The Pharma Legal Handbook

Mexico

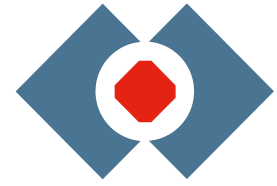
Regulatory, Pricing and Reimbursement Overview · Preclinical and Clinical Trial Requirements · Marketing, Manufacturing, Packaging and Labeling Advertising · Traditional Medicines and OTC Products · Product Liability · Patents and Trademarks · Regulatory Reforms · Cannabinoid Drugs, Medicinal Cannabis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

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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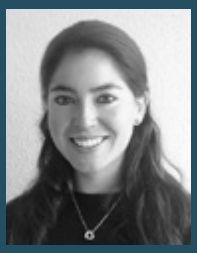
Alejandro joined OLIVARES in 1996 and became a partner in 2005. He Co-chairs the Life Sciences & Pharmaceutical law and industry group and also he coordinates the litigation department. Alejandro has been crucial to the heart of Mexico's intellectual property legal system as one of the few true patent-regulatory litigation experts in Mexico.

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



INGRID ORTÍZ

Ingrid joined OLIVARES in 2011. She studied law at Monterrey Institute of Technology and Advanced Studies (by its acronym in Spanish "ITESM", Tecnológico de Monterrey) in Mexico City.

Ingrid is member of the Life Sciences & Pharmaceutical law at OLIVARES. Her practice is mainly focused on Intellectual Property Litigation, Regulatory and Administrative Litigation; as well as Regulatory and Compliance advisory.

Her main areas of practice allow her to interact with the Mexican sanitary agency, the Federal Commission for Protection against Sanitary Risks (by its acronym in Spanish "COFEPRIS"), the Mexican Patent and Trademark Office (by its acronym in Spanish "IMPI"), and the Courts of law, such as the Federal Court of Tax and Administrative Affairs, the Federal District Courts and the Federal Circuit Courts.

ERWIN CRUZ

Erwin Cruz is member of the Olivares' Life Science Law Group since 2008, assisting clients to add value to their businesses and projects in Mexico. He achieves this commitment, for example, not only by getting exclusive rights to clients, but also by developing and successfully implementing strategies to enforce exclusive rights and fair trade rules against potential infringers. Erwin provides high qualified regulatory assistance related to products' marketing, labelling and advertising.

He has extensive expertise on Intellectual Property Rights and Regulatory compliance related to Pharma, Agro and Software industries. He constantly participates in international and national conferences, and meets key authorities in Mexico for these industries, such as the Patent and Trademark Office (IMPI), the Healthcare Products Regulatory Agency (COFEPRIS), the Plant Breeders' Rights Office (SNICS) and Bureau of Consumer Protection (PROFECO).

Erwin has written several articles over litigation and regulations for pharmaceuticals, biotechnologies, agribusinesses, food and beverages.

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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. These laws and 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 private sector, there is no reimbursement in Mexico.

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. There is a NOM compiling the requirements for granting marketing authorizations for medicinal products (NOM-257-SSA1-2013). In addition, a NOM about the specifics of the stability test (NOM-073-SSA1-2015) was published in 2016. This NOM 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). 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 Molecule 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.

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 (article 2, section XV Health Law Regulations):

- 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 basically 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 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 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, 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). 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.

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 biocomparable must use the corresponding reference biologic to perform comparative and physic-chemical studies. For this, the applicant must have to submit essentially: