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Medicinal product regulation and product liability in Mexico: overview

Alejandro Luna and Armando Arenas
Olivares

global.practicallaw.com/7-376-5204

REGULATORY OVERVIEW

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

Legislation

The primary legislation for medical products is:

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

Regulatory authorities

The regulatory authority in this field is the Federal Commission for Protection against Sanitary Risk (*Comisión Federal para la Protección contra Riesgos Sanitarios*) (COFEPRIS) (*www.cofepris.gob.mx*) which is an administrative agency of the Ministry of Health (*Secretaria de Salud*).

2. Briefly outline how biologicals and combination products are regulated in your jurisdiction.

Both biologics and combination products must have marketing authorisation from COFEPRIS. Roughly, biologics are classified into:

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

Requirements and application timeframes differ in each case.

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. A combination product may require separate drug or biologic and medical device approvals (*see Questions 3 and 9*).

3. Briefly outline how medical devices and diagnostics are regulated in your jurisdiction. Is there any specific regulation of health IT issues and mobile medical applications?

The primary legislation for medical devices and diagnostics is the General Health Law, its regulations and the NOM for good manufacturing practices regarding medical devices (NOM-241-SSA1-2012).

According to their use, Article 262 of the General Health Law classifies medical devices into:

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

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

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

COFEPRIS analyses both medical devices and, if applicable, software that enables them to work. Conversely, mobile medical applications are a new area that COFEPRIS may address in future by particular regulations, especially if they represent health risks.

As an incentive, applicants can benefit from a special procedure for certain devices to be approved in Mexico, which have been previously approved by the:

- US Drug and Food Administration.
- Health Canada.

This procedure is essentially based on the dossier filed with the foreign regulatory agency, to reduce approval timeframes by up to 30 working days. Industry participants have welcomed these new rules, but they are still being tested.

PRICING AND STATE FUNDING

4. What is the structure of the national healthcare system, and how is it funded?

The Ministry of Health:

- Governs the health system in Mexico.
- Manages social security and health insurance.
- Determines the National Formulary for the list of basic drugs (*Cuadro Básico de Insumos para la Salud*).

The Mexican healthcare system comprises public (social security institutions) and private insurers, out-of-pocket payments and informal arrangements.

The major public segments of the Mexican healthcare system are:

- The Mexican Institute of Social Security (*Instituto Mexicano del Seguro Social*) (IMSS). This represents social security for the self-employed and employees in private companies.
- The Institute of Social Security for State Workers (*Instituto de Seguridad y Servicios Sociales de los Trabajadores del Estado*) (ISSSTE).
- The *Seguro Popular*. This is a programme created in 2004 as part of a strategic reform to the General Health Law. It provides a public insurance scheme for those not covered by social security and other formal arrangements. The *Seguro Popular* was created to cover people with lower incomes. The Federal Government pays 70% of the annual family premium, states provide 20% and patients provide 10%.
- Other social security institutes for particular sectors, for example for members of the military and Mexican Navy Force (*Instituto de Seguridad Social para las Fuerzas Armadas Mexicanas ISSFAM and Secretaria de Marina Armada de México SEMAR*), and for Mexican petroleum workers (PEMEX Medical Services).

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

The public health sector normally faces financial problems and 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.

5. How are the prices of medicinal products regulated?

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. There are no established sanctions for violations of the MRP.

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.

6. When is the cost of a medicinal product funded by the state or reimbursed? How is the pharmacist compensated for his dispensing services?

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. Also, 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.

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.

CLINICAL TRIALS

7. Outline the regulation of clinical trials.

Legislation and regulatory authorities

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 taken into account.

