The Pharma Legal Handbook

Mexico

Regulatory, Pricing and Reimbursement Overview · Preclinical and Clinical Trial Requirements · Marketing, Manufacturing, Packaging and Labeling Advertising · Traditional Medicines and OTC Products · Product Liability · Patents and Trademarks · Regulatory Reforms · Cannabinoid Drugs, Medicinal Cannabis and Opioid Drugs · Orphan Drugs and Rare Diseases · Localization · Biosimilars and Biologics

PHARMA BOARDROOM

Mexico

The Pharma Legal Handbook answers essential questions about this environment for pharmaceuticals in Mexico.
It is a must have for any company operating in the country or looking to enter the market.

Prepared in association with Olivares and Associates, a leading Mexcian law firm, it should answer any questions linked to Regulation, Pricing, Clinical and Preclinical Trials, Marketing, Manufacturing, Trademarks and Patents.

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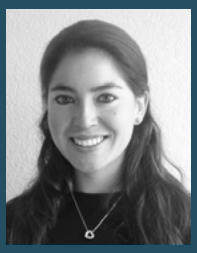
Alejandro has spearheaded a ten-year litigation strategy that has incorporated regulation changes and lobbying which has resulted in an important precedent for the patent linkage regulation and life terms of pipeline patents in Mexico. As a result of his involvement, he has been selected as the delegate to represent AMIIF, the industry association for R&D pharmaceutical companies who do business in Mexico, in the Trans-Pacific Partnership (TPP) negotiations.

Alejandro has successfully litigated for pharmaceutical patents and pioneered administrative court actions to seek recognition of DPE rights (protection for safety and efficacy data), which are not specifically recognized by Mexican laws



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01 REGULATORY, PRICING, AND REIMBURSEMENT OVERVIEW

1. What are the regulatory authorities with jurisdiction over drugs, biologicals, and medical devices in your country?

The authority responsible for applying and enforcing the regulatory framework in relation to drugs, biologicals, and medical devices is the Federal Commission for Protection against Sanitary Risks (COFEPRIS), which is a decentralized agency of the Ministry of Health..

2. What is the regulatory framework for the authorization, pricing, and reimbursement of drugs, biologicals, and medical devices?

The primary legislation for the authorization, pricing, and reimbursement of drugs, biologicals, and medical devices is the General Health Law (Ley General de Salud) (HL) and its Regulations. The laws and its regulations are supplemented by Guidelines and Official Norms (NOMS) published by COFEPRIS.

Price control in the private sector is based on a scheme of self-regulated maximum retail price (MRP) only covering patented products, overseen by the Ministry of Economy. Pharmaceutical companies' participation is voluntary. Under the 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 the private sector, there is no system for reimbursement in Mexico.

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

Public acquisitions are supported by the Committee for the Negotiation of Drug Prices (CNDP).

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 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.

The political party currently governing in Mexico (MORENA) is promoting an amendment to the scheme of self-regulated maximum retail price (MRP). The amendment state, in general terms, that the Ministry of Economy in collaboration with the Ministry of Health shall guarantee, through a transparent process and taking into consideration differentiated policies, the access to medications and inputs to people in situations of poverty. In addition, the price control would be regulated and annually reviewed by these Authorities.

On August 11, 2020, the Mexican Congress published the Decree amending Article 1 of the Public Sector Procurement, Leasing and Services Law, through which the Mexican Government is now empowered to acquire medicines through intergovernmental organizations, such as UNOPS, without having to observe the procedures set forth in the applicable Law and Regulation on public procurement.

According to UNOPS' guidelines, the process is made up of different stages grouped within three phases identified as:

1. Pre-Bidding Process (market research, requirements definition and identification of potential suppliers).
2. Bidding Process (publication of the bases and call for bids and/or invitations for negotiation, bid management, evaluation and award).
3. Post-Bidding Process (contract management and logistics). The distribution to the final destination will be in charge of INSABI.

Therefore, during these proceedings UNOPS is entitled to negotiate the prices of the supplies.

3. What are the steps to obtaining authorization to develop, test, and market a product?

Manufacturers must obtain a marketing authorization from COFEPRIS to sell any medicinal product. Requirements and timeframes vary among new molecules, biologics, and follow-on products.

The Health Law Regulations sets out the following approval timeframes for small molecules:

- 180 calendar days for medicines, including an active pharmaceutical ingredient (API)/therapeutic indication already approved in Mexico.
- 240 calendar days for medicines not approved in Mexico but which are approved abroad.
- 180 calendar days for new drugs (a meeting with the New Molecule Committee is required).

The approval timeframe for biologics and biocomparables is 180 calendar days.

These timeframes may vary in practice.

3.A. NEW MOLECULES

Essentially, applicants for marketing authorizations must prove 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 have to request approval of their products as new molecules by the New Molecules Committee of COFEPRIS. A new molecule is defined as:

- An active ingredient or drug not approved world-wide (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 which is a non-marketed combination of two or more active ingredients; and
- An active ingredient or drug already available in the market, but to be marketed for a new therapeutic indication.

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); and
- The Therapeutic Goods Administration in Australia.

In 2012, COFEPRIS published new rules to set out this procedure. This is essentially based on the dossier filed with the foreign regulatory agency, to reduce approval time frames by up to 60 working days. Industry participants have welcomed and used these new rules.

3.B. GENERICS

Applicants for marketing authorizations have to prove that their products are interchangeable to the innovator product. They have to provide information concerning dissolution profiles or bioavailability studies regarding the reference product. COFEPRIS periodically issues a list of reference medicinal products.

Recently, the NOM that sets out 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 authorization for generics breaching 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 authorizations in violation of exclusive rights. According to the IP Regulations, every six months the IMPI must publish a gazette that includes patents covering allopathic medicines (Linkage Gazette). The initial IMPI position was that only patents relating to a compound were relevant to linkage review (excluding formulation and use of patents). In 2012, the IMPI included, for the first time, formulation patents in the Linkage Gazette, in accordance with a 2010 ruling of the Mexican Supreme Court (Jurisprudence No. 2a./J.7/2010, Federal Judicial Gazette, No. XXXI, page 135). Under the linkage regulations, at the filing of the application, the applicant must prove that it is the owner or licensee of the patent of the active ingredient of the product (recorded with the IMPI), or state under oath that their application does not violate the list of products published in the Linkage Gazette and observes patent law.

As a result of the entry into force of the USMA (July 1, 2020), and the New IP Law (November 5, 2020), the linkage system will be modified, eventually.

The general terms for patent linkage were included in the new IP Law (similarly to the current linkage system). The wording establishes the listing

of patents related to allopathic medicines in terms of the corresponding Regulation. Details and the battle on linkage will follow in the discussion over the eventual amendments in the Regulation.

The USMCA requirement of the notice to the titleholder should be included in the regulation.

Additionally, there are a couple of proposals pushed by the generic associations to limit linkage to compound patents and to patents covering only approved products by COFEPRIS.

3.C. BIOLOGICS (BIOTECH PRODUCTS)

The Mexican jurisdiction already recognises that biotech products deserve special treatment as a result of their distinct characteristics, such as their complex structures, their size in comparison with chemically synthetized drugs and, particularly, their susceptibility to variation during manufacturing. The regulatory scheme distinguishes from other biologics those products that have been manufactured by molecular biotechnology and provides a robust regulatory process to approve them.

The standards to approve biotech products are essentially the same as for other drugs in Mexico: they must be safe, effective and have appropriate quality. The biotech products, however, must comply with a number of additional dossier requirements, in view of their distinct characteristics. Applicants have to prove quality, safety and efficacy requirements under the General Health Law, its regulations and applicable NOMs, particularly, those for biotech products (NOM-257-SSA1-2014), for good manufacturing practices for medicinal products (NOM-059-SSA1-2013) and for active ingredients (NOM-164-SSA1-2013).

For this purpose, biocomparable applicants must submit essentially: **i)** in vitro studies/comparative non-clinical studies, **ii)** 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, **iii)** pharmacodynamics test reports, and **iv)** 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.

3.D. BIOCOMPARABLES (FOLLOW-ONS)

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

The pre-clinical and clinical test used by an applicant for a biosimilar must use the corresponding reference biologic to perform comparative and physic-chemical studies. For this, the applicant essentially have to submit:

- In vitro 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 reference biologic;

- Pharmacodynamics test reports; and
- Comparative efficacy and safety clinical tests to show similarity between both the follow-on and the reference biologic.

Although industry participants welcomed amendments to approve biologics, specific rules to approve follow-ons have caused debate. In Mexican domestic law, there is currently no indication of a data-protection period for biologics. The recognition of data package exclusivity rights for biologics has been achieved through litigation.

Biosimilars have been introduced into the General Health Law and the Mexican Pharmacopeia. In practice, they are approved by a particular procedure, following rules for new molecules when applicable and appropriate, although they do not require approval by the new molecules committee. Specific rules are still pending. The draft of NOM requirements for granting marketing authorizations includes orphan drugs.

4. What are the approximate fees for each authorization?

Government fees for analyzing a manufacturing approval application are around **US$3,000**.

While Government fees for analyzing marketing authorization applications are around:

For new molecules/biologics: **US$8,600**.

Generics/biocomparables: **US$4,800**.

5. For how long are marketing authorizations/registrations valid? How are marketing authorizations/registrations renewed?

Marketing authorizations must be renewed every five years for medications of new molecules, generics, biologics (biotech products) and biosimilars (follow-ons), while orphan drugs must be renewed every two years.

Applicants must prove compliance with good manufacturing practices, safety and efficacy standards, pharmacovigilance, labelling standards and all other applicable provisions.

6. How does the authorization process differ between brand-name products and generic products? Are there differences for local manufacturers versus foreign-owned manufacturers?

The differences between the brand-name and generic product authorization process are mentioned in **question 3**. But in general terms the differences are that for brand-name products it is necessary to demonstrate the safety and efficacy and for generic products it is necessary to demonstrate the interchangeability and biocomparability. (Please see answer to **question 3**).

In Mexico, in general, there should be no differences in the requirements to obtain a marketing authorization for local manufacturers versus foreign-owned manufacturers.

The Mexican President, in an effort to increase the supply of generic medicines and medicines from abroad, ordered the health authorities to take the necessary measures to expedite the granting of marketing authorizations based on the so-called Equivalence Decrees.

As a follow-up to the President's order, the Ministry of Health issued a Decree, published on November 18, 2020, in the Official Federal Gazette, ordering the following:

- COFEPRIS must resolve the applications of marketing authorization of medicines and health supplies coming from abroad within 5 working days.
- If an application is not resolved within the above-mentioned period, it will automatically be understood to have been granted (afirmativa ficta).
- The period of 5 days will be suspended if COFEPRIS requires documents, clarification or additional information from the applicant, with the 5-day period being reactivated immediately following the presentation of the information.
- COFEPRIS must carry out the necessary actions to guarantee the safety, quality and efficacy of the medicines.
- The applicants, importers and marketers are not exempted from complying with the applicable provisions to maintain the marketing authorization.

The Decree has been highly criticized, because in addition to not going through a legislative process, as the nature of the matter requires, a period of 5 working days does not seem reasonable for COFEPRIS to ensure that the medicines and material acquired from abroad comply with regulatory standards that guarantee safety and efficacy for products of various kinds, such as biotechnological medicines, or that patent rights are observed within the framework of the Linkage System in force in Mexico, as well as protection of clinical data.

The Decree has also been criticized for granting facilities to companies and products coming from abroad, specifically, obtaining a marketing authorization within 5 working days, when the procedure for the pharmaceutical industry established in Mexico, according to the applicable regulatory framework, takes approximately between 180 and 240 working days (6 to 8 months). Additionally, for various reasons, including the COVID-19 pandemic, the procedures of such national or international companies established in Mexico have been considerably delayed.

7. How are combination products (drug + drug, drug + biologic, drug + device, biologic + device, drug + biologic + device) regulated?

Combination products must have marketing authorization from COFEPRIS.

Given their particular features, combination products can be classified as either drugs (drug/biologic) and/or medical devices (drug/device). Requirements and application timeframes differ in each case. Depending of the nature of the combination product, it may require separate drug or biologic and medical device approvals.

