Pharmaceuticals in Latin America and the Caribbean

Players, access, and innovation across diverse models

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Abstract

Pharmaceutical products have contributed to longer life expectancy and better quality of life in Latin America and the Caribbean. However, they often account for a significant share of household expenditures, especially among the poor and those facing catastrophic health shocks. And they are not always accessible, as dramatically exposed by the Covid-19 pandemic. This mixed record can be linked to the workings of the pharmaceutical sector, an issue that has not received much attention in policy discussions.

This paper identifies the sector's key domestic and foreign players, and analyzes its local output, international trade, and price levels. It also documents government policies, including intellectual property rights, regulatory oversight, and public procurement. An important contribution of the paper is to show the significant scientific capacity of the region, especially in relation to biological products – including vaccines – whose intrinsic heterogeneity challenges intellectual property rights protection.

Based on this diagnosis, the paper flags three sets of issues for policy makers to consider. Relatively uncontroversial measures include strengthening regulatory authorities, promoting the use of generics, and upgrading public procurement. Other areas, such as supporting R&D and regulating prices, involve tradeoffs. Finally, there are strategic choices to be made, with some countries in the region favoring stringent intellectual property rights, while others support national champions or rely on state entrepreneurship.

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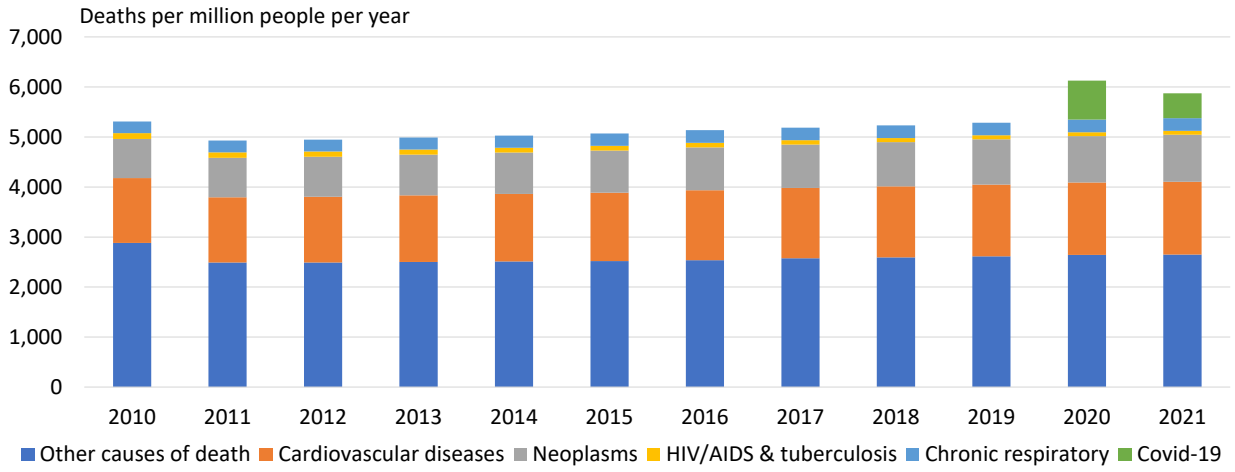
Introduction

Pharmaceutical innovations, together with higher living standards and more effective public health interventions, have been critically important to extend life expectancy and improve population wellbeing in Latin America and the Caribbean.

The largest burden of disease in the region comes from non-communicable conditions that tend to accumulate in aging populations. In 2000, there were approximately 30 million people aged 65 years and older in Latin America and the Caribbean. By 2020, this group had risen to 58 million. And by 2030, the share of the population over 65 could reach 145 million, or almost 19 percent of the total population (United Nations 2020). Not surprisingly, cardiovascular diseases represented 27 percent of total deaths in 2019, followed by cancer at 18 percent, and diabetes and kidney disease at 11 percent (figure 1).

Figure 1. Main causes of mortality in Latin America and the Caribbean



Source: IHME and authors' calculations.

By comparison, communicable diseases typically account for a much smaller share of mortality in Latin America and the Caribbean. At the turn of the decade, AIDS contributed 1.5 percent of total deaths, whereas respiratory infections – including tuberculosis – accounted for another 7 percent. However, the pandemic forcefully brought back the importance of communicable diseases. Based on official statistics, Covid-19 accounted for 12.7 percent of total deaths in 2020. The share would be much higher if data on excess mortality was used instead (World Bank 2020). Based on current trends, the toll could be comparable in 2021.

The greater significance of non-communicable diseases over time and the dramatic surge in communicable diseases during the last two years highlight how important the availability of effective, safe, and affordable medicines is for the region. Considerable progress in access to medicines has been made in the four decades since the introduction of the essential medicines concept by the World Health Organization (WHO) (Laing et al. 2003, Reich 2000, WHO 2004).

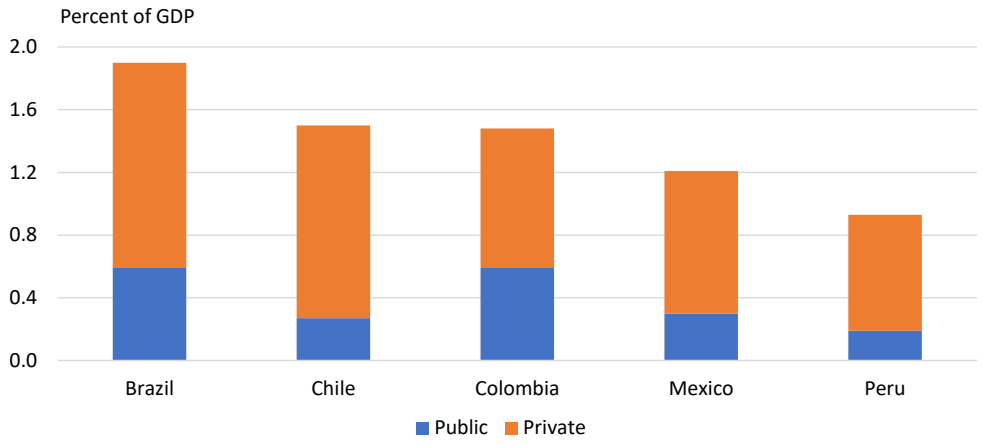
However, about 15 percent of medicines on the current essential list are under patent protection (Hill et al. 2018).

The most significant life-expectancy gains for both women and men in recent times were associated with fewer deaths from cardiovascular diseases, including ischemic heart conditions and cerebrovascular events. Drugs such as statins, antihypertensives, and warfarin were critically important in this respect, but they were not the only ones. Indeed, the list of essential medicines by the WHO includes more than 20 different cardiovascular drugs (Buxbaum et al. 2020, Wirtz et al. 2016). Importantly few new medicines for cardiovascular diseases and cholesterol have been introduced over the last quarter-century, so most treatment relies on generics (IQVIA 2020).

Cancer mortality has also fallen substantially, especially in stomach and colorectal cancer for both sexes, breast cancer for women, and lung cancer for men, with a significant share of the gains linked to new pharmaceuticals (Barrios et al. 2021, Carioli et al. 2020; Mathers et al. 2015). For example, 60 percent of the life extension for breast cancer can be attributed to medicines, and 30 percent for colorectal cancer (Buxbaum et al. 2020). Unlike cardiovascular drugs, most oncological medicines are protected by patents. Together with medicines for immunology and diabetics, they account for about half of the spending on patented pharmaceuticals in advanced economies (IQVIA 2021).

Mortality from communicable diseases has been even more responsive to the availability of effective and safe medicines. The life expectancy of HIV-positive people has been substantially extended thanks to a combined antiretroviral therapy (Buxbaum et al. 2020, Teeraananchai et al. 2017). Meanwhile, as variants of the SARS-Cov-2 virus multiply and non-pharmaceutical interventions such as stay-at-home orders and business closures show their limits, mass vaccination is increasingly seen as the only viable option to transform the pandemic into an endemic disease.

Figure 2. Public and private spending on pharmaceuticals



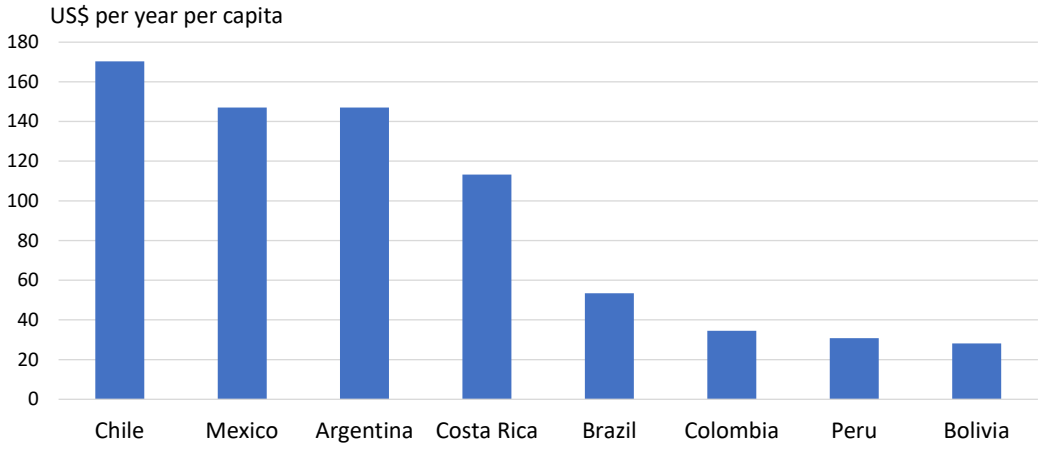
Note: Data are for 2019, except for Chile (2016), Colombia (2017) and Peru (2018).
Source: IBGE for Brazil, Ministry of Health and Ministry of Finance for Chile, Edson (2018) for Colombia, OECD for Mexico, and INEI for Peru.

All Latin American and Caribbean countries have brought almost everyone into a financial protection scheme for health care costs (Atun et al. 2015; Cotlear et al. 2015). And much progress has been made in extending healthcare coverage and access to medicines to increasingly broad segments of the population (Cotlear et al. 2015). However, aging populations and increasingly expensive new drugs have led to the value of pharmaceutical expenditure becoming substantial relative to the size of the economies in the region. In 2020, an estimated 1 to 2 percent of GDP, depending on the countries, was devoted to buying medicines (figure 2).

On average, pharmaceutical revenue accounts for 16 percent of healthcare expenditures in Latin America and the Caribbean, in line with the 15 percent observed among OECD countries. But there is considerable dispersion, with the figure ranging from 6.6 percent in Uruguay to 34.7 percent in Guatemala (Statista 2017). Because lower-income countries tend to spend less on expensive treatment at the hospital level, the relative share of drugs is higher.

How pharmaceutical costs are split between government and households varies depending on the institutional arrangements in force. Out-of-pocket expenditures are influenced by the way the cost of medicines is split between patients and healthcare providers, with the nature of arrangements varying considerably across countries. But households may still bear a considerable financial burden (figure 3).

Figure 3. Out-of-pocket spending on pharmaceuticals in monetary terms



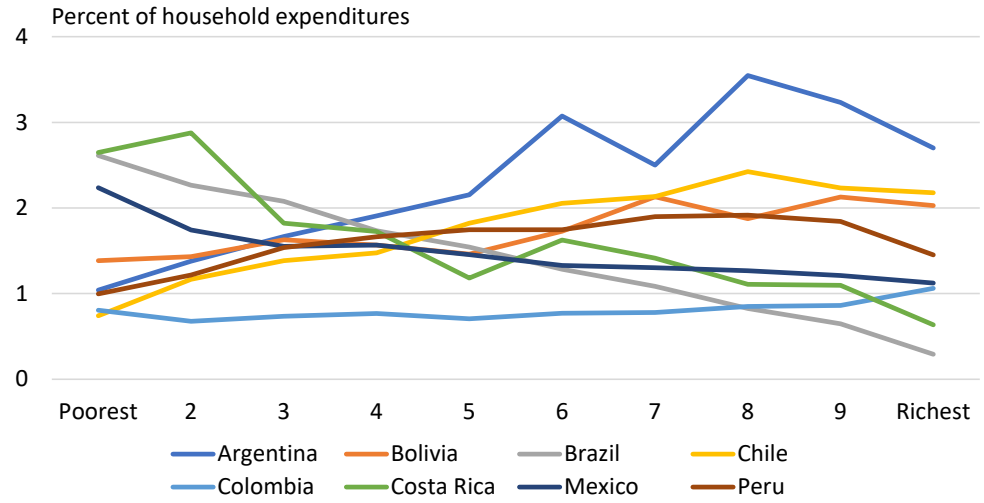
Note: Data are for the year 2018.
Source: World Development Indicators for aggregate data, SEDLAC for household survey expenditure data, and authors' calculations.

The value of medicine purchases in pharmacies more than doubled over a decade in Latin American and the Caribbean, growing from US$ 34.3 billion in 2008 to US$ 69.5 billion in 2017. The region accounts for 6.3 percent of the world pharmaceutical market value (IQVIA 2018). More than three-quarters of this spending takes place in Brazil, Mexico, and Argentina – the three biggest economies in the region (IQVIA 2017).

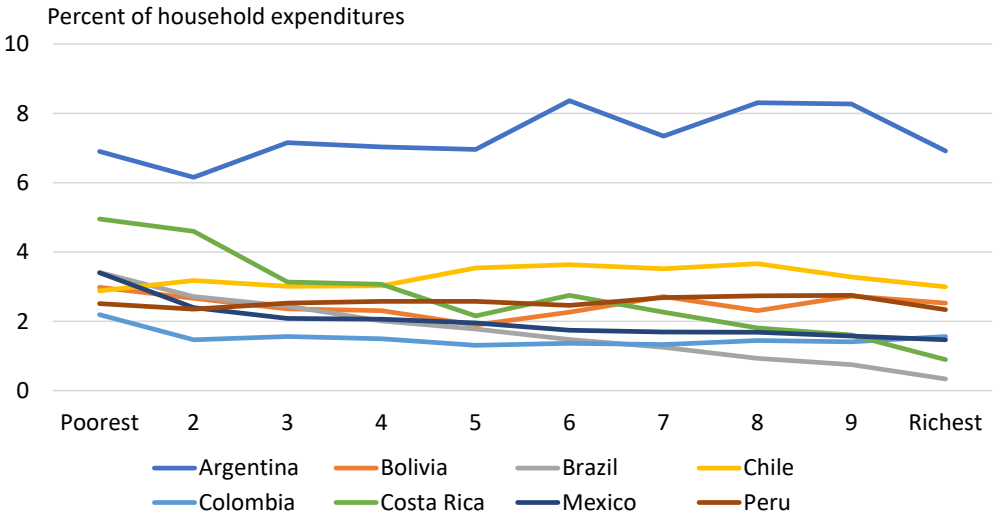
This burden also varies across population groups (figure 4). In some Latin American and Caribbean countries, out-of-pocket expenditures are progressive in the sense of representing a larger share of household expenditures among better-off households. In others, they are regressive, putting a heavier burden on poorer households. But when considering only households that do spend on pharmaceuticals – which includes those experiencing chronic illnesses or catastrophic health shocks – regressivity is the norm.

Figure 4. Incidence of spending on pharmaceuticals on household expenditures

a. All households



b. Households that do spend on pharmaceuticals



Note: Data are for the most recent year available. Deciles are defined based on household expenditure per capita.

Source: SEDLAC and authors' calculations.

Despite the progress in extending healthcare coverage to mostly everyone, no country in Latin America and the Caribbean has eliminated the problem of catastrophic out-of-pocket payments,

where drugs play a significant role World Bank 2020). These payments can impoverish some households and deepen the extent of poverty among others. Although there is a trend toward improved protection, about a decade ago a staggering16.0 million people had incurred catastrophic spending for healthcare in Latin America and the Caribbean (Wagstaff et al. 2015).

Given the contribution pharmaceuticals make to extending life expectancy and to providing a better quality of life, it is worth exploring which pharmaceutical products are available in Latin America and the Caribbean, or whether they are overly expensive. This requires understanding how the pharmaceutical sector is organized and regulated in practice and what is the potential for external and foreign players to meet the needs of the population.

Despite its importance, the pharmaceutical sector has occupied a relatively marginal place in the economic policy debates of the region. A quick exploration of publications by development organizations with a strong regional foothold is revealing. Thus, there are four documents indexed by the word 'pharmaceutical' among the 2.6 thousand entries in the publications' webpage of the Economic Commission for Latin America and the Caribbean. There are nine, out of 10.7 thousand, in the corresponding Inter-American Development Bank webpage; most are briefs, and the last comprehensive overview is two-decades old. And a joint search for the words "pharmaceutical" and "Latin America" yields only four documents among the 33.3 thousand in the World Bank's open knowledge repository; the most recent one is from 2005.

On the other hand, considerable research on pharmaceutical policy is available from a health sector perspective. Both WHO and its regional counterpart, the Pan-American Health Organization (PAHO) have produced a very significant body of knowledge that is extensively cited here. There have also been comprehensive reviews of pharmaceutical policies and regulations in developing countries more generally, with that by Seiter (2010) being an important reference. However, the intersection of the health sector perspective with an industrial organization approach and a region-specific focus remains a relatively empty space.

This paper can be seen as an attempt to fill this void. By jointly analyzing market structure, government policy, and scientific capacity across several countries in Latin America and the Caribbean, the paper tries to shed light on the specificities of the pharmaceutical sector in this region. In the process, it shows that fundamentally different organizational models coexist. Without being prescriptive, the paper identifies the challenges faced by policymakers – especially in the context of the Covid-19 pandemic – and the main choices ahead.

Market structure

The pharmaceutical industry is considered to be one of the sectors with the highest productivity in Latin America and the Caribbean, creating well-paid formal jobs and contributing to economic dynamism more broadly (Carrasco and Harrison 2020). However, what is produced domestically and what is imported differs considerably across countries. To understand these differences, it is useful to distinguish between types of medicines (box 1).

Box 1. Types of pharmaceutical products

Pharmaceutical products can be classified along two main dimensions. From a technical point of view, most approved drugs worldwide are small molecules or **synthetic drugs** with relatively simple chemical structures, which are relatively inexpensive to manufacture. **Biological drugs,** on the other hand, are larger and complex products that build on living organisms. They are much costlier to develop and produce and also harder to standardize, even for the same manufacturer.

Monoclonal antibodies (MAB) stand out among biological drugs, as they are significantly more effective than previously available therapies and often better tolerated by patients. More than 100 MABs have been licensed over the past three decades, most of them for the treatment of non-communicable conditions, such as cancer and autoimmune diseases.

Vaccines can also be treated as a self-standing sub-category of pharmaceuticals, as their production involves various technologies and manufacturing processes with different novelty levels. Four main types of development platforms are usually identified, corresponding to different generations of vaccines.

