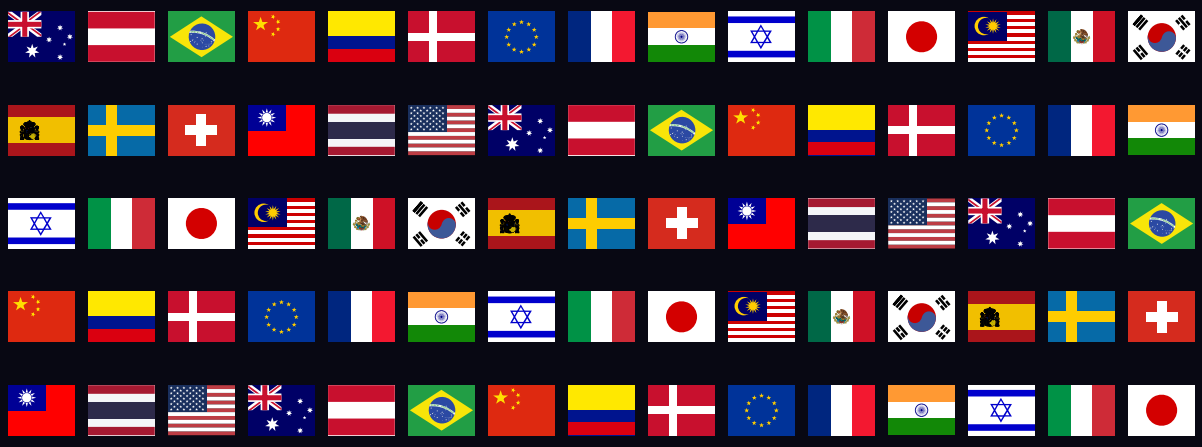
PHARMA & MEDICAL DEVICE REGULATION

Mexico



LEXOLOGY
Getting The Deal Through

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Quick reference guide enabling side-by-side comparison of local insights, including into the regulatory framework; clinical practice; marketing authorisation; amending authorisations; recall; promotion; enforcement of advertising rules; pricing and reimbursement; off-label use and unlicensed products; sale and supply; and recent trends.

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Table of contents

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REGULATORY FRAMEWORK

Competent authorities for authorisation

Identify the competent authorities for approval of the marketing of medicinal products and medical devices. What rules apply to deciding whether a product falls into either category or other regulated categories?

The Mexican authority responsible for enforcing the regulatory framework relating to medical products is the Federal Commission for Protection against Sanitary Risk (COFEPRIS), incorporated in the Undersecretary for Prevention and Promotion of Health of the Ministry of Health. Its Committee on New Molecules and a Subcommittee on Biotech Products assess biological medicinal products.

The regulatory framework is set out in the following federal laws:

- the General Health Law;
- the General Health Law Regulations for Healthcare Products;
- Mexican Official Standards (NOMs);
- the Mexican Pharmacopoeia;
- the COFEPRIS Rules listing healthcare products that do not require a marketing authorisation in view of their low risk to human health; and
- amendments to the Equivalence Decree to import health supplies without marketing authorisation.

The products are classified according to the definitions provided in this legal framework.

Law stated - 15 August 2022

Approval framework

Describe the general legislative and regulatory framework for approval of marketing of medicinal products and medical devices.

Pharmaceutical products

New molecules

Applicants for marketing authorisations must prove the safety and efficacy of their products through standard clinical trials according to the rules set out by the General Health Law, its regulations, and the NOMs of good manufacturing of medicines and active ingredients, as well as the approval of their products as new molecules from the COFEPRIS New Molecules Committee.

Generics

Applicants for marketing authorisations must prove that their products are bioequivalent to the innovator product. On 3 May 2021, the NOM setting the test to prove that a generic drug is interchangeable with a reference drug was updated (NOM-177-SSA1-2013).

There is a linkage system between COFEPRIS and the Mexican Institute of Industrial Property, which aims to prevent the granting of marketing authorisations in violation of patent rights.

Biologics

When it comes to legal and administrative information, the essential dossier submission requirements for innovative products manufactured in Mexico are preclinical and clinical trials, certificates of good manufacturing practices of the active pharmaceutical ingredient and the medicinal product, analytical methods, summaries, manufacturing licence, prescribing information, label, and a pharmacovigilance programme.

For innovative products manufactured abroad, additional requirements apply, particularly a certificate for export, a letter of representation with apostille and a legal representative with address in Mexico. In cases where the good manufacturing practices certificates are not issued by an agency recognised by COFEPRIS, such as the US Food and Drug Administration or the European Medicines Agency, an in-person inspection will be required.

Biocomparables (follow-ons)

The essential dossier submission requirements for biocomparables are almost the same as those for innovative biotech products, except for the requirements to prove safety, efficacy and quality.

For these purposes, biocomparable applicants must submit essentially:

- in vitro studies or comparative non-clinical studies;
- a report of a comparative test of pharmacokinetics if determined by the Ministry of Health to show pharmacokinetic comparability on key parameters between both the follow-on and the product of reference;
- pharmacodynamics test reports; and
- comparative efficacy and safety clinical tests to show similarity between both the follow-on and the product of reference.

Once approved, close pharmacovigilance should be followed.

On 19 August 2020, COFEPRIS announced new operating rules for the approval of generic drugs in Mexico and, in May 2021, they announced some changes to the process of approval for biocomparables.

