

MEXICO PHARMA MARKET & REGULATORY REPORT



Pharmaceuticals Export Promotion Council of India

(Set up by Ministry of Commerce & Industry, Government of India)

CONTENTS

DEMOGRAPHY	89
MARKET REPORT	90
Introduction	90
Updates	90
Swot Analysis	90
Strengths	90
Weaknesses	91
Opportunities	91
Pharma Market	91
Generic drug market	92
Pharmaceutical Trade	93
Epidemiology	94
Intellectual property issues	94
Local Industry	94
Local Generic Industry	95
Statistics	96
REGISTRATION AND REGULATORY REQUIREMENTS	97
KEY REGULATORY INFORMATION	98
REGULATORY APPROACH FOR PRODUCT APPROVAL	98
RISK MANAGEMENT PLAN	104
VALIDITY OF REGISTRATION	107
TIME LINES	107
AGENCY FEE	108
REFERENCES	108

DEMOGRAPHY

SL. No	Parameter	Description
1	Region	LAC
2	Country	Mexico
3	Capital	Mexico City
4	Population	128,645,565(July 2020)
5	Population growth rate (%)	1.09(July(2018))
6	GDP (purchasing power parity)	\$2.463 Trillion(2017est.)
7	GDP - real growth rate (%)	2% (2017 est.)
8	GDP - per capita (PPP)	\$19,900 (2017 est.)
9	Exchange rates	
10	Population below poverty line	46.2%(2014est, no update)
11	Age structure (%)	0-14 years:26.01 %
		15-24 years 16.97%
		25-54years 41.06%
		55-64 years 8.29%
		65 years and over:7.67 (2020est)
<i>Source: CIA World Fact Book updated to July 2020.</i>		

MARKET REPORT

Introduction

An ageing population, a growing middle class and better access to healthcare services are greatly increasing consumer demand for pharmaceutical products. In addition, Mexico has been experiencing an epidemiological transition, from communicable diseases to chronic degenerative diseases which continues to fuel opportunities for drug makers.

The implementation of health reforms will create challenges and opportunities to health sector industries and drug makers operating in Mexico.

The removal of intellectual property extensions from the USMCA precludes the additional revenues that biologic medicine manufacturers could have earned in Mexico and Canada.

Pharma market was of the size \$10.6 billion in 2019 and is forecasted to grow negatively by 9.2% to reach \$9.59 billion in 2020.

Updates

- On January 29 2020, US President Donald Trump signed the amended version of the US-Mexico-Canada Agreement (USMCA) approved by the Senate on January 16 2020. By removing intellectual property clauses, which benefit foreign governments at the expense of US companies, the Democrats are indicating their desire to make changes to the US patent system.
- As of reports in January 2020, Pfizer will invest USD20mn in Mexico in 2020. The resources will be used for clinical research, renovation of production lines and medical education
- In April 2020, Rafael Gual Cosío, director General of the National Chamber of the Pharmaceutical Industry (Canifarma), stated that the industry expected to see increased growth rates in 2020 of up to 2% (from around 4-5% to 6-7%). We highlight that this estimate includes the increased demand for medical devices and consumables required to combat Covid-19 and does not isolate pharmaceutical sales growth.
- The pharmaceutical retail sector is shifting towards increased capacity for sales online and delivery services.
- Despite difficulties in importing raw materials, Canifarma said Mexico is able to produce or import what is required to meet the demand for medicine and medical supplies.
- On April 8 2020, Patrick Devlyn, president of the Health Commission of the Business Coordinating Council, called for the government to streamline procedures in the import of medicines and supplies to treat Covid-19, but also for chronic diseases such as diabetes or cancer.

Swot Analysis

Strengths

- The second-largest drugs market in Latin America, after Brazil.
- One of Latin America's most developed markets, with regulatory standards superior to most of its southern neighbours.
- Strong trade links to the US, Canada and the EU.

- A competitive and well developed pharmaceutical manufacturing industry, including around 200 companies and substantial presence of multinationals

Weaknesses

- Despite recent reforms, the enforcement of domestic patent law remains problematic.
- With about 10% of the population lacking health insurance, Mexico's drug market is sensitive to economic shocks.
- An inefficient coordination of regulatory and healthcare policies and slow generic market entry has contributed to high pharmaceutical prices.

Opportunities

- Health sector reform, as well as the expansion of programmes such as the Seguro Popular, should boost healthcare spending.
- Relaxation of rules on direct-to-consumer advertising should support market growth.
- Growing chronic disease burden - with diabetes products in particular having significant potential to increase sales.

Pharma Market

Despite increased production by the local pharmaceutical industry due to Covid-19, most of the reported increase is on the medical device and consumables segments. Over the long term, Mexico may be an attractive market for multinational pharmaceutical firms, due to the country's large patient base, relatively well-developed regulatory landscape, and rising demand for chronic disease treatment. Forecasts say decelerating growth in pharmaceutical spending over the next decade as the government looks to contain healthcare spending growth.

