Life Sciences Regulation in Mexico: Overview

by Alejandro Luna F, Armando Arenas, and Karla Paulina Olvera Acevedo, *Olivares*

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A Q&A guide to life sciences regulation in Mexico.

This Q&A provides a high-level overview of key practical issues, including life sciences clinical trials, manufacturing, marketing, abridged procedure, pharmacovigilance, data privacy, packaging and labelling, biological medicines, medical devices, health care IT, combination products, borderlines, and natural health products.

Pharmaceuticals

1. What are the main legislation and regulatory authorities for pharmaceuticals in your jurisdiction?

Legislation

The main legislation for pharmaceuticals is:

- The General Health Law (*Ley General de Salud*).
- The General Health Law Regulations (*Reglamentos de la Ley General de Salud*).
- The Health Supplies Regulation (*Reglamento de Insumos para la Salud*).
- The Official Mexican Standards (*Normas Oficiales Mexicanas*) (NOMs).
- The Mexican Pharmacopoeia.

Regulatory Authorities

The regulatory authorities for pharmaceuticals are:

- **The Federal Commission for Protection against Sanitary Risk (*Comisión Federal para la Protección contra Riesgos Sanitarios*) (COFEPRIS).** COFEPRIS is under the authority of the Undersecretary for Prevention and Promotion of Health. COFEPRIS is responsible for:

- the sanitary regulation, surveillance, and control of public social security institutions and private health care institutions;
- the sanitary control of medical products and services, and their import and export;
- the sanitary control of the processing, use, maintenance, import, export, and disposal of medical equipment, prosthetics, orthotics, functional aids, diagnostic agents, dental supplies, surgical materials, and healing and hygiene products;
- preparing and issuing NOMs relating to health facilities, products, and services;
- evaluating, issuing, and revoking sanitary authorisations;
- exercising control and sanitary surveillance of pharmaceuticals and other health products;
- the disposal of organs, tissues, human cells and their components, toxic or dangerous substances, biotechnological products, and raw materials;
- exercising control and surveillance of the advertising of sanitary activities, products, and services; and
- imposing sanctions and implementing security measures.

(General Health Law.)

- **The General Health Council.** This agency is controlled by the executive and funded by the federal government. It is responsible for:
  - preparing, updating, and circulating the National Compendium of Health Supplies through the creation of groups of experts from all public health institutions, which decide on the inclusion of new medicines, therapies, devices, and other products in the compendium;
  - preparing and updating the Guidelines for the Evaluation of Health Supplies; and
  - preparing the Guidelines for Interchangeability Tests of medicines that are submitted to COFEPRIS for the granting of marketing authorisations of generics.

Definition of Medicinal Product

A medicine is defined as any substance or mixture of substances of natural or synthetic origin that both:

- Has therapeutic, preventive, or rehabilitative effect.
- Is presented in pharmaceutical form and is identified as a medicine for its pharmacological activity, and physical, chemical, and biological characteristics.

(General Health Law.)

Where a product contains nutrients, it is considered a medicine if both:

- It is a preparation containing individually or associated vitamins, minerals, electrolytes, amino acids, or fatty acids, which are:
    - present in concentrations higher than in natural foods; and
    - present in any defined pharmaceutical form.
- The indication for use contemplates therapeutic, preventive, or rehabilitative effects.

Clinical Trials

2. Outline the regulation of clinical trials.

Legislation and Regulatory Authorities

The main legislation for clinical trials is:

- The Health Law Regulations for Health Research (*Reglamento de la Ley General de Salud en Materia de Investigación para la Salud*) (RLGSMIS).
- The NOM for Health Research in Human Beings (NOM-012-SSA3-2012).

The Guideline for Good Clinical Practice E6(R1) is taken into account.

The Ministry of Health enforces the legislation, through COFEPRIS.

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

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

Authorisations

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

- 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. These institutions must be approved by COFEPRIS to conduct clinical trials.
- Clinical trial protocol must be drafted (including schedule and approximate amount of medicinal products to be imported).
- Written informed consent templates must be drafted.
- Pre-clinical and clinical data that justifies conducting the research must be provided.
- A description of available resources to conduct the research and to address emergencies (including a statement of sponsorship) must be provided.
- A written letter by the qualified investigator acknowledging their responsibilities, and details of them and their staff, must be provided.
- Medical assistance and financial indemnification for damage caused by the clinical trial must be provided to research participants.

Consent

Investigators must collect informed consent from research participants in a formal written document, which must also be signed by two witnesses. The requirements for valid 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 can leave the trial at any time. Investigators must ensure post-trial care for them, until it is clarified that there is no damage derived from the research.

Trial Pre-Conditions

Pre-clinical data must be collected to justify whether clinical trials can be conducted. The RLGSMIS requires measures to ensure that the investigator does not have conflict of interest, to:

- Protect the rights of research participants.
- Maintain accurate results.
- Allocate resources.

Procedural Requirements

The RLGSMIS and the NOM for Health Research in Human Beings set out the guidelines and standards for the clinical trial protocol, including rules concerning documents, compilation, confidentiality, and reports.

Essentially, any clinical trial must be conducted following ethical guidelines and must always respect the dignity, rights, and welfare of human beings (NOM for Health Research in Human Beings).

Clinical trials can specify certain steps or goals to be achieved. The principal researcher must compile a final technical report for the clinical trial. When clinical trials last longer than one year, annual technical reports must be compiled for health authorities. The following NOMs apply for:

- Medicinal products labelling: NOM- 072- SSA1-2012.
- Pharmacovigilance: NOM-220-SSA1-2012.
- Interchangeability and biocomparability tests: NOM-177-SSA1-2013.
- Biological products: NOM-257-SSA1-2014.
- Good manufacturing practices for medicinal products: NOM-059-SSA1-2015.
- Good manufacturing practices for active ingredients: NOM-164-SSA1-2015.