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

Authorisations

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

- Approval by an independent ethics committee registered with the Ministry of Health.
- Approval by the medical institution or institutions where the clinical trials will be conducted. These institutions must be approved by COFEPRIS to conduct clinical trials.
- Clinical trial protocol (including schedule and approximate amount of medicinal products to be imported).
- Written informed consent templates.
- Preclinical and clinical data that justifies conducting the research.
- Description of available resources to conduct the research and to address emergencies (including a statement of sponsorship).
- Written letter by the qualified investigator acknowledging his responsibilities, and data from both him and his staff.

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

Consent

Investigators have to collect informed consent from research participants in a formal written document, 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 sufficient information (knowing 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.

Trial pre-conditions

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.

Procedural requirements

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-SSA1-2012).
- Good manufacturing practices for medicinal products (NOM-059-SSA1-2013).
- Active ingredients (NOM-164-SSA1-2013).
- Interchangeability and biocomparability tests (NOM-177-SSA1-2013).
- Biological products (NOM-257-SSA1-2014).

MANUFACTURING

8. What is the authorisation process for manufacturing medicinal products?

Application

Companies manufacturing medicinal products must obtain a manufacturing licence/approval (*licencia sanitaria*) from COFEPRIS.

Conditions

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-SSA1-2013) 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 operation procedure.
- Biosafety measures.
- Packaging.
- Equipment.
- Destruction and elimination of waste.

Foreign applicants

To hold a marketing authorisation, applicants must have either (*Article 168, Health Law Regulations*):

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

Key stages and timing

The Health Law Regulations set 60 working days as the timeframe for reviewing an application for a manufacturing approval. This is reduced by up to ten working days if the application has been previously reviewed by an authorised third health institution (private/public company authorised by COFEPRIS to review regulatory submissions).

COFEPRIS ensures that applicable NOMs are followed, beginning when a facility begins production and at least every two years after then.

Fee

Government fees for analysing a manufacturing approval application are around US$6,000.

Period of authorisation and renewals

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

Monitoring compliance and imposing penalties

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

- Ensuring compliance with good manufacturing practices and standard operating procedures.
- Ensuring that activities performed do not exceed either authorised limits nor differ from those authorised activities.
- Ensuring that companies perform validation analyses of their manufacturing processes and systems involved.

COFEPRIS is entitled to implement measures on behalf of public health, such as:

- Seizure of products.
- Ordering partial or total suspension of activities, services or adverts.

Under certain conditions, COFEPRIS 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$74,000), to closure of the establishment.

The imposition of administrative sanctions does not exclude civil and criminal liability.

MARKETING

Authorisation and abridged procedure

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

Application

Manufacturers must obtain a marketing authorisation from COFEPRIS to sell any medicinal product. Requirements and timeframes vary among new molecules, biologics, and follow-on products. A NOM compiling the requirements for granting marketing authorisations for medicinal products (NOM-257-SSA1-2013. In addition, there is a draft NOM about the specifications of stability test (PROY NOM-073-SSA1-2014)) was published in 2015 for public comments and review. This draft specifically addressed the test for stability to be carried out on drugs in Mexico (Climate Zone II subtropical with possible high humidity according to the OMS classification).

New molecules. Essentially, applicants for marketing authorisations 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 (*Article 2, section XV Health Law Regulations*):

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

R&D companies can benefit from a special procedure for drugs to be approved for the first time in Mexico, which have been previously approved by a regulatory authority abroad (*see Question 11*).

Generics. Applicants for marketing authorisations have to prove basically 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 setting the test to prove that a generic drug is interchangeable with a reference drug was updated (NOM-177-SSA1-2013). Legally, COFEPRIS should not grant marketing authorisation for generics breaching exclusivity rights (*see Question 11*).

There is a linkage system between COFEPRIS and the Mexican Institute of Industrial Property (IMPI), which aims to prevent the granting of marketing authorisations in violation of patent rights. According to the IP Regulations, IMPI must publish every six months 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 patents). On 31 July 2012, for the first time the IMPI included 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*).

The use patents are included in the Linkage Gazette by court orders, since IMPI consider that they should not be included in the linkage system.

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.

Biologics. Amendments to the legal framework to regulate the approval of biologics are recent and being tested. Applicants have to prove quality, safety and efficacy of their products, under the General Health Law, its regulations and applicable NOMs, particularly, those for good manufacturing practices for medicinal products (NOM-059-SSA1-2013) and for active ingredients (NOM-164-SSA1-2013).

According to the recent NOM-257-SS1-2014 all biologicals drugs that were authorised before the legal reform that are still on the market must enter a regularisation process to comply with the new standard for biologics. NOM 257 emphasises that key points to ensure safety, efficacy and quality of biologics are already regulated in other Mexican Official Standard Rules currently in effect, such as those for clinical trials and pharmacoviligance. NOM 257 empowers the Assessment Subcommittee on Biotech Products (*Subcomité de Evaluación de Productos Biotecnológicos*, known by its initials in Spanish as SEPB) to:

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

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

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

These provisions only apply to renewal applications submitted before 31 December 2015. COFEPRIS, however, missed an opportunity to address the current uncertainty in respect of Regulatory Data Protection for Biologics, as NOM 257 does not provide for guidelines in this regard.

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

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

- In vitro studies.
- A report of comparative test of pharmacokinetic, 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.
- Comparative efficacy and safety clinical test 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. There is currently no indication of a data protection period for biologics. The recognition of data package exclusivity rights for biologics can only currently be achieved through litigation (*see Question 11*). Accordingly, there are also concerns regarding the accurate application by COFEPRIS of the linkage provisions.

Orphan drugs. They were recently 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. Specific rules are still pending. The draft of NOM compiling requirements for granting marketing authorisations includes orphan drugs.

Key stages and timing

Article 166 of the Health Law Regulations sets out the following approval timeframes:

- 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 Molecules Committee is required).

The approval timeframe for biologics and biocomparables is 180 calendar days (*Articles 177 and 177 bis 4, Health Law Regulations*).

These timeframes may vary in practice, but can be reduced if the application has been pre-examined by a third health institution approved by COFEPRIS to do so.

Fee

Government fees for analysing marketing authorisation applications are around:

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

Period of authorisation and renewals

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

Monitoring compliance and imposing penalties

According to the NOM for good manufacturing practices of medicinal products (NOM-059-SSA1-2013), a marketing authorisation holder is responsible for the quality of the approved product. Therefore, when manufacturing through third parties, the marketing authorisation holder has to supervise the manufacturing of the product and establish in agreements liabilities and duties of each party involved. There must be a programme to recall and destroy products that do not meet quality standards (*see Question 20*).

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

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

COFEPRIS can impose strong administrative sanctions for breaches of the legal framework (*see Question 8*).

10. What commitments and pharmacovigilance obligations apply after a company has obtained marketing authorisation? Are there further conditions concerning how the drug is distributed and accessible to patients?

Post-marketing commitments and pharmacovigilance obligations

The Health Law Regulations and the NOM for pharmacovigilance establish that marketing authorisation holders basically must:

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

Holders of marketing authorisations must submit reports periodically.

Other conditions

Good manufacturing practices, stability, and labelling standards and all other applicable provisions must be complied with. There must be a programme to recall and destroy products that do not meet quality standards (*see Question 20*).

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 authorisation.

11. Which medicinal products can benefit from the abridged procedure for marketing authorisation and what conditions and procedure apply? What information can the applicant rely on?

Generics and data package exclusivity

Generics can be approved by providing dissolution profiles or bioavailability studies relating to the innovator product (*see*

Question 9). Therefore, the General Health Law and its regulations allow indirect reliance on innovators' dossiers by approving generics through interchangeability tests, with no protection period for information provided by the innovator. Mexican domestic law is silent about data package exclusivity.