Mostly driven by an ageing population and the increasing incidence of chronic diseases, forecasts say that over the next 5 years, Mexican pharmaceutical sales will grow at a compound annual growth rate (CAGR) of 2.2% and reach \$10.9 billion. In 2019 Per capita Pharma expenditure stood at \$82.8

The country's rising population and increasing urbanisation, as well as a growing communicable and non-communicable disease burden and the support for universal healthcare coverage, will increase spending on medicines over the forecast period. Per capita drug expenditure is currently low and a large proportion of Mexico's population has extremely low spending power.

In July 2019, the government launched a new public drug procurement system. The purchase of medicines is now made directly with the manufacturers and the distribution is contracted separately. This followed after the government failed to centralise distribution under the Mexican Social Security Institute, owing to a lack of adequate transport and logistics capacity. The first direct purchase of medicines had little success in July 2019, with 62% of the tenders remaining void, in part due to the low reference prices set by the government

Mexico offers distinctive competitive advantages in pharmaceuticals and other manufacturing industries. Among them is a large population, low manufacturing costs, advanced legal frameworks, skilled scientists, and strategic position as a hub for US companies and a natural gateway to Latin American markets. The Mexican government has prioritised growth and innovation in the sector. In particular, it has strengthened the legal and regulatory framework to provide greater certainty to investors, drug makers, care providers and patients. Biotech

clusters are also emerging in several Mexican states as major drivers of the country's biotechnology innovation.

Foreign companies continue to invest in Mexico's emerging market, taking advantage of the country's high consumption rate of branded medicines, as well as its newer uptake in generic drugs. Pfizer, GlaxoSmithKline, Roche, Bayer, and Bristol-Myers Squibb are just a few companies that continue their business in Mexico. Domestic players include Genomma Labs, Laboratorios Diba, and Laboratorios Limont.

As one of the largest consumers of generic medicines in the world, Mexico maintains a significant presence from generic drug manufacturers, including Israel-based Teva, US-based Mylan, Ireland-based Perrigo and Genomma Lab, a domestic company. In upcoming years, the growing consumer demand for more affordable medicines will contribute to the country's increasing rates of generic drug consumption.

The government's efforts to improve competitiveness in Mexico's pharmaceutical sector combined with the country's economic out performance compared with large countries like Brazil will improve Mexico's attractiveness to drug makers. Regulatory changes in particular have been aimed at laying incentives for multinational drug makers to prioritise the country's pharmaceutical market.

In order to begin promoting its own domestic market, the Mexican government is working to develop 'biotech clusters', similar to Cuba's 'scientific poles'. The clusters are meant to operate through public-private partnerships with domestic drug makers and universities and would be used to boost local medicine discovery and production in the country, affording an increase to drug exports. While the continued development of such 'clusters' will ultimately help to further increasing domestic drug development and export opportunities, contributions will likely be minor over the short term and Mexico's negative trade balance will be sustained. This will be compounded by the domestic market's historically sluggish development along with the industry's heavy focus on generic drug production, leaving critical demand for foreign innovative medicines, particularly as the country's burden of chronic diseases grows.

The weakness of the "Peso" over recent years has had a significant negative impact on multinational pharmaceutical revenues through the translation into reporting currencies. The Mexican pharmaceutical market contracted (grew negatively) in US dollar terms for three consecutive years from 2014-2016 and posted weak growth in 2017. Forecast say that the peso weakness is coming to an end and the longer-term outlook for multinationals operating in the country is more positive.

Generic drug market

Mexico's generic drug market will experience strong growth in the long term, driven by a rapidly increasing population and improvements to healthcare insurance coverage. Given state cost-containment measures, the country's historically poor regulatory environment and intellectual property regime, the generic sector will outpace the patented segment, driving sales growth in the wider pharmaceutical market.

The value of the Mexican generic drug market will increase from USD3.2bn in 2019 to USD 6.0bn in 2029, reflecting a compound annual growth rate (CAGR) of 6.2%. In 2019, generic medicines accounted for 30.8% of the total pharmaceutical market. Forecast show that this will increase to 47.8% over the next 10years.

Mexico's generic and biosimilar sector will continue to expand in value as a result of industry and government initiatives. Among the many drivers for the generics industry in Mexico, the regulatory improvement has played an important role. Mexico's regulatory requirements for approving a generic medicine are strict and in alignment with global guidelines. All generic drugs that are currently available in the market have bioequivalent studies that ensure their safety and quality. This unlike many other LAC countries which have locally made products that are copies and not bioequivalent and generally termed as "Similar"

This has ultimately made the industry a more formal one, capable of expanding to other countries and attract foreign investments.