Orphan drugs

Orphan drugs were introduced to the General Health Law and the Mexican Pharmacopeia several years ago. In practice, they are approved by a particular procedure, following rules for new molecules when applicable and appropriate. However, specific rules would be welcomed.

Medical devices

Marketing authorisation requirements for medical devices depend on the level of risk involved in their use, according to a threefold classification:

- Class I encompasses products that are well known in medical practice, for which safety and efficacy have been proven, and are not usually introduced into a patient's body;
- Class II encompasses products that are well known in medical practice but may have material or strength modifications – if introduced, they remain in a patient's body for less than 30 days; and
- Class III encompasses products either recently accepted in medical practice or that remain in a patient's body for

more than 30 days.

COFEPRIS analyses all medical devices and, if applicable, software that enables them to work. Mobile medical applications are a new area that COFEPRIS may address in the future with particular regulations, especially if they present health risks.

Law stated - 15 August 2022

CLINICAL PRACTICE

Applicable rules

What legislation controls and which rules apply to ethics committee approval and performance of clinical trials in your territory for medicinal products and medical devices?

International guidelines – such as the Nuremberg Code, the Helsinki Declaration, World Health Organization guidelines, International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use guidelines, the General Health Law and its Regulations for Health Research, and the Mexican Official Standard (NOM) for Health Research in Human Beings (NOM-012-SSA3-2012) – control and rule ethics committee approval and performance of clinical trials in Mexico.

Moreover, Mexican health authorities have issued guidelines for ethics committees. According to these guidelines, committees shall be integrated from different specialities and shall include professionals from different areas such as psychology, nursing, social work, sociology, anthropology, philosophy and law, among others.

The Federal Commission for Protection against Sanitary Risk (COFEPRIS) approves ethics committees pursuant to the regulatory framework.

Law stated - 15 August 2022

Reporting requirements

What requirements exist for reporting the commencement of a trial and its results to the competent authorities or the public?

Any research on human beings must be approved by COFEPRIS. The research can include testing new medicinal products, or new uses, dosages or administration routes for already approved medicinal products. Essentially, the main requirements for an application for authorisation from COFEPRIS are:

- approval by an independent ethics committee registered with the Ministry of Health;
- approval by the medical institution or institutions where the clinical trials will be conducted, which must be approved by COFEPRIS to conduct clinical trials;
- clinical trial protocols (including schedule and the approximate amount of medicinal products to be imported);
- written informed consent templates;
- preclinical and clinical data that justifies conducting the research;
- a description of available resources to conduct the research and to address emergencies (including a statement of sponsorship); and
- a written letter by the qualified investigator acknowledging their responsibilities, and data from both them and their staff.

Medical assistance and financial indemnification for damage caused by the clinical trial must be provided to research participants.

Trial preconditions

Preclinical data must be collected to justify whether clinical trials can be conducted. The General Health Law Regulations require measures to ensure that the investigator does not have a conflict of interest to protect the rights of research participants, maintain accurate results and allocate resources.

The principal researcher must compile a final technical report for the clinical trial. When clinical trials last longer than one year, annual technical reports for the health authorities must be compiled. Accordingly, the following NOMs apply:

- medicinal products labelling (NOM- 072- SSA1-2012);
- installation and operation of pharmacovigilance (NOM-220-SSA1-2016);
- interchangeability and biocomparability tests (NOM-177-SSA1-2013);
- biological products (NOM-257-SSA1-2014);
- good manufacturing practices for medicinal products (NOM-059-SSA1-2015); and
- good manufacturing practices for active ingredients (NOM-164-SSA1-2015).

Law stated - 15 August 2022

Consent and insurance

Are there mandatory rules for obtaining trial subjects' consent to participate? Must sponsors arrange personal injury insurance to a particular limit?

Investigators must collect informed consent from research participants in a formal written document, which must also be signed by two witnesses. In simple terms, the validity requirements for consent are that a participant grants it on a voluntary basis, with capacity to do so and sufficient information (knowing the potential risks and benefits). Participants maintain the right to withdraw from the study at any time. Investigators must ensure post-care for them until it is clarified that there is no damage derived from the research.

According to NOM-012-SSA3-2012, in relation to clinical trials in human beings, the clinical trial budget should include compensation to which the subject of investigation will be legally entitled in case of damage directly related to the clinical trial. Where appropriate, this financial fund may be covered by study insurance.

Law stated - 15 August 2022

MARKETING AUTHORISATION

Time frame

How long does it take, in general, to obtain an authorisation from application to grant, what fees are payable and what is the normal period of validity of the authorisation?

Time frames

Requirements and time frames vary among new molecules, biologics and follow-on products. Article 166 of the General Health Law Regulations sets out the following approval timeframes:

- 180 calendar days for medicines including an active pharmaceutical ingredient or therapeutic indication already approved in Mexico;
- 240 calendar days for medicines approved abroad but not in Mexico; and
- 180 calendar days for new drugs (a meeting with the New Molecules Committee is required).

The approval time frame for biologics and biocomparables is 180 calendar days (articles 177 and 177-bis 4 of the General Health Law Regulations).

These time frames may vary in practice but can be reduced if the application has been pre-examined by a third examiner (private company) approved by the Federal Commission for Protection against Sanitary Risk (COFEPRIS) to do so.

Government fees

Government fees for analysing marketing authorisation applications are:

- approximately 160,000 Mexican pesos for new molecules and biologics; and
- approximately 80,000 Mexican pesos for generics and biocomparables.