Sponsors and investigators must also comply with privacy and data protection laws (see *Question 12*).

Transparency and Reporting Requirements

The sponsor and principal investigator must report all expected and unexpected suspicions, events, and adverse reactions of which they are aware directly to the centres or pharmacovigilance units within:

- 15 calendar days from identification, for serious events.
- 30 calendar days from identification, for non-serious events.

When three or more similar cases of suspected adverse reactions occur within 24 hours, with the same drug and at the same location, the cases must be reported within 24 hours or the next business day.

Manufacturing and Distribution

3. What is the authorisation process for manufacturing and distributing medicinal products?

Application

Companies manufacturing or distributing medicinal products must obtain an authorisation from COFEPRIS.

COFEPRIS can also issue health permits for the temporary distribution of drugs for strategic purposes.

Conditions

The requirements for manufacturing approval are mainly set out in the General Health Law and the General Health Law Regulations, and NOMs setting good manufacturing practices for medicinal products (NOM-059-SSA1-2015) and health requirements for manufacturing (NOM-176-SSA1-1998). They regulate and provide guidelines and standards for:

- Workforce conditions in the manufacturing facilities (including, for example, responsibilities, uniforms, and medical examinations).
- Legal and technical documents.
- Facility requirements.
- Manufacturing, validity, and quality controls and protocols.
- Standard operation procedure.
- Biosafety measures.
- Packaging.
- Equipment.
- Destruction and elimination of waste.

Restrictions on Foreign Applicants

To hold an authorisation, applicants must have either:

- An approval from COFEPRIS for a manufacturing facility or laboratory for medicines or biologic products for human use in Mexico.
- An equivalent approval (a licence, certificate, or other permit document) for any of these facilities abroad from the competent authority in the country of origin.

(Article 168, Health Law Regulations.)

Fees

Government fees for analysing a manufacturing approval application are about USD5,000.

Authorisations, Variations, and Renewals

Manufacturing approvals are granted without a specific expiration date. However, any modification of the list of manufactured products or change of address must be approved by COFEPRIS.

Monitoring Compliance and Imposing Penalties

COFEPRIS has a permanent pharmacovigilance programme. Under the General Health Law Regulations and NOMs, COFEPRIS's monitoring is focused, among other things, on the following:

- Ensuring compliance with good manufacturing practices and standard operating procedures.
- Ensuring that activities performed do not exceed either authorised limits or differ from those authorised activities.
- Ensuring that companies perform validation analyses of their manufacturing processes and the systems involved.

COFEPRIS can carry out on-site inspection visits of manufacturing, distribution, or storage facilities.

COFEPRIS can implement measures to protect public health, such as:

- Seizure of products.
- Ordering partial or total suspension of activities, services, or adverts.
- Under certain conditions, revoke any manufacturing approval, impose sanctions, or both. Sanctions range from a fine up to 16,000 times the applicable unit of measure (about USD80,000) to closure of the establishment.

The imposition of administrative sanctions does not exclude civil and criminal liability. Affected parties can appeal decisions of COFEPRIS through the relevant administrative or judicial mechanisms.

COFEPRIS can revoke sanitary authorisations in the following cases:

- The products or activities covered by the authorisation pose a risk of harm to human health.
- The exercise of the authorised activity exceeds the limitations set in the authorisation.
- The authorisation is used for different purposes.
- Non-compliance with the General Health Law or the General Health Law Regulations.
- The product covered by the authorisation does not meet or no longer meets specifications or requirements established by the General Health Law, NOMs, or other general provisions.
- The applicant provided false information or documents.
- Reports provided by authorised third parties are false.
- The products no longer possess the attributes or characteristics under which they were authorised or have lost their preventive or therapeutic properties.

Marketing

Authorisation Procedure

4. What is the authorisation process for marketing medicinal products?

Application

New molecules, generics, biologics, biocomparables, and orphan drugs require a marketing authorisation. Requirements and time frames vary among these.

There is a NOM compiling the requirements for granting marketing authorisations for medicinal products (NOM-257-SSA1-2014). In addition, there is a NOM providing the specifications of stability test (NOM-073-SSA1-2015). This NOM specifically addresses the test for stability to be carried out on drugs in Mexico.

New molecules. Applicants for marketing authorisations must prove safety and efficacy of their products through standard clinical trials, according to the rules set out in the General Health Law, the General Health Law Regulations, and NOMs of good manufacturing of medicines and active ingredients.

Concurrently, applicants must request approval of their products as new molecules by the New Molecules Committee of COFEPRIS. A new molecule is:

- An active ingredient or drug not approved worldwide (new molecular entity).
- An active ingredient or drug already available in other countries but with limited clinical experience or disputed information, without approval in Mexico.
- A drug that is a non-marketed combination of two or more active ingredients.
- An active ingredient or drug already available in the market, but to be marketed for a new therapeutic indication.

(Article 2, section XV, General Health Law Regulations.)

Research and development (R&D) companies can benefit from a special procedure for drugs to be approved for the first time in Mexico that have been previously approved by a regulatory authority abroad (see *Question 9*).

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 list of reference medicinal products.

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. Every six months, the IMPI must publish the *Linkage Gazette*, which includes patents covering allopathic medicines (including formulation patents) (Intellectual Property Regulations). Use patents are only included in the *Linkage Gazette* by court orders, since the IMPI consider that they should not be included in the linkage system.

On the filing of the application, the applicant must either:

- Prove that it is the owner or licensee of the patent over the active ingredient of the product (recorded with the IMPI).

- State under oath that its application does not violate the list of products published in the *Linkage Gazette* and complies with patent law.