While the penetration of generic medicines in Mexico has expanded in recent years, it still remains low by international standards. According to COFECE, generic drugs often do not enter the market, even when they have obtained a sanitary registration. In other cases, generic drug entry is late and slow. In Mexico, more than one year elapses between the expiration of the patent and the issuance of the first sanitary registration and it takes on average more than two years between the expiration of a patent and the launch into the market of the first generic product. In the US, the generic product is introduced almost immediately, while in the EU it is launched after approximately seven months.

When the generic equivalents do enter they are unable to exert sufficient competitive pressure on branded drugs. The average number of producers of generic drugs is of 2.8 one year after the patent expired compared to an average 10.1 generic producers in the US. Two years after the entry of the first generic product, the penetration of generic drugs reaches 21.4% of the market in Mexico, compared to 89% in the US, 74% in Canada and 62.1% in the Netherlands. Six months after the entry of the first generic product, the average price of generic drugs is 20% lower than the original drug, and 28.6% 24 months later. However, this difference is less than in other countries. In the EU, the price reduction is of 40% at the 24 months mark. This may be attributable to the fact that the current health legislation in Mexico restricts the possibility of substituting branded drugs for generic drugs when the physician does not write down the generic name in the prescription. (Mexico is dominated by As such, the inability for generic medicines to enter the Mexican market expeditiously and the lack of scope required to discipline the market will continue to benefit multinational innovative drug manufacturers with expired patents.

Pharmaceutical Trade

The country relies heavily on pharmaceutical imports to meet domestic demand for certain medicines.

Mexico's medicine exports will rise from USD1.3bn in 2019 to USD1.6bn in 2024. This will result in a CAGR of 6.0%. Mexico's top five export partners in 2018 were the US (USD420mn), Panama (USD160mn), Colombia (USD89mn), Ecuador (USD63mn) and Chile (USD62mn).

Mexican pharmaceutical imports will grow from a value of USD4.3bn in 2019 to USD4.4bn in 2024, which represents a CAGR of 2.2%. Mexico's top five import partners include the US, Germany, France, Switzerland and Canada. Other top import partners included Spain, and Ireland. Mexico is highly reliant on the US for innovative medicines and pharmaceutical raw materials.

In order to begin promoting its own domestic market, the Mexican government is working to develop 'biotech clusters', similar to Cuba's 'scientific poles'. The clusters are meant to operate through public-private partnerships with domestic drug makers and universities. They

would be used to boost local medicine discovery and production in the country, affording an increase to drug exports. While the continued development of such 'clusters' will ultimately help to further increasing domestic drug development and export opportunities,

Epidemiology

The country will continue to see significant rises in chronic diseases over the coming years, despite national campaigns to improve general healthcare. Mexico's growing chronic disease rates will, therefore generate increased demand for medicines, improving investment opportunities for drug makers. Approximately 75% of all deaths in Mexico are caused by non-communicable diseases, characterized by a high burden of diabetes, cardiovascular disease, cancer, and mental and behavioural disorders

Intellectual property issues

Under the Bolar exemption, generic drug manufacturers in Mexico are allowed to import pharmaceutical active ingredients and other raw materials found in patented drugs for experimental use, three years prior to the expiration of their patents. With no limit imposed on the volume imported, drug makers are worried that some importers may be selling patent infringing medicines in Mexico.

The above facility of Mexico makes many innovative companies sceptical about Mexico's IP Laws.

Local Industry

There are around 400 registered pharmaceutical companies operating in Mexico, employing around 65,000 people. The medicine industry harbours dozens of multinational and domestic companies manufacturing high tech products such as antibiotics, cancer treatment products, a wide variety of over-the-counter medicines, vaccines and many other products. The industry gained a major economic boost with the repeal of the derecho de planta law, which required all companies selling pharmaceuticals in Mexico to have a manufacturing facility in the country, in early 2010, opening the domestic market to numerous new players.

Currently, 20 of the 25 largest pharmaceutical companies in the world have operations in Mexico; names such as MSD, Boehringer Ingelheim, Pfizer, Bayer, AstraZeneca, GlaxoSmithKline and Roche have been operating in the country for decades. This boost has been favored also by improvements in regulation, production practices and certifications. Many foreign companies have made large investments in Mexico over the years. It is estimated that during the period 2005-2014, foreign companies invested a total of USD3.2bn. The largest investments came from the US (36.4% of the total), Luxembourg and Ireland (11.7% each), Germany (11.5%) and Spain (7.8%). Low production cost is one of the reasons for the recent boost of this industry in Mexico: it is estimated that production costs are 17.1% lower than those in the US and the lowest amongst OECD nations.

About 180 firms develop and/or use biotechnology, with important applications in several sectors, including healthcare. Many of such firms are international corporations. There are four strategic life science regions in Mexico: Guanajuato, Jalisco, Morelos, and Nuevo León. Each has strong clinical research clusters, along with other clusters driven by foreign investment oriented particularly to pharmaceutical manufacturing.