8. How is compliance with regulations monitored and evaluated? Is the regulatory regime comparable with the U.S. Food and Drug Administration or

COFEPRIS has a permanent pharmacovigilance programme. This is based on information on possible adverse effects of the drugs given, among others, by:

- Doctors and physicians, on a voluntary basis.
- The pharmaceutical companies that manufactured the products and those who conduct clinical trials, who must both report any health risks.

the European Medicines Agency expectations and requirements?

Under the Health Law Regulations and the NOMs, COFEPRIS´s monitoring is focused, among other things, on the following:

- Ensuring compliance with good manufacturing practices and standard operating procedures.
- Ensuring the activities do not exceed the limits set by the authorization and do not differ from those activities which are authorized.
- Ensuring the performance of validation analysis of the manufacturing processes and systems involved.

9. What is the potential range of penalties for noncompliance?

COFEPRIS is empowered to make on-site visits at any time to inspect premises and verify such compliance, and can initiate ex officio legal proceedings to sanction non-compliance. Ultimately, these legal proceedings can result in the revocation of the marketing authorization, ordering partial or total suspension of activities, services or adverts. Under certain conditions, COFEPRIS also has statutory authority to revoke any manufacturing approval and/or impose sanctions, ranging from a fine of up to 16,000 times the minimum wage (about US $3,523), to closure of the establishment.

10. Is there a national healthcare system? If so, how is it administered and funded?

The public sector comprises of:

- Social security institutions exclusively directed to formal workers, in which the funding comes from contributions by the federal government, the employer and the employee, such as the:
  - o Mexican Institute of Social Security (IMSS);
  - o Institute of Social Security for State Workers (ISSSTE);
  - o Specialised public institutions for members of the military and navy force (ISSFAM);
  - o PEMEX Medical Services, for Mexican petroleum workers; and
- Public institutions exclusively directed to attend people not covered by social security, in which the funding comes from the federal government, states and patients, such as the
  - o Wellness and Health Institute (INSABI). and
  - o State health institutions
- Public institutions exclusively directed to attend people not covered by social security, in which the funding comes from the federal government, states and patients, such as the:
  - o Wellness and Health Institute former People's Health Insurance; (INSABI) and
  - o State health institutions.

In the public sector, social security and public institutions provide medicines. However, if the medicine is not available when required, some public insurers allow private registered drugstores to supply prescribed medicines and to request their refund.

Other social security institutes cater for particular sectors, for example, for members of the military and for Mexican petroleum workers (PEMEX Medical Services).

The public health sector normally faces financial problems and therefore implements measures to limit costs, for example, by pressing for price reductions in public bids and encouraging competition.

On July 31, 2020, the "Specific Agreement between the Institute of Health for the Welfare of the United Mexican States (INSABI) and UNOPS" was signed for the execution of the Implementation Project called "Acquisition of medicines and medical supplies" for the period 2021-2024.

Open international competitive bidding modality (national and international market companies) for the consolidated purchase of medicines is regulated under the procurement policies and procedures of UNOPS.

The Mexican Government transfers all the resources to UNOPS and UNOPS is in charge of implementing, tendering and contracting said activities, as well as managing the respective contracts with third parties.

INSABI will assume responsibility for the actions that UNOPS is in charge of, and will hold it harmless, from and against any action, claim, process or liability of any kind filed by third parties against it.

11. How does the government (or public) healthcare system function with private sector healthcare?

It is worth mentioning that the public and private health sectors function separately, there is no interaction between one and the other.

Private health insurance generally covers professional, executive and higher levels of the private sector. Enrolment in private health insurance has increased considerably over the past few years.

The public health sector normally faces financial problems and therefore implements measures to limit costs, for example, by pressing for price reductions in consolidating public bids (involving the most important health institutions) and encouraging competition.

12. Are prices of drugs and devices regulated and, if so, how?

Price control in the private sector is based on a scheme of self-regulated maximum retail price (MRP) covering patented products, overseen by the Ministry of Economy. Pharmaceutical companies' participation is voluntary. Under the 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. In 2008, the government created the

Committee for the Negotiation of Drug Prices (CNDP) to:

- Support public acquisitions through a process of transparent negotiation between public insurers and pharmaceutical companies.
- Evaluate cost-benefits of new medicines and therapies in view of prices and other comparable products in the market.

On the other hand, at the time this paper is being written, there is a proposal pending to be formally submitted before the Mexican Congress, that is

focused on implementing regulation with respect to the prices of drugs. The aim of this eventual regulation is to warrant access to health. In accordance with the proposal, the prices of drugs would be reviewed and evaluated every year or at any time, if necessary, based on the economic, technical or therapeutic conditions.

On August 11, 2020, the Mexican Congress published the Decree amending Article 1 of the Public Sector Procurement, Leasing and Services Law, through which the Mexican Government is now empowered to acquire medicines through intergovernmental organizations, such as UNOPS, without having to observe the procedures set forth in the applicable Law and Regulation on public procurement.

According to UNOPS' guidelines, the process is made up of different stages grouped within three phases identified as:

1. Pre-Bidding Process (market research, requirements definition and identification of potential suppliers).
2. Bidding Process (publication of the bases and call for bids and/or invitations for negotiation, bid management, evaluation and award).
3. Post-Bidding Process (contract management and logistics). The distribution to the final destination will be in charge of INSABI.

Therefore, during these proceedings UNOPS is entitled to negotiate the prices of the supplies.

13. How are the drugs and devices used by patients paid for? What roles do public and private payers play?

In the private sector, most payments are made on an out-of-pocket basis.

Private insurers are currently improving the level of pharmaceutical coverage as the private market in medicines has grown considerably.

14. Who dispenses drugs and devices to patients and how are those dispensers compensated?

Commonly, public insurers dispense medicinal products prescribed by their healthcare professionals. Products are prescribed from a basic medicinal products list, which public insurers essentially base on the National Formulary issued by the Ministry of Health. Public insurers acquire those listed products mostly by public tender processes. IMSS is the largest public sector buyer of drugs.

For direct purchasing of patented products, CNDP analyses the effectiveness of the drugs and relevant therapeutic alternatives, and the feasibility and implications of an eventual substitution with equivalent medicines.

Furthermore, the CNDP conducts an economic evaluation of the cost-effectiveness of patented medicines compared with those potential substitutes.

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

15. What are the professional and legal responsibilities of those who dispense drugs and devices? What role do they play in providing patient care, information, and safety?

In Mexico, there is a General Health Council that establishes the drugs that can be acquired by the Federal Mexican Government and which therefore can be dispensed by healthcare professionals in the public sector, and, in this way, providing information and safety related to such medications.

Additionally, the General Health Council is entitled to establish the Health Strategy in Mexico and hence, is the one who decides the medications Mexicans should have access to, especially in the public sector.

Under the so-called "Acquisition of medicines and medical supplies" for the period 2021-2024 through UNOPS, INSABI will assume responsibility for the actions UNOPS is in charge of, and will hold it harmless, from and against any action, claim, process or liability of any kind filed by third parties against it.

02

PRECLINICAL AND CLINICAL TRIAL REQUIREMENTS

16. Are clinical trials required to be conducted locally as a condition (stated or implicit) for marketing approval?

17. How are clinical trials funded?

18. What are the requirements for preclinical and clinical trial protocols? Who must approve the protocols?

19. What are the requirements for consent by participants in clinical trials?

20. May participants in clinical trials be compensated?

21. How are participants in clinical trials protected and indemnified against any harm that arises as a result of participation in the trial?

02 PRECLINICAL AND CLINICAL TRIAL REQUIREMENTS

16. Are clinical trials required to be conducted locally as a condition (stated or implicit) for marketing approval?

Clinical trials for innovator biological products must take place in Mexico when the product is to be manufactured in Mexico. For products manufactured abroad, the Ministry of Health can request that a clinical trial takes place in Mexico when the Sub-Committee on Evaluation of Biotechnological Products of COFEPRIS considers that this is necessary.

17. How are clinical trials funded?

The primary 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) and the NOM for Health Research in Human Beings (NOM-012-SSA3-2012). The Guideline for Good Clinical Practice E6(R1) is also taken into account.

18. What are the requirements for preclinical and clinical trial protocols? Who must approve the protocols?

This legislation is enforced by the Ministry of Health through COFEPRIS.

Preclinical data must be collected to justify whether clinical trials can be conducted.

The RLGMIS 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.

The RLGMIS and the NOM for Health Research in Human Beings provide the guidelines and standards for the clinical trial protocol, including rules concerning documentation, compilation, confidentiality and reports.

Essentially, according to the NOM for Health Research in Human Beings, any clinical trial must be conducted following ethical guidelines and must always respect the dignity, rights and welfare of 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 for the Health Authorities must be compiled. Accordingly, the following NOMs apply for:

- Medicinal products labelling (NOM- 072- SSA1-2012).
- 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).

- Active ingredients (NOM-164-SSA1-2015).

Clinical protocols must be approved by COFEPRIS.

19. What are the requirements for consent by participants in clinical trials?

Investigators have to collect informed consent from research participants in a formal written document, which is also signed by two witnesses. Basically, the validity requirements for consent are that a participant grants it on a voluntary basis, with capacity to do so and with sufficient knowledge (knowing the potential risks and benefits). Participants keep the right to give up the research anytime.

Investigators must ensure post-care for them, until it is clarified that there are no damages derived from the research.

20. May participants in clinical trials be compensated?

According to the Official Mexican Standards regarding the Clinical Trials in Human Beings (NOM-012-SSA3-2012), the clinical trials budget should include compensation to which the subject of investigation will be legally entitled.

21. How are participants in clinical trials protected and indemnified against any harm that arises as a result of participation in the trial?

Medical assistance and financial indemnification for damage caused by the clinical trial must be provided to research participants, in case of damages directly related to the trial. Where appropriate, this financial fund may be covered under study insurance.

03

MARKETING, MANUFACTURING, PACKAGING & LABELING ADVERTISING

22. What is the authorization process for the marketing of new drugs, biologics, medical devices, over-the-counter medications, and other medicinal products?

23. What is the authorization process for the marketing of generic versions of these products?

24. What are the typical fees for marketing approval?

25. What is the period of authorization and the renewal process?

26. What are the requirements, if any, for post-approval pharmacovigilance?

27. Are foreign marketing authorizations recognized?

28. Is parallel import of medicines or devices allowed?

29. What are the restrictions on marketing practices such as gifts, sponsorships, consultancy agreements, travel and entertainment, or other incentives for healthcare organizations and individual medical practitioners?

30. How is the manufacturing of medicines and devices regulated and by which agencies?

31. Are local manufacturing requirements compatible with Good Manufacturing Practices (GMPs) as defined by the US Food & Drug Administration (US FDA) and/or the European Medicines Agency (EMA)?

32. What is the inspection regime for manufacturing facilities?

33. Are manufacturing facilities open for inspection by foreign inspectors or third-party inspectors as authorized by the FDA/EMA?

34. What are the requirements for storage, packaging, and handling of medicines and devices and their constituent components?

35. What information must be included in medicine and device labeling?

36. What additional information may be included in labeling and packaging?

37. What items may not be included in labeling and packaging?

38. What are the restrictions and requirements for the marketing and advertising of medicines and devices?

39. Where can medicines and devices be sold or delivered? Can medicines and devices be sold or delivered via post?

40. What are the restrictions and requirements for electronic marketing and advertising via email, by internet, social media, and other channels?

41. May medicines and devices be advertised or sold directly to consumers?

42. How is compliance monitored?

43. What are the potential penalties for noncompliance?

03 MARKETING, MANUFACTURING, PACKAGING AND LABELING, ADVERTISING

22. What is the authorization process for the marketing of new drugs, biologics, medical devices, over-the-counter medications, and other medicinal products?

The authorization process for the marketing of new drugs, biologics, medical devices, over-the-counter medications, and other medicinal products are mentioned in **question 3 in Regulatory, Pricing, and Reimbursement Overview.**

23. What is the authorization process for the marketing of generic versions of these products?

Applicants for marketing authorizations have to prove that their products are bioequivalent to the innovator product. They have to provide information concerning dissolution profiles or bioavailability studies regarding the reference product. COFEPRIS periodically issues a list of reference medicinal products.