Period of validity

Drug manufacturers must renew their licences every five years, subject to the applicable tests, including submission of a certificate of good manufacturing practices.

Law stated - 15 August 2022

Marketing exclusivity

What protections or exclusivities apply to the marketing period of an approved medicinal product or variation?

In Mexico, there is no specific regulation regarding market exclusivity that applies to the marketing period of an approved medicinal product or variation. However, it is possible to obtain data protection exclusivity through litigation. So far, litigation has led to some favourable precedents that recognise at least five years for new chemical molecules, new indications, new formulations, orphan drugs and biologics. For biologics, some even gain over five years of protection. However, because there is no available domestic legislation, there are no guidelines nor provisions that specify the scope of the protection granted through litigation.

Law stated - 15 August 2022

Protecting research data

What protections or exclusivities apply to the data submitted by originators to gain initial approval and, on variation or new application, to add indications or pharmaceutical forms?

There is no specific body of local legislation for data protection exclusivity (RDP) in Mexico. In 2012, COFEPRIS issued internal guidelines to provide a five-year term of protection that only covers new chemical entities. However, the reliability of these guidelines is still uncertain.

Some cases are brought before the federal courts, which decide whether the health authorities have to observe RDP in respect of the product of interest for a five-year period set forth by the North American Free Trade Agreement (NAFTA) and the Mexico–United States–Canada Agreement (MUSCA). Within the corresponding cases, preliminary injunctions are requested so that COFEPRIS observes the requested RDP until the merits of the case are decided. The granting of these injunctions is subject to the criterion and discretion of the court handling the case.

Based on the interpretation of international treaties, RPD for at least five years for new chemical entities, formulations, new indications and orphan drugs have been obtained through litigation.

Concerning biologics, longer periods of RDP have been requested based on NAFTA (which provides that this protection should be at least five years) and international comparative law. However, the analysis in this regard is done on a case-by-case basis.

The new MUSCA entered into force on 1 July 2020. This treaty will have an impact on the current situation concerning RDP in Mexico. The MUSCA used to describe the periods of protection more clearly than the current NAFTA. However, the amendments to the MUSCA completed in December 2019 eliminated the provisions for new formulations or combinations and established a new method of administration: at least three years for new indications, at least 10 years for biologics and at least five years for new chemical molecules, with a transition period of five years. Without those specific provisions and with no domestic law, uncertainty among the generic and innovative pharmaceutical industries continues. To obtain this protection, litigation would still arise against the eventual refusals of COFEPRIS to recognise regulatory protection for more than five years for biologics and at least three years for new indications.

The amendments to the MUSCA will not necessarily result in adverse decisions since the wording of NAFTA 'establishing at least five years of protection' remains the same as it has been since 1994. Moreover, there are favourable precedents with NAFTA's wording obtaining more than five years of RDP for biologics. Therefore, the main grounds for a legal action trying to obtain more than five years RDP for biologics also remain.

The Agreement on Trade-Related Aspects of Intellectual Property Rights is still in force and is implemented through the Code of Commerce. In addition, the internal guidelines issued by COFEPRIS and several favourable legal precedents in this regard remain. Other international treaties will be in force, including the treaty between Mexico and the European Union that binds the parties to recognise at least six years of RDP for both small molecules and biologics, although this treaty is not yet in full force. Finally, the RDP provisions of the Comprehensive and Progressive Agreement for Trans-Pacific Partnership have been suspended.

Law stated - 15 August 2022

Freedom of information

To what extent and when can third parties make freedom of information applications for copies of research data submitted by applicants for authorisation to market medicinal products or medical devices?

According to the General Law of Access to Public Data, all data of applications under assessment and personal data are classified. Thus, Health Authorities usually reject freedom of information applications regarding data contained in marketing authorisation applications for medicinal products and medical devices. However, in some cases, they may allow release of certain information considered public information.

Law stated - 15 August 2022

Regulation of specific medicinal products

What are the specific requirements and processes for marketing approval of the major categories of regulated products?

Pharmaceutical products

New molecules

Essentially, applicants for marketing authorisations must prove the safety and efficacy of their products through standard clinical trials, according to the rules set out by the General Health Law, its regulations and NOMs of good manufacturing of medicines and active ingredients. Concurrently, they also have to request approval of their products as new molecules from the COFEPRIS New Molecules Committee. Research and development companies may benefit from a special procedure for first-time approval in Mexico for drugs that have been previously approved by a regulatory authority abroad.

Generics

Applicants for marketing authorisations must prove that their products are bioequivalent to the innovator product. They must provide information concerning dissolution profiles or bioavailability studies regarding the reference product. COFEPRIS periodically issues a reference list of medicinal products. Recently, the NOM setting the test to prove that a generic drug is interchangeable with a reference drug was updated (NOM-177-SSA1-2013). Legally, COFEPRIS should not grant marketing authorisations for generics that breach exclusivity rights.

There is a linkage system between COFEPRIS and the Mexican Institute of Industrial Property (IMPI), which aims to prevent the granting of marketing authorisations in violation of patent rights. Under the linkage system, at the time of filing the application, the applicant must either prove that it is the owner or licensee of the patent of the active ingredient in the product (recorded before IMPI), or state under oath that their application does not violate the list of products published in the Linkage Gazette and observes patent law.