The first, whole-virus generation, introduced in the 1950s, is at the roots of most of the vaccines in use today and includes two subtypes: inactivated and weakened viruses. Then came protein-based vaccines, which relied on technologies developed in the 1990s, divided into virus-like particles and protein subunit. Finally, viral-vector and nucleic acid vaccines emerged more recently. Two types of viral-vector vaccines, replicating and non-replicating, had been authorized for human use during the last decade, while two nucleic acid Covid-19 vaccines, of the mRNA type, received approval last year (Callaway 2020; Le et al. 2020).

Finally, drug production relies on *Active Pharmaceutical Ingredients* (APIs), which are combined with excipients make the formulation, and then converted into finished dosages under the form of tablets, capsules, or injections. APIs can be of chemical or biological origin; some of them are derived from natural sources extracted from plants and marine ecosystems.

The second important classification of pharmaceuticals concerns their intellectual property rights. **Originator products** are most often protected by either patents or data exclusivities when they first come to market. **Generic products** are based on originator drugs that are either off-patent or have been licensed to other manufacturers to make copies while the patent is valid. A generic drug is intended to be interchangeable with the originator product. It must be identical in terms of safety, quality, efficacy, dosage, strength, and route of administration, and it should have the same intended use (FDA 2019).

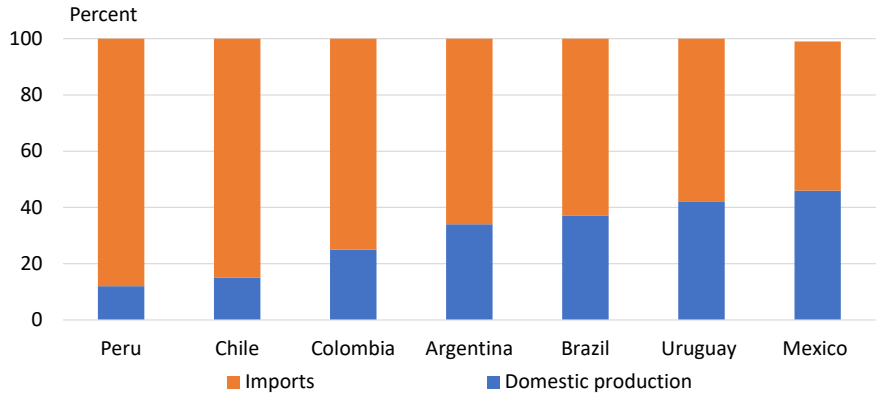
Generics are further grouped into branded and unbranded products. *Unbranded generics* are marketed using the name of the active ingredient, for example, paracetamol. In contrast, *branded generics* use a name other than the active ingredient, such as Tylenol in the previous example. Branded generics are particularly important in Latin America and the Caribbean.

Generic drugs have been advocated as a tool to control healthcare expenditures and improve access to medicines. This approach has worked well in the case of traditional small molecules or synthetic drugs, which are easier to manufacture. However, transforming the last generation of biological drugs into generics is more challenging.

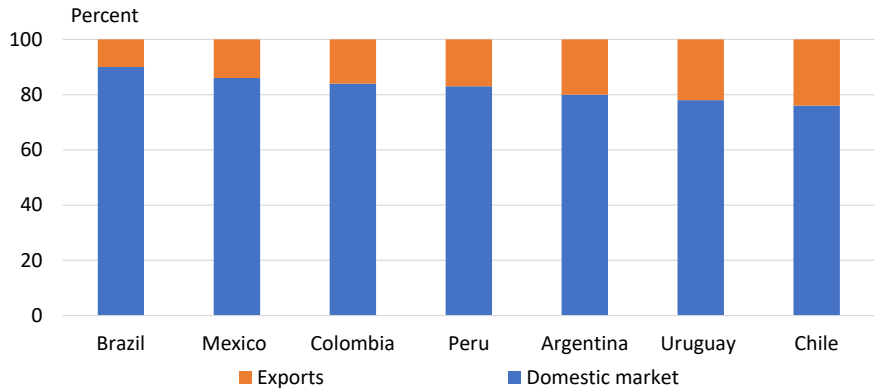
Biosimilars – pharmaceuticals that resemble originator biological drugs – are an important category among generic drugs. To gain approval, their manufacturers must demonstrate very high similarity to the originator product, except for minor differences in clinically inactive components. However, biosimilars are never identical copies, because they are produced from living organisms, and their features are highly dependent on their manufacturing process. Clinical trials are thus needed to demonstrate that any differences are not clinically meaningful. Because their development builds on additional research and takes eight to ten years on average, biosimilars tend to be expensive to produce (Blackstone and Joseph 2013).

Figure 5. Origin of pharmaceutical consumption and destination of pharmaceutical production

a. Consumption by origin



b. Sales by destination



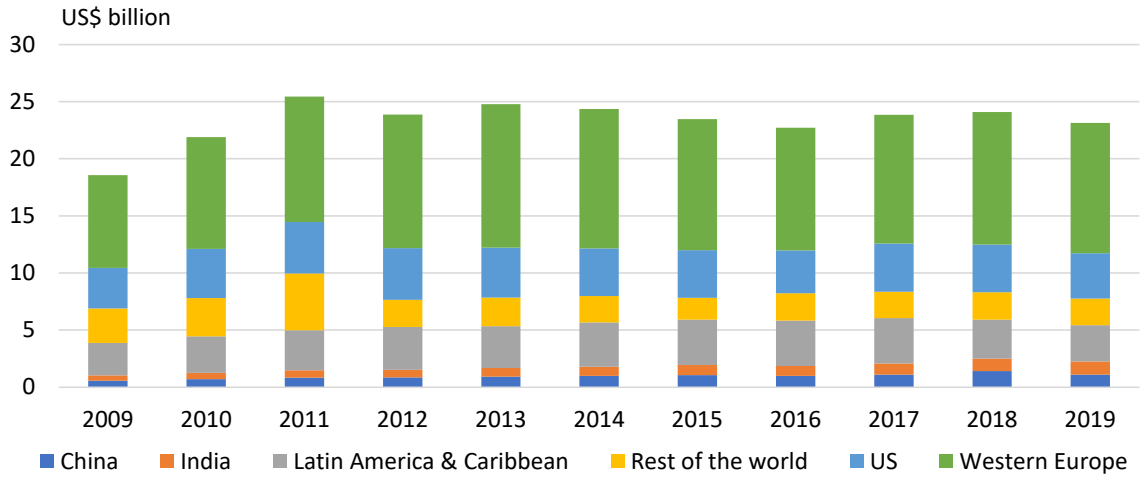
Note: Data are for 2019, except for Colombia, Mexico and Brazil (2018), and Peru (2017).
Source: Brazilian Institute of Geography and Statistics, DANE for Colombia, National Institute of Statistics and Geography for Mexico, INEI for Peru, and International Trade Association for Uruguay.

Output and trade

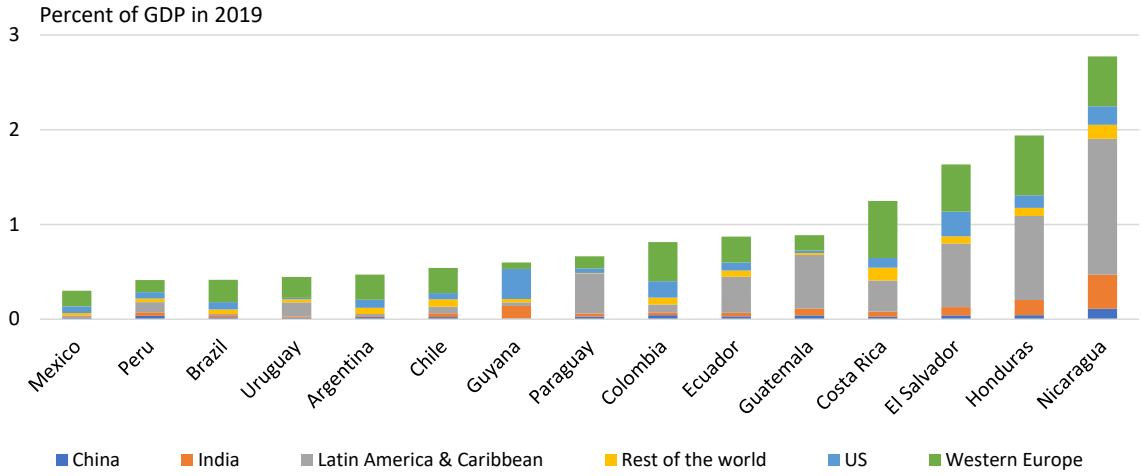
Most countries in Latin America and the Caribbean produce and even export some pharmaceutical products, and all of them are also importers (figure 5). At one end, Mexico and Uruguay have a solid pharmaceutical industry, whose products satisfy 46 and 42 percent of their domestic demand for medicines, respectively. Then follow Brazil and Argentina, meeting around 35 percent of their internal demand. At the other end, Chile and Peru only produce 15 and 12 percent of the pharmaceuticals consumed in the country. Overall, however, the sector does not contribute more than 1 percent of GDP in any of the countries in the region.

Figure 6. Pharmaceutical imports by origin

a. At the regional level



b. At the country level



Source: UN COMTRADE and authors' calculations.

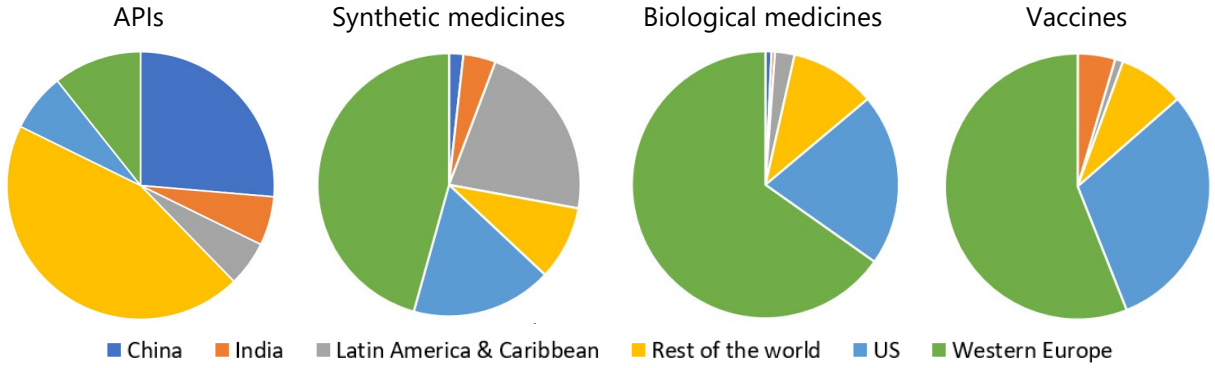
Pharmaceutical imports account for around 70 percent of the local demand for medicines but also for a non-negligible fraction of total country imports (figure 6). The median value of such fraction

across the region is 12.6 percent. About half of the pharmaceutical products imported originate in Western Europe, followed by the US and other Latin American countries, two sources that account for about 20 percent of the total each. The remaining 10 percent is shared roughly equally between China and India.

By value, synthetic drugs account for about two thirds of pharmaceutical imports, followed by biological drugs, at about a quarter. Vaccines and APIs only represent 3 and 7 percent of the value of imports, respectively.

About half of the synthetic drugs imported are from Western Europe and a quarter from other countries in Latin America and the Caribbean (figure 7). APIs are imported to a much greater extent from other developing countries. Western Europe and the US remain important sources, but the rest of the world – including India, Brazil, and Argentina – accounts for 45 percent of the total. Chinese companies are rapidly increasing their participation in this segment through sustained efforts to enhance the quality of their products. The first Chinese API was prequalified by WHO in 2012; 15 more have received prequalification since then (WHO 2020). By now China accounts for more than a quarter of the API imports of the region, with Hungary, South Korea and Singapore being also among the top suppliers.

Figure 7. Pharmaceutical imports at the regional level by type of product and origin

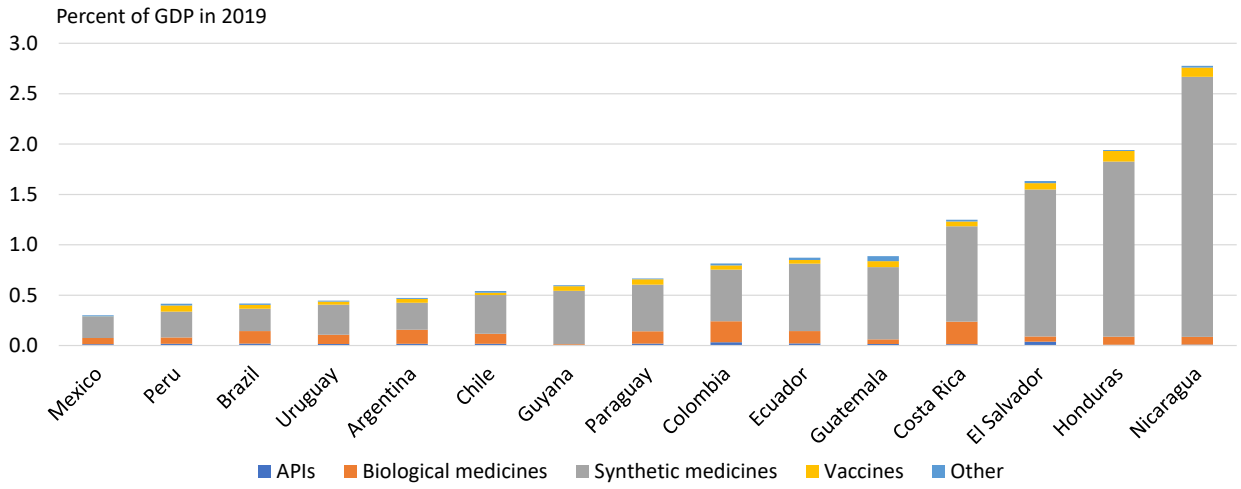


Source: UN COMTRADE and authors calculations.

Biological medicines, mostly under patent protection, originate mainly in Western Europe and the US, which jointly account for 86 percent of the total. Advanced economies are also the main source for vaccines, but India is an emerging supplier, together with other countries in Latin America and the Caribbean, and with the rest of the world. About 50 of the vaccines produced by Indian companies and four from Brazilian and Cuban companies have been prequalified by WHO (WHO 2020).

Import shares by type of product vary with the importer's level of development. In upper-middle-income countries, such as Brazil, Argentina, and Colombia, biologics represent more than 25 percent of total pharmaceutical imports. The share falls below 5 percent in lower-income countries, where synthetic drugs account for the bulk of purchases abroad. (figure 8).

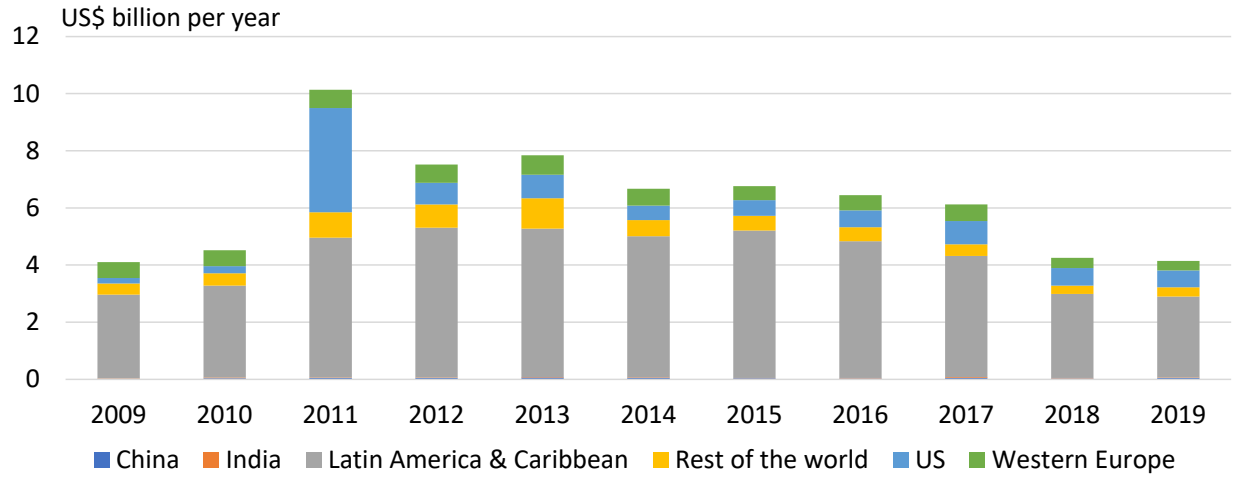
Figure 8. Pharmaceutical imports at the country level by type of product



Source: UN COMTRADE and authors' calculations.

Taken as a whole, Latin America and the Caribbean exports US$ 6 to 8 billion in pharmaceutical products annually. There was a surge in exports in 2011, due to an unusual shortage in the US market. But exports have declined in recent years mainly due to the latest US sanctions on Cuba, traditionally one of the biggest suppliers of medicines in the region (figure 9). About 70 percent of sales abroad are to other countries in Latin America of the Caribbean. The second destination is the US, which absorbs roughly 15 percent of pharmaceutical exports from the region, followed by Western Europe and the rest of the world, at about 8 percent each.

Figure 9. Pharmaceutical exports at the regional level by destination



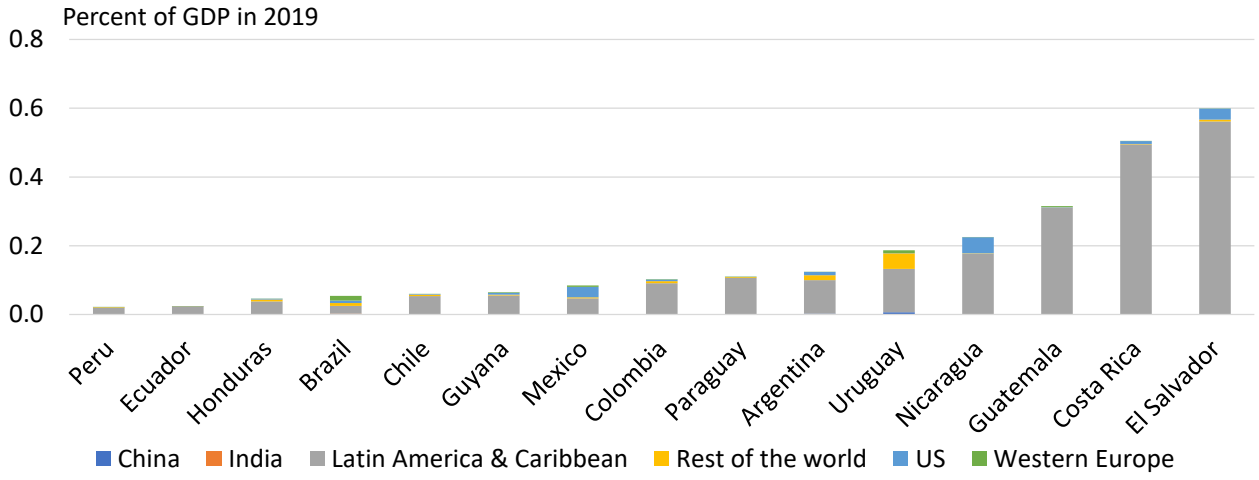
Source: UN COMTRADE and authors' calculations.