Local Generic Industry

As one of the largest consumers of generic medicines in the world, Mexico is home to many prominent generic drug makers, including Teva, Mylan and Perrigo. Other major generic pharmaceutical companies include Aspen Pharmacare Holdings from South Africa. Generic drug makers will continue to be attracted to Mexico, as the country's increasing rates of generic drug consumption will drive its demand for more affordable medicines over the next 10 years. Other domestic pharmaceutical companies include GrupoBruluart, Cinfa, PiSA and Sanfer.

According to reports in July 2019, Mexican generic manufacturers face a new public drug procurement system and lower consumption in some pharmacies, so they are exploring new alternatives to grow. Government sales are one of main issues concerning the sector, according to Rafael Maciel, the president of the Mexican Association of Generic Manufacturers.

Under the new system, the government opened the possibility of buying medicines from laboratories that produce outside of Mexico. In its first tender, the reference prices set by the government were often too low and many producers could not meet them. The delay of the tender also affected the budgets of companies as they calculate tentative sales to the government from January, based on historical data. Maciel added that there is no certainty about future sales.

On January 29 2020, US President Donald Trump signed the amended version of the US-Mexico-Canada trade agreement (USMCA), approved by the Senate on January 16 2020. While the original USMCA included an extension of data protection terms for biologic medicines to 10 years, less than the 12 years currently offered in the US but more than in Mexico (unspecified) and Canada (eight years), the recently agreed version does not.

The USMCA is a successor to the 1994 NAFTA deal. While an agreement was signed by representatives of Mexico, Canada, and the US in 2018, pushback from House Democrats stalled ratification.

The removal of intellectual property extensions from the USMCA precludes the additional revenues that biologic medicine manufacturers could have earned in Mexico and Canada. Pharmaceutical spending in Canada and Mexico will be lower than if the clause had been included. By removing this clause, which benefits foreign governments at the expense of US companies, the Democrats are indicating their desire to make changes to the US patent system.

The deal also removes a provision that would require parties to confirm patents for new uses of known drugs, i.e., the original deal would have created additional pathways for makers of branded drugs to extend their exclusivity periods.

Mexico's bulk drug industry was strong and had 94 manufacturing units at its peak took a major hit and declined to 20 units in 2017, but picked up a bit in the recent years.

Statistics

India Pharma exports to MEXICO by Category \$ Million					
Category	2016-17	2017-18	2018-19	2019-20	Change%
Bulk Drugs & Drug Intermediates	111.68	109.51	104.69	87.85	-16.08
Drug Formulations & Biologicals	28.64	30.26	34.86	42.54	22.03
Ayush	0.00	0.00	0.00	0.01	206.33
Herbal Products	6.05	3.68	3.65	4.00	9.38
Surgical	2.37	3.01	2.98	5.10	71.15
Vaccines	8.73	18.28	13.16	20.46	55.42
Total	157.47	164.73	159.35	159.96	0.38

Mexico's top Ten formulations Importing partners \$ Mn					
Rank	Country	2017	2018	GR %	Share %
1	USA, Puerto Rico and US Virgin Islands	1233.08	1325.51	7.50	31.81
2	Germany	711.84	768.72	7.99	18.45
3	France, Monaco	247.42	367.75	48.63	8.82
4	Switzerland, Liechtenstein	238.50	236.19	-0.97	5.67
5	Canada	158.26	205.76	30.02	4.94
6	Italy	178.73	202.40	13.24	4.86
7	Spain	167.66	166.49	-0.70	4.00
8	Brazil	105.65	128.45	21.58	3.08
9	China	106.62	112.27	5.29	2.69
10	Ireland	71.14	89.15	25.32	2.14
13	India	63.62	68.93	8.34	1.65
	World	3686.09	4167.38	13.06	100.00

Source: Uncomtrade

REGISTRATION AND REGULATORY REQUIREMENTS

- Regulatory Authority : COFEPRIS (Federal Commission for the Protection against Sanitary Risk or Comisión Federal para la Protección Contra Riesgos Sanitarios)
- Website of regulatory Authority : <https://www.gob.mx/cofepris>
- Fees for Drug Registration : For new molecules/biologics: US\$8,600.
Generics/ bio-comparable: US\$4,800.
- Normal time taken for registration : 6 – 8 Months
- Registration Requirement [Dossier Format] : CTD
- Whether plant inspection is mandatory : No
- Requirement of Local agent/ Subsidiary : Local agent is required for registration

Regulatory:

The regulatory body in Mexico responsible for regulating pharmaceuticals and health technologies, occupational and environmental exposures, basic sanitation, food safety and health-related advertisements is known as Federal National Commission for Protection against Health Risks (Comisión Federal para la Protección contra Riesgos Sanitarios [COFEPRIS]).