Biologics

The essential dossier submission requirements for innovative products manufactured in Mexico are preclinical and clinical trials, certificates of good manufacturing practices of the active pharmaceutical ingredient and the medicinal product, analytical methods, summaries, manufacturing licence, prescribing information, label and a pharmacovigilance programme.

For innovative products manufactured abroad, additional requirements apply. In particular, these are a certificate for export, a letter of representation with apostille and legal representative with address in Mexico. In cases where the good manufacturing practices certificates are not issued by an agency recognised by COFEPRIS, such as the US Food and Drug Administration (FDA) or the European Medicines Agency (EMA), an in-person inspection will be required.

As an incentive for innovation, research and development companies can benefit from a special procedure for innovative biotech products that have been approved by the FDA, the EMA, Health Canada, the Swiss Agency for Therapeutic Products (Swissmedic) or the Australian Therapeutic Goods Administration (TGA).

Biocomparables (follow-ons)

The essential dossier submission requirements for biocomparables are almost the same as those for innovative

biotech products, except for the requirements to prove safety, efficacy and quality.

For these purposes, biocomparable applicants must essentially submit:

- in vitro studies or comparative non-clinical studies;
- a report of comparative test of pharmacokinetics if determined by the Ministry of Health to show pharmacokinetic comparability on key parameters between both the follow-on and the product of reference;
- pharmacodynamics test reports; and
- comparative efficacy and safety clinical tests to show similarity between both the follow-on and the product of reference.

Once approved, close pharmacovigilance should be followed.

COFEPRIS has been working on guidelines to perform biocomparability studies. They have issued guidelines for etanercept, filgrastim, infliximab, insulin and its analogous, rituximab, and somatropin.

Orphan drugs

Orphan drugs were introduced into the General Health Law and the Mexican Pharmacopeia several years ago. In practice, they are approved by a particular procedure, following rules for new molecules when applicable and appropriate. However, specific rules would be welcomed.

Medical devices

Marketing authorisation requirements for medical devices depend on the level of risk involved in their use, according to a threefold classification:

- Class I encompasses products that are well known in medical practice, for which safety and efficacy have been proven, and are not usually introduced into a patient's body;
- Class II encompasses products that are well known in medical practice but may have material or strength modifications – if introduced, they remain in a patient's body for less than 30 days; and
- Class III encompasses products either recently accepted in medical practice or that remain in a patient's body for more than 30 days.

COFEPRIS analyses all medical devices and, if applicable, software that enables them to work. Mobile medical applications are a new area that COFEPRIS may address in the future with particular regulations, especially if they present health risks.

As an incentive, applicants can benefit from a special procedure for first-time approval in Mexico for certain devices that have been previously approved by the US FDA and Health Canada. This procedure is essentially based on a dossier filed with the foreign regulatory agency and can reduce approval time frames in Mexico by up to 30 working days. Industry participants have welcomed these new rules, but they are still being tested.

Dietary supplements

Dietary supplements do not require a marketing authorisation. Manufacturers or those responsible for their marketing in the country must submit an operation notice 30 days before starting operations.

Traditional herbal remedies

A herbal remedy can be described as the preparation of medicinal plants or their parts, individually or in combination, and their derivatives presented in pharmaceutical form, to which the relief for some participating or isolated symptoms of a disease is attributed by popular or traditional knowledge.

These products do not require a marketing authorisation per se, but it is necessary to submit an application before the regulatory agency to obtain an alphanumeric key prior to commercialisation.

Herbal medicines

This encompasses products made with plant material or some derivative of it. The main ingredient is the aerial or underground part of a plant or extracts and tinctures, as well as juices, resins, fatty oils and essential oils, presented in pharmaceutical form, the therapeutic efficacy and safety of which have been scientifically confirmed in national or international literature. These type medicines require a marketing authorisation to be commercialised.

Homeopathic products

This encompasses a homeopathic medicine, any substance or mixture of substances of natural or synthetic origin that has a therapeutic, preventive or rehabilitative effect and that is prepared in accordance with the manufacturing procedures described in the Mexican Homeopathic Pharmacopoeia, or in those of other countries or other sources of national and international scientific information. These types of products require a marketing authorisation.

Law stated - 15 August 2022

Rewards and incentives

What rewards or incentives for approval are applicable to the major product categories, including orphan drugs, drugs for paediatric use, generic drugs and biosimilars?

New molecules

Research and development companies relating to new molecules may benefit from a special procedure for first-time approval in Mexico for drugs that have been previously approved by a regulatory authority abroad.

Biologics

As an incentive for innovation, research and development companies can benefit from a special procedure for innovative biotech products that have been approved by the US FDA, the EMA, Health Canada, Swissmedic or the TGA.

Medical devices

As an incentive, applicants can benefit from a special procedure for first-time approval in Mexico for certain devices that have been previously approved by the US FDA and Health Canada. This procedure is essentially based on a dossier filed with the foreign regulatory agency and can reduce approval time frames in Mexico by up to 30 working days. Industry participants have welcomed these new rules, but they are still being tested.

Orphan drugs

Orphan drugs were introduced into the General Health Law and the Mexican Pharmacopeia several years ago. In practice, they are approved by a particular procedure, following some of the rules for new molecules when applicable and appropriate, yet it is not necessary to go through the New Molecules Committee as a requirement to submit an approval application.