At present, pharmaceutical exports from the region originate mainly in two distinct geographical areas: Mexico plus Central American countries on the one hand and South America on the other. Each of these two areas accounts for roughly the same export value. Exporting Central American

countries include Costa Rica, Guatemala, and El Salvador, while South America's leading exporters are Brazil, Argentina, Colombia, and Uruguay.

Pharmaceutical exports account for a bigger share of GDP in Central American countries and Uruguay. The destination markets are different as well. Mexico and Central American countries lean toward the US market. In contrast, South America has more diversified destinations, primarily Western Europe, followed by the US, China, and India (figure 10).

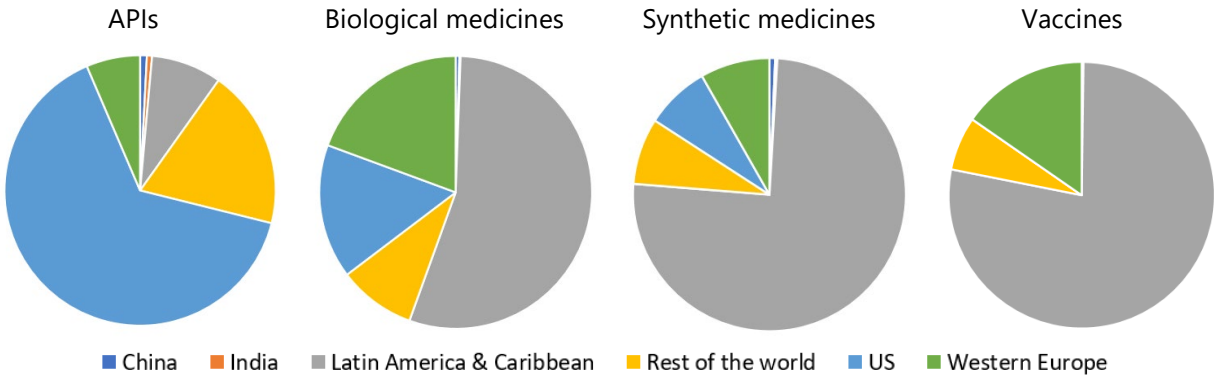
Figure 10. Pharmaceutical exports at the country level by destination



Source: UN COMTRADE and authors' calculations.

Most of the pharmaceutical products exported by countries in Latin America and the Caribbean are generics and they are mainly sold to other countries in the region. In terms of total export value, APIs are the only other significant export item. Their main market is China. Biological medicines, vaccines and other drugs, taken together, account for far less than US$ 1 billion in exports annually (figure 11).

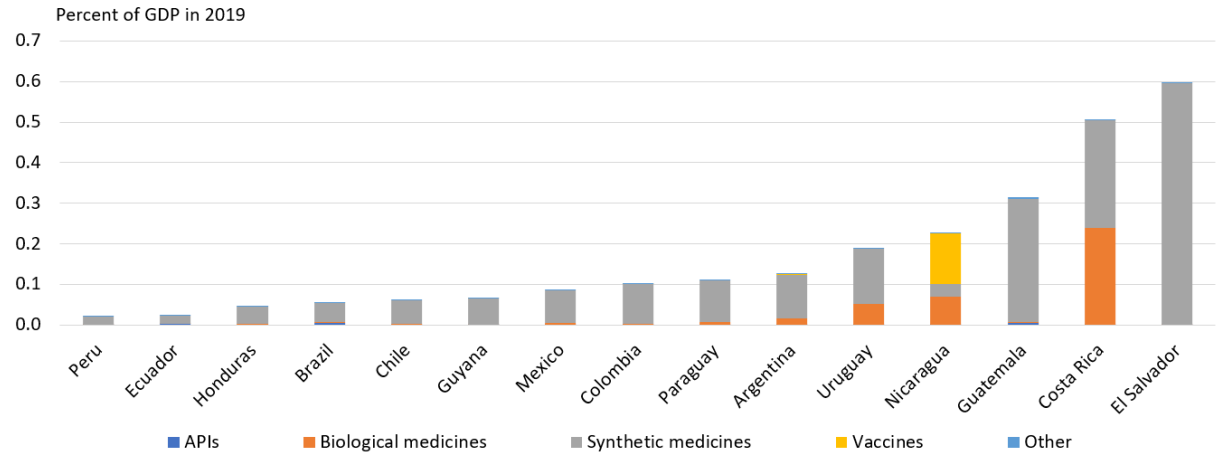
Figure 11. Pharmaceutical exports at the regional level by type of product and destination



Source: UN COMTRADE and authors' calculations.

A few countries, mostly small, display a more diversified export mix. Foreign sales of biological products account for a non-negligible share of GDP in Costa Rica, Nicaragua, Uruguay, and, to a lesser degree, in Argentina. Nicaragua is also a significant exporter of vaccines (figure 12).

Figure 12. Pharmaceutical exports at the country level by type of product



Source: UN COMTRADE and authors' calculations.

Pharmaceutical companies

The pharmaceutical industry is intensive in capital. The production of innovative drugs is also intensive in research and development (R&D), resulting in large sunk costs. The main actors are large traditional multinationals from Western Europe and the US. But new players have emerged in recent years, including multinationals from China, India, and South Korea, and local firms from a relatively narrow group of developing countries. Players belonging to these three groups of firms can be found, to varying extents, in the pharmaceutical sectors of most countries in Latin American and the Caribbean (Table 1).

Pharmaceutical companies differ in the types of products they develop and sell. Multinationals operating in the region focus on marketing and selling originator products and branded generics developed by their parent companies, some of which may be produced domestically. Local firms, conversely, use mostly imported APIs to produce generic drugs, which they sell at lower prices than imported products. Increasingly, they also produce biosimilar products.

In Argentina, Brazil, and Mexico, local firms play a leading role in manufacturing pharmaceuticals. Measured by their share of market sales, only two out of the top ten pharmaceutical companies operating in Argentina are foreign multinationals. Their number increases to four in Brazil, including Medley from India, and six in Mexico, where local firms are still important players. By contrast, in Chile and Colombia, nine of the top ten pharmaceutical companies are multinationals. A cursory look at the top local firms gives a sense of their product mix and R&D potential (box 2).

Table 1 — Top ten pharmaceutical companies by revenue

Argentina	Brazil	Chile	Colombia	Mexico
Roemmers	Aché	Abbott	Pfizer	Sanofi
Elea Phoenix	EMS	Sintex	Sanofi	Genomma Lab
Gador	Eurofarma	Roche	Novartis	Liomont
Casasco	Sanofi	TEVA/ Laboratorio Chile	Roche	Pfizer
Montpellier	Takeda	Saval	Bayer	Boehringer Ingelheim
Bagó	Neo Química	Bayer	Abbott	Roche
Baliarda	Novartis	Andromaco-Grunenthal	GlaxoSmithKline	Probiomed
Raffo	Mantecorp Farmasa	Merck	Technoquimicas	Farmaceutica Maipo
Sanovi	Medley	GlaxoSmithKline	Janssen	Novartis
Bayer	Libbs	Pharma Investi/Megalabs	Merck	Bauch Health

Note: Cells in yellow indicate multinational pharmaceutical companies, cells in white are for domestic ones, and those in gay to joint ventures and subsidiaries, mostly specializing in generics. Data are for 2021, except for Colombia (2020).

Source: CILFA for Argentina, Interfarma for Brazil, América Economía for Chile, Superintendencia de Industria y Comercio for Colombia, and Statista for Mexico.

With around 65 biotech companies working on human health, Argentina's pharmaceutical industry has shown strengths in the development of generics and biosimilars (Papini and Morinigo 2020). Over a dozen of these companies, including the Insud group, Bago, Cassara, ELEA, Gador, Roemmers, and Wiener, are exporting biosimilars, primarily to other countries in the region and to Asia (Gutman and Lavarello 2017). Sales to China, India, and Vietnam increased by 179 percent between 2003 and 2017. Some of these companies manufacture their products in Asia. For example, Bago, through a joint venture, produces biosimilars in Pakistan. Others such as BioNovis S.A. fill and finish local products that were developed abroad. Thus, the Insud group recently entered an agreement with AstraZeneca and Liomont of Mexico to produce a Covid-19 vaccines (Ortiz-Prado et al. 2020, Vargas 2020a).

Brazil, Mexico, and Uruguay are all active in life sciences research, publications, manufacturing, and exports. These countries have access to a large regional market through trade agreements such as Mercosur or US-Mexico-Canada. In Mexico, among the few companies, Probiomed, SA stands out, conducting research with the support of academic institutions to innovate. Brazil's local companies, such as Libbs and, Biomm are successfully supplying trastuzumab's biosimilars at half the originator biological's price.

Box 2. Outstanding domestic pharmaceutical companies in the region

Argentina

Roemmers is an Argentinean-German firm that manufactures generics, biosimilars, and innovative products. It exports to other countries in the region and has a presence in Mexico, Brazil, Ecuador, Peru, Colombia, Chile, Venezuela, and Paraguay. It also exports to Western Europe and Asia. Roemmers has significant R&D capabilities and has developed an innovative anti-inflammatory molecule, clonixinato lisina.

Gador manufactures biologics, biosimilar products, branded generics, and APIs. It exports to other countries in the region, as well as to Western Europe and Asia. Its R&D focuses on endocrinology and bone diseases. As an innovative firm, it has invested in developing a vaccine for Chagas disease.

Bago manufactures generics, biosimilars, and innovative products. It exports to the rest of the region, Asia and Western Europe. It has a joint-venture partnership in Pakistan for the R&D and manufacturing of cancer biosimilars. Bago has significant R&D capabilities, including a unit dedicated exclusively to multiple sclerosis. It has discovered the anti-inflammatories talniflumate and trifamox, and an antibiotic that it exports primarily to Asia.

Elea Phoenix is a top Argentinian pharmaceutical company with an R&D unit and a primary interest in oncology. It manufactures MABs and therapeutic vaccines. In 1997 it was the first company to launch a MAB in Argentina, followed by the first biosimilar for rituximab in 2014 and bevacizumab in 2016.

Grupo Insud includes the companies Chemo, Exeltis, and mAbxience, which integrate a pharmaceutical industry chain. Chemo manufactures APIs and generics. It owns 16 manufacturing sites and nine R&D centers worldwide. mAbxience is a biotech engaged in the research, development, and manufacturing of biosimilars. It has two production plants, in Buenos Aires and in León, Spain, both compliant with Good Manufacturing Practices (GMP). Group Insud is also a shareholder of Elea, Biogénesis Bagó, Sinergium Biotech, Chemotecnica S.A, and Inmunova.

Pablo Cassara is one of the top Argentinian pharmaceutical companies with a biotechnology R&D unit and closely associated with public research centers. It has developed seven biosimilar drugs, primarily for cancer – for example, filgrastim. and an innovative MAB under patent.

Brazil

EMS S.A. is one of Brazil's largest domestic companies. It focuses on generics and branded generics, exporting to other countries in the region and to Western Europe, Australia, and Asia. In addition, it has partnered with Chinese companies to access technologies for manufacturing biologics and especially MABs.

Aché manufactures generics, branded generics, and plant-based medicines, specializing in oncological and dermatological drugs. It exports to other countries in the region, Asia, Africa and the US. It is one of the most innovative pharmaceutical companies in the region, with two molecules in the market and half a dozen molecules out of Brazil's biodiversity in its R&D pipeline. In 2016 Aché joined the Structural Genomics Consortium (SGC), an international partnership between universities, governments, and pharmaceutical industries to develop new oncological and anti-infectious drugs under an open innovation model.

Hypermarcas manufactures and commercializes generics and branded generics pharmaceuticals, with a focus on the domestic market. It started an R&D center in 2012.

BioNovis S.A is a public-private partnership between the government of Brazil and some of the most prominent local companies – including Aché, EMS, Hypermarcas, and União Química – to develop biosimilars. It has already launched a MAB biosimilar for the drug infliximab. Its pipeline includes oncological and anti-inflammatory drugs, such as trastuzumab, rituximab, bevacizumab, etanercept, and adalimumab.

Chile

Saval is the fourth-largest company in Chile by market value. It specializes in generics, branded generics, and biosimilars. It exports to ten countries in the region, focusing on medicines for infectious diseases, ophthalmology, and oncology.

Colombia

Tecnoquímicas manufactures generics and branded generics in eight production sites in Colombia and two in El Salvador. In addition, it has entered the production of biosimilars in alliance with *mAbxience*, an Argentinean firm. It exports to Central American countries and to the US.

Mexico

Pisa Farmacéutica is one of the largest manufacturing companies in Mexico, but it is also vertically integrated, including medical centers and pharmacies. It has around 20 specialties, with nephrology and diabetes standing out. Its unit Pisa Biotech has developed a biosimilar for insulin in partnership with Becton Dickinson AB, an American company. It also exports generics to other countries in the region and to the US.

Sanfer is a company producing generics and branded generics, with manufacturing plants in Mexico, Colombia, and Chile. Partnerships with various other companies facilitate its exports to the US, the rest of the region, Western Europe, and Asia.

Senosiain manufactures generics, such as antibiotics, antirheumatic and antiulcer drugs. It exports to other countries in the region and, since 2016, to the US market.

Siegfried Rhein – a subsidiary of Argentina's Roemmers – manufactures around 90 generics for antibiotics, analgesics, and medicines for cardiovascular diseases. In 2019 the company received a US$ 160 million loan from the World Bank's International Finance Corporation to expand its operations to other countries in the region.

Another case in point is that Brazil's government partnered with a Cuban Research Center, which led to a technology transfer agreement to manufacture locally pegylated interferon, a biological product used for treating hepatitis C (Azevedo et al. 2012). Finally, Uruguay also has some companies developing and manufacturing biosimilars for filgrastim and interferon in a joint venture with an Italian company.

For Costa Rica, biotechnology is a fundamental pillar of the country's strategic development plan, promoting the collaboration between the state, academia, research centers, and the domestic and international private sector (Álvarez 2020). In contrast to other Latin American and Caribbean countries, the pharmaceutical industry includes local companies in tandem with international companies, having as the primary target markets in Western Europe and the US. Costa Rica and Argentina, independently, under a public-private collaboration, have developed a serum therapy for the treatment of COVID-19. Both are in clinical trials (Barquero 2021; Zylberman et al. 2020).

Cuba stands out in the region because of the 'full-cycle,' vertically integrated organization of its pharmaceutical sector (box 3). There are close to ten companies responsible for the entire innovation process, starting from basic science and then moving into clinical trials, all the way from Phase 1 to Phase 4 studies. Once the various regulatory authorities approve a drug, it is produced for the internal and international market (Lage 2008, Wright 2016, Radcliffe Institute 2020). Cuba is currently trying to establish a legal regime more conducive to attracting investors into its biotechnology sector.

Box 3. The Cuban pharmaceutical sector

The biotechnology and the pharmaceutical industry in Cuba are managed and coordinated by Bio Cuba Farma. At the core, there are more than 30 closely related organizations involved in R&D and the production of vaccines and drugs. Altogether they employ about 20,000 people. The most prominent organizations are the Center for Genetic Engineering and Biotechnology (CIGB), the Finlay Institute, and the Center for Molecular Immunology (CIM).

The CIGB, founded in 1986, is the flagship of the Cuban biotechnology sector and the most prominent institute. CIGB produces vaccines and other medical, industrial, and agricultural biotech products. Its main expertise is in recombinant technologies based on single cell organisms. CIM's focus is cancer research and includes cutting-edge recombinant therapeutic cancer vaccines. The Finlay Institute emerged from a 1980s vaccine development project. It is through this project that the country successfully combated a meningitis epidemic by developing its own meningococcal group B vaccine. Finlay's product portfolio is dominated by traditional vaccine technologies (Plahte and Reid-Henry 2013).

Cuba's biotechnology sector is also actively involved in international research collaboration, including joint publications and research with American, European, Latin American, China, and Indian scientists (Palacios-Callender, Roberts, and Roth-Berghofer 2016). Some examples are the tripartite Canada-Cuba-China research collaboration for the study of Alzheimer's (The Ludmer Centre 2018). Cuba's Molecular Immunology Center (MIC) partnership with New York's Roswell Park Cancer Institute implementing the island's first clinical trial in the USA. The clinical trial is for the lung cancer drug, CIMAvax-EGF, currently in phase 2 (Evans et al. 2018).

MIC has established joint venture companies in Canada, Thailand, China, India, and Spain. The activities of these companies include the development, production, and commercialization of therapeutic cancer vaccines, monoclonal antibodies, and erythropoietin (Thorsteinsdóttir et al. 2010). Commercial contracts are subscribed under international law, for example, under the Swiss or the British legal systems (Radcliffe Institute 2020).

Overall, more than 100 new products – originators and generics – have been developed, and another 60 are in the pipeline. Most of them are protected by intellectual property rights. About 200 patents have been issued in Cuba, leading to the filing of 1,800 patents overseas, including in the US (García Delgado, Di Fabio, and Vidal Casanovas 2020; WHO 2015).

Cuba biotech earns revenue from technology licensing agreements. For instance, CIGB has licensed its yeast-based recombinant hepatitis B expression system to Indian Panacea Biotec. Also, CIM has established a joint venture company with Biocon India to manufacture its own biological products, including nimotizumab, itolizumab, and monoclonal antibodies (Radcliffe Institute 2020).

In recent years, the arrival of Chinese, Indian and South Korean companies has transformed the pharmaceutical sectors of Latin America and the Caribbean. But there are important differences between them, both in terms of their products and the way they operate.

South Korean companies export generics and biosimilar products to Brazil, Chile, Mexico, and Ecuador, among others. Three of them stand out. Dong-A, one of the largest pharmaceutical companies in the country, has developed innovative products for cancer and infectious diseases. Celltrion specializes in biosimilars for MABs, focusing on autoimmune diseases such as rheumatoid arthritis. And ISU Abxis develops and manufactures MABs for cancer, inflammations, and rare diseases.

