Sector", August, 2015.
16 Erik Vance, "Why can't Mexico make science pay off?" Scientific American, October 2013, vol. 309, Issue 4, p. 6.
17 United States Census Bureau, Population Data 2010.

ABOUT THE AUTHORS

Giulia Salieri is Director at Fundación IDEA where she has worked since 2010. Her research focuses mainly on education and innovation. She is also a partner of C230 Consultores, Fundación IDEA's public policy consulting arm. Previously, she worked as consultant for McKinsey and Company.She has a MBA and a MA in Education from Stanford University, as well as a MS in Financial Economics from the Bocconi University (Italy).

Sandra Fuentes has been a Senior Analyst at Fundación IDEA since 2013, participating in a range of innovation and technology-transfer related projects, particularly related to IT and healthcare. She has a bachelors' degree in International Relations from the Instituto Tecnológico Autónomo de México (ITAM) and has completed studies at the Institut d'Etudes Politiques of Paris. Prior to Fundación IDEA, she worked at the French Embassy in Mexico City.

Fundación IDEA is one of the oldest public policy think tanks in Mexico. It is an independent non-profit organization whose mission is to design and promote the implementation of innovative public policies and programs which will foster economic development, poverty reduction and equal opportunities, in Mexico and within the Latin-American region; as well as to be a reliable source of information and analysis for government officers and the general public. For more information: **www.fundacionidea.org**

Giulia Salieri - Director at Fundación IDEA

Sandra Fuentes - Senior Analyst at Fundación IDEA

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