Law stated - 15 August 2022

Post-marketing surveillance of safety

What pharmacovigilance or device vigilance obligations apply to the holder of a relevant authorisation once the product is placed on the market?

The Mexican Official Norm for Pharmacovigilance, NOM-220-SSA1-2016 (NOM-220), establishes mandatory provisions regarding pharmacovigilance that apply to all medicines.

NOM-220 requires marketing authorisation holders to have a pharmacovigilance plan, which must include provisions for monitoring adverse effects in patients caused by the product at every stage of treatment.

The National Commission for Pharmacovigilance should verify the plan to manage risks, and, if applicable, require the implementation of an intensive pharmacovigilance plan.

Regarding medical devices, the marketing authorisation holder is required to have registered a Technovigilance Unit before COFEPRIS. The unit should have manuals and standard operating procedures. A qualified person should be in charge of the unit who should receive, sort and report adverse effects.

Law stated - 15 August 2022

Other authorisations

What authorisations are required to manufacture, import, export or conduct wholesale distribution and storage of medicinal products and medical devices? What type of information needs to be provided to the authorities with an application, what are the fees, and what is the normal period of validity?

Companies manufacturing medicinal products and medical devices in Mexico must be approved by COFEPRIS through a manufacturing licence or authorisation. Manufacturers must renew their licences every five years, subject to the relevant tests, particularly regarding good manufacturing practices.

Any import of drugs, health products or raw materials for drugs must be approved by COFEPRIS. A marketing authorisation is needed unless an exemption applies. The import of a minimal quantity of products without a marketing authorisation can be approved in certain circumstances (eg, clinical trials, personal use and orphan drugs).

As mentioned, applicants for marketing authorisations must prove the safety and efficacy of their products through standard clinical trials and comply with all requirements established in articles 167, 177 and 177-bis 4 of the General Health Law Regulations for Healthcare Products and NOMs of good manufacturing of medicines and active ingredients.

Government fees for analysing marketing authorisation applications are:

- approximately 160,000 Mexican pesos for new molecules and biologics; and
- approximately 80,000 Mexican pesos for generics and biocomparables.

Foreign marketing authorisations are not valid in Mexico. However, COFEPRIS has developed a special procedure for drugs requiring first-time approval in Mexico, but that have been approved by equivalent regulatory authorities abroad. In this procedure, the approval requirements of the foreign agencies are recognised as equivalent to those in Mexico.

Law stated - 15 August 2022

Sanctions

What civil, administrative or criminal sanctions can authorities impose on entities or their directors and officers for breach of the requirements concerning controlled activities?

COFEPRIS can request reports from marketing authorisation holders and make on-site inspection visits to the manufacturing, distribution or storage facilities.

COFEPRIS can initiate ex officio legal proceedings to sanction non-compliance. Ultimately, these legal proceedings can result in the revocation of authorisations. COFEPRIS is also entitled to implement measures on behalf of public health, such as the seizure of products and ordering partial or total suspension of activities, services, or advertisements. Under certain conditions, COFEPRIS has the statutory authority to revoke any manufacturing approval or impose sanctions, ranging from a fine of up to 16,000 times the minimum wage or unit of measure for sanctions to the closure of the corresponding establishment or facility.

The imposition of administrative sanctions does not exclude civil and criminal liability. Administrative infringers can incur penalties ranging from a fine up to 50,000 times the minimum wage to final closure of the establishment. Repeated infringement is also considered to be a criminal offence.

COFEPRIS has broad jurisdiction to seize counterfeit or illegal medicines. The General Health Law classifies the manufacturing and sale of counterfeit or falsified medicine as a crime. In addition, COFEPRIS commonly enters into collaboration agreements with the general attorney and the Customs Office to investigate and prevent counterfeit and illegal medicines.

Law stated - 15 August 2022

Exemptions

What, if any, manufacture and supply of medicinal products is exempt from the requirement to obtain an approval to market?

No medicinal product is exempt from the requirement of having a marketing authorisation in Mexico, apart from a magistral formula, which article 115 of the General Health Law Regulations for Healthcare Products defines as a medicine compounded in a local pharmacy to fit the unique need of a patient according to a detailed facultative prescription of a physician, under certain conditions and requirements, such as the requirement that the pharmacy needs regulatory approval to do so.

Law stated - 15 August 2022

Parallel trade

Are imports allowed into your jurisdiction of finished products already authorised in another jurisdiction, without the importer having to provide the full particulars normally required to obtain an authorisation to market? What are the requirements?

The import of medicinal products requires a marketing authorisation unless an exemption applies. These exemptions for medicines are essentially lab tests, clinical trials, raw materials for assembly processes for export, special treatments for illnesses with low prevalence and social interest, personal use, and donations.

Regarding medical devices, the exceptions are essentially lab tests, clinical trials, personal use, physician use, donations and used devices.

In January 2020, the Ministry of Health published a decree in the Official Gazette whereby the government allows the importation of medicinal products already authorised in another jurisdiction (ie, the United States, Canada, Switzerland or the European Union). Certain requirements must be complied with prior to importation.

On 22 June 2021, a decree was published amending the Equivalence Decree published on 28 January 2020 in the Official Gazette by the Ministry of Health. The decree contains amendments to make the process of importation easier, with the aim to expedite the granting of marketing authorisations of health supplies (eg, drugs, vaccines) into Mexico.

Law stated - 15 August 2022

AMENDING AUTHORISATIONS

Variation

What are the main requirements relating to variation of authorisations for medicinal products and medical devices?