Chinese firms have been increasing their presence by supplying APIs and, more recently, vaccines. Some of the most important players are Biomabs, a pharmaceutical laboratory from Shanghai, and Guojian, a company established in 2002 which focuses on R&D, manufacturing, and commercialization of MABs. Guojian has grown into one of China's leaders in this area, providing drugs for cancer and autoimmune diseases, as well as immunosuppressants for organ transplantations. Another is Sinovac, which focuses on vaccines against infectious diseases, including the Covid-19 vaccine CoronaVac.

Table 2. Indian pharmaceutical companies with presence in the region

Indian company	Regional affiliate	Location	Year	Entry mode	Ownership	Activities
Aurobindo AB	Farmo Quimica	Brazil	2000	Greenfield	100	R&M&M
Dr Reddy's	Dr Reddy's Farmaceutica	Brazil	1999	Greenfield	100	R&M
Glenmark	Glenmark	Brazil	2003	Greenfield	100	R&M
Glenmark	Laboratorios Klinger	Brazil	2004	Acquisition	100	R&M&M
Glenmark	Serveycal	Argentina	2000	Acquisition	100	R&M&M
Ipca	Ipca do Brasil	Brazil	2003	Greenfield	100	R&M
Orchid Chemicals	Ogna Farma	Brazil		Greenfield		R&M
Ranbaxy	Ranbaxy Farmaceutica	Brazil	2000	Greenfield	94	R&M&M
Ranbaxy	Ranbaxy do Brasil	Brazil		Greenfield	100	R&M
Ranbaxy	Ranbaxy Panama, SA	Panama	2001	Greenfield	100	R&M
Ranbaxy	Ranbaxy PRP	Peru		Greenfield	100	R&M
Ranbaxy	Ranbaxy Mexico S.A. de C.V	Mexico	2004	Greenfield	100	R&M
Strides Arcolab	Strides Latina	Uruguay	2000	Greenfield	67	R&M
Strides Arcolab	Cellofarm Farmaceutica	Brazil	2000	Merger	100	R&M&M
Strides Arcolab	Infabra Industria Farmaceutica Brasileria Ltda	Brazil	2001	Acquisition	50	
Strides Arcolab	Goodlanza	Uruguay	2000	Greenfield	67	
Strides Arcolab	Biopharma	Venezuela	2006	Acquisition	80	R&M
Strides Arcolab	Solara SA de CV	Mexico		Greenfield	74	R&M&M
Torrent	Torrent do Brasil	Brazil	2002	Greenfield	100	R&M
Unichem	Unichem Farmaceutica do Brasil	Brazil	2004	Greenfield	100	R&M
Wockhardt	Wockhardt Farmaceutica do Brasil	Brazil	2004	Greenfield	100	R&M
Wockhardt	Wockhardt Mexico SA de CV	Mexico	2004	Joint Venture	51	R&M
Zydus Cadila	Zydus Cadila	Brazil	2000	Greenfield	100	R&M
Zydus Cadila	Quimica e Farmaceutica Nikkho do Brasil	Brazil	2007	Acquisition	100	R&M&M
Zydus Cadila		Mexico				

Note: R&M stands for registration and marketing and R&M&M for registration, marketing, and manufacturing. Data are for 2020.
Source: Sweet (2010) and National Stock Exchange of India Limited.

Chinese companies are not only growing suppliers to Latin America and the Caribbean. Increasingly, they are also establishing joint ventures with local firms. For example, the Brazilian company EMS, in partnership with Biomabs and Guojian, manufactures etanercept, a MAB to treat rheumatoid arthritis.

Globally, Indian companies are playing a growing role in the formulations segment of the industry. In Latin America and the Caribbean, however, they primarily supply APIs, followed by high-quality generics, with few companies focusing on biosimilars. All the leading Indian manufacturers – Dr. Reddy's Labs, Biocon, Cadila Pharma, and Aurobindo – are currently operating in the region. Smaller ones are working through local subsidiaries. In all, 23 pharmaceutical companies from India have entered the region since 2000. Their largest number is in Brazil, followed by Mexico (table 2).

A common characteristic of these engagements is the mode of investment. Indian pharmaceutical companies have entered the region predominantly through greenfield investments. In contrast with acquisitions, licensing, mergers, or joint ventures, greenfield investments involve a parent firm establishing a local subsidiary. From the viewpoint of the investing company, an advantage of this mode of entry is greater control of business operations. Still, it comes at the cost of not tapping into existing networks and customer bases.

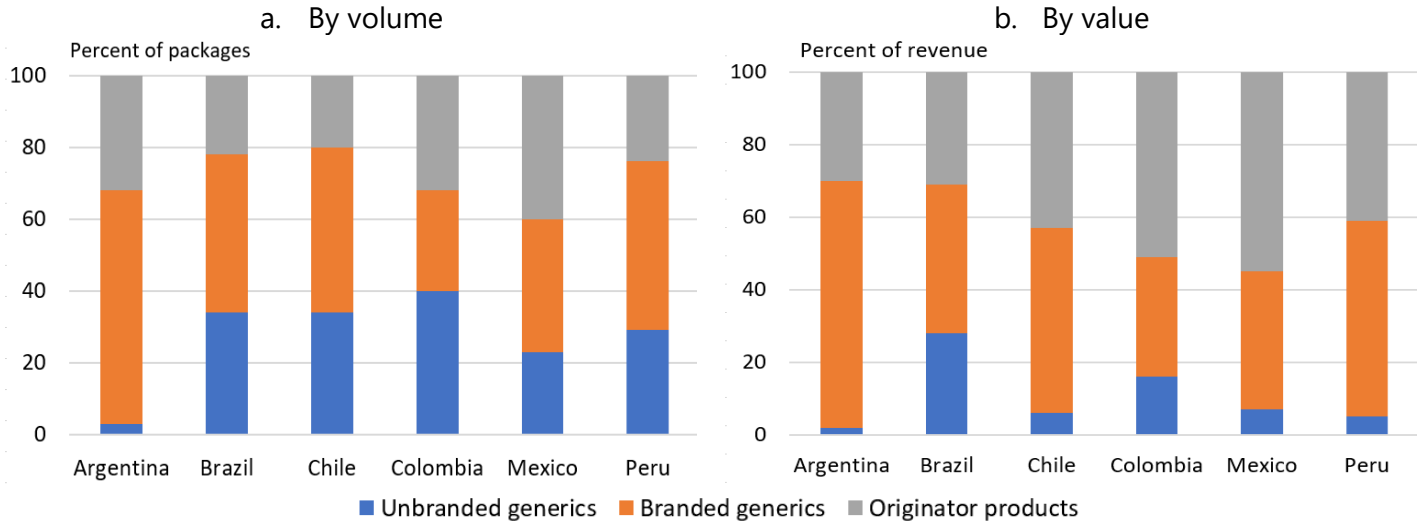
Product mix and prices

Countries in Latin America and the Caribbean produce mainly generic versions of synthetic products, using APIs as inputs and selling their outputs mainly to domestic and regional markets. These drugs are manufactured by local pharmaceutical companies in Argentina, Brazil, and Mexico and by multinationals such as Abbot and TEVA in Chile and Colombia. Among them, the market share of unbranded generics – measured by volume – has decreased among the countries in the region for which data are available. That of branded generics has increased accordingly, reaching 45 percent of the packages sold in pharmacies over the period 2015-2019 (figure 13a).

The main exceptions to this pattern are Colombia, where unbranded generics represent a more significant share of the market, and Mexico, where originator products dominate. The highest market share of branded generics can be found in Argentina, where it reaches almost 70 percent of the total, compared to barely 3 percent for unbranded generics. Measured by value, the market shares of branded generics, and especially of originator products, are even larger, due to the higher unit prices they fetch (figure 13b).

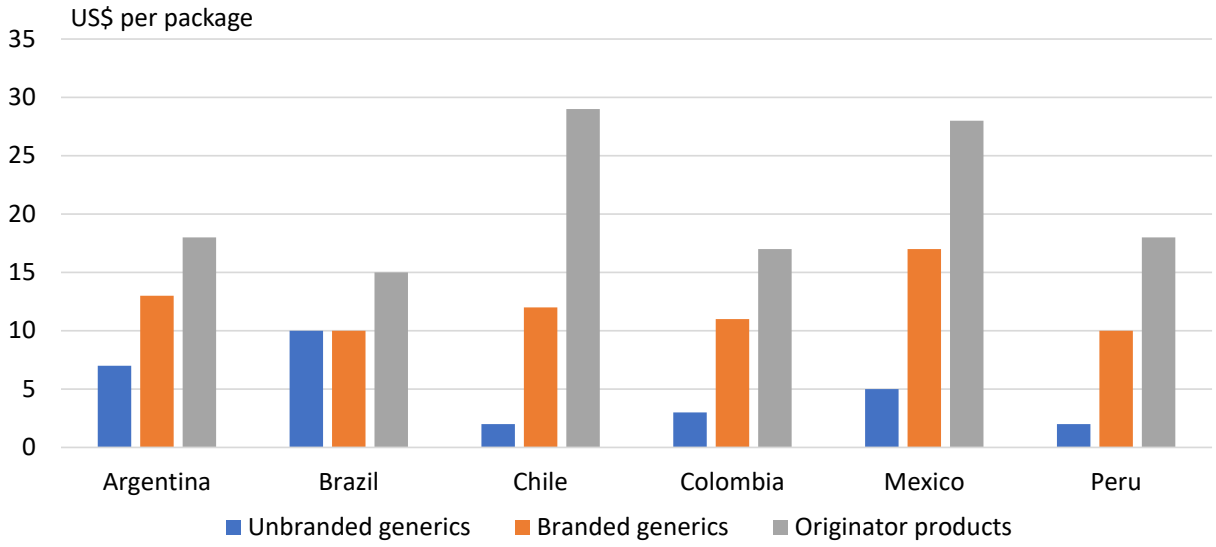
Predictably, there is a stepwise increase in unit prices when moving from unbranded generics to branded generics to originator products. However, the price gradients vary widely across the countries for which data are available. The cheapest unbranded generics, but also the most expensive originator products, can be found in Chile. The gradient is also steep in Mexico and Peru. At the other end, unbranded generics are more expensive, and originator products cheaper, in Argentina and Brazil. Colombia occupies an intermediate position (figure 14).

Figure 13. Sales of pharmaceutical products



Note: Excludes biological products and biosimilars. Data are for 2019.
Source: IQVIA.

Figure 14. The average price of pharmaceutical products



Note: Excludes biological products and biosimilars. Data are for 2019.
Source: IQVIA.

These differences can be attributed to the extent of competition in the markets for each of the different types of pharmaceuticals. At one end, Chile has entered into deep trade agreements with advanced economies that ensure a robust protection of intellectual property rights for originator products. But Chile also has a very open economy, which allows international manufacturers of generics – including Indian companies – to have an active presence, bringing prices down in that

segment. Conversely, domestic companies are more sheltered from international competition in both Argentina and Brazil, resulting in a greater availability of cheaper originator products, but also in more expensive generics.

Globally, the relative importance of biological products has been on the rise during the last two decades. Of the 313 new drugs approved by stringent regulatory authorities around the world between 2015 and 2019, 95 were biologics, and 38 were vaccines (Newman and Cragg 2020). The market value for small-molecule drugs has been growing by 4 percent per year, compared to 8 percent for biological products. As a result, biological drugs now represent about one quarter of the total market value of pharmaceuticals and around 30 percent of new therapeutic products for cancer treatment.

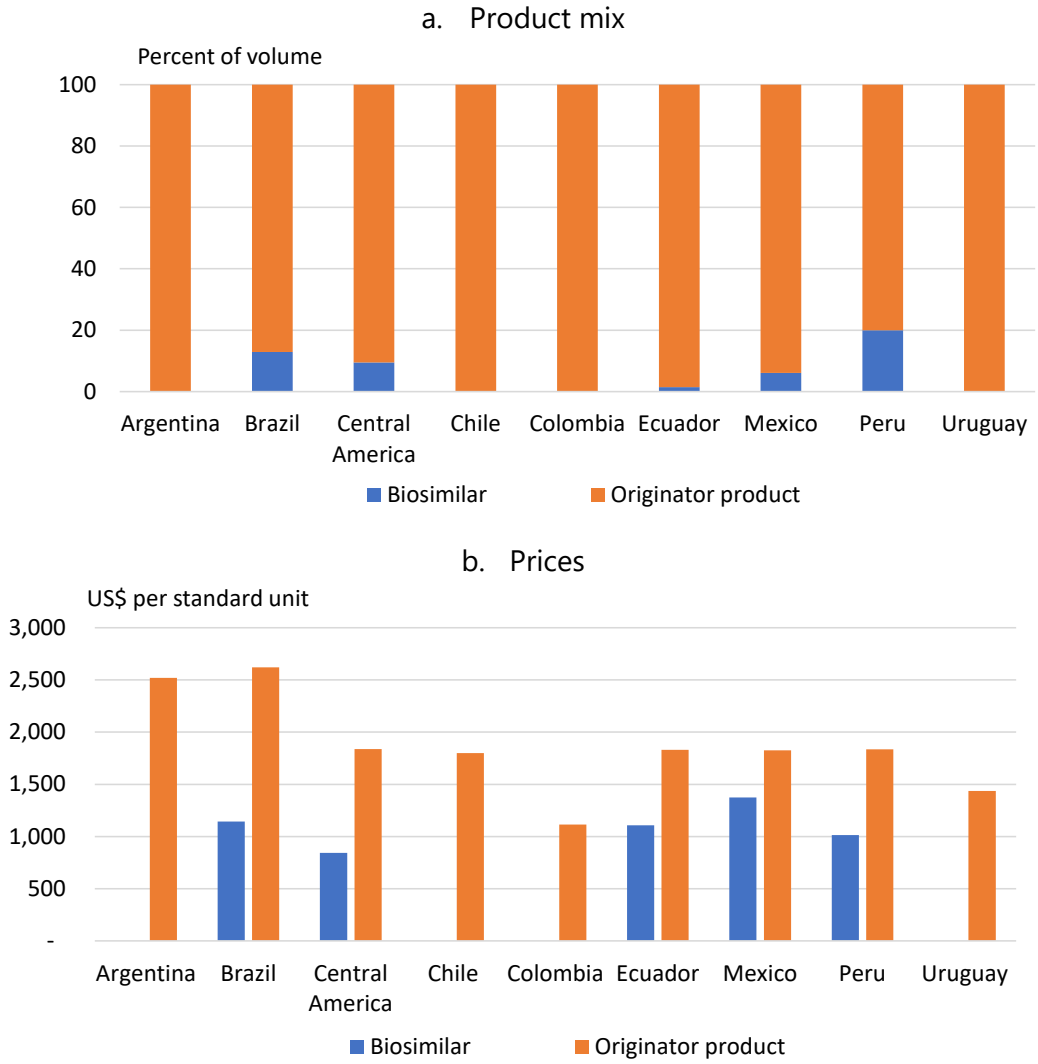
Biosimilars, the generic version of biological products, have the highest growth potential for the pharmaceutical sector of the region. While they are costlier to produce, they feature higher sale prices than generics, with their attractiveness coming from being cheaper than the originator products they compete with. However, the growth of this segment also encounters institutional barriers. Pharmaceutical companies may try to hold off biosimilars by extending intellectual property right protection, whereas the medical profession may resist their use on the grounds that they are not close enough in terms of efficacy and safety.

Oncology is the therapeutic area with the highest sales in the prescription drug market globally, steadily increasing over the past decade (Paliouras, Pearson, and Barkalow 2021). Growth in spending has been driven by new drugs under patent protection and has not been offset by lower costs from patent expiration (IQVIA 2020). The trend is similar in Latin America and the Caribbean. In Chile, for example, public spending on cancer medicines increased by 19 percent per year in 2013-2017 (Vargas 2020b).

There are also significant price differences for the same biological product across countries. The case of the cancer treatment drug trastuzumab is informative in this respect. Trastuzumab is one of the most effective drugs to improve survival outcomes for a particular type of breast cancer (Blackwell et al. 2018). First approved in the US in 1998, the patent for its branded product Herceptin expired in Europe in 2004. The European Medicines Agency (EMA) approved the first biosimilar for trastuzumab in 2017. At present, there are seven trastuzumab biosimilars available to countries in Latin America and the Caribbean. Brazilian companies Libbs and Biomm are among the regional manufacturers. Mexico and Peru are volunteering to host clinical trials by Pfizer and Biocon as a path to access new biosimilars (Wellcome Trust 2019).

In the countries where trastuzumab biosimilars are available, they are on average 63 percent cheaper than the originator product. And yet, trastuzumab biosimilars account for only 10 percent of the total volume of this medicine used in the region. Out of the nine countries for which data are available, four use only the originator product. Brazil, countries in Central America, and Peru lead in the utilization of biosimilars (figure 15).

Figure 15. Product mix and prices for oncological drug trastuzumab



Note: Data are averages for 2017-2020.
Source: IQVIA.

Government stewardship

The functioning of a market depends not only on the number of players but also on the way policies and institutions shape their interaction. Choices related to ownership and regulation play an especially important role in markets characterized by oligopolistic competition, information asymmetry, and large sunk investments. Some of the relevant policies and institutions are set at supranational levels, as is the case with the international trade agreements that protect intellectual property rights or with the multilateral funds that support aggregated procurement of medicines. Other important forces shaping pharmaceutical markets, from quality control to price regulation to government purchases, operate mainly at the domestic level.

Intellectual property rights

Originator drugs are protected by patents or data exclusivities when they first come to market. Patents allow their holders to exclude others from manufacturing or selling the product for 20 years from the patent filing date. In contrast, data exclusivity prevents new generics or biosimilar products from being registered and marketed based on data previously submitted by the originator company, and usually lasts for five to ten years after the approval of the drug.

The main international framework regulating patents and data exclusivities is the agreement on Trade-related Aspects of Intellectual Property Rights (TRIPS), by the World Trade Organization (WTO). The TRIPS agreement came into force in 1995, requiring all WTO member countries in Latin America and the Caribbean to enforce intellectual property rights for all trade products, including pharmaceuticals.

Following its adoption, many Latin American and the Caribbean countries signed international trade agreements that usually carry an even more stringent protection of patents and data exclusivities (Sweet 2017, Rodrik 2018, Mattoo et al. 2020). In the region, the strongest protection of intellectual property rights for pharmaceuticals can be found among the countries that entered into deep trade agreements with the European Union or the US, including Chile, Colombia, Mexico, Peru, and countries in Central America (Smith, Correa, and Oh 2009, World Bank 2019).