Biologics. Amendments to the legal framework to regulate the approval of biologics are recent and being tested. Applicants must prove quality, safety, and efficacy of their products (General Health Law, General Health Law Regulations, and NOMs (particularly those for good manufacturing practices for medicinal products (NOM-059-SSA1-2015) and for active ingredients (NOM-164-SSA1-2015)).

All biological drugs that were authorised before the legal reform, that are still on the market, must enter a regularisation process to comply with the new standard for biologics (NOM-257-SSA1-2014). NOM-257-SSA1-2014 emphasises that key points to ensure safety, efficacy, and quality of biologics are already regulated in other NOMs currently in effect, such as those for clinical trials and pharmacoviligance. NOM-257-SSA1-2014 empowers the Assessment Subcommittee on Biotech Products (*Subcomité de Evaluación de Productos Biotecnológicos*) (SEPB) to:

- Assess technical and scientific data in connection with clinical trials, and approval or renewal of innovator biologics or follow-on biologics (biocomparables).
- Issue opinions to classify biologics as innovators, reference products, or biocomparables.

NOM-257-SSA1-2014 provides transitional provisions for the renewal of marketing authorisations of biologics granted before the amendments to the Health Law Regulations for Biologics issued in 2011 came into force. These provisions establish that:

- COFEPRIS assesses whether biologics refer to innovators or biocomparables.
- Renewal applications for innovators do not require assessment by the SEPB.
- Renewal applications for biocomparables require prior assessment by the SEPB to identify the product of reference for applicants to submit the corresponding tests.

These provisions only apply to renewal applications submitted before 31 December 2015. However, COFEPRIS has not addressed the current uncertainty in respect of regulatory data protection for biologics, as NOM-257-SSA1-2014 does not provide guidelines in this regard.

Biocomparables (follow-ons). Applicants must submit clinical tests and, when appropriate, in-vitro tests, to prove safety, efficacy, and quality of the product comparable (similar) to those of the reference biologic.

COFEPRIS published guidelines for biocomparability tests for Etanercept, Filgrastim, Infliximab, Insulin, and its analogues Rituximab and Somatropin. These guidelines are only recommendations, since the corresponding evaluation is conducted on a case-by-case basis.

The pre-clinical and clinical tests used by an applicant for a biocomparable must use the corresponding reference biologic to perform comparative and physico-chemical studies. For this, the applicant must submit:

- In vitro studies.
- A report of a comparative test of pharmacokinetics, if determined by the Ministry of Health, to show pharmacokinetic comparability on key parameters between the follow-on and the reference biologic.
- Pharmacodynamics test reports.

- Comparative efficacy and safety clinical test to show similarity between the follow-on and the reference biologic.

Although industry participants welcomed amendments to approve biologics, specific rules to approve follow-ons have caused debate. There is currently no indication of a data protection period for biologics. The recognition of data package exclusivity rights for biologics can only currently be achieved through litigation (see *Question 9*). Accordingly, there are also concerns regarding the accurate application by COFEPRIS of the linkage provisions.

Orphan drugs. Orphan drugs were recently expressly recognised by the General Health Law and the Mexican Pharmacopeia. In practice, they are approved through a particular procedure, following the rules for new molecules when applicable and appropriate. Specific rules are pending. The NOM compiling requirements for granting marketing authorisations includes orphan drugs.

Authorisation Conditions

A marketing authorisation consists of the necessary sanitary authorisation so that a pharmaceutical product can be manufactured and commercialised in Mexico, either in the public or private sector. COFEPRIS does not interfere in the regulation of drug prices. Therefore, the economic considerations associated with drugs are independent of the marketing authorisation.

Applicants must prove quality, safety, and efficacy of their products, under the General Health Law, the General Health Law Regulations, and applicable NOMs, particularly those relating to good manufacturing practices for medicinal products. Marketing authorisation holders must ensure compliance with good manufacturing practices, stability, labelling standards, and all other applicable provisions.

Key Stages and Timing

General approval time frames. The following approval time frames apply:

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

  (Article 166, General Health Law Regulations.)
- 180 calendar days for biologics and biocomparables (Articles 177 and 177bis 4, General Health Law Regulations).

These time frames can be reduced if the application has been pre-examined by a third health institution approved by COFEPRIS to do so.

Approval time frame for foreign medicines. In January 2020, the Ministry of Health published an official administrative decree, establishing an expedited procedure for applications for marketing authorisation and import of medicines into Mexico (Equivalence Decree). The Equivalence Decree confirms that both:

- The requirements and evaluation procedures applied by various foreign regulatory health authorities to allow the sale, distribution, and use of allopathic and biological medicines are equivalent to those under the General Health Law, the Health Supplies Regulation, and other instruments.

- Compliance with these foreign requirements and procedures is sufficient to evidence the levels of quality, safety, and efficacy required to obtain a marketing authorisation in Mexico.

On 22 June 2021, the Ministry of Health published a Decree amending the Equivalence Decree. The Decree includes the following amendments:

- Regardless of the country of origin of a medicine, COFEPRIS must process marketing authorisation applications submitted in accordance with the Decree within 45 working days. If COFEPRIS fails to provide a response within that time frame, the application will be presumed to have been denied.
- Mexican authorities can import medicines that do not have a marketing authorisation in Mexico, if this is necessary to guarantee the supply of medicines for the correct and timely provision of health services to the population. In this case, the foreign marketing authorisation holder or its legal representative must initiate the sanitary authorisation process with COFEPRIS within ten working days after import of the product. COFEPRIS must then decide on the application within 45 working days.

Authorisations, Variations, and Renewals

Marketing authorisations must be renewed every five years. Applicants must prove continued compliance with good manufacturing practices, safety and efficacy standards, pharmacovigilance, labelling standards, and all other applicable provisions.

Any modification to the authorised product, including transfers of rights, must be notified and approved by COFEPRIS on a case-by-case basis.