Marketing authorisation holders can apply for adjustments to their marketing authorisations, but applicable requirements depend on the type of adjustment (for example, legal, technical or administrative information, manufacturing site and indication of use, among others).

Law stated - 15 August 2022

Renewal

What are the main requirements relating to renewal of authorisations for medicinal products and medical devices?

Marketing authorisations must be renewed every five years. According to article 190-bis of the General Health Law Regulations for Healthcare Products, as amended on 31 May 2021, to obtain an extension of a marketing authorisation drug, the applicant must submit the following documents:

- payment;
- a number or simple copy for which extension is required;
- in cases of major modifications that impact the pharmacokinetics of a drug, the applicant must submit the technical report issued by units of interchangeability; and
- a pharmacovigilance report of the drug.

On the other hand, the main requirements for the renewal of a medical device are the following:

- payment;
- the document that certifies a legal representative domiciled in Mexico; and
- the good manufacturing practices certificate of the product, issued by a national regulatory agency recognised by the Federal Commission for Protection against Sanitary Risk (COFEPRIS).

Law stated - 15 August 2022

Transfer

How easy is it to transfer the existing approvals or rights to market medicines and medical devices? How long does this take in general?

The transfer of a marketing authorisation requires compliance with certain formalities and proceedings, which should not be difficult if the applicant meets applicable requirements. To transfer a marketing authorisation to a new holder, an application must be submitted to COFEPRIS.

The transfer of a marketing authorisation must be communicated through a written document before COFEPRIS by the new holder, within a period not exceeding 30 days from the date on which it was made. The applicant must attach the documents where the transfer is evidenced and the label projects where the new owner is expressed.

According to the General Health Law Regulations for Healthcare Products, COFEPRIS must decide a transfer application within a period of 20 calendar days following the filing date. In practice, this period varies and it can be extended if further data or documents are requested.

COFEPRIS may serve the applicant during this 20-day period with a request for information or documents, granting the applicant with a term to respond that cannot be less than five working days. If no response is provided within the granted term, the application will be considered cancelled.

If COFEPRIS does not serve any request or decision on the applicant during that 20-day period, the regulations rule that the application should be considered approved.

Law stated - 15 August 2022

RECALL

Defective and unsafe products

What are the normal requirements for handling cases of defective or possibly unsafe products, including approvals required for recall and communication with health professionals?

The Mexican Official Standard (NOM) for the good manufacturing practice of medicinal products (NOM-059-SSA1-2015) requires a programme to recall products that do not meet quality standards in an appropriate and efficient manner. This programme must include:

- activities planned for recalling products in a rapid and effective manner;
- storage; and
- a list of authorities to be notified according to the product distribution.

Marketing authorisation holders must report any product recall decision to the Federal Commission for Protection against Sanitary Risk, providing details of the products and the causes leading to the recall.

Law stated - 15 August 2022

ADVERTISING AND PROMOTION

Regulation

Summarise the rules relating to advertising and promotion of medicinal products and medical devices, explaining when the provision of information will be treated as promotional. Do special rules apply to online advertising?

The primary legislation on advertising of medicinal products and medical devices is the General Health Law's regulations regarding advertising (RLGSMP) and opinions issued by the Advertising Council. The Intellectual Property Law and the Federal Consumer Protection Law also have provisions on advertising.

The Federal Commission for Protection against Sanitary Risk (COFEPRIS) and the Federal Consumer Bureau (consumer legal framework) are the regulatory authorities in this field.

The National Chamber of the Pharmaceutical Industry has a code of ethics that includes provisions on advertising. Although these provisions are not mandatory, failure to comply can result in a suspension of rights as a member of the chamber or exclusion from it.

The RLGSMP defines advertising as an activity covering all creation, planning, performance and distribution processes of advertisement to promote the sale or consumption of products and services. Thus, we consider that providing information will be treated as advertising when it promotes the sale or consumption of products.

Electronic advertising falls under the general rules for advertising in article 2 of the RLGSMP. COFEPRIS is increasing its monitoring of online advertisements for medicinal products and medicinal devices, which to date has been less stringent than advertising on television and radio. The Code of Good Practices of Promotion (the Code of GPP) states that online promotion of prescription only medicines addressed to healthcare professionals must be duly approved by the corresponding authorities. The advertising must be disclosed on scientific websites. The sponsor must be clearly identified.

Law stated - 15 August 2022

Inducement

What regulations exist to discourage the provision of inducements to healthcare professionals to prescribe, sell, supply or recommend use of a particular medicinal product or medical device?

There are several bodies of law that refer in general terms to the relationship between the pharmaceutical industry and healthcare professionals, such as the Health Law and Health Law Regulations (including those that concern the regulatory control of healthcare activities, establishments, products and services). Industry codes of practice complement these regulations.

The Council of Ethics and Transparency of the Pharmaceutical Industry (CETIFARMA) has issued the following self-regulatory instruments:

- the Code of Ethics and Transparency of the Pharmaceutical Industry (the Code of Ethics and Transparency);
- the Code of GPP; and
- the Code of Good Practices of Interaction of the Pharmaceutical Industry with Patient Organisations (Code of GPI).

Affiliate members of the National Chamber of the Pharmaceutical Industry (CANIFARMA) are required to follow these

codes. CETIFARMA supervises members' and adherents' compliance.