Based on the WTO Agreement on Trade-Related Aspects of Intellectual Property Rights 1994 (TRIPS) and the North America Free Trade Agreement (NAFTA), and the hierarchy of international treaties in the Mexican legal system, the authors' firm has devised a legal strategy to obtain recognition of data package exclusivity for products that deserve this protection, and obtained court precedents recognising and ordering COFEPRIS to observe data package exclusivity.

On 19 June 2012, COFEPRIS published an internal decree on its website, providing guidelines to observe and protect data package exclusivity in Mexico. According to the guidelines (and a minimum term set by NAFTA), a marketing authorisation holder has a five year exclusive right, where his information cannot benefit or be used to support a third party application for registration of a generic drug.

These guidelines show that COFEPRIS is now willing to recognise and protect data package exclusivity, according to NAFTA and TRIPS, and the decree provides a higher degree of confidence for innovators, which has been done and obtained in some cases specifically new small molecules. However, certain issues are not clear and require further clarification, for example:

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

The main issue is the weight and strength of the decree versus the lack of domestic statutory law recognising data package exclusivity (*see Question 26*).

Expedited procedure

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

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

In 2012, COFEPRIS published new rules to set out this new procedure. This is essentially based on the dossier filed with the foreign regulatory agency, to reduce approval timeframes by up to 60 working days. Industry participants have welcomed these new rules, but they are still being tested.

Third institutions approved for pre-examination

A pre-examination of formal and substantive requirements of applications for marketing authorisations by an authorised health institution reduces approval timeframes. A pre-examination does not bind COFEPRIS, but it should indicate the outcome of an application.

12. Are foreign marketing authorisations recognised in your jurisdiction?

Foreign marketing authorisations are not valid in Mexico. However, COFEPRIS has set a special procedure for drugs to be approved for the first time in Mexico, already approved by equivalent regulatory authorities abroad. In this procedure, the requirements for approval of these agencies are recognised as equivalent to those in Mexico (*see Question 11*).

Parallel imports

13. Are parallel imports of medicinal products into your jurisdiction allowed?

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

Regarding IP rights, parallel imports are allowed in Mexico in relation to trade marks 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. However, it is likely that the principle of exhaustion of rights also applies to patents.

For information on pharmaceutical patents, trade marks, competition law, patent licensing, generic entry, abuse of dominance and parallel imports, visit *Pharmaceutical IP and Competition Law in Mexico: overview*.

RESTRICTIONS ON DEALINGS WITH HEALTHCARE PROFESSIONALS

14. What are the restrictions on marketing practices such as gifts, sponsoring, consultancy agreements or incentive schemes for healthcare establishments or individual medical practitioners?

Government officers must not request, accept or receive any gifts or donations from persons whose commercial or industrial activities they are directly linked to, or that they 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 or 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* (CANIFARmarketing authorisation). The corresponding sanctions range from a warning to a fine.

Similarly, CANIFARmarketing authorisation'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.

SALES AND MARKETING

15. What are the restrictions on selling medicinal products? Are there specific regulations for the sale of medicinal products on the internet, by e-mail and by mail order?

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

For advertising on the internet, see *Question 16*.

ADVERTISING

16. What are the restrictions on advertising medicinal products?

Legislation and regulatory authority

The primary legislation on advertising of medicinal products is the General Health Law, its regulations regarding Advertising (*Reglamento de la Ley General de Salud en Materia de Publicidad*) (RLGSMP), and opinions issued by the Advertising Council. The Industrial Property Law (IP Law) and the Federal Consumer Protection Law also have provisions on advertising.

COFEPRIS (health legal framework) and the Federal Attorney's Office of Consumer (PROFECO) (consumer legal framework) are regulatory authorities in this field.

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

Restrictions

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

Prescription medicines cannot be advertised to the general public (*Article 310, General Health Law*).

Any visual or audio advert for non-prescription medicines must bear the message "Consult your physician", and must mention any required precautions when use of the medicine represents any danger, in case of an existing pathology (*Article 43, RLGSMP*).