COFEPRIS has introduced an electronic system for product registration applications, using the National Register of Accredited Persons (RUPA), the Advanced Electronic Signature (FIEL), and the electronic payment tools. It is believed to make a significant contribution to saving time and resources, while improving the speed of patients' access to medicines

The approval time in Mexico lags behind its regional peer, Brazil (average 3.4 years) and developed markets such as the US, where approval takes one year. From September 2016, COFEPRIS began accepting English-written documentation for the registration of innovative drugs, highlighting the theme of streamlined pharmaceutical regulation. COFEPRIS estimates that accepting English-written submissions will reduce the administrative burden of drug registration by 60% allowing drugs to reach the market faster.

In the case of new molecules, local trials are mandatory for molecules produced in Mexico; if new molecules are manufactured abroad, the COFEPRIS New Molecules Committee may decide whether local trials are required. For biosimilars, the obligation to perform trials in Mexico also depends on the committee's decision.

KEY REGULATORY INFORMATION

Drugs are termed as Allopathic Medicines in Mexico, product should be Registered (Sanitary Registry/Health Record) with COFEPRIS before marketing in Mexico.

<http://www.cofepris.gob.mx/AS/Paginas/Registros%20Sanitarios/RegistroSanitarioMedicamentos.aspx>

S. No	Regulatory parameters	Details
1.	Classification	New Molecules or Generic
2.	Legal Representative	Mandatory (Sanitary responsible person)
3.	Notice of Operation	It is the registration of the local entity (Client's local office in Mexico or distributor's office in Mexico) with COFEPRIS
4.	Registration Documents requirements (Language)	Spanish ²
5.	Labelling Requirements (Language)	Spanish ²
6.	On-site Audit	Conducted if GMP certificate not issued by Recognized Country (Refer section 2 above)
7.	Submission Online	Not Available; Physical Submission of the dossier Required
8.	Registration Phases	Phase 1: Notice of Operation and Sanitary Responsible Person Phase 2: Product Classification Phase 3: Application to the Committee of New Molecule, for New Molecules Phase 4: GMP Inspection Phase 5: Product Registration Phase 6: Import

REGULATORY APPROACH FOR PRODUCT APPROVAL

1. The pre-requisite for product registration is Notice of Operation and Notice of Sanitary Responsible Person. This must be performed before product registration is started for Generic Drugs.

2. New Molecule need to be presented before the Committee of New Molecules for their opinion before applying for Notice of Operation and Notice of Sanitary Responsible Person. The product registration application should be submitted to COFEPRIS after receiving the opinion of the Committee and the required Notices are submitted.
3. Classification of the product as a New Molecule or as a Generic should be done, if required a Formal Classification by COFEPRIS can be requested.
4. Prepare technical document as per checklist and submit to COFEPRIS for Sanitary Registry.
5. GMP audit by COFEPRIS is required for manufactures who obtained GMP certificate from countries other than recognized countries. The legal representative of the client has to request COFEPRIS for a GMP audit.

The detail of the various phases is presented below.

Phase 1: Notice of Operation and Sanitary Responsible Person

1. Notice of operation³ is required for establishments that want to sell or distribute medicines in Mexico.
2. It should be performed by the client if they have an establishment in Mexico, or by a distributor based in Mexico.
3. Application for Notice of operation should be submitted to COFEPRIS.
4. The notice of operation is performed only once for a product category by the client or distributor:

For example, an Establishment with a Notice of Operation for – Cardiovascular Drugs, need not apply for Notice of Operation for a specific product that it intends to supply/distribute in Mexico.

5. The Sanitary Responsible Person oversees the monitoring of the product, signing documents related to the product and attend some notification for the authority.
6. The Notice of Sanitary Responsible Person should be made to COFEPRIS along with the Notice of Operation.

Generic Drugs: To market a drug in Mexico, a company should apply for a health registration that certifies the efficacy, safety and quality of the drug. It is issued by the Mexican Commission for Health Risks (Cofepris).

7. Cofepris grants the health registration to generics if they contain the same amount of the active ingredient and have the pharmaceutical form of the “original” and checks that the pharmacopeia specifications, dissolution profiles or bioavailability are equivalent to the original.
8. It has a maximum term of 180 days to conclude the procedure; the term is cut in half if the application is accompanied by a favourable technical report issued by a third party authorized by the Ministry of Health. However, the reality is different: the average time for concluding the procedure is usually 347 days, and 214 days in case of a pre-assessment by an authorized third party.