These bodies of law and codes set important sanctions to discourage the provision of inducements to healthcare professionals to prescribe, sell, supply or recommend use of particular products.

Law stated - 15 August 2022

Reporting transfers of value

What requirements apply to recording and publishing details of transfers of value to healthcare professionals and organisations by companies marketing medicinal products or medical devices?

The Codes of GPP and GPI allow CETIFARMA to require members to record any valuable support given to healthcare professionals, institutions or patient organisations. According to their guidelines, members will make information concerning donations granted available to the public on a yearly basis to promote transparency.

Law stated - 15 August 2022

Enforcers

Describe the bodies involved in monitoring and ensuring compliance with advertising controls for medicinal products and medical devices, distinguishing between any self-regulatory framework and control by the authorities.

In accordance with the General Health Law, COFEPRIS is in charge of monitoring and ensuring compliance with advertising controls.

The primary legislation for the advertising of medicinal products and medical devices is the General Health Law and its regulations. These norms are supplemented by guidelines published by COFEPRIS. This agency is part of the Ministry of Health and controls the advertising of medicinal products and medical devices. Industry codes of practices complement this regulation. CETIFARMA has issued the following self-regulatory instruments:

- the Code of Ethics and Transparency;
- the Code of GPP; and
- the Code of GPI.

Affiliate members of CANIFARMA are required to follow these codes. CETIFARMA supervises members' and adherents' compliance. There are also opinions issued by the Advertising Council, which include representatives from the Ministry of Health, the academic and scientific communities, the business sector, the media, and consumer groups.

Law stated - 15 August 2022

Sanctions

What are the possible financial or other sanctions for breach of advertising and promotional controls for medicinal products or medical devices?

COFEPRIS has specific authority to order the suspension of an advertising activity in breach of the legal framework. This order must be followed by both the responsible party and the media channel within a term of 24 hours. COFEPRIS may warn companies with approved products to modify ads that are presumably in breach of the legal framework. If

not modified or the modification is considered to not comply with the legal provisions, COFEPRIS may suspend the advertising activities and impose a fine. The decision and orders issued by COFEPRIS may be appealed before itself or the federal courts.

The penalties for failing to comply with the rules related to advertising are the suspension of advertising activities ordered either to the responsible party or directly to the media, and the imposition of a fine to each one, which can range from 2,000 to 16,000 units of measure for sanctions. The responsibility for imposing these penalties falls directly on the Ministry of Health through COFEPRIS.

COFEPRIS constantly monitors advertising activities throughout Mexico, particularly regarding drug-like products. COFEPRIS directs the efforts of coordination agreements related to publicity and the enforcement of the same. There has also been a strong coordinated effort between COFEPRIS and pharmaceutical companies tending to the self-regulation of advertising, which is still monitored. COFEPRIS has imposed large fines against specific over-the-counter medication manufacturers for using misleading advertising related to its products, inciting the public to self-medicate and taking their products at the first symptom without consulting a doctor.

Law stated - 15 August 2022

OFF-LABEL USE AND UNLICENSED PRODUCTS

Off-label use

May health professionals prescribe or use products for 'off-label' indications? May pharmaceutical companies draw health professionals' attention to potential off-label uses?

The Code of Good Practices of Promotion sets forth that information about medicinal products must be grounded on scientific evaluation and related empirical evidence, which must be kept at the disposal of healthcare professionals, if required. It must not induce confusion by means of distortion, unjustified pressure, omission or any other means. This code also states that, when scientific information is provided and is not part of the prescribing information duly approved or authorised in the marketing authorisation of a product, it should be strictly limited to a scientific audience, avoiding the promotion, directly, indirectly or through a third party, of any unauthorised directions of use.

Whereas there is no specific provision in the General Health Law Regulations concerning advertisements for off-label use, advertisement activities addressed to health professionals do not require a permit from the Federal Commission for Protection against Sanitary Risk – a notice of such an advertisement is sufficient. However, off-label advertisements should be avoided.

Law stated - 15 August 2022

Unlicensed products

What rules apply to the manufacture and importation and supply to healthcare providers of unlicensed medicines or medical devices?

The manufacturing, importation and supply of a medicinal product or medical device to a healthcare professional requires that such a product has been approved.

Law stated - 15 August 2022

Compassionate use

What rules apply to the establishment of compassionate use programmes for unlicensed products?

The applicable legislation concerning compassionate use programmes is mainly the following:

- the General Health Law;
- the General Health Law Regulations;
- health research in human beings (Mexican Official Standard (NOM) NOM-012-SSA3-2012);
- the Code of Good Practices of Advertising of the National Chamber of the Pharmaceutical Industry (CANIFARMA);
- the CANIFARMA Code of Ethics; and
- several other NOMs.

Law stated - 15 August 2022

SALE AND SUPPLY

Regulation

Are there special rules governing the dispensing or sale of particular types of medicinal products or medical devices?

Despite the marketing authorisations requirement to sell products, prescription medicines, such as antibiotics, can be dispensed only if the consumer gives the received written prescription to a pharmacy. Dispensing over-the-counter medicines does not require a specific permit. Psychotropic and narcotic drugs are prescribed using a special notebook monitored by the Federal Commission for Protection against Sanitary Risk (COFEPRIS) and dispensed through local pharmacies authorised by COFEPRIS.

Law stated - 15 August 2022

Online supply

What laws and guidelines govern online dispensing, sale and supply of medicinal products and medical devices?