Recently, the NOM which sets out 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 authorization for generics breaching exclusivity rights.

24. What are the typical fees for marketing approval?

Government fees for analyzing marketing authorization applications are around:

- For new molecules/biologics: US$8,600.
- Generics/biocomparables: US$4,800.

25. What is the period of authorization and the renewal process?

The periods of authorization may vary in practice, yet the average time is one to two years.

Marketing authorizations must be renewed every five years for medications of new molecules, generics, biologics (biotech products) and biosimilars (follow-ons), while Orphan drugs must be renewed every two years.

Applicants must prove compliance with good manufacturing practices, safety and efficacy standards, pharmacovigilance, labelling standards and all other applicable provisions.

26. What are the requirements, if any, for post-approval pharmacovigilance?

Under the Health Law Regulations and the NOMs, COFEPRIS´s monitoring is focused, among other things, on the following:

- Ensuring compliance with good manufacturing practices and standard operating procedures.
- Ensuring the activities do not exceed the limits set by the authorization and do not differ from those activities which are authorized.

- Ensuring the performance of validation analysis of the manufacturing processes and systems involved.

27. Are foreign marketing authorizations recognized?

Foreign marketing authorizations are not valid in Mexico. However, COFEPRIS has set a special procedure for drugs to be approved for the first time in Mexico, that have already been approved by equivalent regulatory authorities abroad.

In this procedure, the requirements for approval set out by these foreign agencies are recognized as equivalent to those in Mexico. According to the equivalence agreement, marketing authorizations which have been approved by the following agencies, are also approved in Mexico:

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

28. Are parallel imports of medicines or devices allowed?

Any import of drugs, health products or raw material for drugs must be approved by COFEPRIS. Marketing authorization in Mexico is required. In certain circumstances, for example, clinical trials and orphan drugs, import of a minimal quantity of products without marketing authorization can be approved.

Regarding IP rights, parallel imports are allowed in Mexico in relation to trademarks where both:

- The product was legally introduced in the country of origin.
- The trade mark is owned by the same company or a related company in Mexico.

The Intellectual Property Law does not specifically address patents in this context as it does for trademarks. However, it is likely that the principle of exhaustion of rights also applies to patents.

29. What are the restrictions on marketing practices such as gifts, sponsorships, consultancy agreements, travel and entertainment, or other incentives for healthcare organizations and individual medical practitioners?

Government officers must not request, accept or receive any gifts or donations from persons whose commercial or industrial activities are directly linked to the government official, or that the official regulate or supervise (Article 8, Federal Law of Responsibilities for Government Officers).

Doctors working for the IMSS or ISSSTE are considered to be government officers and are therefore not allowed to receive gifts or donations from pharmaceutical companies when on duty and working in the name of facilities of IMSS or ISSSTE.

The General Health Law and its regulations do not address doctors in private practice, although they specify that private doctors must act according to professional ethics.

Companies must not provide doctors with goods or incentives of any kind to use, prescribe, purchase or recommend a medicinal product or to influence the result of a clinical trial (Article 4.9.1, Code of Good

Practices of Advertising of the National Chamber of the Pharmaceutical Industry (CANIFARMA). The corresponding sanctions range from a warning to a fine.

Similarly, CANIFARMA's Code of Ethics indicates, in general terms, that companies should act responsibly in relation to sponsorships and donations.

Mexico does not currently have any anti-bribery laws to limit these practices, and there is no domestic legislation to regulate these cases beyond Mexico's jurisdiction. However, Mexico has ratified certain international treaties which do regulate, and in some cases prohibit, these practices.

30. How is the manufacturing of medicines and devices regulated and by which agencies?

The Mexican authority responsible for enforcing the regulatory framework relating to medical products, is the Ministry of Health and the Federal Commission for Protection against Sanitary Risks (COFEPRIS). COFEPRIS can request reports from marketing authorization holders, and make on-site inspection visits in the manufacturing, distribution or storage facilities.

The requirements for manufacturing approval are set out mainly in the General Health Law, its 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 essentially for:

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

The authority responsible for enforcing the regulatory framework in relation to medicines is COFEPRIS.

31. Are local manufacturing requirements compatible with Good Manufacturing Practices (GMPs) as defined by the US Food & Drug Administration (US FDA) and/or the European Medicines Agency (EMA)?

Yes, they are. In Mexico, the certificates of Good Manufacturing Practices issued by those agencies shall be recognized and validated, as well as the ones issued by Health Canada (Canada), Therapeutic Goods Administration (TGA, Australia), Swissmedic (Switzerland), Ministry of Health, Labour and Welfare (MHLW, Japan) and Ministry of Food and Drug Safety of the Republic of Korea (MFDS, South Korea).

32. What is the inspection regime for manufacturing facilities?

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

Good manufacturing practices, stability, and labelling standards and all other applicable provisions must be complied with. There must be a programmer to recall and destroy products that do not meet quality standards.

33. Are manufacturing facilities open for inspection by foreign inspectors or third-party inspectors as authorized by the FDA/EMA?

Yes, in Mexico COFEPRIS can authorize foreign inspectors or third party inspectors to make on-site visits.

34. What are the requirements for storage, packaging, and handling of medicines and devices and their constituent components?

In Mexico, establishments must obtain a health license from COFEPRIS and a certificate of Good Storage Practices in order to demonstrate that they comply with the requirements. Depending of the nature of the activities of the establishment, it may require such a license or just an operation notice.

35. What information must be included in medicine and device labeling?

The labelling of medicinal products should include essentially 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 authorization number.
- Batch number.
- Expiration date.
- Manufacturer's and, if applicable, distributor's information, including address.
- Content.
- Maximum price to the public.

In cases of drugs with a biological origin, 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 the revised international nomenclature, must be given.

36. What additional information may be included in labeling and packaging?

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

Moreover, a Decree that has been issued amending article 26 of the Health Law Regulation (HLR) is now pending publication in the Official Gazette of the Federation and its eventual entry into force.

This decree details the guidelines for the labelling of drugs for the public sector. In general terms, it indicates that the primary and secondary packaging of a medicine must be differentiated from that destined for the public sector and the labelling must include the captions "its sale prohibited" or "property of the Public Health Sector." Likewise, the general provisions regarding labelling will be maintained.

Overall, this reform provides greater certainty regarding the requirements that must be met in the labelling of medicines destined exclusively for public health and social security institutions. However, it imposes an additional obligation on holders of sanitary registration.

37. What items may not be included in labeling and packaging?

The labelling of medicinal products may not include the following information:

- Additives present in the medicinal product.
- The number of the marketing authorization of the country or countries to be exported.
- Graphics that impede or impair the legibility and importance of the legends.
- Graphics that lead to confusion or quality criteria, or with food and beverages and that are caricatured according to the Mexican Official Standard (NOM-072-SSA1-2012).

38. What are the restrictions and requirements for the marketing and advertising of medicines and devices?

Only non-prescription medicines can be advertised to the general public, and they are subject to approval by COFEPRIS. Media channels must have certified copies of the relevant marketing authorizations for medicines, before publishing related adverts.

Prescription medicines cannot be advertised to the general public.

Any visual or audio advert for non-prescription medicines must bear the message "Consult your physician", and must mention any required precautions when the use of the medicine represents any danger, in case of an existing pathology.

Prescription medicines can be advertised to health professionals. However, advertising directed to health professionals can only be published in specialized media and it must be based on medical prescription information.

39. Where can medicines and devices be sold or delivered? Can medicines and devices be sold or delivered via post?

Unless they are over-the-counter products, medicines can only be available in authorized drug stores and can only be sold to patients with a physician's prescription.

The parcel companies can only store and deliver medicines if they have a Sanitary License, Notice of a Sanitary Responsible and a special area for the storage and conservation of said medicines.

40. What are the restrictions and requirements for electronic marketing and advertising via email, by internet, social media, and other channels?

The Health Law Regulations apply to any advertising activity, including ads through electronic means and other forms of technological media.

COFEPRIS is in charge of monitoring ads on the internet. It has been strongly monitoring drug-like products, known as "miracle products" (products with non-proven health-related claims).

The internet 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.

Companies must adopt the proper measures to ensure the promotion of prescription medicines on their websites will only be accessible to healthcare professionals.

Recently, COFEPRIS issued guidelines for digital advertising that apply to any product subject to be monitored/approved by COFEPRIS. These guidelines clarify that digital advertising campaigns must be approved by COFEPRIS before being used on any digital media.

41. May medicines and devices be advertised or sold directly to consumers?

Only non-prescription medicines can be advertised to the general public, and they are subject to approval by COFEPRIS.

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

42. How is compliance monitored?

COFEPRIS has a permanent pharmacovigilance programme. The strictness on the imposition of fines, in our experience, has been steadily increasing. COFEPRIS constantly monitors advertising activities throughout the country, particularly regarding drug-like products. COFEPRIS has been directing the efforts of coordination agreements related to publicity, and the enforcement of the same.

There has also been a strong coordination effort between COFEPRIS and pharmaceutical companies in the self-regulation of advertising, which is still monitored.

43. What are the potential penalties for noncompliance?

The penalties for failing to comply with the rules related to advertising are the suspension of advertising activities, either directed 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 minimum wages (around US $14,000 to US

$115,000). The responsibility for imposing these penalties falls directly on the Ministry of Health, through COFEPRIS.

04

TRADITIONAL MEDICINES AND OVER-THE-COUNTER PRODUCTS

44. What are the regulatory requirements for traditional, herbal, complementary, or alternative medicines and devices?

45. Can these traditional, herbal, complementary, or alternative products be advertised directly to the public?

46. What health, advertising, and marketing claims may be made for traditional, herbal, complementary, or alternative products?

47. What are the regulatory requirements for over-the-counter (non-prescription) medications?

48. Are there any limitations on locations or channels through which OTC products may be sold?

49. What health, advertising, and marketing claims may be made for OTC products?

50. Can OTC products be marketed or advertised directly to the public?

51. What is the mechanism by which a prescription-only product can be converted to an OTC product?

52. What are the requirements for the importation of either traditional medicines or OTC products?

04 TRADICTIONAL MEDICINES AND OVER-THE-COUNTER PRODUCTS

44. What are the regulatory requirements for traditional, herbal, complementary, or alternative medicines and devices?

Traditional herbal medicinal products are regulated by the General Health Law and its regulations.

These types of products can contain excipients and additives besides vegetable materials, but they must not:

- Be isolated or chemically defined active ingredients.
- Be injectable.
- Include psychotropic or narcotic substances.
- Be mixed with conventional medicines or other substances that represent a health risk.

45. Can these traditional, herbal, complementary, or alternative products be advertised directly to the public?

Yes, they can be advertised to the general public. Any visual or audio advert must bear the message "consult your physician". Adverts must limit themselves to indicating the general characteristics of the product, its therapeutic properties and use.

46. What health, advertising, and marketing claims may be made for traditional, herbal, complementary, or alternative products?

The advertising of traditional, herbal, complementary, or alternative products directed to the general population may include the description of the diseases specific to the human being, diagnosis, treatment or rehabilitation expressed in the terms of their sanitary registration and in a language appropriate to the target audience. These messages must identify the issuer with the brand of the product or its business name.

Information on how to use the medication may be included on the label.

Advertising of herbal products must comply with the following requirements:

- The generic denomination will be the scientific name and will be printed according to the botanical nomenclature.
- The phrase "herbal medicine" should be included at the bottom of the main display surface.
- The declaration of the formula must be expressed by indicating the physicochemical form of the ingredient (dry extract, fluid extract, essential oil, powder, etc.) the part of the plant used, the scientific name, the name in parentheses common and the amount of the active ingredient.

47. What are the regulatory requirements for over-the-counter (non-prescription) medications?

The over-the-counter medication should meet certain requirements; initially it should have demonstrated efficacy and safety over time (at least 5 years) to be used in the relief of symptoms and signs of mild and short-term

illnesses and be easily recognizable by to the consumer. It should be indicated for common, self-limiting, easy self-diagnosis, self-management and simple self-assessment of response; it has to demonstrate efficacy and safety in all age groups of the population or at least in the majority, as well as in the paediatric, geriatric, pregnant and lactating population. The over-the-counter medication must possess a wide therapeutic margin, so that voluntary or involuntary administration with a higher dose than recommended or for an unapproved use, does not represent a direct or indirect serious harm to the health of the consumer. This means that the drug must have a low toxicity, it should not mask serious or non-serious diseases that delay the diagnosis and timely treatment of an underlying disease.

48. Are there any limitations on locations or channels through which OTC products may be sold?

Medications can be dispensed at establishments other than pharmacies, so the medical advice or recommendation focuses on the labelling of the product or its instructions.

The General Health Law states that no over-the-counter or other health supplies can be sold in semi-finished, mobile or semi-mobile facilities.

49. What health, advertising, and marketing claims may be made for OTC products?

The advertising of OTC products directed to the general population may include the description of the diseases specific to the human being, diagnosis, treatment or rehabilitation expressed in the terms of their sanitary registration and in a language appropriate to the target audience. These messages must identify the issuer with the brand of the product or its business name.

50. Can OTC products be marketed or advertised directly to the public?

Over-the-counter products can be advertised to the general public. Any visual or audio advert must bear the message "consult your physician", and must mention any required precautions when use of the medicine represents any danger, in the case of an existing pathology.

COFEPRIS's advertisement guidelines state that this regulatory agency will not approve an ad providing disease awareness to be followed by another ad of an over-the-counter medicinal product related to that disease, unless both ads are approved jointly.

51. What is the mechanism by which a prescription-only product can be converted to an OTC product?

There is no an expressly established process by COFEPRIS in order to convert a prescription-only product to an OTC product, but if there is a change in its production process and it have demonstrated efficacy and safety over time (at least 5 years) to be used in the relief of symptoms and signs of mild and short-term illnesses and easily recognizable by the consumer, the marketing authorization holder may present a written request to COFEPRIS asking to reclassify the prescription-only product to an OTC product.

52. What are the requirements for the importation of either traditional medicines or OTC products?

In order to import either traditional medicines or OTC products, it is necessary to obtain a sanitary authorization from COFEPRIS, have a marketing authorization for the product, the person who will import the product must have the proper installation, and, the medicines expiration date must be greater than twelve months, counting from the entry of medicines to the country.

05

PRODUCT LIABILITY

53. What types of liability are recognized in your jurisdiction?

54. How do these types of liabilities apply to the manufacturers of medicines and devices?

55. Does potential liability extend to the manufacturer only or could claims extend to corporate executives, employees, and representatives?

56. How can a liability claim be brought?

57. What defenses are available?

05 PRODUCT LIABILITY

53. What types of liability are recognized in your jurisdiction?

A. LEGAL PROVISIONS

In general terms, liability arises from provisions in federal or local civil codes in Mexico. Liability can also arise from statutory terms. The NOM for good manufacturing practices of medicinal products (NOM-059-SSA1-2015) has provisions regarding liability. Recently, the Federal Consumer Protection Law has been amended to allow class actions.

B. SUBSTANTIVE TEST

Liability claims are mainly regulated by statutes and not by court precedents.

Therefore, there is no clear substantive test. The standards to determine damages are high. According to precedents from the Federal Courts, the cause-effect relationship between actions/omissions and damage has to be fully proved.

54. How do these types of liabilities apply to the manufacturers of medicines and devices?

Accordingly, the NOM for good manufacturing practices of medicinal products (NOM-059-SSA1-2015) states that, when manufacturing through third parties, the marketing authorization holder has to supervise the manufacturing of the product and establish in agreements the liabilities and duties of each party involved.

55. Does potential liability extend to the manufacturer only or could claims extend to corporate executives, employees, and representatives?

All those involved in selling and/or distributing medicinal products can be liable in civil actions for harm derived from a defective medicinal product.

56. How can a liability claim be brought?

A. LIMITATION PERIODS

Depending on the conduct and cause of action, the limitation periods are two to ten years for civil actions, and one to nine years for certain criminal actions.

B. CITIZEN ACTIONS

The federal procedural laws have been amended to allow class actions before the federal courts. The Federal Agency for Protection of Consumers (Procuraduría Federal de Protección al Consumidor) (PROFECO), the Attorney General's Office, non-profit associations and a common representative of a group of at least 30 members can now pursue class actions. These

amendments are subject to testing in the courts and apparently there are no precedents of class actions for product liability.

In addition, there is an action available called "accion popular", whereby any individual with or without proper legal standing can file a complaint before COFEPRIS, arguing and proving that there are certain health risks in a product in the market. However, the claimant's procedural rights are very limited, and these actions are intended to cease a health risk and not to obtain compensation.

57. What defences are available?

Equitable defenses are available. Available defenses include

- Assumption of the risk and contributory negligence.

06

PATENTS AND TRADEMARKS

58. What are the basic requirements to obtain patent and trademark protection?

59. What agencies or bodies regulate patents and trademarks?

60. What products, substances, and processes can be protected by patents or trademarks and what types cannot be protected?

61. How can patents and trademarks be revoked?

62. Are foreign patents and trademarks recognized and, if so, under what circumstances?

63. Are there any non-patent/trademark barriers to competition to protect medicines or devices?

64. Are there restrictions on the types of medicines or devices that can be granted patent and trademark protection?

65. Must a patent or trademark license agreement with a foreign licensor be approved or accepted by any government or regulatory body?

06 PATENTS AND TRADEMARKS

58. What are the basic requirements to obtain patent and trademark protection?

To obtain the protection of a trademark for a sign, it is required to file an application before the Mexican Intellectual Property Office (IMPI) and to comply with the formalities established by the IP law.

As for patents, it is also necessary to file an application before the IMPI and to comply with the formalities established by the IP law.

59. What agencies or bodies regulate patents and trademarks?

In Mexico patents and trademarks are regulated by the Mexican Intellectual Property Office (IMPI).

60. What products, substances, and processes can be protected by patents or trademarks and what types cannot be protected?

TRADEMARKS

In accordance with the IP Law, any sign perceptible by the senses can be protected, provided that they are sufficiently distinctive and that one is able to identify the products or services to which they apply or intend to apply with respect to those in the same class.

The following signs may constitute a trademark:

- The denominations, letters, numbers, figurative elements and color combinations, as well as the holograms.
- The three-dimensional shapes;
- Trade names and denominations or company names
- The proper name of a person.
- Audible perception.
- Olfactory perception.
- The plurality of operational or image elements, including, among others, size, design, color, shape arrangement, label, packaging, decoration or any other than when combined, distinguish products or services in the market.

Taste perception cannot be protected in Mexico.

PATENTS

According to IP Law, the inventions that are new, involve inventive steps, and are capable of industrial application are patentable. In Mexico, methods and process claims are considered patentable subject-matter as long they fulfil the patentability requirements, with exception of: i) Cloning procedures ii) essentially biological processes for obtaining, reproducing and propagating plants and animals; iii) methods for carrying out mental processes, playing games or doing business, and mathematical methods; iv) methods of presenting information; v) methods of surgical, therapeutic or diagnostic treatment

applicable to the human body and to animals, and vi) vegetable varieties and animal breeds.

Regarding therapeutic treatment methods, please note that the patentability thereof can be dependent upon the formulation of the claims. IMPI, for example, allows Swiss type claims (Use of Compound/Composition X for the manufacture of a medicament for treating Y), or purpose-limited product claims (Compound/composition X for use in ...). In this respect, please note that there currently is an absence of criteria and guidelines in IMPI about which medical use claims can be accepted, since some Examiners accept both purpose-limited product claims and Swiss type claims. Taking into consideration that IMPI usually follows EPO's criteria, and that it is easier to argue that purpose-limited product claims encompass products, we preferably recommend filing the purpose-limited product claim format. Please note that product claims are easily listed in the patent linkage gazette in order to prevent the violation of the patent through approvals before the regulatory agency.

According to the IP Law, computer programs are not considered as inventions.

Software is protected under the copyright laws. It is worth mentioning that they can be patentable as computer-implemented processes.

61. How can patents and trademarks be revoked?

TRADEMARKS

I. INVALIDITY ACTION

The grounds of invalidation established by the IP law are:

1. The trademark has been granted in contravention of the provisions of the IP Law.
2. The trademark is identical or confusingly similar to another one that has been used in Mexico or abroad prior to the date of filing the application, and it is applied to the same or similar products or services, provided that the party who asserts the greater right for prior use proves the they have used the trademark continuously in Mexico or abroad prior to the mentioned filing date or declared use. The applicable statute of limitations is three years from the date that the Trademark Gazette which published the disputed registration, was put into circulation;
3. The registration was granted on the basis of false information in the application. The applicable statute of limitations is five years from the date that the Trademark Gazette which published the disputed registration, was put into circulation;
4. The existence of a senior registration for a trademark identical or similar to that covered by a junior registration, and the goods or services covered thereby are similar or identical in nature. The applicable statute of limitations is five years from the publication date of the Trademark Gazette detailing the disputed registration;
5. Registration is obtained by the agent, representative, user or distributor without the authorization of the owner of the foreign trademark registration. No statute of limitations applies to this action; or

6. A general cause of invalidity is available and it relies on the granting of registration against any provisions of the IP law or the law in force at the time when the registration was granted. This cause of cancellation has no statute of limitations.
7. Thetitle holder of the trademark registration does not prove the veracity of the date of first use declared in the application.

II. CANCELLATION ACTIONS

The IP law establishes as that if a trademark is not used for three consecutive years on the products or services for which it was registered, the trademark registration will be subject to cancellation for lack of use, unless the holder or the user of a recorder-granted license has used it during the three consecutive years' lack of use.

Furthermore, a cancellation action can be brought against a registration when the owner of it has provoked or tolerated that a trademark has become a generic term.

PATENTS

The IP law establishes several grounds on which a patent can be invalidated:

1. When the patent was granted in contravention of the provisions or requirements and conditions for the grant of patents.
2. When the protected subject matter is not considered an invention, the invention is not patentable, or lacks novelty, inventive activity or an industrial application.
3. Whenthe invention is not disclosed in a sufficiently clear and complete manner, so that it can be carried out by a person skilled in the art.
4. When the claims exceed the disclosure contained in the application, as it was initially presented to the Institute.
5. When, by error or serious oversight, a right of priority has been recognized and thereby unduly determined the novelty or inventive activity of the subject matter protected by the patent.
6. When it has been granted to those who did not have the right to obtain it.

The invalidity actions may be filed at any time, from the date on which the publication of the patent in the Gazette takes effect.

If the grounds for invalidity partially affect the patent, it will be declared partially invalid.

62. Are foreign patents and trademarks recognized and, if so, under what circumstances?

TRADEMARKS

When the registration of a trademark is applied for in Mexico within the periods specified in international treaties or, failing that, within six months of the filing of applications in other countries, the filing date in the country of first filing may be recognized as the priority date.

For the referred priority to be recognized, the following requirements must be met:

I. The priority must be claimed, and proof given of the country of origin and of the filing date of the application in that country, when applying for registration;
II. The application filed in Mexico must not seek to cover products or services additional to those provided for in the application filed abroad, in which case priority will be recognized only for those specified in the application filed in the country of origin;
III. The requirements specified in international treaties, the IP Law and the regulations thereunder must be met within three months of the filing of the application.

Additionally, if a trademark is identical or confusingly similar to another that has been used in the country or abroad prior to the filing date of the application of the registered trademark and has been applied to the same or similar products or services, provided that the person who asserts the stronger right by virtue of prior use proves uninterrupted use of the trademark in the country or abroad prior to the filing date or, where applicable, prior to the date of first declared use by the person who has registered it; it shall be invalid.

PATENTS

Where a patent is requested having been applied for abroad, the filing date in the country of first filing may be recognized as the priority date, provided that filing in Mexico occurs within the periods specified by international treaties or, otherwise, within 12 months after the application for a patent in the country of origin.

To give priority referred shall meet the following requirements:

I. The Mexican application must include which priority that is to be claimed, the country of origin of the priority, the date on which the application was filed in that country and the application number in that country;
II. A certified copy of the priority claimed must be submitted and, where appropriate, translated into Spanish, at the latest within a period of three months from the filing of the application in Mexico.
III. The requirements specified in international treaties, the IP Law and the regulations thereunder shall be complied with within 3 months after filing the application.

It is worth mentioning that parallel imports are not recognized by the IP Law in Mexico.

63. Are there any non-patent/trademark barriers to competition to protect medicines or devices?

In Mexico there is not a specific body of legislation for Data package exclusivity (DPE), but in 2012 COFEPRIS issued some internal guidelines to provide 5 years of protection for new chemical entities.

However, the reliability and legal value of these guidelines is still uncertain.

Based on the interpretation of international treaties, along with the Mexican legislation specifically related to the approval of new molecules (new chemical

entities, formulations and new indications), in addition to the New Molecules Committee's (NMC) regulation (which assists COFEPRIS with the analysis of technical and scientific data in connection with clinical trials, approval of new molecules and biologics) of regulatory data exclusivity for 5 years for new chemical entities, formulations and new indications has been obtained through litigation.

Regarding biologics, there have been precedents involving longer periods of protection, although the period has been decided on a case-by-case basis. It is worth noting that NAFTA mentions that the protection should be for at least 5 years. Furthermore, some countries grant a wider length in regulatory exclusivity for biologics such as the United States and, Canada, among others.

The agreement between the U.S., Canada and Mexico (USMCA/T-MEC) came into force on July 1st, 2020. This new agreement kept similar wording as NAFTA, providing at least 5 years of protection for new chemical molecules.

64. Are there restrictions on the types of medicines or devices that can be granted patent and trademark protection?

No, there are no restrictions to any types of medicines or devices that can be granted patent and trademark protection

65. Must a patent or trademark license agreement with a foreign licensor be approved or accepted by any government or regulatory body?

The only requirement established by the IP law is that for the license to have effect on third parties, it has to be duly recorded before IMPI.

Likewise, according to the linkage regulation established in article 147 BIS of the Mexican Industrial Property Regulations and article 167 BIS of the Health

Law Regulations, COFEPRIS is bound to observe the patents which are listed in the gazette, listing those patents in force that cover allopathic medicines, according to the generic name of the active ingredient, prior to granting marketing authorizations to third parties different to the titleholder, and alternatively to present the corresponding license.

07

REGULATORY REFORMS

66. Are there proposals for reform or significant change to the healthcare system?

67. When are they likely to come into force?

07 REGULATORY REFORMS

66. Are there proposals for reform or significant change to the healthcare system?

INITIATIVE BIOTECHNOLOGY MEDICINES

Reform various regulations of the General Health Law)

The initiative aims to regulate the use of medical devices. Among what is proposed, it is worth noting that: 1) prosthetics, diagnostic agents and dental supplies should be considered as medical devices; 2) the term "essential accessories for health" will be replaced with the term "medical devices"; 3) for sale or supply, as well as for importation, the retailers must have a sanitary authorization from the department of health; and, 4) the indications of the medical device´s use will be detailed in the instructions of the corresponding product, in printed or electronic form.

On December 20, 2021, the new version of the Official Mexican Standard NOM-241-SSA1-2021, Good medical device manufacturing practices, was published in the Official Gazette.

In general terms, this new version of the standard clarifies seems clearer than the previous other one since 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, i.e., in each step of the manufacturing chain until its distribution and marketing. In particular, the chapter on the "Quality Management System" is 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 "…any instrument, device, utensil, machine, software, implantable product or material, diagnostic agent, material, substance or similar product to be used, alone or in combination, directly or indirectly in human beings with any of the following purposes of use indicated in the document itself".

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. highlighted since, until now, this category was not included in the current legislation even though nowadays there are various programs and applications (apps) 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 standard, 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.

INITIATIVE TELEMEDICINE

(Amends article 77 Bis of the General Health Law)

The initiative aims to implement telemedicine through electronic means. For this purpose, it suggests: 1) to specify that the medical prescriptions will be issued in digital form; and 2) determine that this modality may be implemented by the public and private agencies and entities of the National Health System, subject to Mexican regulatory and official regulations issued by the COFEPRIS.

Recently, the Mexican government approved several amendments to the Tax Law. In summary, digital health platform providers could be taxed even though the medical service itself is exempt from tax. Agreements between Telemedicine providers and digital platforms can help to determine whether these entities fall within the scope of the law.

INITIATIVE CANNABIS REGULATION

(New General Health Law Regulation on Sanitary Control of Cannabis)

On January 12, 2020, the General Health Law Regulation on Sanitary Control for the Production, Research and Medicinal Use of Cannabis and its Pharmacological Derivatives was published in the Federal Official Gazette.

The new Cannabis Regulation is intended to regulate, promote, and monitor the use of cannabis and its derivatives for medicinal use. The regulation includes provisions regarding primary production, research, manufacturing of pharmacological derivatives and medicines, distribution, advertising, prescription, and commercialization. This regulation entered into force on January 13, 2020.

INITIATIVE PRICE REGULATION

The aim of this eventual regulation is to regulate the prices of drugs in order to ensure the proper access. The prices of drugs would be reviewed and evaluated every year or at any time, if necessary, based on the economic, technical or therapeutic conditions.

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 HSTI aimed at influencing priority issues for national development, with the purpose of guaranteeing that public benefits of the development of sciences and technologies result in social welfare and contribute to the care and restoration of the environment, as well as to promote the strengthening of national sovereignty and the integral development of the country.

67. When are they likely to come into force?

It is worth mentioning that rules and practices are changing almost on a day-by-day basis, yet it is also uncertain when and how the relevant proposals would be decided and enacted. At this point of time, considering the recent change of government, there are a lot of proposals for reform in several other fields than health. The proposals concerning health are being carefully reviewed and often discussed, and may conclude this process of evaluation in an average time of 6 months, since this government is very active in these matters.

08

CANNABINOID DRUGS, MEDICINAL CANNABIS AND OPIOID DRUGS

68. Are Cannabinoid Drugs authorized in your country?

69. What are the regulatory authorities with jurisdiction over Cannabinoid Drugs?

70. Is there a specific regulatory framework for the authorization pricing, and reimbursement of Cannabinoid Drugs?

71. Which are the Cannabinoid Drugs that have received market approval to date?

72. Who can prescribe Cannabinoid Drugs?

73. Is there a list of doctors authorized to prescribe Cannabinoid Drugs?

74. What approvals or notifications are required to prescribe Cannabinoid Drugs?

75. Which organizations are authorized to sell/distribute Cannabinoid Drugs available?

76. Is there a list of retailers/ distributors authorized to sell Cannabinoid Drugs?

77. Are there proposals for reform or significant change to the regulation of Cannabinoid Drugs?

78. When are they likely to come into force?

79. Is Medicinal Cannabis authorized in the country?

80. What are the regulatory authorities with jurisdiction over Medicinal Cannabis?

81. What is the regulatory framework for the authorization, pricing, and reimbursement of Medicinal Cannabis?

82. How is the production and import of Medicinal Cannabis regulated and by which agencies/authorities?

83. What approval or notifications are necessary to produce or import Medicinal Cannabis?

84. What is the regulatory framework for the marketing and distribution of Medicinal Cannabis?

85. How can patients obtain Medicinal Cannabis?

86. Who can prescribe Medicinal Cannabis?

87. Is there a list of doctors authorized to prescribe Medicinal Cannabis?

88. What approvals or notifications are required to prescribe Medicinal Cannabis?

89. Where is Medicinal Cannabis available?

90. Is there a list of retailers authorized to sell Medicinal Cannabis?

91. Are there proposals for reform or significant change to the regulation of Medicinal Cannabis?

92. Are Opioid Drugs authorized in your country?

93. What are the regulatory authorities with jurisdiction over Opioid Drugs?

94. Is there a specific regulatory framework for the authorization, pricing, and reimbursement of Opioid Drugs?

95. Which are the Opioid Drugs that have received market approval to date?

96. Who can prescribe Opioid Drugs?

97. Is there a list of doctors authorized to prescribe Opioid Drugs?

98. What approvals or notifications are required to prescribe Opioid Drugs?

99. Which organizations are authorized to sell/distribute Opioid Drugs available?

100. Is there a list of retailers/ distributors authorized to sell Opioid Drugs?

101. Are there proposals for reform or significant change to the regulation of Opioid Drugs?

102. When are they likely to come into force?

08 CANNABINOID DRUGS, MEDICINAL CANNABIS AND OPIOID DRUGS

CANNABINOID DRUGS

68. Are Cannabinoid Drugs authorized in your country?

The use of cannabis is authorized for medicinal use, including investigational activities, and granting marketing authorizations is also allowed for medicines where the active ingredient is THC.

On January 12, 2020, the General Health Law Regulation on Sanitary Control for the Production, Research and Medicinal Use of Cannabis and its Pharmacological Derivatives was published in the Federal Official Gazette.

The new Cannabis Regulation is intended to regulate, promote, and monitor the use of cannabis and its derivatives for medicinal use. The regulation includes provisions regarding primary production, research, manufacturing of pharmacological derivatives and medicines, distribution, advertising, prescription, and commercialization. This regulation came into force on January 13, 2020.

69. What are the regulatory authorities with jurisdiction over Cannabinoid Drugs?

So far, the authority responsible for applying and enforcing the regulatory framework in relation to Cannabinoid Drugs is the Federal Commission for Protection against Sanitary Risks (COFEPRIS), which is a decentralized agency of the Ministry of Health. On the other hand, it is worth mentioning that the proposal of this new law refers to the creation of the "Mexican Institute for Regulation and Cannabis Control". This proposal may impact the role of COFEPRIS as the main regulatory authority. Additionally, this Institute will be in charge of the creation of specific regulations and guidelines concerning the permitted activities with cannabis.

70. Is there a specific regulatory framework for the authorization pricing, and reimbursement of Cannabinoid Drugs?

The recently published General Health Law Regulation on Sanitary Control for the Production, Research and Medicinal Use of Cannabis and its Pharmacological Derivatives only established the authorization of Cannabinoid Drugs for investigation, production, and medicinal use. The primary legislation for the authorization, pricing, and reimbursement of these kinds of drugs, is the General Health Law (Ley General de Salud) (HL), and its Regulations. The law and its regulations are supplemented by Guidelines and Official Norms (NOMS) published by COFEPRIS.

Price control in the private sector is based on a scheme of self-regulated maximum retail price (MRP) only covering patented products, overseen by the Ministry of Economy. Pharmaceutical companies' participation is voluntary. Under the 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 the private sector, there is no system for reimbursement in Mexico.

Public acquisitions are supported by the Committee for the Negotiation of Drug Prices (CNDP).

71. Which are the Cannabinoid Drugs that have received market approval to date?

The official Website of COFEPRIS does not show any registrations concerning cannabinoid drugs which have an approval in force. However, there have been authorizations granted concerning cannabinoid drugs.

72. Who can prescribe Cannabinoid Drugs?

Healthcare professionals who have registered before COFEPRIS and have been granted with the specialized prescription forms concerning narcotic substances, are authorized to prescribe Cannabinoid Drugs.

73. Is there a list of doctors authorized to prescribe Cannabinoid Drugs?

So far, there is no list of doctors authorized to prescribe Cannabinoid Drugs.

74. What approvals or notifications are required to prescribe Cannabinoid Drugs?

There is no express regulation in this regard.

75. Which organizations are authorized to sell/distribute Cannabinoid Drugs available?

As of today, there is no available official information on whom that are authorized to sell and distribute Cannabinoid Drugs.

COFEPRIS may authorize drugstores, apothecaries, and/or pharmacies to supply the public with Cannabinoid Drugs.

76. Is there a list of retailers/distributors authorized to sell Cannabinoid Drugs?

So far, there is no list of retailers/distributors authorized to sell Cannabinoid Drugs

77. Are there proposals for reform or significant change to the regulation of Cannabinoid Drugs?

On January 12, 2020, the General Health Law Regulation on Sanitary Control for the Production, Research and Medicinal Use of Cannabis and its Pharmacological Derivatives was published in the Federal Official Gazette.

It is worth mentioning that the proposal of this new law refers to the creation of the "Mexican Institute for Regulation and Cannabis Control". This proposal may impact the role of COFEPRIS as the main regulatory authority. Additionally, this Institute will be in charge of the creation of specific regulation and guidelines concerning the permitted activities with cannabis.

78. When are they likely to come into force?

The proposal is still under discussion by the Mexican Congress. Since the cannabis path has taken quite a while, we expect at least one more year for these documents to be approved and enter into force.

MEDICINAL CANNABIS

79. Is Medicinal Cannabis authorized in the country?

The use of cannabis has been authorized for medicinal use, including investigational activities, and the granting of marketing authorizations for medicines whose active ingredient is THC, is allowed. On January 12, 2020, the General Health Law Regulation on Sanitary Control for the Production, Research and Medicinal Use of Cannabis and its Pharmacological Derivatives was published in the Federal Official Gazette.

The new Cannabis Regulation is intended to regulate, promote, and monitor the use of cannabis and its derivatives for medicinal use. The regulation includes provisions regarding primary production, research, manufacturing of pharmacological derivatives and medicines, distribution, advertising, prescription, and commercialization. This regulation came into force on January 13, 2020. However, the issuance of specific and specialized regulation is still missing.

80. What are the regulatory authorities with jurisdiction over Medicinal Cannabis?

So far, the authority responsible for applying and enforcing the regulatory framework in relation to Medical Cannabis is the Federal Commission for Protection against Sanitary Risks (COFEPRIS), which is a decentralized agency of the Ministry of Health,

81. What is the regulatory framework for the authorization, pricing, and reimbursement of Medicinal Cannabis?

The recently published General Health Law Regulation on Sanitary Control for the Production, Research and Medicinal Use of Cannabis and its Pharmacological Derivatives only established the authorization of Medicinal Cannabis for investigation, production, and medicinal use. So far, there is no specific regulatory framework for pricing, and reimbursement of Medicinal Cannabis. The primary legislation for the authorization, pricing, and reimbursement of these kinds of drugs, is the General Health Law (Ley General de Salud) (HL), and its Regulations. The law and its regulations are supplemented by Guidelines and Official Norms (NOMS) published by COFEPRIS.

82. How is the production and import of Medicinal Cannabis regulated and by which agencies/authorities?

According to the new General Health Law Regulation on Sanitary Control for the Production, Research and Medicinal Use of Cannabis and its Pharmacological Derivatives, the production and import of Medicinal Cannabis is regulated by the National Service for Agro-Food Safety and Quality (SENASICA) and the Federal Commission for Protection against Sanitary Risks (COFEPRIS), which is a decentralized agency of the Ministry of Health, and by the Ministry of Economy.

83. What approval or notifications are necessary to produce or import Medicinal Cannabis?

The new General Health Law Regulation on Sanitary Control for the Production, Research and Medicinal Use of Cannabis and its Pharmacological Derivatives, establishes that the authorization to sow cannabis for research and manufacturing purposes, must be processed before SENASICA having attached the research protocol, or the marketing authorization of the drug that is intended to be produced.

COFEPRIS may authorize public and private establishments that are used for the manufacturing process, or that import, export, or use Raw Material, Pharmacological Derivatives or Cannabis Medicines. Furthermore, such establishments MUST have control books which are authorized by COFEPRIS, in which the manufacture of the batches of Raw Material, Pharmacological Derivatives or Cannabis Medicines that are used to obtain the sanitary registration for commercialization for research, must be registered.

A permit for commercialization issued by COFEPRIS is required to apply for a sanitary importation permit.

However, the General Health Law Regulation on Sanitary Control for the Production, Research and Medicinal Use of Cannabis and its Pharmacological Derivatives, establishes that for the import and export of Raw Material, Pharmacological Derivatives and Cannabis Medicines, it is required to have a prior sanitary permit for Import or Export, granted by the Ministry of Agriculture and Rural Development (SADER) or COFEPRIS, within the scope of their nature. Furthermore, there is still lack of harmonization in the current sanitary legislation and the International Trade legislation. In the International Trade legislation field, despite it consisting of tariff schedules allowing importation for certain forms of cannabis, there are some other tariff schedules concerning cannabis that are still forbidden, which keeps causing problems for e the importation of certain types of products.

84. What is the regulatory framework for the marketing and distribution of Medicinal Cannabis?

The primary legislation for the marketing and distribution of Medicinal Cannabis is the General Health Law (Ley General de Salud) (HL) and its Regulations. The law and its regulations are supplemented by Guidelines and Official Norms (NOMS) published by COFEPRIS.

85. How can patients obtain Medicinal Cannabis?

Patients can obtain Medicinal Cannabis as long as they have a valid and codified prescription.

86. Who can prescribe Medicinal Cannabis?

Healthcare professionals who have registered before COFEPRIS and have been granted with the specialized prescription forms concerning narcotic substances.

87. Is there a list of doctors authorized to prescribe

There is a database of authorized healthcare professionals. However, so far, there is no list of doctors authorized to prescribe Medicinal Cannabis.

Medicinal Cannabis?

88. What approvals or notifications are required to prescribe Medicinal Cannabis?	The healthcare professionals must be registered before COFEPRIS, and been granted with the specialized prescription forms concerning narcotic substances. The healthcare professionals interested in obtaining the barcode for special prescription recipes for Cannabis Medications, must file an application before COFEPRIS for this purpose.
89. Where is Medicinal Cannabis available?	As of today, there is no official information on where medicinal cannabis is available. COFEPRIS may authorize drugstores, apothecaries, and/or pharmacies to supply the public with Cannabis Medications.
90. Is there a list of retailers authorized to sell Medicinal Cannabis?	So far, there is no list of retailers authorized to sell Medicinal Cannabis.
91. Are there proposals for reform or significant change to the regulation of Medicinal Cannabis?	Not at this point of time. However, it is important to note that the new Cannabis Regulation only entered into force in January 2020, shortly before the pandemic put an end to a lot of legal work. Once the pandemic has calmed down, we at least expect more specialized regulation, and maybe reforms or changes to the regulation of Medical Cannabis.

OPIOID DRUGS

92. Are Opioid Drugs authorized in your country?	Yes.
93. What are the regulatory authorities with jurisdiction over Opioid Drugs?	So far, the authority responsible for applying and enforcing the regulatory framework in relation to Opioid Drugs is the Federal Commission for Protection against Sanitary Risks (COFEPRIS), which is a decentralized agency of the Ministry of Health.
94. Is there a specific regulatory framework for the authorization, pricing, and reimbursement of Opioid Drugs?	The primary legislation for the authorization, pricing, and reimbursement of drugs, biologicals, and medical devices is the General Health Law (Ley General de Salud) (HL) and its Regulations. The law and its regulations are supplemented by Guidelines and Official Norms (NOMS) published by COFEPRIS. Price control in the private sector is based on a scheme of self-regulated maximum retail price (MRP) only covering patented products, overseen by the Ministry of Economy. Pharmaceutical companies' participation is voluntary. Under the 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 the private sector, there is no system for reimbursement in Mexico.
95. Which are the Opioid Drugs that have received market approval to date?	Morphine.
96. Who can prescribe Opioid Drugs?	The healthcare professionals must be registered before COFEPRIS, and been granted with the specialized prescription forms concerning narcotic substances.
97. Is there a list of doctors authorized to prescribe Opioid Drugs?	There is a database of authorized healthcare professionals. However, so far there is no list of doctors authorized to prescribe Opioid Drugs.
98. What approvals or notifications are required to prescribe Opioid Drugs?	The healthcare professionals must be registered before COFEPRIS, and been granted with the specialized prescription forms concerning narcotic substances.
99. Which organizations are authorized to sell/distribute Opioid Drugs available?	As of today, there is no available official information on whom that are authorized to sell and distribute Opioid drugs. Pharmacies are allowed to sell and distribute available opioid drugs, but only to those with a valid prescription.
100. Is there a list of retailers/ distributors authorized to sell Opioid Drugs?	There is no list of retailers/distributors authorized to sell Opioid Drugs.
101. Are there proposals for reform or significant change to the regulation of Opioid Drugs?	No.
102. When are they likely to come into force?	Not applicable.

09

ORPHAN DRUGS AND RARE DISEASES

103. What is the definition of Rare Diseases in your country?

104. Does the designation of 'Orphan Drug' exist in your country? (Does it correspond with the definition of Rare Diseases?)

105. What is the regulatory framework for the authorization of an Orphan Drug? (Is this regulatory framework based on Rare Disease status or can it alternatively be based on Orphan Drug foreign status?)

106. Does your country have provisions for relaxed clinical trial/scientific evidence requirements in respect of Orphan Drugs as compared to other drugs?

107. Is there an expedited pathway for Orphan Drugs?

108. Are foreign marketing authorizations recognized in your jurisdiction for Orphan Drugs? If yes, marketing authorizations from which countries are recognized?

109. Can Orphan Drugs be reimbursed? If so, is there a specific reimbursement procedure for Orphan Drugs?

110. How are the prices of Orphan Drugs regulated?

111. In case of reference price based on a basket of countries, what countries are included?

112. Have there been any significant legal/judicial developments in relation to Orphan Drugs in your country?

113. Are there proposals for reform or significant change to the regulation of Orphan Drugs? If yes, when are they likely to come into force?

09 ORPHAN DRUGS AND RARE DISEASES

103. What is the definition of Rare Diseases in your country?	In accordance with the General health law, rare diseases are those that have a prevalence of not more than 5 people for every 10,000 inhabitants.
104. Does the designation of 'Orphan Drug' exist in your country? (Does it correspond with the definition of Rare Diseases?)	Yes, in Mexico there is a designation of Orphan Drugs contemplated in the General Health Law and these drugs are intended for the prevention, diagnosis or treatment of rare diseases.
105. What is the regulatory framework for the authorization of an Orphan Drug? (Is this regulatory framework based on Rare Disease status or can it alternatively be based on Orphan Drug foreign status?)	The regulatory framework for the authorization of an Orphan Drug are: • General Health Law (Ley General de Salud). • General Health Law Regulations for Healthcare Products (Reglamento de Insumos para la Salud). • Official Mexicans Standards (NOMs). • Mexican Pharmacopoeia; Foreign marketing authorizations are not valid in Mexico.
106. Does your country have provisions for relaxed clinical trial/ scientific evidence requirements in respect of Orphan Drugs as compared to other drugs?	Orphan drugs were introduced into the General Health Law and the Mexican Pharmacopeia some years ago. However, they follow the main principles and general rules as other drugs.
107. Is there an expedited pathway for Orphan Drugs?	Orphan drugs were introduced into the General Health Law and the Mexican Pharmacopeia some 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. Despite the fact that this procedure has worked reasonably well, more specific rules would be welcomed.
108. Are foreign marketing authorizations recognized in your jurisdiction for Orphan Drugs? If yes, marketing authorizations from which countries are recog-	Foreign marketing authorizations are not valid in Mexico. However, COFEPRIS has set out a special procedure for drugs to be approved for the first time in Mexico, as long as they are already approved by equivalent regulatory authorities abroad. In this procedure, the requirements for approval of these agencies are recognized as equivalent to those in Mexico. According to the equivalence

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agreement, marketing authorizations which have been approved by the following agencies, are also approved in Mexico:

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

Yet, as for Orphan Drugs, there are no express provisions to consider as reference for these foreign approvals. Thus, in these cases it would be under the authority's discretion to consider them in the evaluation process.

109. Can Orphan Drugs be reimbursed? If so, is there a specific reimbursement procedure for Orphan Drugs?

The primary legislation for the reimbursement of these kinds of drugs, is the General Health Law (Ley General de Salud) (HL), and its Regulations. The law and its regulations are supplemented by Guidelines and Official Norms (NOMS) published by COFEPRIS.

In the private sector, there is no system for reimbursement in Mexico. For the 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.

110. How are the prices of Orphan Drugs regulated?

Price control in the private sector is based on a scheme of self-regulated maximum retail price (MRP) only covering patented products, overseen by the Ministry of Economy. Pharmaceutical companies' participation is voluntary. Under the 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 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.

Public acquisitions are supported by the Committee for the Negotiation of Drug Prices (CNDP).