9. The time taken by COFEPRIS to issue Notice of operation is

10. Valid for:

11. Fee to COFEPRIS:

12. Requirement for the Establishment:

Documents Required for Notice of Operation and Sanitary Responsible Person

S. No	Document Required	Details
1.	Constitutive Act of the company in Mexico	This document is to prove that the facility is registered in Mexico. It will have the legal representative person's name and the kind of business that the company is doing in Mexico.
2	Company data including the 1. Company's registered address, 2. Contact phone number 3. Email id	a) Role - manufacturer/ distributor in Mexico b) All the contract warehouse details to be shared. c) Free Sale certificate from the country of origin with the manufacturer's details. d) GMP certificate e) Distribution letter - Document that manufacture should issue in the company letter head that is authorizing the distributing company to distribute its products in Mexico. If the distributor is the same company, then this letter is not required. f) All the legal documents to be apostilled by Mexican Embassy.
3	Legal Representative Person data and ID	This is the details of the same person whose name will appear on the Constitutive act document The ID proof can be Passport/ Mexico electoral documents/Driving licence.
4	Schedule of the establishment (hours of operation)	The details about the working days and hours of the warehouse. The same information is required for your registered office also.
5	Confirmation to Appoint Clients affiliate as Sanitary responsible person.	E-mail confirmation about appointing clients affiliate is acceptable. No other documentation needed.

Phase 2: Product Classification

1. Drugs are Classified as New Molecules or Generics

S. No	Class	Criteria
1.	New Molecules	a) Drugs that does not have a worldwide registration and that is intended to be registered in Mexico (new molecular entity); b) That drug or medication that is approved in other countries, with limited clinical experience, but does not have a registry in Mexico. c) Combination Drug of two or more drugs that does not exist in the national market. d) Drug or medication existing in Mexico but intends to be marketed with another therapeutic indication.
2.	Generic	Drugs that include active and therapeutic indications already registered in Mexico

2. Check from published list if there is a product already registered with COFEPRIS <https://www.gob.mx/cofepris/documentos/15-paquete-de-liberacion-de-genericos>

<http://www.cofepris.gob.mx/AS/Paginas/Registros%20Sanitarios/RegistroSanitarioMedicamentos.aspx>

3. Formal Classification can be requested from COFEPRIS, if required

4. The Cost for Formal Classification is:

5. Documents Required for Formal classification:

6. Time Taken by COFEPRIS for formal classification:

Phase 3: Committee of New Molecule Application, for New Molecules

1. Clients with New Molecules should apply to the Committee of New Molecules and obtain conclusion/opinion regarding the safety, efficacy and quality of the molecule presented, as well as the feasibility or not of the commercialization of said molecule in the country, before applying for sanitary registration.
2. The opinion/conclusion of the Committee must be included in Sanitary Registry Application for New Molecules.
3. The request for the meeting with the Committee must be made via COFEPRIS.

4. The cost involved for the Application to the committee is:
5. The time-taken by the committee for giving its opinion is:
6. Validity of the opinion/report, if any:
7. How should the request to the committee be made:
8. Who should submit the document:
9. Is there any physical meeting required by the client and the committee, if yes who should be present at the meeting?
10. For more information, call 50805200 Ext. 1011, 1392 or 1224

4.3.1 Documents/Information Required for Submission to the Committee

S. NO	Document/Information	Details
1.	Applicant Details	Corporate name, legal representative, address, telephone, e-mail
2.	Information of the Molecule	<ol style="list-style-type: none"> a) Generic name b) Distinctive denomination (if applicable) c) Pharmaceutical form d) Concentrations e) Route of administration f) Consideration of use
3.	Classification	<ol style="list-style-type: none"> a) Type of request (finished product or product under development) b) Type of molecule: New molecule, new indication, new combination, biotechnological, bio-comparable, other. c) Origin of the molecule: Pharm-chemical, biological, biotechnological
4.	Information of the molecule	<ol style="list-style-type: none"> a) Indication of the molecule b) Summary of pre-clinical and clinical evidence (phase I, II and III studies) c) Summary Risk management plan and summary of adverse events d) Summary of analytical methodology
5.	Regulatory status:	<ol style="list-style-type: none"> a) New registry worldwide b) Registration in other countries indicating regulatory agency and authorization date.

The list is prepared according to 'Meeting requirements to apply to the Committee on New Molecules document. Appendix-xxx

Phase 4: GMP Inspection⁸

In Mexico, GMP Inspection is required prior to submission (the certificate is an important document to be annexed to the submission dossier, it must be ready beforehand) and it will be conducted by the Health Authority COFEPRIS or by a Third Authorized Party. COFEPRIS also accepts certificates issued by the following countries, inspection by Mexico is not required if certification by these high-sanitary surveillance countries is submitted: USA, Brazil, Canada, countries of the EU, Japan and Australia.

Mexico is currently participating in workgroups and has created taskforces to allow the possibility in the future of collaboration regarding GMP certification with other countries of the Pacific Alliance (Chile, Colombia, Costa Rica and Peru) and other Health Authorities of Regional Reference. (Regulators from Argentina, Brazil, Colombia and Cuba).

The legal representative must have GMP certificate at the time of submitting the application dossier by:

- COFEPRIS (Mexican Health Authority)
- One of the Health Authorities recognized by COFEPRIS: FDA (USA), ANVISA (BRAZIL), Health Canada (CANADA), EMA (EU), Pharmaceutical and Safety Bureau (Japan) and TGA (Australia) or
- Health Authority of Origin

The GMP certificate must be presented in original or notary-certified copy, be written in Spanish or have attached the Spanish translation by an authorized translator (perito traductor autorizado). It must be apostilled or legalized.

If the GMP certificate issued by the health authority of origin is not recognized by COFEPRIS, an analysis with focus on risk assessment will be performed to assess the compliance with GMP standards. This analysis will consider the record of the manufacturing site, its pharmacovigilance reports, other GMP certificates issued by COFEPRIS or other health authorities, sanitary alerts, and any other information that the authority might consider relevant.

In the analysis results, if there is no enough information to consider the foreign GMP certificate as valid. Then COFEPRIS will visit and inspect the manufacturing site to verify the compliance with GMP guidelines. This inspection will have to be requested by the solicitor via the established administrative processes, and the receipt for the application for inspection must be evidenced to the Commission of Sanitary Authorization.

The solicitors will then be able to request to COFEPRIS a note (constancia) stating that a certain GMP certificate has been recognized as acceptable, which will be attached to the submission dossier.

GMP Verification is required by COFEPRIS in the following cases:

- For new registration and manufacturing changes of biologic, biotech and hemoderivate products.
- For new registration or renewal of drug products or drug substances of any kind manufactured in countries not considered as high sanitary surveillance by COFEPRIS.

The application should be made to COFEPRIS by the legal representative. GMP issued by COFEPRIS is Valid for 30 months.

Documents Required for GMP inspection

1. Application form
2. Proof of payments
3. Letter of Authorization to the Legal Representative.
4. Technical documentation of the manufacturing line to be verified

Note: All documents that accompany the applications must be submitted in Spanish, or otherwise, must be attached to the same translation into Spanish, endorsed with the signature of the sanitary responsible person.

Phase 5: Pharmacovigilance Requirement^{9w}

Pharmacovigilance is an activity destined to the detection, evaluation, understanding and prevention of adverse events, suspected adverse reactions, reactions of adverse events, the events supposedly attributable to vaccination or immunization, or any other problem of safety related to the use of medicines and vaccines. Therefore, pharmacovigilance is a shared responsibility between the Regulatory Authority, the members of the National Health System, health professionals, institutions that carry out research in humans, holders of the sanitary registry or their legal representatives, distributors and marketers of the product and patients or users. In relation to the above, there is a need for timely risk management and the creation of a tool for its evaluation, management and mitigation.

Mexico joined the International Drug Monitoring Program in 1999. The National Center for Pharmacovigilance (CNFV) is part of the Commission of Evidence and Risk Management (CEMAR) within the Federal Commission for the Protection against Health Risks (COFEPRIS) since 2001 and has the purpose of receiving information on Suspected Adverse Reactions of Medicines, vaccines and medical devices, by the members of Pharmacovigilance in the country, as well as the evaluation, analysis and feedback of information.

Legal Representative: The producing laboratories or their legal representatives have the responsibility to guarantee the quality, safety and efficacy of the medicines that they commercialize in the country and the National Regulatory Authority (COFEPRIS) must verify this guarantee, as well as establish policies, and guidelines in this matter, in concordance with international regulations.

RISK MANAGEMENT PLAN

Definition: The Risk Management Plan is a document that includes information about the safety profile of medicines or vaccines and describes the measure to be taken to monitor, prevent and minimize risks.

In accordance with the regulations in force, the categories for medicines and vaccines are divided into the following categories:

Type	Description
Category I	Generic drugs, including your reference medicine.
Category II	Medications and vaccines marketed, of which there is a concern or issue of security at a national or international level that affects the benefit / risk balance.
	Drugs and vaccines with modifications that impact on the therapeutic scheme and / or route of administration.
	New, biological or biotechnological molecules that have a sanitary registry issued by a health authority recognized by COFEPRIS and information from clinical trials that allows to establish a favorable security profile.
	Orphan drugs that have a sanitary registry / recognition of an orphan issued by a regulatory authority recognized by COFEPRIS and information from studies that allows establishing a favorable safety profile.
	Drugs and vaccines of which your safety profile is already known in other conditions and that have undergone modifications that impact their safety.
Category III	New, biological or biotechnological molecules that do not have a sanitary registry issued by a regulatory authority recognized by COFEPRIS and that information from studies clinical trials does not allow establishing a favorable safety profile.
	Orphan drugs that do not have a sanitary registry / recognition of an orphan issued by a regulatory authority recognized by COFEPRIS and that the information from clinical studies does not allow to establish a favorable safety profile.
	Medicines and vaccines marketed in Mexico where there is evidence of a risk at the national or international that potentially can exceed the benefit.