Unless they are over-the-counter products, medicines must be made available only through authorised drug stores and prescription medicines can be sold to patients only with a physician's prescription. Dispensers must keep original prescriptions regarding antibiotics.

Law stated - 15 August 2022

Pricing and reimbursement

What are the controls imposed on pricing of medicines and medical devices and reimbursement by national social security systems that are applicable to manufacturers, distributors and pharmacists?

Price control in the private sector is based on a self-regulated maximum retail price (MRP) scheme covering patented products, overseen by the Ministry of Economy. Under price control, each product's MRP must not exceed an international reference price, estimated as the average price in six major markets, plus a market factor. There are no established sanctions for violations of the MRP.

In 2008, the government created the Committee for the Negotiation of Drug Prices (CNDP). Until 2018, recommended prices for patented and unique drugs (or those with exclusive distributors) for all public institutions were negotiated with the CNDP under the supervision of the Ministry of Public Function and the Mexican Antitrust Authority.

Under that scheme, price reviews and eventual changes were done annually. The new administration is implementing modifications frequently, which may impact the frequency of price change. The austerity measures that have recently been taken by the government will continue and may result in more frequent price reviews.

Public insurers dispense medicinal products prescribed by their healthcare professionals. Products are prescribed from a basic medicinal products list, which public insurers base on the national formulary issued by the Ministry of Health. Public insurers acquire those listed products mostly by public tender processes. The Mexican Institute of Social Security is the largest public sector buyer of drugs.

For direct purchasing of patented products, the CNDP analyses the effectiveness of the drugs and relevant therapeutic alternatives, and the feasibility and implications of an eventual substitution with equivalent medicines. The CNDP also conducts an economic evaluation of the cost-effectiveness of patented medicines compared with potential substitutes.

For the Institute of Social Security for State Workers (ISSSTE), a prescribed medicinal product can be dispensed in a private drug store registered with a public insurer, provided that this is not available within ISSSTE facilities and under certain conditions. The ISSSTE reimburses the cost of that product according to previous agreements.

In the private sector, most payments are made on an out-of-pocket basis. Private insurers are improving the level of pharmaceutical coverage as the private market in medicines has grown considerably.

Law stated - 15 August 2022

UPDATE AND TRENDS

Forthcoming legislation and regulation

Is there any current or foreseeable draft legislation or other rules that will affect the regulation of pharmaceuticals and medical devices? What is likely to change, and what steps need to be taken in preparation?

Medical devices

The initiative to reform various regulations of the General Health Law aims to regulate the use of medical devices. Among what is proposed, it is worth noting that:

- prosthetics, diagnostic agents and dental supplies should be considered medical devices;
- the term ‘essential accessories for health’ will be replaced with the term ‘medical devices’;
- for sale or supply, as well as for importation, the retailers must have a health authorisation from the Ministry of Health; and
- the indications of the medical device’s use will be detailed in the instructions of the corresponding product, in printed or electronic form.

In addition, on 20 December 2021, the new version of the Mexican Official Standard (NOM) NOM-241-SSA1-2021 on

good medical device manufacturing practices was published in the Official Gazette.

In general terms, this new version of the NOM seems clearer than the previous one as it focuses on giving a greater order to the specifications that must be considered in each of the stages of the life cycle of a medical device (eg, in each step of the manufacturing chain until its distribution and marketing.) In particular, the chapter on the quality management system was strengthened.

Among the modifications, it is important to highlight that the scope of the definition of a medical device is extended because of technological advances, now including:

The inclusion of the definitions of 'software' as a medical device is of high relevance and solves the old loop in the regulation of software in connection with medical devices. Until now, this category was not included in the current legislation despite the fact that there are various programmes and applications that address health matters.

Likewise, reference is made to the use of digital media, including digital records and the use of electronic signatures. Simultaneously, following the changes and inclusions throughout the new NOM, these are reflected in the inclusion of various terms to be compatible with the new figures.

This standard will leave NOM-241-SSA1-2012 without effect until it enters into force in 2023.

Proposal for a general law on humanities, sciences, technologies and innovation

This proposal promotes the continuous generation of new knowledge, as well as the articulation of basic science and frontier research with activities in the field of humanities, sciences, technologies and innovation. This is aimed at influencing priority issues for national development with the purpose of guaranteeing that public benefits gained from the development of sciences and technologies will result in social welfare, and contribute to the care and restoration of the environment. It also aims to promote the strengthening of national sovereignty and the integral development of Mexico.

Law stated - 15 August 2022

Jurisdictions

Australia	Clayton Utz
Austria	Preslmayr Attorneys at Law
Brazil	Kasznar Leonardos
China	East & Concord Partners
Colombia	OlarteMoure
Denmark	Accura Advokatpartnerselskab
European Union	DLA Piper
France	Intuity
India	ANA Law Group
Israel	Pearl Cohen Zedek Latzer Baratz
Italy	Avvocati Associati Franzosi Dal Negro Setti
Japan	Atsumi & Sakai
Malaysia	Raja, Darryl & Loh
Mexico	OLIVARES
South Korea	Lee & Ko
Spain	Faus & Moliner
Sweden	Advokatfirman Hammarskiöld
Switzerland	Wenger Vieli Ltd
Taiwan	Formosa Transnational Attorneys at Law
Thailand	Baker McKenzie
USA	DLA Piper