COFEPRIS has the power to revoke authorisations in certain circumstances (see *Question 3*, *Authorisations, Variations, and Renewals*).

Protection of Confidential Information

Information disclosed in an application for marketing authorisation is treated as classified and confidential. The marketing authorisation application process only involves COFEPRIS and the applicant. Third parties are not entitled to intervene in the process or to access related information.

However, COFEPRIS publishes on its website a list of marketing authorisation applications received over certain periods of time, indicating the name of the active ingredient, the pharmaceutical form, the name of the applicant, and the date of filing. However, this information is not reliable or consistently updated.

Exceptions

5. Are there additional or alternative regulations for special types of medicines or medicines intended for particular types of patients or diseases?

The use in human beings of medicines for which there is not yet sufficient scientific evidence of therapeutic efficacy, can be authorised for preventive, therapeutic, rehabilitative, or research purposes (General Health Law).

Marketing authorisation, import, and release of vaccines are prioritised due to their importance for public health and national security. In cases of emergency, these procedures are undertaken immediately (General Health Law).

6. Can products be marketed without a marketing authorisation in certain circumstances?

Generally, all medicines must have a marketing authorisation to be manufactured and commercialised in Mexico (General Health Law and Health Supplies Regulation).

In certain circumstances (for example, in relation to clinical trials and orphan drugs), import of a certain quantity of products without a marketing authorisation can be approved. COFEPRIS can also grant permission for the import of finished products that do not have a marketing authorisation in the following cases:

- When required by a contingent event.
- When required by health policy.
- For purposes of scientific research, registration, or personal use.
- For laboratory tests.

Additionally, Mexican authorities can import medicines that do not have a marketing authorisation in Mexico, if this is necessary to guarantee the supply of medicines for the correct and timely provision of health services to the population (Ministry of Health official administrative decree of January 2020).

Monitoring Compliance and Penalties

7. What powers does the regulator have to monitor compliance with marketing authorisations and impose penalties for a breach?

A marketing authorisation holder is responsible for the quality of the approved product (NOM-059-SSA1-2015). Therefore, when manufacturing through third parties, a marketing authorisation holder must supervise the manufacturing of the product and set the liabilities and duties of each party involved. There must be a programme to recall and destroy products that do not meet quality standards.

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

- Verify that their products meet the approved specifications and do not represent a risk to public health.
- Ensure that good manufacturing practices, stability, pharmacovigilance, and labelling standards are complied with.

COFEPRIS can impose strong administrative penalties for breaches of the legal framework (see *Question 3*, *Monitoring Compliance and Imposing Penalties*).

Data and Marketing Exclusivity Protections

8. What exclusivity does a marketing authorisation holder benefit from?

Mexican laws and regulations do not provide marketing exclusivity or distinguish between data exclusivity and marketing exclusivity, and they do not provide any other type of exclusivity for new innovator drugs. In addition, the Data Protection Guidelines do not provide parameters or rules as to how data package exclusivity (DPE) protection is obtained, recognised, observed, or enforced. However, data required to determine the safety and effectiveness of pharmochemical products that use new chemical components must remain protected under the terms of international treaties to which Mexico is a party (Industrial Property Law).

DPE is not automatically conferred on approval. A petition must be filed with COFEPRIS and in many cases it is necessary to start proceedings to obtain a court decision ordering DPE.

International Treaties

The United States-Mexico-Canada Agreement (USMCA), which replaces NAFTA, entered into force on 1 July 2020. The USMCA will have an impact on DPE in Mexico. However, the current text of the USMCA only recognises five years of DPE for new chemical molecules. The provisions on new indications, formulations, or combinations and biologics were removed, which will lead to difficulty in obtaining DPE in Mexico for these products.

Additionally, the Mexico-EU Trade Agreement requires at least six years of DPE for both small molecules and biologics, although the Agreement has not yet fully entered into force.

COFEPRIS Guidelines

COFEPRIS has published an internal decree on its website, providing guidelines to observe and protect DPE. According to the guidelines (and minimum requirements under the North American Free Trade Agreement (NAFTA)), a marketing authorisation holder benefits from a five-year exclusivity period during which their information cannot benefit or be used to support a third party application for registration of a generic drug. These guidelines show that COFEPRIS is willing to recognise and protect DPE by reference to NAFTA and the Agreement on Trade-Related Aspects of Intellectual Property Rights (TRIPS). The decree provides a higher degree of confidence for innovators. However, certain issues are not clear and require further clarification, for example:

- Whether the guidelines apply to biological products.
- Whether other key approvals, such as new formulations and indications, are protected.
- The proceedings and measures to enforce and observe DPE rights, which are not covered by the decree.

Abridged Procedure for Marketing Authorisation

9. Outline the abridged procedure for marketing authorisation.

Generics

Generics can be approved by providing dissolution profiles or bioavailability studies relating to the innovator product. Therefore, the General Health Law and its regulations allow indirect reliance on innovators' dossiers, by approving generics through interchangeability tests, with no protection period for information provided by the innovator.

R&D Companies

As an incentive, R&D companies can benefit from a special procedure for drugs to be approved for the first time in Mexico, if they have been previously approved by:

- The European Medicines Agency.
- The US Drug and Food Administration.
- Health Canada.
- The Swiss Agency for Therapeutic Products (Swissmedic).
- The Therapeutic Goods Administration of Australia.

In 2012, COFEPRIS published rules for the new procedure. Essentially, a dossier is filed with the foreign regulatory agency, to reduce approval time frames by up to 60 working days.

Ministry of Health Decrees

There is an abridged procedure for marketing authorisation for foreign medical products (see *Question 4*, *Key Stages and Timing: Approval time frame for foreign medicines*).