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 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.

The political party currently governing in Mexico (MORENA) is promoting an amendment to the scheme of self-regulated maximum retail price

(MRP). This amendment state, in general terms, that the Ministry of Economy in collaboration with the Ministry of Health shall guarantee, through a transparent process and taking into consideration differentiated policies, the access to medications and inputs to people in situations of poverty. In addition, the price control would be regulated and annually reviewed by these Authorities.

On August 11, 2020, the Mexican Congress published the Decree amending Article 1 of the Public Sector Procurement, Leasing and Services Law, through which the Mexican Government is now empowered to acquire medicines through intergovernmental organizations, such as UNOPS, without having to observe the procedures set forth in the applicable Law and Regulation on public procurement.

According to UNOPS' guidelines, the process is made up of different stages grouped within three phases identified as:

1. Pre-Bidding Process (market research, requirements definition and identification of potential suppliers).
2. Bidding Process (publication of the bases and call for bids and/or invitations for negotiation, bid management, evaluation and award).
3. Post-Bidding Process (contract management and logistics). The distribution to the final destination will be in charge of INSABI.

Therefore, during these proceedings UNOPS is entitled to negotiate the prices of the supplies.

111. In case of reference price based on a basket of countries, what countries are included?

As mention in **answer 110**, under the 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.

112. Have there been any significant legal/judicial developments in relation to Orphan Drugs in your country?

In 2014, the Mexican Supreme Court of Justice ruled that the refusal to supply orphan drugs is not unconstitutional if they have not been approved, prior to the examination and analysis, by the interinstitutional commission of the so-called National formulary, which is the document containing all medicines, medical supplies, instruments used by the public health institutions in Mexico.

The Second Chamber of the Supreme Court issued a partial favourable decision in this case. First, the decision recognized that the right to health is a constitutional right of primary importance. Yet, secondary laws shape the access to health services. Therefore, the denial of providing basic health services, such as medical care for conditions that require "orphan" drugs for their treatment, directly affect the fundamental right to protection of health.

On the other hand, the Chamber considered it was necessary to follow the procedure to include the product in the National Formulary, as this is a mechanism through which the State guarantees that the drugs necessary to treat the diseases of the population are safe, efficient and effective.

Thus, the Supreme Court recognizes that the health institution that should be providing these to the patients can and should request the evaluation and

analysis of the drug to be included in such list, in order to be able to provide the orphan drug.

In conclusion, the Supreme Court mainly stated that the applicable procedures should be observed in order to be able to supply the drug. Yet, the Second Chamber may have omitted to consider that it would take a while, which would eventually put the health of the patients in danger.

113. Are there proposals for reform or significant change to the regulation of Orphan Drugs? If yes, when are they likely to come into force?

No, there are no proposals to reform or significantly change the regulation. Nevertheless, specific rules would be welcomed.

10

LOCALIZATION

114. Are there any rules or regulations requiring and/or encouraging localization in your country? What is the legal framework defining these localization rules and policies?

115. Have there been any recent significant changes involving localization rules? If yes, when did they take place and what did they involve?

116. Is the process of obtaining a marketing authorization impacted by localization policies in your country? If yes, how so (what are the incentives received or the requirements)?

117. Is the pricing process for pharmaceutical products impacted by localization policies in your country? If yes, how so (what are the incentives received or the requirements)?

118. Is the reimbursement of pharmaceutical products impacted by localization policies in your country? If yes, how so (what are the incentives received or the requirements)?

119. Is the access to public or public tenders of pharmaceutical products impacted by localization policies in your country? If yes, how so (what are the incentives received or the requirements)?

120. Are import tariffs, importation and/or exportation permits, trade and/or taxation of pharmaceutical products impacted by localization policies in your country? If yes, how so?

121. Are there any other incentives or advantages offered by the current local localization rules in your country? If yes, what are they?

122. Are there discussions about the possibility of implementing localization policies in your country? If yes, what are the proposed reforms and when should they come into place?

10 LOCALIZATION

114. Are there any rules or regulations requiring and/ or encouraging localization in your country? What is the legal framework defining these localization rules and policies?	Largely, there are no specific rules or regulations requiring and/or encouraging localization in Mexico. Thus, there is no legal framework defining localization rules and policies in Mexico. Although the legal framework may involve a slight advantage if part of a specific process is carried out in Mexico or may be appointed as a requirement.
115. Have there been any recent significant changes involving localization rules? If yes, when did they take place and what did they involve?	No.
116. Is the process of obtaining a marketing authorization impacted by localization policies in your country? If yes, how so (what are the incentives received or the requirements)?	Despite the lack of a specific legal framework defining localization rules and setting policies in Mexico There are some provisions, which may fall under localization policies in relation to marketing authorization process Concerning drugs containing new molecular entities which are not authorized in other countries and are intended to be registered in Mexico, it is possible to file the report of clinical studies with the participation of the Mexican population demonstrating the safety, quality and efficacy of the product. This can be submitted instead of a Free Sale Certificate or its equivalent in other countries. Even though such provision does not necessarily mentions that the study should be conducted in Mexico, it was amended in 2014 in order to stimulate the participation of foreign companies in Mexico. Moreover, for the authorization of biologics it is required to conduct clinical trials in Mexico. If the eventual MAH is a foreign company with no establishment in Mexico, the MAH must submit a license/certificate/document issued by the local corresponding Sanitary authority that proves that it has an authorized manufacturing facility in that country. It is not necessary to have a subsidiary, however it is necessary to have a legal representative in Mexico. The local representative must have a warehouse authorized by COFEPRIS (or a contract with an existing warehouse, in order to be able to be considered as legal representative of the MAH holder within the eventual authorization. In general, the warehouse should mainly be an authorized site and have a registered Sanitary Responsible (a person in charge of supervising and managing the activities at the facilities).

	Is not mandatory that the legal representative is a subsidiary or an affiliate of the Marketing Authorization Holder (MAH).
117. Is the pricing process for pharmaceutical products impacted by localization policies in your country? If yes, how so (what are the incentives received or the requirements)?	No.
118. Is the reimbursement of pharmaceutical products impacted by localization policies in your country? If yes, how so (what are the incentives received or the requirements)?	No.
119. Is the access to public or public tenders of pharmaceutical products impacted by localization policies in your country? If yes, how so (what are the incentives received or the requirements)?	No. In fact, on July 31, 2020, the "Specific Agreement between the Institute of Health for the Welfare of the United Mexican States (INSABI) and UNOPS" was signed for the execution of the Implementation Project called "Acquisition of medicines and medical supplies" for the period 2021-2024, which allows open international competitive bidding modality (national and international market companies) for the consolidated purchase of medicines under the procurement policies and procedures of UNOPS. The Mexican Government transfers to UNOPS all the resources and UNOPS oversees implementing, tendering and contracting said activities, as well as managing the respective contracts with third parties. Also, on January 28, 2020 a Decree was published in the Federal Official Gazette by the Ministry of Health which states the sanitary requirements equivalence and allows the importation of drugs without marketing authorization into México. If the product has met all the requirements and procedures of the foreign regulatory agency, i.e., if they were granted a MA, this is considered equivalent to having complied with all the requirements of the Mexican legislation. In addition, products which have previously been approved by the EMA, FDA, Health Canada, the Swiss Agency for Therapeutic Products (Swissmedic) or the TGA in Australia can benefit from an expedited MA approval process with time frames up to 60 working days.
120. Are import tariffs, importation and/or exportation permits, trade and/or taxation of pharmaceutical products impacted by localization policies	The General Import and Export Tax Law was amended in July 2020 to create a table that showed a 5 % import tax per kilogram of vaccine and tax exemption on export. The law was further amended in February 2021 to make both the import and export of vaccines tax-free.

in your country? If yes, how so?

No.

121. Are there any other incentives or advantages offered by the current local localization rules in your country? If yes, what are they?

122. Are there discussions about the possibility of implementing localization policies in your country?
If yes, what are the proposed reforms and when should they come into place?

There are no specific discussions about the possibility of implementing localization policies.

On the other hand, some amendments have been proposed that may fall under the shadow of localization polices, such as "plant requirement". The Mexican legislation used to state a "plant requirement". Thus, it was required to have a manufacturing or conditioning plant in our country, in order to obtain a marketing authorization (even if the product was manufactured abroad and imported). This caused different pharmaceutical companies to sign hosting agreements with national companies to be able to sell their products, these national companies were, then, the holders of the marketing authorizations.

The plant requirement was eliminated in 2008. According to the current regulation, the holder of a marketing authorization still needs to have a manufacturing plant, but that plant may be located abroad.

Recently, a proposal to amend the Health Law Regulations was published. This project has proposed to include the "plant requirement" again.

In this regard, the Mexican Association of Pharmaceutical Research Industries (AMIIF), has conducted lobbying efforts in order to prevent the approval of such reform.

Moreover, there is a legal precedent issued by an International Court, ordering Mexico to eliminate said requirement. The International Court considered that Mexico violated the international treaty concluded with Central America, by demanding the "plant requirement", since the principle of "national treatment" was violated, in relation to El Salvador.

Thus, we believe that the chances of such an initiative being approved are few, however, we continue to follow up.

RECAP TABLE

MEXICO	RESEARCH	CLINICAL TRIALS	API CONTENT	FILL AND FINISH	PACKAGING
Require/Benefit	0	R/B	0	0	0
Requirement	MA	MA			
Benefits					

Line 1
0 - if neutral
R - if a requirement
B - if provides benefit

Line 2 and 3 Fill in (according to answer in Line 1)
MA - Market Access
P - Pricing
R - Reimbursement
T - Tenders
Tx - Taxes and import tariffs

11

BIOSIMILARS AND BIOLOGICS

123. Are biosimilar medicines considered the same as generic medicines in your country?

124. Are all biologic medicines, including biosimilar medicines, patentable in your country?

125. Is there a specific regulatory framework for the marketing authorization of biosimilar medicines in your country? If yes, what is the regulatory framework for the authorization of biosimilar medicines?

126. What kind of data package is needed to obtain approval for a biosimilar drug? Is this any different to the requirements for the original Biologics drug?

127. What are the requirements for the choice of the reference comparator product?

128. Can the comparator product be sourced from another regulatory jurisdiction? If yes, what are the data needed to support this approach?

129. How are the prices of biosimilar medicines regulated? Is this any different from the requirements for the original Biologics drug?

130. What is the reimbursement policy for biosimilar medicine? Is this any different from the requirements for the original Biologic drug?

131. Does biosimilar competition impact the reimbursement policy of the originator reference products?

132. What is the legal framework for biosimilar medicines prescribing (clinical decision maker) and dispensing (pharmacy level, hospital or retail)? Is this any different to the requirements for the original Biologics drug?

133. Is the system considering physician-led switching and/or pharmacy-level substitution (without involvement of the clinical decision maker)?

134. What are the post - authorisation requirements (including pharmacovigilance, risk management plans, post-approval studies) for biosimilar medicines? Is this any different to the requirements for the original Biologics drug?

135. Are there specific policies and requirements for labelling biosimilar medicines in the event of second medical use patents? Is this any different from the requirements for the original Biologic drug?

136. Have there been any significant legal/ judicial developments in relation to biosimilars in your country? (Including but not limited to IP, procurement, competition, misleading information campaign, access to reference comparator product)

137. Are there proposals for reform or significant change to the legal, regulatory, procurement of biosimilars? If yes, when are they likely to come into force?

11 BIOSIMILARS AND BIOLOGICS

123. Are biosimilar medicines considered the same as generic medicines in your country?

No, biosimilars are not considered the same as generic medicines. Biosimilars are regulated by specific provisions within the sanitary legislation.

The Mexican General Health Law defines a "biologic product" as any substance that: has been manufactured by molecular biotechnology; has therapeutic, preventive, or rehabilitative effects; is provided in a dosage form; and is identified as such by its pharmacological activity and physical, chemical and biological properties.

Article 222 Bis of the Health Law names follow-on biotechnology products (biosimilars) as "biosimilars", since they must be comparable to reference products with regard to safety, efficacy and quality.