Deep trade agreements are especially relevant for biological drugs, mostly imported from Western Europe and the US. Their provisions often include data exclusivity for a minimum period of five years in the case of small molecule drugs, and eight years for biologics (Branstetter 2016, Shadlen et al. 2020). These regulations have been shown to improve the availability of patented biological drugs but also to increase their price and delay the introduction of biosimilars (Palmedo 2021; Trachtenberg et al. 2020).

Under justified public health circumstances, the TRIPS agreement grants countries some room to facilitate the manufacturing of generic drugs by making a patent subject to a compulsory license. The latter has to be issued by the government or a court. While compulsory licensing doesn't require the holder's consent, it has to ensure the payment of royalties. The holder can also sue the country if the justification provided is seen as questionable. In the region, this TRIPS option has been used by Brazil (2007), Colombia (2017), and three times by Ecuador (2010, 2012, and 2021) (Nowak 2017).

In the context of the Covid-19 pandemic, several countries around the world have also taken steps to facilitate the compulsory licensing of pharmaceuticals if needed. Two countries in Latin America and the Caribbean – Chile, and Ecuador – belong in this group (Bassi and Hwenda 2020).

Another flexibility allowed by the TRIPS agreement is the so-called Bolar exception, which allows a domestic manufacturer to register a generic drug before the patent of the originator product expires. The Bolar exception is intended to increase access to medicines and lower their cost. In Latin America and the Caribbean, it has been enacted by Brazil in 1996, Argentina in 1997, Colombia, Dominican Republic and Uruguay in 2000, Peru in 2009, and Chile in 2012.

There is evidence that these flexibilities make a difference in practice. For example, a study reviewing the Chilean experience after 2012 found that the branded generics entering the market — 47 molecules in all — cost on average a third of the originator products, propping up the combined sales by 148 percent in the following four years (Álvarez et al. 2019).

All countries in Latin America and the Caribbean have adopted policies to incentivize imports, registration, and production of generics. For example, Colombia applies lower tariffs, Mexico awards tax exemptions to the businesses involved, Ecuador offers streamlined bureaucratic processes, and El Salvador financially supports production by small and medium-sized pharmaceutical companies. Trade in generics is also facilitated by regional integration agreements such as Mercosur (Trachtenberg et al. 2020).

To boost the entry of generics into domestic pharmaceutical markets, WHO and UNITAID – a global health initiative bringing together several development partners – created a Medicine Patent Pool. The goal is to leverage multilateral collaboration to increase competition and lower the price of pharmaceuticals. This initiative manages the patents associated with specific technologies – such as the various antiretroviral drugs for HIV/AIDS – and makes them available to generic producers through a joint licensing platform. More recently, the Medicines Patent Pool has signed licensing agreements for a Covid-19 oral antiviral treatment candidate with Pfizer. The evidence suggests that the Medicines Patent Pool has led to an increase in the supply of generic drugs in the region (Wang 2019).

However, it is in relation to biosimilars that Latin America and the Caribbean stands out. Because these medicines are never identical to the originator biological product, they are less vulnerable to intellectual property rights challenges. Thus, about 60 percent of the biosimilar MABs authorized in Latin America and the Caribbean have been developed and manufactured locally, with pharmaceutical companies from Argentina and Cuba in the lead. Next come companies from the US and Germany, availing about a quarter of all registered biosimilars. Finally, Asian pharmaceutical companies have inscribed 15 percent of all biosimilars, with South Korean firms at the forefront.

Regulatory oversight

The development and use of a therapeutic depend on the assessment of its benefits and risks, first by pharmaceutical companies, then by regulatory bodies, and finally, millions of times over, by individual physicians and patients (Avorn and Kesselheim 2020). Ensuring that this chain is successful at delivering effective and safe medicines requires a trusted regulatory authority with the scientific capacity to determine that the products on the market meet accepted standards, and the enforcement capacity to ensure compliance with its decisions.

There are important differences in what regulatory authorities do in practice in Latin America and the Caribbean (table 3). Six of them – those of Argentina, Brazil, Chile, Colombia, Cuba, and Mexico – are recognized as a reference by WHO or by its regional counterpart (PAHO 2021).

Table 3. Key features of the regulatory regime for pharmaceutical products

		Argentina	Brazil	Chile	Colombia	Mexico	Peru
Licensing	Registry meets all the WHO criteria	No	Yes	No	No	No	No
	Clinical trial results are publicly available	Yes	No	No	No	Yes	No
Quality control	APIs with bioequivalence	Low	High	Medium	Low	High	Low
	Traceability - Number of inspections	High	Medium	Low	n/a	n/a	n/a
Price regulation	Generics	No	Yes	No	Yes	No	No
	In-patent	No	Yes	No	Yes	Yes	No
Promotion	Doctors mandated to prescribe generics	Yes	Yes	No	Yes	No	No
	Pharmacies mandated to offer generics	No	No	No	No	No	No

Source: PAHO (2021) and websites of the regulatory authorities.

The regulatory phase of this process entails the **licensing** of pharmaceuticals. The drug prequalification program created by WHO in 2001, which evaluates product quality and inspects the relevant manufacturing sites, plays an important role in this respect. As a result of it, around 900 products have been approved already. Among these prequalified medicines, 379 are from India and 42 from China. However, 130 of India's products on this list depend on APIs sourced from China (Guerin et al. 2020).

The licensing process varies across pharmaceutical products of different types. In the case of generics, it usually relies on bioequivalence, a certification not requiring clinical trials to assess effectiveness and safety. Brazil has been the leader in the region, launching two distinct pathways to bioequivalence in 2010. One, less stringent, is for simple small-molecule drugs; the other, more demanding, is for more complex products such as MABs. Argentina and Cuba followed suit in 2011, Chile, Colombia, and Mexico in 2014, and Peru in 2016.

On the other hand, clinical trials are required to license innovative or repurposed drugs. While most of these trials occur in high-income countries, the share conducted in Latin America and the Caribbean has been growing fast (PAHO 2021). If the preclinical trials of new drugs demonstrate their safety and efficacy in a laboratory with animals, the research can move into the next stage, which consists of three phases involving humans. Phase 1 and 2 are conducted in a small population to rule out safety issues. In contrast, Phase 3 aims to include thousands of subjects, including diverse demographic profiles, ethnic backgrounds, and medical histories, to test the efficacy and provide additional safety assurance.

Clinical trials are usually demanding. Their duration ranges from 5.9 to 7.2 years for most pharmaceutical products but extends beyond a decade for oncology treatments. And their probability of success is low, reaching barely 13.8 percent in the US and Western Europe (Wong, Siah, and Lo 2019). The process is faster for drug repurposing. When assessing new therapeutic uses for existing drugs, information on safety is already available, allowing clinical trials to move directly to Phase 3.

Because biosimilars are more complex and more heterogeneous in nature than small-molecule drugs, their licensing process falls somewhere in between those for generics and for originator products. The first regulation on biosimilars was issued by the EMA in 2005, while the FDA began approving them only in 2015 But the number has increased rapidly since then (Darrow 2020; Frank et al. 2021; Sarpatwari et al. 2019). The first biosimilar to enter the WHO prequalification list did so in 2019, and a biosimilar registration guide is only being finalized at present (WHO 2021).

Regulatory regimes for biosimilars vary across Latin America and the Caribbean, with phase 3 clinical trials required in some countries. For example, in Brazil and Cuba, the registry of clinical trials meets all the WHO criteria, and in Argentina and Mexico, regulatory authorities make clinical trials' results public.

The biosimilars approved so far have been primarily oncological medicines. Out of 100 originator MABs commercialized in Latin American and Caribbean countries, 39 have at least one biosimilar available, resulting in a total of 88 biosimilars on the market. (IQVIA 2020, Ortiz-Prado et al. 2020). The countries with the highest number of authorized biosimilars are Argentina, Mexico, Chile, Cuba, Brazil, and Ecuador. The biologics with the highest number of authorized biosimilars are filgrastim, rituximab, and erythropoietin (Annex).

The need to counter substandard pharmaceutical products and outright falsification makes **quality control** another important role of regulatory authorities (PAHO 2021; Seiter 2010). Drug quality is on average better in Latin America and the Caribbean than in other developing regions, but concerns remain. A study across ten cities in the region found that 7 percent of pharmaceutical products did not meet technical standards (Bate and Mathur 2018). Safety issues with biosimilars have also been reported in Brazil, Chile, and Mexico (Azevedo et al. 2012).

A growing number of medicines are manufactured in one country, packaged in a second one, and sold and distributed to consumers in a third one. With the growing unbundling of the production process, ensuring drug quality can be challenging in such a context. As a first step in that direction, manufacturers are typically required to prove the integrity of their upstream, supply chain to the regulatory authority, in order to get licenses for their products.

In addition, there must be traceability, understood as the capacity for the regulatory authority to track a finished product from the factory door to the patient. Less demanding than full traceability, point-of-sale verification is an approach that is making inroads in Latin America and the Caribbean. Argentina, Brazil, and Colombia have been its early implementers in the region (Pisa and McCurdy 2019).

Whether to embrace some form of **price regulation** for pharmaceutical products is more controversial Generics and biosimilars typically enter the market at cheaper prices than the originator products they compete with. However, gathering price data on medicines carrying different names is time-consuming, especially because it requires checking that they are equivalent in strength, efficacy, and safety. This imperfect consumer information plays a crucial role in keeping many pharmaceutical products more expensive than they should be.

Regulatory authorities in Latin America and the Caribbean have tried to address this problem by increasing market transparency. Brazil, Colombia, and Peru publish retail prices in online price observatories (Kaplan et al. 2016). In Mexico, the state-funded consumer organization publishes prices of a selection of medicines (originator products and some generics) in their monthly electronic consumer information report (Mexico Federal Consumer Agency, 2010).

Public procurement can also be used to increase price transparency. Electronic tenders, in particular, can support much-improved data management systems, thus reducing wastage and the risk of corruption (Seidman and Atun 2017). In the region, Argentina, Brazil, Chile, Colombia, Costa Rica, Ecuador, Mexico, Panama, Paraguay, Peru, and Uruguay have developed e-tender procurement systems with different integration levels. All of them report data on public drug transactions online (Acosta et al. 2018; Hawkins and Seiter 2007).

Some regulatory authorities in the region have also tried to directly influence drug prices, through a combination of external benchmarking and cost-plus price caps. Brazil, Mexico, and Colombia fall in this category. In contrast, Others, including Argentina, Chile, and Peru allow pharmaceutical companies and pharmacies to set most drug prices freely (Tordrup et al. 2020; World Health Organization 2015). Among the countries in Latin America and the Caribbean whose, policies and institutions were reviewed, none regulates the price of APIs.

In Brazil price caps are determined by the Câmara de Regulação do Mercado de Medicamentos for in-patent, similar, and generics drugs after they have gained marketing authorization from the National Health Surveillance Agency (ANVISA). In the case of generics, the cap is calculated as the manufacturer's cost plus a profit margin. Brazil also uses an external reference price based on a basket of comparator countries. The law mandates that generic drug prices should be at least 35 percent lower than the price of the corresponding originator product.

In Colombia, the National Price Commission of Medicines and Medical Devices (CNPMDM) benchmarks externally the price of originator products if they are deemed to have a substantial impact on budgets, do not have a therapeutic substitute, and suffer from high market concentration. The price of such drugs cannot exceed the 25^{th} percentile of the price distribution across a set of 17 reference countries (Prada et al. 2018). Under this policy, the prices of 2,513 medicines had been capped as of September 2021 (Ministerio de Salud de Colombia 2021).

In Mexico, finally, the regulation of the pharmaceutical sector is in the hands of the Federal Commission, which also uses international benchmarking to cap the prices of in-patent drugs.

Institutional mechanisms are also required to align the incentives of the doctors who prescribe the medicines, the pharmacists who sell them, and the patients who use them (Kaplan et al. 2016). Through **promotion**, regulatory authorities seek to coordinate institutions with diverse and sometimes conflicting goals, so that affordable medicines are chosen whenever their equivalence with originator drugs and their quality is ensured (Aivalli et al. 2018; Dunne and Dunne 2015; Maceira and Palacios 2016).

Economic incentives are often used in advanced economies, where agencies specialized in health technology assessments select the medicines worth funding based on scientific evidence and cost-effectiveness analysis. In Latin America and the Caribbean, on the other hand, a careful analysis of policies and institutions related to the pharmaceutical sector across a set of selected countries also reveals that the regulation of doctors and pharmacies is still incipient.

Beyond economic incentives, guidance by physicians makes a difference. Numerous studies and surveys have shown that patients prefer originator products and branded generics over unbranded generic medicines. Nevertheless, patient trust in their physician often helps them overcome their mistrust (Hellerstein 1998).

Not surprisingly, pharmaceutical companies spend significant resources sending sales representatives into physicians' offices to promote their drugs. Such promotion has come under increased public scrutiny, with critics contending that physicians may play a role in raising healthcare costs by prescribing more expensive products.

To counter this bias, regulations governing the prescribing of medicines by physicians have been introduced by several countries in the region. For example, Colombia, Cuba, Panama, and Uruguay require physicians to write prescriptions with the generic name. This requirement is limited to the public sector in Brazil and Chile, but in the latter case, there is an ongoing discussion on promoting generics consumption (Azevedo et al. 2012, Stojanova et al. 2020, Sweet 2017). In Argentina, Mexico, and Peru, on the other hand, doctors are allowed to opt for a branded name (da Fonseca and Shadlen 2017, C. M. Sweet 2017).

Pharmacies are the first line of health care for many in Latin America and the Caribbean, and especially for the poor. Regulations instructing pharmacies to recommend generic medicines whenever they are available could thus have a significant impact on the out-of-pocket health expenditures of their customers (Homedes and Fugh-Berman 2019). However, no country in the region makes it mandatory for pharmacists to remind patients that a generic alternative exists or even encourages them to sell more generics through targeted incentives. Besides, evidence from Argentina suggests that customers are often unwilling to pick the cheapest generic alternative, even when the pharmacist suggests options at the point of sales (Maceira and Palacios 2016).

Public procurement

With the pharmaceutical market being oligopolistic and the government being the single biggest purchaser, the cost of medicines is generally influenced by public procurement practices. Price

discrimination by suppliers and bargaining power by the government typically result in discounts. Instead of uniform pricing across markets, medicines are sold to low- and middle-income countries at prices below those in force in advanced economies, a practice known as tiered pricing. However, the magnitude of such discounts depends on how public tenders are designed.

In developing countries, there is evidence that centralized procurement lowers pharmaceutical prices relative to decentralized purchases. The estimated magnitude of the effect is significant, as savings can attain 50 to 75 percent of the price of originator products (Silverman et al. 2019). However, the price reduction is smaller when the supply side is more concentrated, and it vanishes when public buyers face a monopolistic supplier (Dubois, Lefouili, and Straub 2019).

The aggregation of tenders can take place across hospitals and primary health care centers, across districts and geographical units, and across medicines. However, in the region it rarely reaches the point of a single public purchaser. For example, in Argentina, drugs in an essential list of medicines are procured through the Remediar program (Gertler, Giovagnoli, and Martinez 2014). In Brazil, medicines are purchased at federal, state, and municipal levels of government, with the Intermunicipal Health Consortium operating as an aggregator in practice (Sweet 2017). And in Mexico, the Coordinating Commission for Negotiating the Price of Medicines and other Health Inputs (CCPNM) sets single procurement prices for patented medicines in the public sector (Gómez-Dantés et al. 2012).

Another way to increase the bargaining power of the government is to implement a centralized price negotiation with the pharmaceutical industry. This approach may work when the government has a high technical capacity, and the risk of corruption is low. Examples of procurement agencies with negotiation authority in the region include the National Supply Centre (CENABAST) in Chile, the Office for Logistical Support and Program for the Supply of Essential Medicines in the Dominican Republic, and the General Directorate of Medicines, Supplies, and Drugs (DIGEMID) in Peru (Tobar and Martichb 2014).

Most countries in the region also participate in regional purchasing agreements, and especially in the two led by PAHO. These are the PAHO's Revolving Fund for Access to Vaccines, launched in 1979, and the Strategic Fund, established in 2000. In both cases, empirical studies report significant procurement discounts compared to market prices (Li 2013).

The Revolving Fund is a cooperation mechanism that centrally procures vaccines on behalf of 41 countries in Latin America and the Caribbean. Participating vaccines are typically part of national childhood immunization programs, targeting diseases such as polio, measles, yellow fever, rotavirus, and human papillomavirus. Most countries in the region order all of these vaccines from the Revolving Fund. Those with significant manufacturing capacities, such as Brazil, Cuba, and Mexico, only order the vaccines that they do not produce domestically (PAHO 2014).

The Strategic Fund currently has 34 Latin American and Caribbean country members. It provides pooled procurement of medicines for communicable diseases such as HIV and hepatitis C, for

non-communicable health conditions such as cardiovascular diseases, and for neglected tropical illnesses such as malaria.

A precursor of these two regional purchasing agreements by PAHO is the Organization of Eastern Caribbean States Pharmaceutical Procurement Scheme (OECS), established in 1986. The OECS serves nine small Caribbean states and procures a standardized list of essential medicines, including drugs for infectious and chronic diseases, as well as neglected infectious diseases. The scheme is financed with a surcharge to member states. Suppliers, identified through a restricted international e-tender, enter into 18-month framework agreements during which they can ship medicines directly to member states at fixed prices (Nemzoff, Chalkidou, and Over 2019).

Finally, the Central America poling mechanism (CAMSICA) has also entered pooled procurement for personal protective equipment in response to the pandemic.