Pre-Examination by Authorised Health Institutions

A pre-examination of the formal and substantive requirements of applications for marketing authorisations by an authorised health institution reduces approval time frames.

Pharmacovigilance and Other Commitments

10. What pharmacovigilance obligations and other commitments apply after a company has obtained marketing authorisation? Are there further conditions on how the medicinal product is distributed and made accessible to patients?

Post-Marketing Commitments and Pharmacovigilance Obligations

The General Health Law Regulations and NOM-220-SSA1-2002 provide that marketing authorisation holders must:

- Report to the health authorities any adverse event, or suspected adverse reaction, that they are aware of and that may have been caused by their products manufactured or marketed in Mexico.
- Have standard operating procedures.
- Obtain any report of suspected adverse reactions from any possible source.
- Record, validate, and identify any reports of misuse or abuse reported by health professionals or patients.
- Record and monitor any information related to any product used during lactation and pregnancy.
- Investigate serious and unexpected adverse events or reactions.
- Estimate the frequency of suspected adverse reactions and investigate the possible risk factors with intensive pharmacovigilance studies (at the request of the health authorities).
- Ensure the confidentiality of the identity of patients and reporters.
- Submit periodic reports on adverse reactions.

Other Commitments

Marketing authorisation holders must ensure compliance with good manufacturing practices, stability, labelling standards, and all other applicable provisions. There must be a programme to recall and destroy products that do not meet quality standards.

COFEPRIS can conduct on-site visits at any time to inspect premises and verify compliance, and can initiate *ex officio* legal proceedings to sanction non-compliance. Ultimately, these legal proceedings can result in the revocation of the marketing authorisation.

Foreign Marketing Authorisations

11. Are foreign marketing authorisations recognised in your jurisdiction?

Foreign marketing authorisations are not valid in Mexico. However, COFEPRIS has a special procedure for drugs to be approved for the first time in Mexico, if these are already approved by equivalent regulatory authorities abroad. Under this procedure, the requirements for approval of these agencies are recognised as equivalent to those in Mexico (see *Question 9*).

Data Privacy

12. Do privacy and data protection laws impact on pharmaceutical regulation in your jurisdiction?

The existing regulations on personal data protection have an impact on pharmaceutical regulation, for example, in the case of clinical trials and pharmacovigilance.

The sponsor of a clinical trial is the data controller of participants' personal data under:

- The Federal Law for the Protection of Personal Data Held by Private Parties (*Ley Federal de Protección de Datos Personales en Posesión de Particulares*), for information collected, used, and handled by a private party.
- The Federal Law for the Protection of Personal Information Held by Public Entities (*Ley Federeal de Protección de Datos Personales en Posesión de Sujetos Obligados*), for information collected by authorities or public entities and organisations that are funded by the government.

Data controllers must comply with requirements relating to consent, quality, purpose, loyalty, proportionality, responsibility, security, and confidentiality:

- The trial institution must protect participants' personal data at the research and publishing stages.

- Investigators must obtain informed valid consent from research participants to share data.
- Public authorities must maintain the confidentiality of reports they receive from investigators (Health Law Regulation on Research for Health).
- Investigators must ensure that reports do not identify research subjects and maintain the confidentiality of their personal information.

Research participants have rights of access, rectification, cancellation, and opposition rights, in line with the Personal Data Protection Law (Federal Law for the Protection of Personal Information Held by Public Entities and NOM-012-SSA3-2012).

The NOM for pharmacovigilance (NOM-220-SSA1-2002) also recognises the protection of personal data of research participants and health care professionals submitting reports, by deferring this to the Personal Data Protection Law.

Packaging, Labelling, and Tracking

13. Outline the regulation of the packaging and labelling of medicinal products.

Legislation and Regulatory Authority

Packaging and labelling of medicinal products are regulated by:

- The General Health Law.
- The General Health Law Regulations.
- The NOM 072-SSA1-2012 relating to the labelling of medicinal products.

COFEPRIS is responsible for enforcing provisions concerning the packaging and labelling of medicinal products.

Information Requirements

The labelling of medicinal products must include the following information:

- Distinctive brand name.
- Generic name.
- Pharmaceutical form.
- Drug concentration.
- Formulation.

- Formula description.
- Dose.
- Mode of administration.
- Conservation and storage information.
- Precaution and warning legends, including risks in case of pregnancy.
- Marketing authorisation number.
- Batch number.
- Expiration date.
- Manufacturer's and, if applicable, distributor's information, including address.
- Content.
- Maximum retail price.
- For biological drugs, the specifications of the live organism that was used for the preparation of the medicinal product, and the name of the disease for which it is indicated, according to international nomenclature.

Serialisation

Batches must be identified in accordance with the applicable NOMs. Medicine containers must have closure systems that make it clear to the user that they have not been opened before purchase and that prevent accidental manipulation.

Other Conditions

The label information can be additionally stated in another language, provided it does not contradict the information in Spanish.

The decree amending Article 26 of the General Health Law Regulations, published on 31 May 2021, sets out rules on the labelling of drugs for use in the public sector. The decree provides that the primary and secondary packaging of a medicine destined for the public sector must include the words "sale prohibited" or "property of the public health sector." The other general provisions regarding labelling otherwise apply.

Biological Medicines

14. What is the definition of biological medicines in your jurisdiction? Are there any additional or alternative regulations that apply specifically to them?

Definition of Biological Medicines

A biological medicine is any substance that meets all of the following requirements:

- It is produced by molecular biotechnology.
- It has a therapeutic, preventive, or rehabilitative effect.
- It is presented in pharmaceutical form.
- It is identified as a biological medicine by its pharmacological activity and physical properties (chemical and biological).

(General Health Law.)

Broadly, biologicals are classified as:

- Biologicals of reference (usually innovators).
- Biocomparables, a term used instead of biosimilars, in view of social context issues with the term "similars" in Spanish (similares).

Regulation of Biological Medicines

Both biological and combination products must have marketing authorisation from COFEPRIS.

Medical Devices

Legislation and Regulatory Authorities

15. What are the main legislation and regulatory authorities for medical devices in your jurisdiction?

Legislation

The main legislation for medical devices is:

- The General Health Law (*Ley General de Salud*).
- The General Health Law Regulations (*Reglamentos de la Ley General de Salud*).
- The Health Supplies Regulation (*Reglamento de Insumos para la Salud*).

- The NOMs dealing with particulars of specific medical devices.
- The Mexican Pharmacopoeia.

Regulatory Authorities

The regulatory authorities in this field are:

- COFEPRIS.
- The General Health Council.

Medical Devices Definition

16. What is the definition of a medical device (or equivalent) in your jurisdiction?

Medical devices are defined as the substance, mixture of substances, material, apparatus, or instrument (including any computer program necessary for its appropriate use or application), used alone or in combination in:

- The diagnosis, monitoring, or prevention of diseases in humans, or auxiliary in the treatment of disease or disability in humans.
- The replacement, correction, restoration, or modification of human anatomy or human physiological processes.

Classification of Medical Devices

17. Briefly outline any classification system and the main classifications of regulated medical devices.

According to their use, the General Health Law categorises medical devices as:

- Medical equipment.

- Prosthetics, orthotics, and functional supports.
- Diagnostic agents.
- Dental supplies.
- Surgical and healing materials.
- Hygiene products.

Medical devices are classified according to the level of risk involved in their use:

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

Requirements to Manufacture and Market Medical Devices

18. What are the requirements to manufacture and market medical devices?

Application for Marketing Authorisation

To obtain a marketing authorisation for a medical device, it is necessary to submit an application in the official format, to which the following documentary information must be attached:

- A copy of the notice of operation of the factory or production laboratory, warehouse for storage, or distribution or conditioning facility, established in the national territory. These must comply with the applicable requirements for establishments that manufacture, store, condition, or import the relevant products.
- Scientific and technical information to demonstrate that the product meets safety and efficacy requirements.
- A draft label in Spanish, in the terms of the corresponding Mexican Official Standards.
- Instructions, if applicable, for its use or operation manual in Spanish.
- A description of the product's manufacturing process.
- A description of the structure, materials, parts, and functions, in the case of medical equipment.

- A certificate of good manufacturing practice.
- Laboratory tests to verify the product's specifications.
- Bibliographic references.
- The payment of rights.

(Health Supplies Regulation.)

If the product is manufactured abroad, the following documents must also be attached to the application:

- The manufacturer's letter of representation, if the product is not manufactured by the parent company or factory or laboratory requesting the authorisation in Mexico.
- The certificate of good manufacturing practice issued by the health authority of the country of origin. COFEPRIS recognises certificates of good manufacturing practice from certain foreign regulatory agencies, including the Food and Drug Administration (FDA) (US), Health Canada, the Ministry of Health, Labour, and Welfare (Japan), the Therapeutic Goods Administration (Australia), the European Medicines Agency, the National Health Surveillance Agency (Brazil), and the Agency for Therapeutic Products (Swissmedic).
- The original certificate of analysis issued by the company that manufactures the product, with the letterhead of its company name, signed by the responsible chemists of the foreign company.

Additional requirements may apply, depending on the place of manufacture and classification of the medical device.

General Certification Requirements

Medical device manufacturing companies in Mexico require the following certificates and regulatory documents from the Ministry of Health to operate:

- A notice of operation. A company's legal representative can submit this to COFEPRIS. Unless COFEPRIS requires documents or clarifications, this notice needs no approval and has effect as soon as filed.
- A notice of the principal health care professional in charge of health law regulations compliance (*Aviso de Funcionamiento de Responsible Sanitario*). The health care professional must submit this to COFEPRIS. Unless COFEPRIS requires documents or clarifications, this notice needs no approval and has effect as soon as filed.
- Certificate of good manufacturing practice. A company's legal representative can request this from COFEPRIS.

Medical device importer/distributor companies in Mexico require the following documents from the Ministry of Health to operate:

- A notice of operation.
- A notice of the principal health care professional in charge of health law regulations compliance. The health care professional must submit this to COFEPRIS. Unless COFEPRIS requires documents or clarifications, this notice needs no approval and has effect as soon as filed.

Time Frames

The time frame for COFEPRIS to resolve marketing authorisation applications depends on the class of product the authorisation relates to:

- Class I products: 30 working days.
- Class II products: 35 working days.
- Class III products: 60 working days.

If the applicant submits a favourable opinion issued by an authorised third party to demonstrate that the product meets the relevant safety and efficacy conditions, COFEPRIS will authorise the registration within 15 working days.

19. Are there exceptions to the requirements (for example, for clinical studies, special individual patient use, custom devices, and compassionate use)?

The use in human beings of materials for which there is not yet sufficient scientific evidence of their therapeutic efficacy, may be authorised for preventive, therapeutic, rehabilitative, or research purposes (General Health Law).

COFEPRIS can also grant permission for the import of products that do not have a marketing authorisation in the following cases:

- When required by a contingent event.
- When required by health policy.
- For purposes of scientific research, registration, or personal use.
- For laboratory tests.

20. Are there fewer or different requirements for medical devices that have already been licensed or approved in another jurisdiction?

The Ministry of Health and COFEPRIS has determined that the regulatory and technical requirements to approve medical devices in the US, Canada, and Japan are equivalent to the requirements established by Mexico (Executive Rules). COFEPRIS therefore approves medical devices based on dossiers evidencing quality, safety, and efficacy submitted in those countries, with reduced approval time frames.