For instance, applicants for marketing authorizations of generics basically only have to prove that their products are interchangeable to the innovator product. They have to provide information concerning dissolution profiles or bioavailability studies regarding the reference product. COFEPRIS periodically issues a list of reference medicinal products.

However, the essential dossier submission requirements for biosimilars are the same as those for innovative biotech products, except for extra the requirements to prove safety, efficacy and quality. Applicants for biosimilars must submit clinical tests and, when appropriate, in-vitro tests, to prove that the safety, efficacy and quality of their t biosimilar (biosimilar) product is comparable to the reference biologic.

124. Are all biologic medicines, including biosimilar medicines, patentable in your country?

Biologic medicines are patentable in Mexico. Biosimilar medicines may be protected under IP rights if the specific product, somehow fulfils, among others, the patentability requirements.

125. Is there a specific regulatory framework for the marketing authorization of biosimilar medicines in your country?
If yes, what is the regulatory framework for the authorization of biosimilar medicines?

The primary legislation for the authorization of biosimilars is the General Health Law (Ley General de Salud) (HL) and its Regulations. The law and regulations are complemented by Guidelines and Official Mexican Standards (NOMS) published by COFEPRIS.

Biologics are treated differently to non-biologic drugs for the purposes of gaining regulatory approval. The biologics-specific path is mainly provided in the Mexican official standard Rule, NOM-257-SSA1-2014 "Regarding biologic medicines".

In addition, the Mexican official standard Rule NOM-177-SSA1-2013 regarding "Interchangeability and biosimilarity tests" mainly establishes the

126. What kind of data package is needed to obtain approval for a biosimilar drug? Is this any different to the requirements for the original Biologics drug?

guidelines for generating clinical protocols, quality management systems, pharmacovigilance, biosimilarity and establishes the reference products.

In general terms, the standard dossier submission requirements for marketing authorization applications for drugs usually comprise legal and administrative information, summaries, chemical, pharmaceutical and biological information, nonclinical reports and clinical study reports.

The additional dossier requirements for biotech products include, for example, a description of the manufacturing process, the provision of information concerning the starting and biological origin materials, and a description of the manufacturing facilities and equipment.

Innovative biotech products may be used as the reference product for the approval of non-innovative products. The General Health Law calls these products 'biosimilars', since they must be comparable to reference products regarding safety, quality and efficacy. The Health Law Regulations stipulate that a biosimilar may be a reference product for another one, where an innovative product has not been approved in Mexico yet.

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

The pre-clinical and clinical test used by an applicant for a biosimilar must use the corresponding reference biologic to perform comparative and physic-chemical studies. For this, the applicant essentially has to submit:

- In vitro 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 reference biologic;
- Pharmacodynamics test reports; and
- Comparative efficacy and safety clinical tests to show similarity between both the follow-on and the reference biologic.

127. What are the requirements for the choice of the reference comparator product?

According to the Health Law Regulations, reference medicinal products are those indicated by the Ministry of Health as such, that has the registry of said agency, that is commercially available and is selected according to the criteria established in the Standards.

In 2018, the Federal Commission for Protection against Sanitary Risks (COFEPRIS) issued the guidelines that establishes the requirements for the recognition and selection of a reference medicine. The guidelines establish that the medicine which has its marketing authorization and that was presented through the New Molecules Committee, may be recognized as a reference medicine by COFEPRIS. Furthermore, in case there already is a patent in force, the medicine can be designated as a reference medicine, but only three years before of the expiration of the patent that is already in force, and only if the medicine complies with the following:

- It has a current marketing authorization issued by the Federal Commission for Protection against Sanitary Risks (COFEPRIS).

- It has the information of the clinical trials that support the safety and efficacy of the product or with the official communication of the resolution issued by the New Molecules Committee.
- They have submitted a letter under oath stating that the drug and its different concentrations are currently marketed, which must be signed by the Legal Representative.
- They have provided the information to prescribe the authorization in non-editable electronic format.
- It complies with the provisions of the current Official Mexican Standard NOM-2020-SSA1-2016 "Installation and operation of pharmacovigilance".

https://www.gob.mx/cms/uploads/attachment/file/295040/Lineamientos_MedRef_31ene2018.pdf

128. Can the comparator product be sourced from another regulatory jurisdiction? If yes, what are the data needed to support this approach?

Under the guidelines that establish the requirements for the recognition and selection of a reference medicine, and if the reference product (comparator) is not included within the corresponding list, or it is included but not commercially available in Mexico, it is possible to have the comparator product sourced from one of the following regulatory jurisdictions:

- The European Medicines Agency;
- The US Drug and Food Administration;
- Health Canada;
- The Swiss Agency for Therapeutic Products (Swissmedic); and
- The Therapeutic Goods Administration in Australia.
- The National Agency of Sanitary Vigilance (ANVISA) in Brazil.
- The Pharmaceutical and Food Safety Bureau.

129. How are the prices of biosimilar medicines regulated? Is this any different from the requirements for the original Biologics drug?

Price control in the private sector is based on a scheme of self-regulated maximum retail price (MRP) only covering patented products, overseen by the Ministry of Economy. Pharmaceutical companies' participation is voluntary. Under the 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 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.

Public acquisitions are supported by the Committee for the Negotiation of Drug Prices (CNDP).

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 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.

On August 11, 2020, the Mexican Congress published the Decree amending Article 1 of the Public Sector Procurement, Leasing and Services Law, through which the Mexican Government is now empowered to acquire medicines through intergovernmental organizations, such as UNOPS, without having to observe the procedures set forth in the applicable Law and Regulation on public procurement.

According to UNOPS' guidelines, the process is made up of different stages grouped within three phases identified as:

1. Pre-Bidding Process (market research, requirements definition and identification of potential suppliers).
2. Bidding Process (publication of the bases and call for bids and/or invitations for negotiation, bid management, evaluation and award).
3. Post-Bidding Process (contract management and logistics). The distribution to the final destination will be in charge of INSABI.

Therefore, during these proceedings UNOPS is entitled to negotiate the prices of the supplies.

130. What is the reimbursement policy for biosimilar medicine? Is this any different from the requirements for the original Biologic drug?

The primary legislation for the reimbursement of these kinds of drugs, is the General Health Law (Ley General de Salud) (HL) and its Regulations. The law and its regulations are complemented by Guidelines and Official Mexican Standards (NOMS) published by COFEPRIS.

In the private sector, there is no system for reimbursement in Mexico. For the 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.

131. Does biosimilar competition impact the reimbursement policy of the originator reference products?

In general terms it should not have any impact as the Institution would prescribe the product that has been appointed in previous agreements. Yet, those agreements may only appoint the biosimilar as the product to be reimbursed.

132. What is the legal framework for biosimilar medicines prescribing (clinical decision maker) and dispensing (pharmacy level, hospital or retail)? Is this any different to

- General Health Law (Ley General de Salud).
- General Health Law Regulations for Healthcare Products (Reglamento de Insumos para la Salud).
- Official Mexicans Standards (NOMs).

No, the requirements are the same for both drugs.

the requirements for the original Biologics drug?

133. Is the system considering physician-led switching and/ or pharmacy-level substitution (without involvement of the clinical decision maker)?

The regulations do not prevent automatic switching/substitution. Thus, pharmacists may choose to dispense any product with the same non-proprietary name (INN). Physicians may not prohibit substitution, but in the private sector, patients may prohibit substitution.

In the private sector or out-of-pocket acquisitions, patients can prevent substitution by requesting that the pharmacist not make the substitution. If the pharmacist insists on making the substitution, the patient may choose not to purchase the medicine and may search for the prescribed product in a different pharmacy.

However, under a public insurer, patients cannot prevent substitution, and a pharmacist may dispense any product with the same non-proprietary name (INN).

There was a proposal published in 2013 to amend the Health Law to prevent automatic substitution/switching from innovative biological products to biosimilars, and vice versa. However, the proposal was not further discussed in the Mexican Senate, and has since lapsed.

134. What are the post - authorisation requirements (including pharmacovigilance, risk management plans, post-approval studies) for biosimilar medicines? Is this any different to the requirements for the original Biologics drug?

Post-authorisation requirements are the following:

- Comply with the Official Mexican Standards such as:
  - Pharmacovigilance, NOM-220-SSA1-2016 (NOM-220).
  - Good manufacturing practices for medicinal products (NOM-059-SSA1-2015).
  - Good manufacturing practices for Active ingredients (NOM-164-SSA1-2015).
  - Interchangeability and biocomparability tests (NOM-177-SSA1-2013).
  - Medicinal products labelling (NOM- 072- SSA1-2012).

- Drug manufacturers must renew their marketing authorization every five years, subject to the relevant tests, including submission of a certificate of good manufacturing practices in force.

135. Are there specific policies and requirements for labelling biosimilar medicines in the event of second medical use patents? Is this any different from the requirements for the original Biologic drug?

The requirements for the labelling of medicines are established in the Official Mexican Standard NOM-072-SSA1-2012, Labelling of medicines and herbal remedies.

Between the requirements of biologics and biosimilars there are the following differences or exceptions:

- In labeling of secondary packaging the distinctive denomination is optional in the case of generic or biocomparable drugs.
- The labeling must bear the acronyms M.B. in the case of innovative biotech drugs, and M.B.B. in the case of biocomparable biotech drugs.

136. Have there been any significant legal/judicial developments in relation to biosimilars in your country? (Including but not limited to IP, procurement, competition, misleading information campaign, access to reference comparator product)

On August 19, 2020, the regulatory agency in Mexico (COFEPRIS), announced new operating rules for the approval of generic drugs in Mexico, based on the following guidelines:

- COFEPRIS will have a special procedures window for the generic pharmaceutical industry.
- These applications for approvals could be filed the day after the granting of the patent related to the innovative medicine.
- The respective applications would be decided at any time, prior to the expiration of the patent. If the registration or approval is given, COFEPRIS will provide a provisional official communication, which would be exchanged for the definitive sanitary registration or approval the day after the expiration or the validity of the patent.

COFEPRIS indicates that they are complying with the elimination of the temporality of 3 years (for chemically synthesized drugs) and 8 years (for biotechnological) to research and develop generics or biosimilars, according to the reforms to the so-called Bolar Exception in the new Federal Law for the Protection of Industrial Property (New IP Law) which entered in force November 2020.

The communication also mentions that the rules for granting sanitary registrations of generic drugs, "second-use patents, which refer to the therapeutic indication, are no longer allowed," which seems to mean that the patents of new uses will not be considered as part of the linkage system.

These rules announced by COFEPRIS are still without a legal basis, since it is only a statement on its official website.

137. Are there proposals for reform or significant change to the legal, regulatory, procurement of biosimilars? If yes, when are they likely to come into force?

Concerning significant changes to the legal, regulatory, procurement of biosimilars, last year (2021), the Ministry of Health issued a decree in the Official Gazette, amending several articles of the Health Law Regulations. The most relevant points of this decree were the following:

- COFEPRIS allows the submission of documentation in English, without translation into Spanish within sanitary approval applications. In the case of documents issued by a foreign Authority, they must be legalized.
- The labels of products destined for the public sector must now be differentiated from those of the private.
- For the approval of biosimilar medicines, the participation of the Subcommittee for the Evaluation of Biotechnological Products was eliminated, now it is sufficient the New Molecules Committee opinion.
- Clinical studies in the country of origin of biosimilar medicines can be submitted as evidence for the Marketing Authorization application. When applying for a renewal of the Marketing Authorization, clinical studies in Mexico must be submitted.
- The first extension must be requested 5 years after the approval and must be resolved within 120 days.

- To obtain the first Marketing Authorization renewal, all products will be monitored by the regulatory agency, taking into account the effects of the product during its first years in the market.
- For further renewals must be requested/ informed to COFEPRIS every five years, and no later than 150 calendar days before the expiration of the Marketing Authorization.
- The statutory terms regarding applications to modify the Marketing Authorization have changed, the regulatory agency shall issue a response within 45 days for technical modifications and 20 days for administrative modifications.
- If the modification of the Marketing Authorization is authorized, the holder will have a period up to 240 calendar days to eliminate the stock of the product.

Aside from those modifications, there are no significant changes that will impact these products any time soon.

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