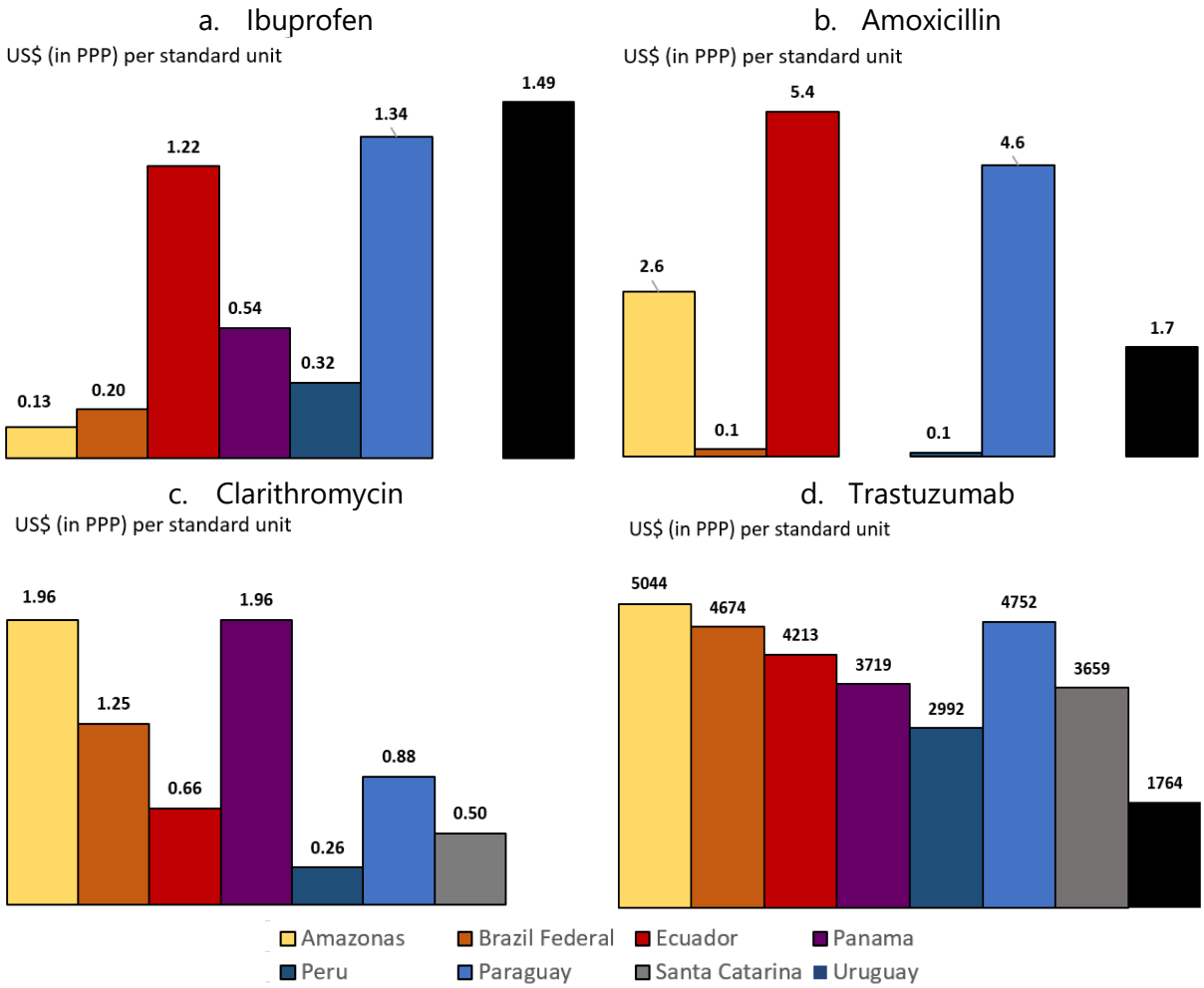
Despite these efforts, a striking dispersion of procurement prices across tenders remains, as revealed by a big data analysis across nine jurisdictions in Latin America and the Caribbean covering 235 matched pharmaceutical products. The jurisdictions covered by the study were Ecuador, Brazil (federal), Paraguay, Panama, Uruguay, Peru, and Costa Rica, plus two Brazilian states (Amazonas and Santa Catarina). For each of the 235 matched products, prices per dose were gathered across half a million procurement contracts, together with the technical features of the corresponding tenders (Fazekas et al. 2021).

Among these 235 matched products, trastuzumab, sodium chloride, amoxicillin, ibuprofen, and clarithromycin accounted for almost 6 percent of government purchases across the nine jurisdictions considered. For each of these products, a comparison between contracts in the 25th and 75th percentile of the price distribution is revealing. In one of the jurisdictions in the database, a purchase of Trastuzumab is 44 percent more expensive in the 75th percentile of the distribution than in the 25th percentile and 159 percent for clarithromycin. The price gap reaches 845 percent for sodium chloride in another jurisdiction in the sample, 925 percent for amoxicillin in a third one, and 3,156 percent for Ibuprofen in a fourth one. These are the most extreme examples of price gaps for each of the five top-spending medicines, but the dispersion of prices is considerable for most products in all jurisdictions.

In addition to the high dispersion of procurement prices within a jurisdiction, the study also revealed significant differences in average prices across them (figure 16). These differences are due not only to the features of public procurement in each jurisdiction: they were also influenced by the different market structures and diverse policies and institutions across jurisdictions and across segments of the pharmaceutical sector.

Public procurement can also be used as a tool akin to advance purchase commitment, thus encouraging R&D efforts by key market players (Kremer et al. 2020). For example, in Argentina, a new vaccine production facility, Sinergium Biotech S.A., was constructed in response to the 2009 influenza pandemic, supported by a purchasing guarantee issued by the Argentinian government.

Figure 16. Average procurement prices for selected pharmaceutical products



Note: PPP stands for Purchasing Power Parity. Data are for the period 2012-2018.
Source: Fazekas et al. (2021).

At the time, Argentina, like many other developing countries, faced supply vaccine shortages. With an entirely private investment and a technology transfer partnership with multinational Novartis, Sinergium established a new production facility for flu and pneumococcal vaccines. The government granted Sinergium a ten-year exclusivity supply contract to meet the demand of public-sector vaccine procurement. In exchange, Sinergium committed to providing free vaccines to all risk groups, reaching annual targets in line with public vaccination plans, delivering vaccination cards, building cold chambers at the provincial level, and supplying computers to vaccination centers for registration purposes (Radcliffe Institute 2020; WHO 2018).

Today Argentina is among the few countries in Latin America and the Caribbean with the technology to produce vaccines. This capacity underlies the recent technology transfer agreement with PAHO to develop the new COVID-19 mRNA vaccines for the region (Radcliffe Institute 2020, WHO 2018).

Scientific capacity

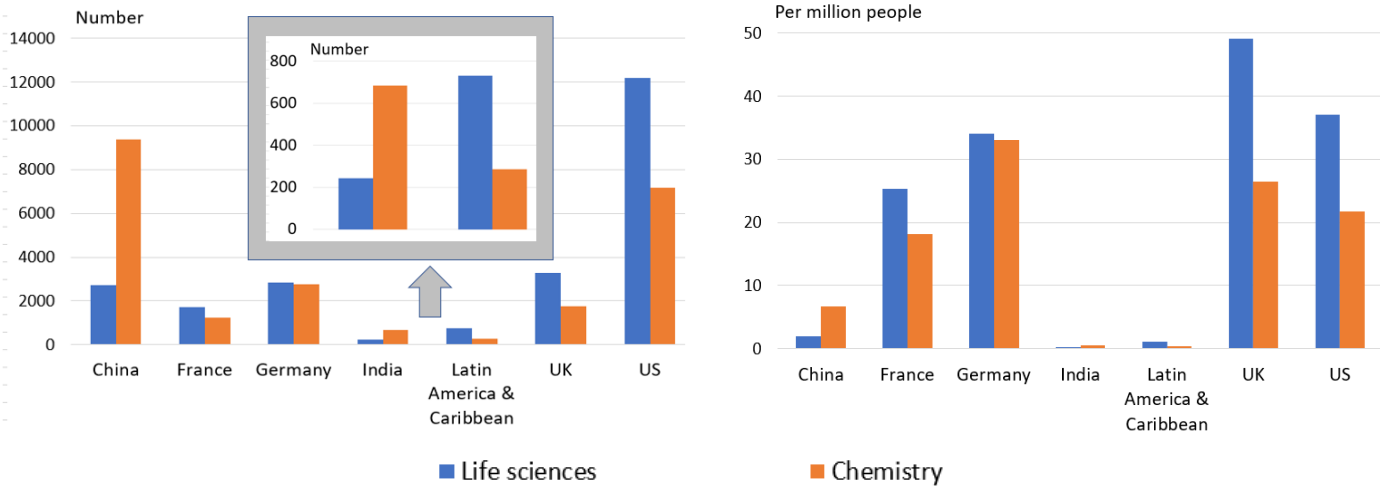
Spending on R&D by countries in Latin America and the Caribbean is relatively low by international standards; taken altogether, it amounts to only one-tenth of US spending. But in real terms, it grew by about 3.3 percent per year over the period 2007-2017. On average, countries in the region spend 0.67 percent of their GDP on R&D, with the maximum corresponding to Brazil, at 1.26 percent. Argentina, Colombia, Chile, Cuba, Mexico, Peru, and Uruguay are also active in this front (UNESCO 2020). However, how this R&D spending translates into frontier research, product innovation, and the development of marketable drugs very much depends on how scientific activities are organized in each country.

Academic publications

Research capacity in life sciences is particularly important for the last generation of biological drugs. Unlike chemically synthesized drugs, biological products build on living systems and molecular engineering. As a result, the chemistry–human biology interface holds a growing place in the pharmaceutical industry (Khosla 2014). In line with the growth in its R&D spending, the region is becoming more innovative in life sciences, including biotechnology.

An index developed by the journal *Nature* to track articles published in 43 high-quality periodicals in life science and chemistry provides a measure of local research capacity (figure 17). The list of top publications is selected by an independent panel of experts. While this is only a small fraction of total research papers, the index is useful to assess scientific output and institutional collaboration. The index adds one count per country and per institution for every article that features a researcher from such country and institution, regardless of the number of authors involved. As a result, there are more counts than articles.

Figure 17. Relevant publications in high-quality journals at the global level



Note: Data are for the period 2015-2019.
Source: Based on the journal *Nature*.

Based on this index, the US leads global research in life sciences by a significant margin, with Harvard University and the National Institutes of Health as the top contributors to the discipline over the last four years. Harvard is also a prolific academic collaborator around the world. The US is followed by a group of countries with comparable scientific output, namely the UK, China, Germany, and France. Behind them are India and countries in Latin America and the Caribbean, with a similar number of publications in absolute number, and a strong complementarity in terms of scientific disciplines.

In chemistry, high-quality research is led by China and the US, followed by the UK, Germany, and France. China overtook the US in this ranking for the first time in 2019, with the University of the Chinese Academy of Sciences in Beijing as the fastest-rising institution in the field. Once again, India and countries in Latin America and the Caribbean come further down in the list (figure 18).

Among countries in Latin America and the Caribbean, Mexico displays the greatest dynamism, with its scientific output growing by 16 percent per year between 2015 and 2019. It is followed by Chile and Brazil. Taken together with Argentina and Colombia, these countries account for 82 percent of the region's top scientific publications in life sciences and biotechnology (table 4).

Table 4. Relevant publications in high-quality journals at the country level

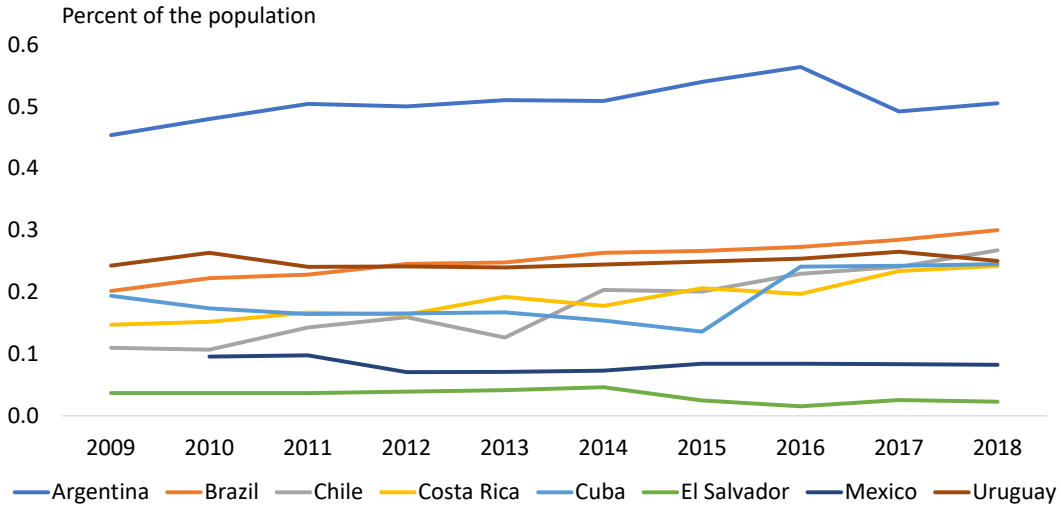
Country	2015	2016	2017	2018	2019	Total
Argentina	97	77	88	90	98	450
Bolivia	4	3	2	3	9	21
Brazil	179	201	192	222	236	1030
Colombia	40	37	33	30	50	190
Costa Rica	10	13	1	6	16	46
Chile	61	51	51	65	83	311
Ecuador	12	11	8	19	24	74
Guyana	3	1	0	0	3	7
Mexico	63	70	84	93	116	426
Nicaragua	0	0	3	5	7	15
Panama	30	26	36	31	35	158
Paraguay	1	0	1	0	3	5
Peru	17	19	14	18	29	97
Uruguay	12	11	12	9	8	52
Venezuela	9	4	3	5	11	32
Suriname	0	1	0	0	3	4

Note: Data are for the period 2015-2019.
Source: Based on the journal *Nature*.

Research organizations

The number of researchers in life sciences in the region roughly doubled over a decade, from about 60 thousand in 2007 to 113 thousand in 2018 (RICYT 2020). Researchers included in this count have five or more years of tertiary education and focus on chemistry, biology, computer and information sciences, mathematics, or other natural sciences. Not surprisingly, more than half of the scientific researchers of the region are in Brazil, followed by Argentina with about one-fifth (Ministry of Sciences of Brazil 2021). Relative to the population, however, Argentina comes in the first place, followed by Brazil and Uruguay (figure 18).

Figure 18. Researchers active in areas relevant to the pharmaceutical sector



Note: Includes researchers with five years of tertiary education or more in chemistry, biology, computer science, mathematics, and natural science.

Source: RICYT and own estimates.

Universities and research centers employ most of these researchers and generate most of the research in the life sciences. Indeed, around 40 percent of the R&D projects in the region are implemented by public or private universities, sometimes in collaboration with pharmaceutical companies. An additional third of the projects is undertaken by public laboratories. The remainder of R&D projects is in the hands of private pharmaceutical companies and not-for-profit institutions.

Based on the index developed by the journal *Nature*, the leading research institutions in the region are the University of São Paulo in Brazil, the National Scientific and Technical Research Council in Argentina, the National Autonomous University in Mexico, and the Pontifical Catholic University in Chile. In addition, Argentina holds the unique position of having three Nobel Prize awards, in medicine and chemistry. The 1984 award was in recognition for discovering the principle to produce MABs.

Local research laboratories are generally established by scientists who completed doctoral studies in centers of knowledge in the US or Europe – or in the former Soviet Union in Cuba's case. These relationships shape scientific collaborations and build international networks for funding, publication, licensing, and technology transfers. For example, an agreement between with the US National Institutes of Health (NIH) allowed the Butantan Institute from Brazil to lead clinical trials of the dengue and pentavalent rotavirus vaccines. Another example is the joint development of vaccines by Oxford University and Mexico's Instituto Politécnico Nacional.

Biotechnology companies emerge primarily in the neighborhood of universities that provide access to highly qualified personnel and research infrastructure, such as specialized laboratories (Evens and Kaitin 2015). However, only a few R&D initiatives build on a collaboration across the public, private sectors, and academia from the onset.

It is different in the later development stages of pharmaceutical products, where joint ventures and public-private partnerships involving intellectual property arrangements and licensing become essential. Collaboration also plays an important role in resolving complex problems amid rapidly changing knowledge and technology, especially when financial resources are limited. Thus, the strong complementarity in terms of scientific disciplines between India and Latin America and the Caribbean has already contributed to speeding up the innovative process in the region.

An illustration is the collaboration between Biocon — one of India's largest pharmaceutical companies, specializing in affordable biosimilars and complex APIs — and Cuba's CIM. In the early 2000s, CIM had developed a novel drug for the treatment of psoriasis called itolizumab. After thorough testing in Cuba, the drug was licensed to Biocon, which conducted more clinical trials and added improvements to the original concept. As a result, the drug was approved in India, where it has been manufactured since 2013 and has recently been authorized for treating moderate-to-severe Covid-19 patients.

Products and pipeline

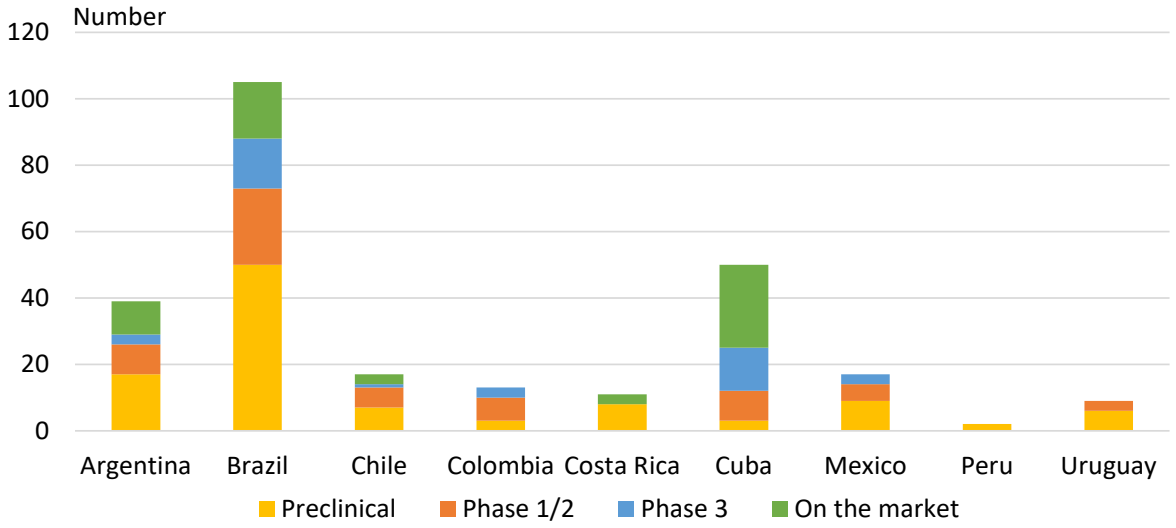
The region is becoming more innovative in life sciences, including biotechnology (Nature 2020). This is a significant development for the pharmaceutical sector, given that biologic drugs and vaccines are increasingly at the core of the industry. After decades of reverse engineering and licensing pharmaceutical products developed in advanced economies, a growing number of institutions from the region, mostly academic in nature, have begun developing new medicines of their own.

The process of developing an innovative product starts with basic research identifying modifiable factors in a disease process, which makes them suitable targets for new therapeutic drugs or vaccines. This identification leads to the selection of potential drugs for prevention or treatment. Next, the potential drugs must go through clinical trials before being approved. The whole process can take an average of 10 years.