The structure of the RMP is not affected by the product category, however there are differences in the scope of pharmacovigilance and risk minimization actions.

Type	Elements to include in RMP
Category I	<ul style="list-style-type: none"> - Product description - distinctive description - Generic description - Pharmaceutical forma and formulation - Therapeutic indications - Security specifications - Description of populations for which there is no safety information - Usage information outside of authorized indication, overdose, illegal use, medication errors - summary of Security problems - list of important risks - International alerts - pharmacovigilance plan

Category II	- Pharmacovigilance Plan - Additional activities (does not include clinical studies) - Risk Management Plan
Category III	- Pharmacovigilance Plan - Additional activities (may include pharmacovigilance or clinical studies) - Risk Management Plan - Additional activities

In Mexico in general, the RMP must contain the following elements:

- Submission brief
- Product description
- Security specifications
- Pharmacovigilance plan
- Risk minimization plan

Structure of the RMP:

It is divided into four parts:

1. Product Description

- General and regulatory information
- Basic pharmacological information

2. Security Specifications

- **Description of populations for which there is no safety information:** this includes description of the disease and its epidemiological characteristics, pre-clinical and clinical development of the product and populations for which there is no safety information.
- **Post-marketing security information available:** this includes update security concerns, post-marketing studies, post-marketing use,
- **Safety information for uses outside authorized indication, overdose, illegal use, medication errors**
- **List of important risks:** significant identified and potential risks, interactions, pharmacological effects associated with the therapeutic class
- **Summary of security problems**
- **International alerts**

3. Pharmacovigilance Plan

- Routine pharmacovigilance activities
- Additional pharmacovigilance activities

4. Minimization Plan for Risks

- Routine risk minimization activities

- Activities to minimize additional risks

The pharmacovigilance plan describes the routine activities and, in some cases, the additional activities according to the safety specifications of the medicine or vaccine, designed to monitor, identify and characterize the risks of the drugs or vaccines and requiring routine activities for all categories, while additional activities will be considered for categories II and III.

The risk minimization plan describes the activities and interventions that aim to prevent or reduce the probability or severity of occurrence of RAM associated with the use of the product.

Phase 5: Product Registration

1. There no format for the Dossier.
2. The dossier should be prepared according to the checklist provided by COFEPRIS for New Molecules and Generic.
3. Dossier is divided into 4 modules:
 - a) Module I: Administrative and Legal
 - b) Module II: Quality Information
 - c) Module III: Pre-clinical (for New Molecules) or Interchangeability /Bioequivalence (for Generic)
 - d) Module IV: Clinical (only for New Molecules)

Document Required for Product Registration are Appendix-xxx

VALIDITY OF REGISTRATION

The registration (Health Record) is valid for 5 years

TIME LINES

S. No	Category	Time (Days)
1	Generic (Drugs that include active and therapeutic indications already registered in Mexico)	180
2	Drugs whose active ingredients not registered in the United Mexican States, but are registered and sold freely in their country of origin	240
3	New Molecule	180*

*The time taken to resolve New Drugs Application is after a technical meeting between the applicant and the Committee on New Molecules is held, and once the application is submitted for registration.

AGENCY FEE

S.NO	Category	FEE (mxn)
1	Generic	71,334.41
2	New molecule	127,549.79
3.	GMP inspection fee	84,080.88

REFERENCES

1. Certificates of good manufacturing practices, Appendix 1
2. Regulation of Health Products, Article 16 and Article 24, Appendix 2
3. Notice of Operation, Appendix 3
4. General Law of Health, Article 226
5. Regulation of Health Products, Article 376
6. Regulation of Health Products, Article 166
7. Index of Documentation for Application Income for Generic Health Registration
8. <https://latampharmara.com/2013/10/18/mexico-new-guidelines-for-the-acceptance-of-gmp-certificates/>
9. Pharmacovigilance Guide for the preparation of the Periodic Safety Report

<http://siga.impi.gob.mx/newSIGA/content/common/principal.jsf> patents search

https://www.researchgate.net/publication/303279229_OVERVIEW_OF_DRUG_REGISTRATION_REQUIREMENTS_FOR_PHARMACEUTICALS_IN_EMERGING_MARKET

<https://pharmaboardroom.com/legal-articles/regulatory-pricing-and-reimbursement-mexico/>

<http://www.ijpacr.com/files/21-07-2017/29.pdf>

Details of Indian Embassy abroad: <https://mea.gov.in/indian-mission.htm?151/Mexico>

Details of importing country Embassy in India: <https://embamex.sre.gob.mx/india/>