21. What are the main requirements to import medical devices from or export medical devices to other jurisdictions?

Import Permits

For medical devices with marketing authorisation. To obtain a sanitary import permit for new medical devices with marketing authorisation, it is necessary to submit the payment of government fees and the sanitary licence or notice of operation. Additional requirements apply to the import of radiation sources.

For medical devices without marketing authorisation. The requirements for obtaining a sanitary import permit for medical devices without marketing authorisation or in the experimentation phase, depend on the type of use the device is imported for:

- **For assembly.** The following must be submitted:
  - the payment of rights; and
  - the authorisation letter from the Ministry of Economy.
- **For personal use.** The current medical prescription (including a professional licence number and the product and quantity) must be exhibited.
- **For medical use.** The following must be submitted:
  - the payment of rights;
  - the sanitary licence or notice of operation;
  - the professional licence of the physician in charge; and
  - the sanitary licence issued by COFEPRIS, in the case of radiation sources, with the corresponding line of business.

In the case of x-ray devices, it is also necessary to exhibit the sanitary licence issued by COFEPRIS and the authorisation of the person responsible for the operation and functioning of the x-ray equipment.

In the case of class II and III (see *Question 17*) medical devices, the following is also required:

- a certificate of good practice, issued by the health authority of the country of origin; and
- a certificate of free sale issued by the health authority of the country of origin.

In the case of used equipment, the following is also required:

- an invoice certified before a notary public or public broker (or its equivalent abroad) indicating that the equipment is used; and
- proof of facts before a notary public or public broker (or its equivalent abroad) of the guarantees of effectiveness and evidence of the correct functioning of the used equipment and that it is suitable for use.

- **For human research.** The following must be exhibited:
  - the payment of rights;
  - the sanitary licence or notice of operation; and
  - the official letter of approval of the research protocol authorised by COFEPRIS.

Export Permits

COFEPRIS is in charge of issuing certificates of support for the export of health supplies (export certificate) that comply with the health legislation. The export certificate guarantees that a product complies with current health regulations in Mexico.

To obtain an export certificate, an application must be submitted attaching the acceptance letter from the final importer on letterhead. COFEPRIS has five days to resolve the petition.

Health Care IT

22. Is there any specific regulation of medical software, health care IT, or e-health products (such as mobile health apps)?

There are no specific regulations on medical software, health care IT, or e-health products. Due to the current gap in legislation, COFEPRIS has implemented a process to review these types of products on a case-by-case basis. It is recommended applicants comply with the standard process established for these types of products before COFEPRIS, to obtain an official confirmation by the corresponding sanitary authority that no approval is necessary.

Combination Products and Borderlines

23. Does your jurisdiction recognise combination products? Are there any additional or alternative regulations that apply specifically to them?

Types of Combination Products

Combination products can be classified as either drugs (drug/biologic) or medical devices (drug/device).

Regulation of Combination Products

There are no specific regulations regarding combination products.

A combination product may require separate drug or biologic and medical device approvals. Requirements and application time frames differ in each case.

Borderlines

24. What product type determinations are relevant and are there specific mechanisms for determining which regulatory regime applies to a borderline product?

In the applicable legislation, borderline products are not identified as such, so there are no specific provisions or mechanisms for determining which regulatory regime applies. COFEPRIS has implemented a process to review these types of products on a case-by-case basis.

Natural Health Products

25. Is there a separate regulatory regime for natural health products (or equivalent) (for example, traditional medicines, homeopathic medicines, supplements, vitamins, and minerals)?

There is a separate regulatory regime for natural health products.

26. Which authorities regulate the manufacture and marketing of natural health products?

The regulatory authorities in this field are:

- COFEPRIS.
- The General Health Council.

27. What notifications, registrations, approvals, and licences are required to manufacture and market natural health products?

Application Requirements

Vitamins. Vitamins require a marketing authorisation for manufacture and commercialisation. The application must include the following:

- The monograph of the finished product with control methods, qualitative and quantitative, of all the components.
- The conditions for handling, conservation, and storage.
- The description of the primary and secondary containers and tests of atoxicity.
- Labelling with precautionary legends.
- Instructions for use, where appropriate.
- Stability tests.
- The certificate of analysis of the raw materials and finished product, containing the physicochemical and microbiological specifications.
- The certificate of free sale or equivalent, if the product is imported, issued by the health authority or agency authority from the country of origin, and a letter of representation from the supplier.

Homeopathic medicines. Homeopathic medicines require a marketing authorisation for manufacture and commercialisation. The application must include the following:

- Technical and scientific information that demonstrates:
    - the identity and purity of the product's components according to what is established in the Homeopathic Pharmacopoeia and their supplements or, failing that, the pharmacopoeias from other countries or sources of international scientific information; and

    - the stability of the finished product.

- Therapeutic indications.
- Labelling.
- The pathogenesis of the active ingredients.
- Instructions for use.
- A description of the manufacturing process.
- Prescribing information.

Herbal medicines. Herbal medicines require a marketing authorisation for manufacture and commercialisation. The application must include the following:

- Technical and scientific information that demonstrates:
    - the identity and purity of the product's components according to what is established in the special pharmacopoeias or, failing that, sources of international scientific information;
    - the stability of the finished product; and
    - taxonomic identification.

- Therapeutic indications.
- Labelling.
- Instructions for use.
- A description of the drug manufacturing process.

Foreign homeopathic and herbal medicines. To obtain marketing authorisation for homeopathic and herbal medicines manufactured abroad, the following must also be exhibited:

- The certificate of free sale issued by the competent authority of the country of origin.
- The certificate of analysis issued by the manufacturer of the medicine, on letterhead and endorsed by the health officials of the foreign and national companies.
- The manufacturer's letter of representation, only when the laboratory that manufactures it abroad is not a subsidiary or parent company of the laboratory requesting registration.