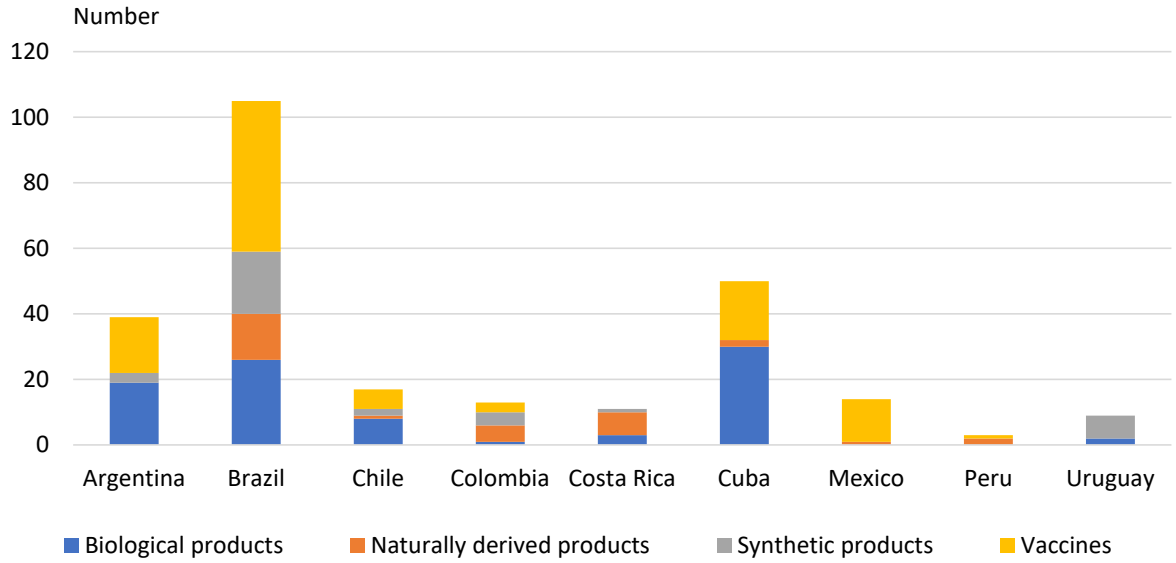
More than 200 pharmaceutical products from the region were in pre-clinical or clinical trials by May 2021, and almost 60 are already on the market (supplemental documentation). These products include both innovative and repurposed drugs. From a technical point of view, they cover the entire spectrum, from synthetic drugs to biological products, including MABs. Naturally derived products, stand out thanks to the region's enormous biodiversity (Desmarchelier 2010; Radcliffe Institute 2021).

Figure 19. Pharmaceutical products at the country level

a. By development phase



b. By type of product



Note: Includes biosimilars and innovative or repurposed drugs. Data are as of June 2021.
Source: Vargas and Rivera-Ottenberger (2021).

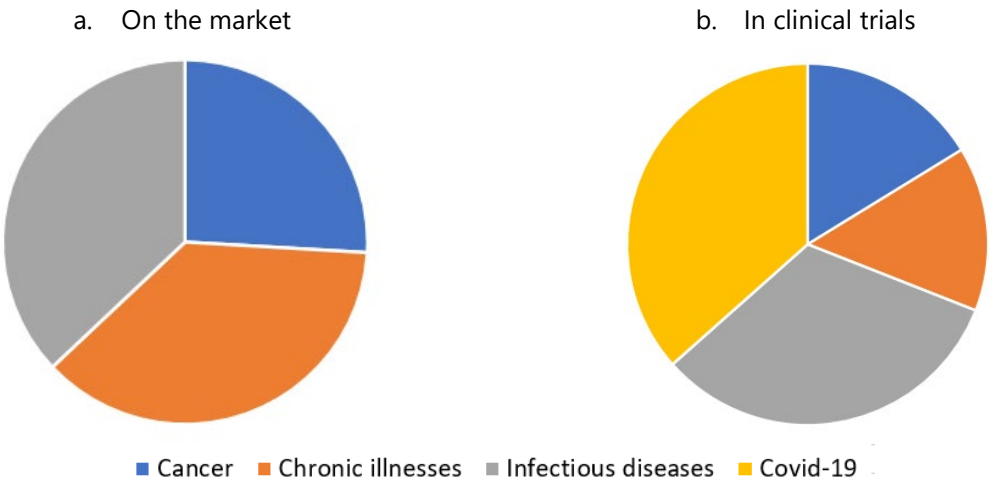
The countries with the highest number of products on the market are Cuba, Brazil, and Argentina, while the countries with the greatest number of pharmaceutical products in the pipeline are Brazil and Argentina, followed by Cuba and Mexico (figure 19). Relative to their population, Uruguay, and Cuba are the most prolific countries in the region.

Several of the new pharmaceuticals from Latin America and the Caribbean are innovation breakthroughs. Among them is nimotuzumab, an anti-cancer MAB developed by Cuba's CIM and commercialized through a joint venture with India's Biocon. Another outstanding product currently completing phase 3 clinical trials is the dengue vaccine developed by Brazil's Butantan Institute. Meanwhile, the Colombian Pontificia Universidad Javeriana has initiated clinical trials for naturally derived co-adjuvants for cancer treatments, while Uruguay is testing innovative synthetic molecules for chronic diseases such as diabetes. Finally, Brazil and Colombia are at the forefront of innovations using naturally derived compounds.

Most of the new products on the market are biosimilars, primarily developed to treat cancer and other chronic diseases. The regional leaders in this area are Argentina and Cuba. Another third of the products is intended to treat infectious diseases. The remaining are naturally derived and synthetic drugs. In contrast, most of the products in the pipeline are vaccines, using traditional and new technologies, followed by innovative products, and then a new set of repurposed products.

On the other hand, about 70 percent of the medicines in development target infectious diseases. This shift is largely due to the Covid-19 pandemic. Several research laboratories and companies were forced to postpone clinical trials to comply with lockdowns and social distancing rules. At the same time, developing a Covid-19 vaccine and being able to produce it and distribute it became a priority for most companies with manufacturing capacity.

Figure 20. Pharmaceutical products on the market and in clinical trials by type

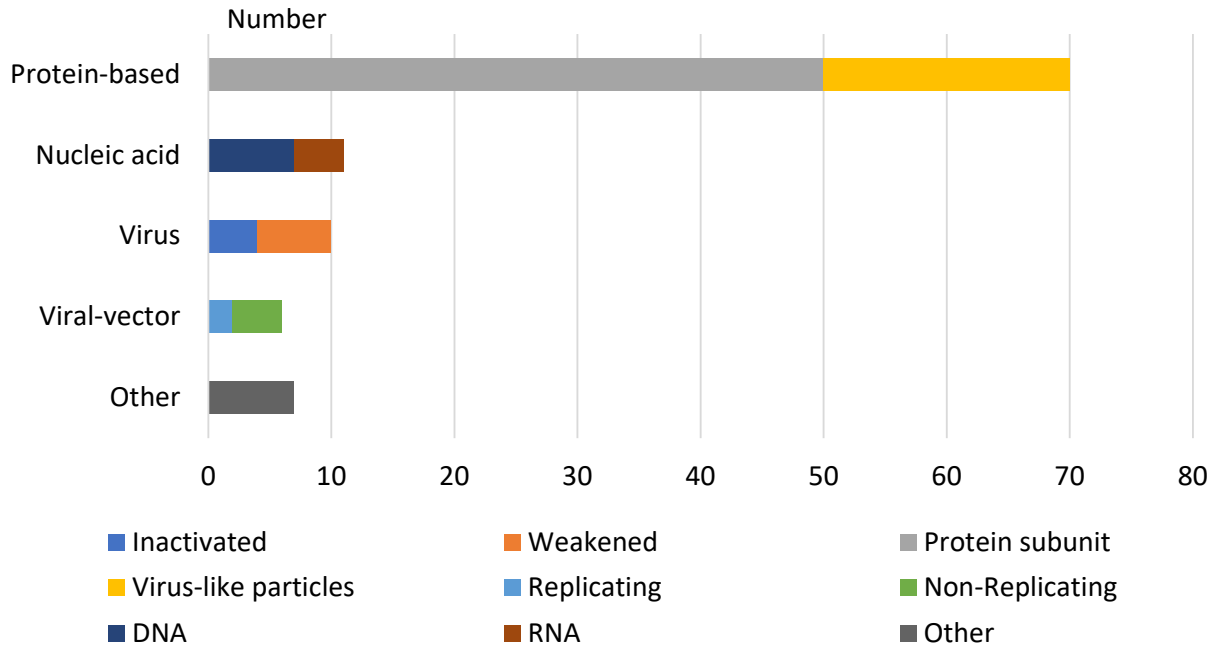


Note: Includes biosimilars and innovative or repurposed drugs. Data are as of June 2021.
Source: Vargas and Rivera-Ottenberger (2021).

As a result, more than one third of the drugs being developed to treat infectious diseases at this point are therapeutics against the SARS-CoV-2 virus (figure 20). This rapid transition of scientists from one field of research to the other was facilitated by the similarity of the immune-based strategies underlying the development of vaccines and many other biological products.

About 70 vaccines are currently in different stages of development in Latin America and the Caribbean. In terms of the platforms they use, most of them belong to the first and second generations, with a limited number from the last generation. However, Mexico, Brazil, and Argentina are developing nucleic acid (DNA and RNA) vaccines, thanks to technology transfer agreements facilitated by PAHO/WHO (figure 21).

Figure 21. Research and development of vaccines at the regional level by technology



Source: Vargas and Rivera-Ottenberger (2021).

The regional front-runners for Covid-19 vaccines at this point are Abdala, Mambisa, Soberana 1, and Soberana 2, all from Cuba (Burki 2021).They have completed phase 3 trials and are under accelerated production, while they seek final regulatory approval. In addition, the Abdala vaccine is being exported to Venezuela and Vietnam.

In parallel, there is research on the use of MABs to prevent Covid-19 infections. Unlike vaccines, which prompt the immune system to "learn" about the virus and build longer-lasting defenses against it, MABs directly deliver human-made antibodies to help fight off infection. So far, the FDA has approved two MAB treatments for emergency use against Covid-19 – bamlanivimab and the casirivimab-imdevimab antibody 'cocktail'.

In the region, clinical trials to repurpose several MABs are being conducted by the Butantan Institute in Brazil and CIM in Cuba. There were also a few repurposed synthetic drugs on the market and in the pipeline before the pandemic, but Brazil initiated a new trend with many clinical trials searching for a treatment for mild-to-severe Covid-19 using existing approved small molecules.

Finally, about a third of the pharmaceuticals being developed in the region at present targets neglected diseases, such as dengue, zika, and leishmaniasis. Therapeutics against Chagas are being studied in Argentina, Brazil, and Mexico, and drugs against the Hantavirus in Chile. Some of these neglected diseases are exclusive to Latin America and the Caribbean and are not part of the mainstream research programs in advanced countries.

The choices ahead

Pharmaceutical products have been essential to reduce mortality and increase the quality of life. From effective generics to treat cardiovascular diseases, to innovative drugs for cancer, to vaccines increasing Covid-19 immunity, new medicines have substantially improved health outcomes in the region. Yet, as this paper shows, effective and safe medicines are not always available, their price dispersion across and within countries is staggering, their cost and weighs heavily on government budgets.

Moreover, as shown above, pharmaceuticals account for a high share of household expenditures, and they tend to be regressive, in the sense of representing a heavier burden for the poorest segments of society. The impact of pharmaceutical payments for households hit by a catastrophic health shock, and the percentage of the population driven into poverty because of high drug expenditures are increasingly on the discussion (Cid et al. 2021).

Understandably, public policy efforts in Latin America and the Caribbean have been geared toward building technically strong and financially sustainable healthcare systems, organized around a common vision (Atun et al. 2015). Universal coverage, partial or near-total financing by government budgets, standardized benefits packages, competition among healthcare providers, and the availability of a public sector default option for those not able to defray healthcare costs are some of the key principles guiding public health policy in the region (Cotlear et al. 2015; Dmytraczenko and Almeida 2015; OECD and The World Bank 2020).

Less attention has been devoted in the public debate to the organization and regulation of the pharmaceutical sector, and by now substantially different models have taken shape across countries. The review in this paper can be seen as an attempt to spot the differences between these models and to identify how those differences matter for key outcomes, including the scientific and manufacturing capacity of the countries, the mix of pharmaceutical products available in each of them, and their cost to the government and the public at large.

Based on this review, there are three policy choices that seem relatively uncontroversial, implying that all countries in the region would gain if they embraced them. Another two policy choices

entail tradeoffs that may play out differently across countries, depending on the characteristics of their economies and their pharmaceutical sectors in particular. Finally, there is a broader strategic choice to be made regarding the structure of the sector and the nature of its relationship with the global pharmaceutical industry.

Starting with the **relatively uncontroversial policy choices**, *regulatory authorities* must have strong technical and enforcement capacity, given their mandate to prevent the circulation of unsafe pharmaceutical products and to boost public trust in the products that are on the market, including generics and biosimilars.

If anything, the Covid-19 crisis has made this first priority even more salient, by seriously testing the ability of regulatory authorities in the region to rapidly assess clinical trials for treatments, authorize new vaccines and repurposed drugs, and evaluate local vaccine manufacturing capacities (PAHO 2021, Vargas 2020a)

Building stronger regulatory authorities require embracing science-based decision-making processes, upgrading the capacity to inspect local manufacturing sites, and conducting more systematic point-of-dispense verifications. A first step in this direction, one not requiring high capacity, is to adopt the WHO essential list of medicines.

A robust framework to encourage the use of *generics and biosimilars* is needed to contain healthcare costs without undermining the effectiveness of treatment. Certifying the strength, efficacy, and safety of generic medicines is relatively straightforward in the case of small synthetic molecules, but it is more demanding in the case of, more complex and heterogeneous biological drugs. However, biosimilars are increasingly important in Latin America and the Caribbean, whereas precedents from advanced economies, are limited and WHO guidelines for biosimilars are yet to be issued.

Moreover, given the financial impact of generics and biosimilars on the pharmaceutical industry, their certification alone may be insufficient to encourage their use Clear guidance – and potential incentives – should be in place for physicians and pharmacists to propose first the most affordable option. On the other hand, the ability of pharmaceutical companies to provide monetary and non-monetary incentives to physicians who promote their products among patients should be effectively curtailed.

Several options to encourage the uptake of generics and biosimilars are used in advanced economies. One of them is to set the maximum reimbursement rate for each medicine within the same active substance group (Carone et al. 2012; Vogler et al. 2021). A more radical version of this policy is to only reimburse one such medicine, selected through a public tendering process (Panteli et al. 2016; The World Bank 2016). Another tool that has been shown to increase compliance from doctors and pharmacies is e-prescription, with the software starting with the preferred generic variant (Carone et al. 2012; Deetjen 2016).

The third relatively uncontroversial policy choice concerns the need for efficient *public procurement* of medicines, to reduce government waste and strengthen competition in the

markets for medicines, especially for high and low volume generics and for innovative drugs. While the dispersion between procurement prices for identical medicines across countries reflects the different bargaining power of pharmaceutical companies, price dispersion within countries is very much linked to the features of the corresponding tenders.

Thus, the length of the advertisement process or the reviewing mechanisms for the bids submitted have a demonstrable impact on procurement prices. And the impact can be sizeable: a recent simulation based on procurement data from nine jurisdictions in seven countries in the region shows that better designed tenders could reduce the average procurement price of pharmaceutical products by about 12 to 15 percent (Fazekas et al. 2021, World Bank 2020). Pooled international procurement, as in the PAHO regional purchasing agreements, is conducive to price reductions as well, provided that countries plan ahead of time.

Managed entry agreements are a new option for procuring high-priced originator drugs. These are deals with pharmaceutical companies guaranteeing financing in exchange for discounts, with or without disclosure of the magnitude of the discounts. A less common variant of these arrangements makes payments conditional on product performance (Ferrario et al. 2017; Wenzl and Chapman 2019). In Latin America and the Caribbean, this option is being considered by Argentina, Brazil, Chile and Uruguay (Castro E et al. 2019; Dias et al. 2020; Poblete 2020).

The findings from the review in this paper are less clear-cut on **policy choices involving tradeoffs** because the preferred option may vary across countries depending on their characteristics.

Government support for R&D is in principle needed as fundamental research has the characteristics of a public good: it is beneficial to society, but the benefits cannot be fully appropriated by any actor, which results in less private investment than is socially optimal. If those benefits matter in normal times, they become even more valuable when confronting a health emergency such as the Covid-19 crisis.

However, it is unlikely that R&D support can succeed in the absence of a scientific foundation to build upon. Thus, research on biological products – including vaccines and biosimilars – in Argentina, Brazil, and Cuba leans on strong capacities in life sciences. And naturally derived products in Brazil, Colombia, Costa Rica, and Peru are anchored in their remarkable biodiversity.

The ability to repurpose existing medicines could be another important foundation of R&D success. Repurposing has been fundamental for the development of transformative drugs in the US during the last decades (Kesselheim and Avorn 2013). More recently, strong scientific capacity has been vital to the development of vaccines against the SARS-Cov-2 virus, with success linked to the combined efforts of academia and private pharmaceutical companies. In Latin America and the Caribbean, research efforts could be quickly redirected to the fight against Covid-19 thanks to the region's strong scientific tradition on vaccines for neglected diseases and on biological products, including MABs for oncological and immune therapies.

However, the impact of government support for R&D on local scientific capacity is likely to depend on the terms under which resources are channeled to universities and pharmaceutical companies.

Untied budget support for research organizations may provide stability to researchers but not ensure the development of innovative drugs. Grants for specific research projects and advance purchase commitments may be successful at the product level but less so in terms of building general research capacity. Strengthening the manufacturing base may help respond more quickly to emergencies, but some countries may be better positioned than others to serve as regional hubs and forge international partnerships.

In sum, an appropriate mix of resources and incentives is needed. Competitive bidding for scientific grants has shown some promise, and there are successful cases of direct government investment in research institutions. But it is fair to say that no general recipe exists, and what works in one country may not work in another.

Another policy choice involving clear tradeoffs is *pharmaceutical price regulation*. A relatively straightforward option is to increase transparency in the pricing of pharmaceuticals and to benchmark the domestic price of medicines against relevant comparator countries. New digital tools and e-procurement can help on the first count (WHO 2021b).

However, aggregating the information and presenting it in a user-friendly require a deliberate effort. Similar challenges arise in the case of benchmarking, where choosing the appropriate reference markets and points of sale and updating the information regularly can be demanding tasks. It has also been argued that increasing price transparency for on-patent medicines could slow the diffusion of innovative products to low-income countries (Berdud et al. 2019).