Prescription medicines can be advertised to health professionals. However, advertising directed to health professionals can only be published in specialised media and it must be based on medical prescription information (*Article 42, RLGSMP*).

The RLGSMP was amended on 19 January 2012, granting COFEPRIS strong powers to require media channels to remove any suspicious illegal advert within 24 hours, and to impose a fine up to 16,000 times the minimum wage (about US$74 ,000).

Internet advertising

Electronic advertising falls under the general rules for advertising in Article 2 of the RLGSMP. COFEPRIS is currently increasing its monitoring of internet adverts for medicinal products, which had been less stringent than those by television or radio.

DATA PROTECTION

17. Do data protection laws impact on pharmaceutical regulation in your jurisdiction?

The primary legislation is the Personal Data Protection Law and its rules. This legal framework requires the person/entity in charge of compliance to observe consent, quality, purpose, loyalty, proportionality, responsibility, security and confidentiality requirements. It relates to the pharmaceutical legal framework, such as in the case of health research and pharmacovigilance.

The NOM for Health Research in Human Beings requires protection of access, rectification, cancellation and opposition rights (ARCO rights) of research participants, by deferring this to the Personal Data Protection Law. Investigators and committees of the institution where the research is conducted must protect personal data of participants, in the research stages and the publishing stages. Investigators must collect informed valid consent from research participants.

The NOM for pharmacovigilance also recognises the protection of personal data of research participants and of healthcare professionals submitting reports, by deferring this to the Personal Data Protection Law.

PACKAGING AND LABELLING

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

Legislation and regulatory authority

Packaging and labelling of medicinal products is regulated by the:

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

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

Information requirements

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 authorisation 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.

Other conditions

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

PRODUCT LIABILITY

19. Outline the key regulators and their powers in relation to medicinal product liability.

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

- Ensuring compliance with good manufacturing practices.
- Ensuring that activities performed do not exceed either authorised limits nor differ from authorised activities.
- Ensuring that companies perform validation analyses of their manufacturing processes and systems.

In case of potential non-compliance, COFEPRIS has statutory authority to:

- Evaluate them *ex officio*, granting procedural rights to those involved.
- Inspect at reasonable times, subject to reasonable limits and in a reasonable manner any place where products are manufactured, packed and/or held for marketing.
- Impose measures to prevent harm, such as seizure and orders to recall products and adverts.
- Impose fines up to 16,000 times the minimum wage (around US$74,000).
- Revoke marketing authorisations and other approvals.

The imposition of administrative sanctions does not exclude civil and criminal liability.

20. Are there any mandatory requirements relating to medicinal product safety?

The NOM for good manufacturing practices of medicinal products (NOM-059-SSA1-2013) requires a programme to recall products that do not meet quality standards to be implemented in an appropriate and efficient manner. This programme should essentially include those activities planned for recalling products in a rapid and effective manner, storage, and a list of authorities to be notified according to the distribution of the product. Marketing authorisation holders must report to COFEPRIS any product recall decision, providing details of these products, causes and a store centre.

In addition, COFEPRIS has a permanent pharmacovigilance programme, based on information on possible adverse effects of the drugs provided, among others, by:

- Doctors and physicians, on a voluntary basis.
- Those who conduct clinical trials. They must submit periodical reports according to the relevant phase (*see Question 7*).
- Pharmaceutical companies. They must submit periodical safety reports each six months or year, according to the year after the granting of the marketing authorisation (*see Question 10*).

For clinical trials and approved health products, severe harmful effects must be reported within 15 days of identification of the effects.

21. Outline the key areas of law applicable to medicinal product liability, including key legislation and recent case law.

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-SSA1-2013) has provisions regarding liability. Recently, the Federal Consumer Protection Law has been amended to allow class actions (*see Question 24*).

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.

22. Who is potentially liable for defective medicinal products?

All those involved in selling and/or distributing medicinal products can be liable in civil actions for harm derived from a defective medicinal product. In this regard, the NOM for good manufacturing practices of medicinal products (NOM-059-SSA1-2013) states that the marketing authorisation holder is responsible for the quality of the approved product. Accordingly, the NOM states that, when manufacturing through third parties, the marketing authorisation holder has to supervise the manufacturing of the product and establish in agreements the liabilities and duties of each party involved.

Physicians are also subject to liability for malpractice. In this case, patients can opt between filing a civil action or require medical arbitration from the National Commission of Medical Arbitration (CONAMED). The latter is a quick alternative where a non-judicial solution is proposed.

23. What defences are available to product liability claims? Is it possible to limit liability for defective medicinal products?

Equitable defences are available. Available defences include:

- Statutes of limitations (which ranges from two to ten years). Under the Civil Code, liability for any illicit action (excluding criminal offences) expires after two years.
- Assumption of the risk and contributory negligence.

24. How can a product liability claim be brought?

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.

Class 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.

25. What remedies are available to the claimant? Are punitive damages allowed for product liability claims?

Preliminary injunctions can be ordered to stop the commercialisation and distribution of a product. Monetary compensation is the most common remedy but equitable remedies are also available.

Punitive damages are not subject to regulation and there are no public precedents to make estimations in this regard.

REFORM

26. Are there proposals for reform and when are they likely to come into force?

Data package exclusivity

Since data package exclusivity periods were not expressly included in amendments to the General Health Law (as was expected, to bring domestic law in line with international treaties), a proposed amendment to the law was published in the *Gazette of the Congress* in February 2011. The proposed amendment concerns Article 376 of the General Health Law, and intends to create a five-year data package exclusivity period for innovator products. The following points should be considered:

- The word "interchangeable" in Article 376 should be removed, since there is no longer any distinction made between "generics" and "interchangeable generics".
- The proposal does not make specific distinctions between the protection of new chemical entities, formulations and new indications.
- The proposal limits the scope of data package exclusivity to five years, while NAFTA establishes the five-year period as a minimum.
- The proposal seems to be limited to allopathic medicines of a chemical nature, as there is no specific mention of biological drugs. In other jurisdictions, biological drugs obtain a longer protection period.

Transpacific Partnership

In November 2011, during the Asia Pacific Economic Cooperation (APEC) meeting, Mexico showed its interest to initiate consultations to participate in the Trans-Pacific Partnership (TPP). On 18 June 2012 during the G20 in Los Cabos, Mexico, the countries participating in the TPP decided to invite Mexico to participate.

Regarding intellectual property, the TPP partners remain confident that copyrights, patents and trade marks will be enforced. There appears to be general consensus that the standard of protection for intellectual property should go beyond TRIPS.

The terms, conditions and wording of the TPP remain confidential. However, it has been made public that the main topics regarding intellectual property include effective customs measures, pharmaceutical patents, and agrochemical patents.

In the case of pharmaceutical patents and regulation, the main topics appear to be that the countries commit to have additional mechanisms of intellectual property protection such as:

- Patent linkage.
- Extensions or compensation for the life term of patents due to regulatory delays.
- Data package exclusivity for new chemical compounds and formulation and second uses.

Mexico has implemented the first steps towards TPP, since the WIPO Protocol Relating to the Madrid Agreement Concerning the International Registration of Marks 1989 (Madrid Protocol) entered into force in Mexico at the beginning of 2013. The rushed approval of this, without a full review of the trade mark system (and assuming IMPI is prepared to properly adopt the Madrid Protocol system) is a good indication that the Mexican government is willing to fulfil the standards of the TPP, and replicate the enactment of the IP Law 1991 when NAFTA started to be discussed.

Due to the negotiations and eventual integration of Mexico into the TPP, Mexico has a new and valuable opportunity to review and change its entire intellectual property system and adopt higher, and more importantly, more efficient standards of intellectual property protection.

For information on pharmaceutical patents, trade marks, competition law, patent licensing, generic entry, abuse of dominance and parallel imports, visit *Pharmaceutical IP and Competition Law in Mexico: overview*.

ONLINE RESOURCES

The COFEPRIS website (Federal Commission for Protection against Sanitary Risk (COFEPRIS) (*www.cofepris.gob.mx*) and the Mexican Institute of Industrial Property (IMPI) website (*www.impi.gob.mx*) contain official updated of life sciences related legislation, in Spanish. As far as the authors know, there are no websites that provide reliable and up to date English translations.

Practical Law **Contributor profiles**

Alejandro Luna Fandiño, Partner

Olivares & Cia
T +52 55 5322 3080
F +52 55 5322 3001
E alf@olivares.com.mx
W www.olivares.com.mx

Professional qualifications. Mexico, Bachelor Degree, Universidad Latinoamericana 1996; four diplomas, Universidad Panamericana.; IP LLM, Franklin Pierce Law Center, US

Areas of practice. Biotechnology/pharmaceutical law; intellectual property litigation; anti-piracy; anti-counterfeiting; alternative dispute resolution and IP enforcement.

Recent transactions

- Participated in cases against the unconstitutionality and inefficiency of certain amendments to the Federal Law of Administrative Proceedings in Mexico, which have affected the venues for challenging resolutions by the Mexican Institute of Industrial Property.
- Sponsor of a proposal to modify the litigation system of industrial property, limiting the Mexican Institute of Industrial Property to an exclusive registration authority, transferring jurisdiction to civil courts for infringement cases, and to administrative courts for cases related to the annulment of trade mark registrations and patents.

Languages. English, Spanish

Professional associations/memberships. Former Vice-President of the Mexican Association for IP Protection (AMPPI); member of the International Trademark Association (INTA).

Publications

- *Imports shine the spotlight on experimental use defence, 2013, Intellectual Asset Management magazine issue, published by the IP Media Group.*
- *Maximising IP rights in the life sciences industry, 2012, Intellectual Asset Management magazine issue 54, published by the IP Media Group.*
- *New Regulations Pending, 2011 edition of Life Sciences, Mexico Chapter: Biologic Drugs; published by Managing Intellectual Property Magazine.*
- *Supreme Court upholds the worth of formulation patents, 2010, IAM Life Sciences 250, Formulation patents in Mexico.*
- *Pharmaceutical trademarks. World Trademark Review, Country correspondent: Mexico, October/November 2009.*

Armando Arenas, Associate

Olivares & Cia
T +52 55 5322 3000
F +52 55 5322 3001
E ara@olivares.com.mx
W www.olivares.com.mx

Professional qualifications. Mexico, Bachelor Degree by National Autonomous University of Mexico (UNAM), 1995.

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

Recent transactions

- First case in Mexico where a marketing authorisation of a pharmaceutical product was revoked for being in violation of a formulation patent listed in the Linkage Gazette.
- First case in Mexico of a use patent being effectively enforced in Mexico related to public tender.
- The unconstitutionality of Article 167bis of the Health Supplies Regulation, as it does not provide the right of the titleholder of a patent to be heard during the prosecution of the marketing authorisation.

Languages. English, Spanish

Professional associations/memberships. Mexican Association for IP Protection (AMPPI).

Publications

- *Preliminary injunctions and infringement actions. Intellectual Property and Pharmaceutical Research*, January 2012.
- *Approval of follow-on biologics in Mexico. Intellectual Asset Management.* July/August 2011.
- *Reform of preliminary injunctions. Managing Intellectual Property.* October 2010.
- *Trademark enforcement. World Trademark Review.* June/July 2009.
- *Composite trademarks. Managing Intellectual Property.* January 2009.
- *COFEPRIS ordered to cancel marketing authorisation. Managing Intellectual Property.* March, 2015.