Food supplements. Food supplements do not require marketing authorisation. Manufacturers or those responsible for their marketing must submit an Operation Notice at least 30 days before starting operations in Mexico.

Timeline for Authorisation

COFEPRIS has 45 days to resolve marketing authorisation applications for homeopathic medicines, vitamins, and herbal medicines. If the applicant submits a favourable opinion issued by an authorised third party, the registration will be authorised within 15 days.

COFEPRIS will verify compliance with good manufacturing practices and the drug production process, as well as the certification of the product's active ingredients, in accordance with the corresponding legislation.

28. Are there fewer or different requirements for natural health products that have already been licensed or approved in another jurisdiction?

COFEPRIS has implemented a process to review natural health products that have already been licensed or approved in another jurisdiction on a case-by-case basis.

29. Is it possible to sell natural health products to or buy natural health products from other jurisdictions?

To import a natural health product:

- It is necessary to obtain a sanitary authorisation from COFEPRIS and a marketing authorisation for the product.
- The person who will import the product must have the appropriate premises for their activities.
- The product's expiration date must be in more than 12 months' time, counting from the product's entry into the country.

COFEPRIS is in charge of issuing certificates of support for the export of health supplies (export certificates) that comply with the health legislation. The export certificate guarantees that a product complies with current health regulations in Mexico. To obtain the certificate of export, an application must be submitted in the official format. The original of the acceptance letter of the final importer, on letterhead paper, must be attached to the application.

Recent Developments and Reform Proposals

30. Have there been any significant recent developments or proposals for reform?

On 1 July 2020, as a result of the entry into force of the USMCA, the new Federal Law for Protection of the Industrial Property (new IP Law), was enacted. The new IP Law represents an important legislative change, as it aims to align domestic law with the standards set by the new trade and co-operation agreements signed by Mexico in recent years. As a result of this, amendments to the health laws are expected in the near future.

COFEPRIS is currently taking steps to make regulation more efficient in matters relating to drugs and medical devices, encouraging the use of regulatory decisions from other jurisdictions, and formulating and implementing strategies to strengthen its regulatory system.

Contributor Profiles

Alejandro Luna F, Partner

Olivares
T +52 55 5322 3080
E *alejandro.luna@olivares.mx*
W *www.olivares.com.mx*

Professional qualifications. Lawyer, Mexico

Areas of practice. IP litigation; alternative dispute resolution; regulatory law; anti-piracy; anti-counterfeiting; enforcement.

Recent transactions

- Participated in questioning the constitutionality of certain provisions of the Industrial Property Law and the Federal Copyright Law.
- Sponsor of an important proposal to modify the system of litigation and enforcement of intellectual property rights in Mexico.
- Spearheaded a ten-year litigation strategy that has incorporated regulation changes and lobbying, which has resulted in precedent for patent linkage regulations and life terms of pipeline patents in Mexico.

Non-professional qualifications. Universidad Latinoamericana, Juris Doctor, 1996; Franklin Pierce Law Center, LL.M., Intellectual Property Law, 2002; UNAM, Ph.D., 2020

Languages. English, Spanish

Professional associations/memberships. Part-time professor at the National Autonomous University of Mexico (UNAM).

Publications. Author of several articles on patents, litigation, and regulatory issues.

Armando Arenas, Partner

Olivares
T +52 55 5322 3000
E *armando.arenas@olivares.mx*
W *www.olivares.com.mx*

Professional qualifications. Lawyer, Mexico

Areas of practice. Pharmaceutical law; IP litigation; civil and commercial litigation; anti-piracy; anti-counterfeiting; enforcement.

Recent transactions

- Obtaining through litigation the correction of the life term of pharmaceutical patents granted under transitory Article 12 of the Law for the Promotion and Protection of Industrial Property, representing more than seven innovative companies.
- The declaration of infringement of patents that protect active ingredients, medical uses, pharmaceutical formulations, and production processes of biotechnological drugs, to maintain the market exclusivity of their clients.
- Obtained the nullity of marketing authorisations (more than seven successful cases) of generic medicines for violating the Mexican Linkage System for the benefit of patent holders that protect active ingredients, pharmaceutical formulations, and medical uses.
- Secured a judgment declaring the unconstitutionality of Article 167 *bis* of the Health Supplies Regulation, as it does not provide the right of the titleholder of a patent to be heard during the prosecution of the marketing authorisation.
- Successfully participated in civil actions for damages to obtain the payment of compensation for violating the Industrial Property rights of the clients.

Non-professional qualifications. National Autonomous University of Mexico (UNAM), Bachelor Degree, 1995

Languages. English, Spanish

Karla Paulina Olvera Acevedo, Associate

Olivares
T +52 55 5322 3000
E *karla.olvera@olivares.mx*
W *www.olivares.com.mx*

Professional qualifications. Lawyer, Mexico

Areas of practice. Pharmaceutical law; IP litigation and enforcement.

Recent transactions

- Legal advice to clients from different industries through the preparation and implementation of innovative strategies to protect their intellectual property rights in Mexico.
- Litigation related to patents, trade marks, unfair competition, and regulatory and administrative matters.
- Participated in the first case in Mexico in which it was decided to revoke the granting of a marketing authorisation of a medicine in violation of a formulation patent derived from the non-compliance by the regulatory authority of the existing linkage system between the granting of marketing authorisations and patents in force. Also involved in the first case in which the application of this system was recognised in relation to a use patent and its defence in public tenders.
- Involved in various litigations related to government procurement, data protection of biologics medicines, and in infringement actions involving those products and the granting of marketing authorisations for biocomparable medicines.

Non-professional qualifications. LLM International and European Intellectual Property Law, Trinity College Dublin, Ireland, 2017; Bachelor Degree, Universidad Iberoamericana, Mexico, 2010

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