Outright price regulation is potentially more problematic. Capping pharmaceutical prices can improve access to medicines, provided that the volumes available are sufficient. However, determining the right level for the caps is challenging, and the regulatory process itself may distort competition, discourage research, and encourage rent-seeking behavior by pharmaceutical companies.

The growing judicialization of access to medicines further complicates attempts to regulate prices. As patients resort to the courts to ensure that they get high-cost pharmaceuticals at affordable prices, decision making has gradually shifted from the regulatory authority to the judiciary. The outcome has often been weaker governance, budget misallocations, and sometimes inequitable coverage (Freiberg and Espin 2021; Uribe et al. 2021).

Finally, the most **strategic policy choices** concern intellectual property rights. Options were clearer when large numbers of essential medicines were small molecules off-patent. In their case, the TRIPS agreement under WTO, as well as international trade agreements, do not leave much room for disagreement. But the surge in innovative biological products and vaccines have somewhat blurred the lines.

These products are more complex and more heterogeneous, their development involves new research, clinical trials, and manufacturing processes. All this limits the reach of intellectual property rights, creating ambiguity on whether biosimilars are subject to originator product

patents, hence not subject to the payment of royalties (Sarpatwari et al. 2019). Data exclusivities for originator products go some way towards addressing this challenge. However, they will not deter the emergence of biosimilars in Latin America and the Caribbean, given the strong scientific capacity of the region, and its proven track record in the development of vaccines for neglected infectious diseases and biological products, including MABs for oncological treatments.

At the risk of caricaturing, countries in Latin America and the Caribbean have addressed this challenge through three fundamentally different models. One model – exemplified by Chile, Colombia, and Peru – is characterized by stringent intellectual property rights protection, as enshrined in deep international trade agreements. Another model – illustrated by Argentina and Brazil – is built around national champions, private pharmaceutical companies with strong scientific capacity benefitting from an advantageous policy environment. Finally, Cuba stands out as a model of state entrepreneurship, relying on international joint ventures and vertical integration. Other countries in Latin America and the Caribbean combine, in varying degrees, features of these three distinct ways of organizing the pharmaceutical sector.

The *stringent intellectual property* model is anchored in a new generation of deep trade agreements with advanced economies. The salient feature of these agreements is that they go beyond the areas traditionally covered by the WTO – such as tariff and non-tariff barriers – to deal with behind-the-border issues such as market competition, government subsidies, or public procurement (Mattoo et al. 2020).

Pharmaceutical issues have increasingly dominated trade agreement discussions since TRIPS was adopted in 1995. It is telling that a significant portion of these deep trade agreements, as measured by the number of pages, deals with pharmaceutical products. And lobbyists from the industry association and major pharmaceutical companies from advanced economies have played an important role in the negotiation (Drutman 2014; Weissman 2017).

This model supports strong competition for small-molecule generics, allowing, in particular, a vibrant market participation by Indian companies. As a result, generics are the cheapest in this model. On the other hand, innovative products are mainly supplied by multinationals from advanced economies, with a limited presence of biosimilars. High-quality originator products – including biologics – are thus available, but they are considerably more expensive than in other countries. It may not be by chance that many pharmacies were burned in Chile during the social unrest wave of late 2019 (Vargas 2020b).

The *national champions* model builds on a long inward-looking tradition and can be found in counties that have not engaged in deep trade agreements with advanced economies, preferring instead regional integration initiatives. With a weaker protection of intellectual property rights, a less stringent certification of biosimilars, national priority policies for public procurement, or advance purchase commitments for traditional medicines and vaccines, local pharmaceutical companies are partially sheltered from international competition.

This model has led to a flatter price gradient across types of pharmaceuticals, compared to the stringent intellectual property rights model. Unbranded generics are among the most expensive in the region, but branded medicines produced locally are among the cheapest.

The national champions model has also supported a strong local scientific capacity, as reflected in the high number of publications in the life sciences and the numerous innovative pharmaceutical products developed. It has also resulted in a strong manufacturing capacity, one that can, among other things, be mobilized to produce Covid-19 vaccines locally.

Finally, Cuba's *state entrepreneurship* model does not have equivalents in the region. Market institutions there are still incipient, which makes it challenging to build private pharmaceutical companies and to abide by international agreements on intellectual property. Instead, R&D investments are coordinated by the highest levels of government, whereas creative institutional arrangements are used to compensate for the difficulties of mobilizing private capital and enforcing contracts through the legal system.

Cuban pharmaceutical companies have thus been strategic in entering joint ventures with companies abroad whose expertise and financial resources complement local capacities well. For example, Cuban laboratories have the R&D base to develop innovative medicines, but not the deep pockets and the legal capacity to conduct large-scale trials, especially in advanced economies. Partnering up with pharmaceutical companies in advanced economies and emerging markets allows overcoming these constraints. But for this approach to work, the joint ventures need to be incorporated in advanced economies, under the law of the land, so as to provide the reassurance to foreign investors that deals will be honored.

Cuba's state entrepreneurship model has led to a significant R&D capacity and manufacturing power base, especially when considering the country's small economic size and considerable international isolation. Innovation goes beyond delivering biosimilar products and has led to the development of fundamentally new medicines. It is telling that before the most recent US sanctions, Cuba's ratio of pharmaceutical exports to GDP was among the highest in the region. Pharmaceutical products are also affordable domestically, but in an economy where market mechanisms are underdeveloped, it is difficult to tell whether affordability reflects efficiency or distortions.

This paper does not intend to advocate for one model over the others, as there are significant tradeoffs. For example, local scientific capacity and manufacturing potential are arguably higher in the national champions and the state entrepreneurship models. Integration into world markets, in turn, is greater under the stringent intellectual property rights and the state entrepreneurship models. Generics such as those used to treat cardiovascular diseases are less expensive in the stringent intellectual property rights model, but innovative drugs like those showing promise with cancers are more expensive. The significance of these tradeoffs is likely to vary across countries, depending on their characteristics, collective preferences regarding the various potential outcomes (scientific capacity, global integration, or price affordability) may vary as well.

These three models also have potentially different political economy implications. In the national champions and state entrepreneurship models, the relationship between pharmaceutical companies and the government plays a very important role, creating the scope for strategic policies. But they also raise the usual pitfalls associated with picking winners, something governments are not particularly good at, while at the same time encouraging rent-seeking behavior by local companies. These risks are contained in the stringent intellectual property rights model, but in its case, the power sits with multinational companies from advanced economies and emerging markets. And there may not be a consensus in the region on whether empowering big government is preferable to empowering big pharma or the other way around.

Finally, the three models may differ in their resilience during health emergencies, as was made clear by the Covid-19 crisis. Stringent intellectual property rights can ensure lower costs for generics in normal times, by concentrating production among manufacturers in large markets such as China and India. The national champions and state entrepreneurship models rate higher when having to respond fast to a pandemic, because they ensure access to medicines in times of constrained supplies. This tradeoff somewhat calls for greater regional integration of the pharmaceutical sector, a way to reconcile the advantages of scale and autonomy in Latin America and the Caribbean (ECLAC 2021)

What is clear, however, is that these strategically important choices should not be made by default. Giving priority to effectively universalizing healthcare coverage is the right choice, However, given the social impact of out-of-pocket spending on medicines, decisions on how to organize and regulate the pharmaceutical sector matter as well.

The review in this paper highlights some of the most important tradeoffs that governments in Latin America and the Caribbean face. It can only be hoped that the evidence presented will encourage a dispassionate discussion consistent with an evidence-based approach to policymaking. Making progress in practice may require a multisectoral approach involving the health sector, production, science, and intellectual property (WHO, WTO, and WIPO 2020).

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Annex - Biosimilar products registered in Latin America and the Caribbean

Country	Molecule	Biosimilar name	Manufacturing company	Country origin
Argentina	Filgrastim	Neupogen	Laboratorio Varifarma SA	Argentina
Argentina	Filgrastim	Neutropine	Gemabiotech	Argentina
Argentina	Erythropoietin	Hemastin	MR Pharma SA	Argentina
Argentina	Bevacizumab	Bevax	Elea	Argentina
Argentina	Adalimumab	Amgevita	Amgen	US
Argentina	Enoxaparin sodium	Fada enoxaparina	Fada Pharma	Argentina
Argentina	Rituximab	Novex	Elea	Argentina
Argentina	FSH	Fostimon	Laboratorios Buxton SA	Argentina
Argentina	Filgrastim	Neutrofil	Laboratorio Pablo Cassara SRL	Argentina
Argentina	Interleukin 2	Ilcass	Laboratorio Pablo Cassara SRL	Argentina
Argentina	Enoxaparin sodium	Loparine	Rivero	Argentina
Argentina	HCG	Gonacor	Laboratorios Ferring SA	Argentina
Argentina	Molgramostim	Molcass	Laboratorio Pablo Cassara SRL	Argentina
Argentina	Racotumomab	Vaxira	Elea	Argentina/Cuba
Argentina	Filgrastim	Filgrastim	Elea	Argentina
Argentina	Filgrastim	Neutromax	BioSidus SA	Argentina
Argentina	Erythropoietin	Epogen	Laboratorio Pablo Cassara SRL	Argentina
Argentina	Nimotuzumab	Cimaher	Elea	Argentina
Argentina	Somatotropin	Omnitrope	Novartis	Switzerland
Argentina	Rituximab	Truxima	Teva Tuteur	Israel
Argentina	Somatotropin	Somactive	Gemabiotech	Argentina
Argentina	Enoxaparin sodium	Heparinox	Denver Farma SA	Argentina
Argentina	Filgrastim	Filgen	Bioprofarma Bago SA	Argentina
Argentina	Enoxaparin sodium	Enoxanorth	Laboratorio Internacional Argentino SA	Argentina
Argentina	Somatotropin	HHT	BioSidus SA	Argentina

(Continued)

Country	Molecule	Biosimilar name	Manufacturing company	Country origin
Argentina	FSH	Menopur	Laboratorios Ferring Sociedad Anonima	Argentina
Argentina	Enoxaparin sodium	Omatex	Laboratorios Phoenix Saic y F	Argentina
Argentina	Enoxaparin sodium	Dilutol	Dr Lazar y CIA SA Quimica e Industrial	Argentina
Argentina	Filgrastim	Filgrastin Duncan	Duncan	Argentina
Argentina	Recombinant human insulin	Densulin R	Denver Farma SA	Argentina
Argentina	FSH	Lifecell	Laboratorios Buxton SA	Argentina
Argentina	Somatotropin	Zomacton	Ferring	Switzerland
Argentina	Interferon alfa-2b	Interferon Alfa 2B	Laboratorio Pablo Cassara SRL	Argentina
Brazil	Rituximab	Truxima	Celltrion	South Korea
Brazil	Nimotuzumab	Cimaher	Eurofarma Laboratorios SA	Brazil
Brazil	Adalimumab	Amgevita	Amgen	US
Brazil	Trastuzumab	Kanjinti	Amgen	US
Brazil	Rituximab	Vivaxxia	Libbs	Brazil
Brazil	Trastuzumab	Zedora	Libbs	Brazil
Brazil	Trastuzumab	Trazimera	Pfizer	US
Brazil	Alemtuzumab	Lemtrada	Sanofi	France
Brazil	Infliximab	Infliximab Bionovis	Bionovis	Brazil
Brazil	Infliximab	Inflectra	Pfizer	US
Brazil	Infliximab	Remsima	Celltrion	South Korea
Brazil	Filgrastim	Fiprima	Eurofarma Laboratorios SA	Brazil
Brazil	Bemiparin	Hibor	Farmacéuticos Rovi SA	Spain
Brazil	Insulin glargine	Basaglar	Eli Lilly	France
Brazil	Trastuzumab	Herzuma	Biomm	Brazil
Brazil	Adalimumab	Hyrimoz	Sandoz GmbH	Germany
Central America	Rituximab	USMAL	Roemmers	Argentina
Central America	Trastuzumab	Canmab	Biocon	India
Chile	Recombinant human interferon alfa-2a	Interferon alfa 2b hm	Dong-A ST Co, Ltd	South Korea
Chile	Filgrastim	Neutrofil	Laboratorio Pablo Cassara SRL	Argentina
Chile	Filgrastim	Ior Leukocim	CIM	Cuba

(Continued)

Country	Molecule	Biosimilar name	Manufacturing company	Country origin
Chile	Adalimumab	Amgevita	Tecnofarma	Chile
Chile	Alemtuzumab	Lemtrada	Sanofi	France
Chile	Rituximab	Reditux	Abbott	US
Chile	Interferon alfa-2b	INF	Laboratorios Bioprofarma SA	Argentina
Chile	Filgrastim	Foltran	Laboratorios Clausen SA	Uruguay
Chile	Recombinant human interferon alfa-2a	Alpha 2a	Blau Farmacêutica SA	Brazil
Chile	Filgrastim	Blautrim	Blau Farmacêutica SA	Brazil
Chile	Filgrastim	Lioplim	Dong-A ST Co, Ltd	South Korea
Chile	Filgrastim	Zarzio	Sandoz GmbH	Germany
Chile	Insulin glargine	Basaglar	Eli Lilly	France
Chile	Interferon alfa-2a	Histocan	Dong-A ST Co, Ltd	South Korea
Chile	Rituximab	Reditux	Dr Reddy's Laboratories	India
Chile	Filgrastim	Filgen	Bioprofarma Bago SA	Argentina
Chile	Recombinat human interferon alfa-2b	Heberon Alfa R	Herber Biotec	Cuba
Chile	Recombinant human interferon alfa-2b	Biofigran	BioSidus SA	Argentina
Colombia	Etanercept	Etanar	Shanghai CP Guojian Pharmaceutical Co, Ltd	China
Colombia	Human chorionic gonadotropin	Prolugyn	LG Chem Ltd	South Korea
Colombia	Nimotuzumab	Cimaher	CIM	Cuba
Colombia	Insulin glargine	Basaglar	Eli Lilly	France
Costa Rica	Filgrastim	Heberon Alfa R	Sandoz/CIM	Cuba
Costa Rica	Erythropoietin	Epoyet	BioSidus SA	Argentina
Costa Rica	Erythropoietin	Ior Epocim*	CIM	Cuba
Cuba	Recombinant human interferon-α 2B	Heberon Alfa R	CIGB/Changchun Heber Biological Technology Co Ltd	Cuba/China
Cuba	Recombinant human γ interferon	Heberon	CIGB	Cuba
Cuba	Somatotropin	Saizen	Merck SL Madrid	Spain
Cuba	Interferon-α 2b polyethylene	Peg-Heberon®	CIGB/Changchun Heber Biological Technology Co Ltd	Cuba/China
Cuba	Racotumomab	Vaxira	CIM	Cuba/Argentina
Cuba	Extract of leukocyte	Hebertrans	CIGB	Cuba
Cuba	Human insulin (recombinant DNA)	Insulatard	Laboratotrios Liorad/Novo Nordisk	Cuba/Denmark

(Continued)

Country	Molecule	Biosimilar name	Manufacturing company	Country origin
Cuba	Erythropoietin	Ior Epocim*	CIM	Cuba
Cuba	Recombinant Interferon-β 1b	Betaferon®	Bayer	Germany
Cuba	Recombinant human erythropoietin	Heberitro	CIGB/Siam Biosciences Co Ltd	Cuba/Thailand
Cuba	Recombinant human epidermal growth factor	Heberprot-p	CIGB	Cuba
Cuba	Interferon alfa-2b	HeberPAG	CIGB	Cuba
Cuba	Granulocytic colony-stimulating factor	Ior Leukocim	CIM	Cuba
Cuba	Interferon β-1a	Rebif NF	Ares/Merck Serono	Uruguay/Italy
Cuba	Somatotropin	Norditropin®	Novo Nordisk A/S Gentofte	US
Cuba	Filgrastim	Hebervital	CIGB	Cuba
Cuba	Human insulin monocompetent DNA	Actrapid®	Laboratotrios Liorad/Novo Nordisk	Cuba/Denmark
Dominican Republic	Alemtuzumab	Lemtrada	Sanofi	France
Ecuador	Filgrastim	Ior Leukocim	CIM	Cuba
Ecuador	Filgrastim	Zarzio	Sandoz GmbH	Germany
Ecuador	Erythropoietin	Epogen	Laboratorio Pablo Cassara SRL	Argentina
Ecuador	Rituximab	Truxima	Celltrion	South Korea
Ecuador	Erythropoietin	Hemastin	Mr Pharma SA	Argentina
Ecuador	Erythropoietin	Ior Epocim*	CIM	Cuba
Ecuador	Trastuzumab	Herzuma	Celltrion	South Korea
Ecuador	Etanercept	Etanar	Shanghai CP Guojian Pharmaceutical Co, Ltd	China
Ecuador	Bevacizumab	Bevax	Grunenthal	Germany
Ecuador	Infliximab	Remsima	Celltrion	South Korea
Mexico	Rituximab	Rigetuxer	PharmADN, SA	Argentina
Mexico	Somatotropin	Omnitrope	Sandoz GmbH	Germany
Mexico	Bevacizumab	Mvasi	Amgen	US
Mexico	Insulin glargine	Abasaglar	Eli Lilly	US
Mexico	Insulin glargine	Galactus	Biocon Limited	India
Mexico	Alemtuzumab	Mabcampath	Bayer	Germany
Mexico	Filgrastim	Filatil	Probiomed	Mexico
Mexico	Nimotuzumab	Nimotuzumab	Pisa	Mexico

(Continued)

Country	Molecule	Biosimilar name	Manufacturing company	Country origin
Mexico	Trastuzumab	Trazimera	Pfizer	US
Mexico	Rituximab	Rituximab GI PIS	Pisa	Mexico
Mexico	Follitropin alpha	Corneumon	Laboratorios Corne, SA de CV	Mexico
Mexico	Infliximab	Remsima	Celltrion	South Korea
Mexico	Rituximab	Kikuzubam	Probiomed	Mexico
Mexico	Alemtuzumab	Lemtrada	Sanofi	France
Mexico	Infliximab	Inflectra	Pfizer	US
Mexico	Bevacizumab	Mvasi	Amgen	US
Mexico	Filgrastim	Zarzio	Sandoz GmbH	Germany
Mexico	Insulin glargine	Valvey	Wockhardt Limited	India
Paraguay	Rituximab	Reditux	Farmasa	Paraguay
Perú	Rituximab	Kikuzubam	Probiomed	Mexico
Perú	Rituximab	Reditux	Dr Reddy's Laboratories	India
Perú	Abciximab	Clotinab	ISU Abxis Co, Ltd	South Korea
Uruguay	Filgrastim	Foltran	Laboratorios Clausen SA	Uruguay
Venezuela	Abciximab	Clotinab	Abbott	US

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