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CLINICAL TRIALS HANDBOOK
Americas

MEXICO

Mexico

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Introduction

Prior authorization from the Mexican authorities is required for any experimental use in Mexico of novel drugs, materials, devices or procedures that is conducted on human beings for scientific research and for demonstrating preventive, therapeutic or rehabilitative properties.

Competent authorities

In Mexico, the two main competent authorities for clinical trials and health research are the following[1]:

- The Federal Commission for Protection against Sanitary Risks (**COFEPRIS**)[2]
- National Bioethics Commission (**CONBIOÉTICA**)

Regulatory framework

The regulatory framework governing clinical trials in Mexico includes the following:

- General Health Law (**GHL**)
- Health Research Secondary Regulations (**CRSR**)
- Official Mexican Standard NOM-012-2012 on health research projects in humans ("**NOM 012**")
- Official Mexican Standard NOM-177-SSA1-2013 on bioequivalence and biocomparable studies ("**NOM 177**")
- 2012 COFEPRIS' Guidelines for Good Clinical Practice ("**Clinical Trials Guidelines**")
- The 2012 Decree for the Operation of Ethics Committees ("**Ethics Committee Decree**")
- Federal Law for the Protection of Personal Data Held by Private Entities ("**FDPL**") and its implementing regulations

In general, clinical trials (Phases I to IV) should: (i) be preceded and supported by pre-clinical data; (ii) be conducted in accordance with scientific and ethical principles; (iii) be performed with the informed consent of the participating human subjects; (iv) be executed under a research protocol; (v) be overseen by a principal investigator; (vi) be performed in sites that are licensed healthcare institutions; and (vii) obtain the relevant approvals of the healthcare institution, the ethics committee and COFEPRIS.

For a long time, the operation of ethics committees at each healthcare institution was largely self-regulated and based on international best practice. There was also a lack of coordination between COFEPRIS and CONBIOÉTICA. However, since the Ethics Committee Decree was issued in 2012, there is now a clearer legal framework for these

[1] The regulation foresees that the General Health Council is also competent for issuing general provisions in relation to clinical trials; however, it has not exercised such authority in practice.
[2] State-level sanitary agencies can conduct inspection visits according to the relevant Coordination Agreement signed with COFEPRIS.

committees, thereby establishing its structure, objectives, the roles of its members, and the applicable requirements for their registry before both CONBIOÉTICA and COFEPRIS.

The Clinical Trials Guidelines make a clear reference to international best practice and guidelines, including standards developed by the International Conference on Harmonisation (ICH). The guidelines are the basis for the current certification system, for which COFEPRIS is responsible to authorize the research centers to conduct clinical research and the research protocols.

In addition, other regulatory measures promote Mexico as a place for conducting clinical research. These include the following:

- Article 170 of the Health Supplies Secondary Regulations RIS requires the submission of a clinical trial report, provided that the Mexican population was included in the trial to obtain a marketing authorization of a drug produced abroad. This allows Mexico to be the first country of registration of the product.
- COFEPRIS has authorized several public hospitals and one public university — all with extensive experience in clinical research — as Third Authorized Parties for the pre-approval of research protocols. If their report is positive, approval times at COFEPRIS are reduced significantly.

Clinical researches are classified according to the potential risk they represent:

1. Research without risk (e.g., questionnaires, interviews and revision of clinical files)
2. Research with minimum risk (e.g., weighing the subject; obtaining placenta during birth; the collection of saliva and extraction of blood from generally healthy adults)
3. Research with higher risk (e.g., radiologic studies, experimental drugs)

Moreover, clinical evidence gathered from authorized clinical trials is required to obtain the marketing authorization (MA) of drugs and medical devices. Whereas innovative drugs require full clinical data (Phases I-III), subsequent entry products require less clinical information. In the case of generic drugs, only bioequivalence studies on healthy subjects are required. In the case of biosimilar drugs, only biocomparable clinical trials are required.

Securing authorization

The procedure for securing authorization to undertake a clinical trial of a pharmaceutical involves three basic steps, which are sequential and cannot be applied for in parallel:

- Favorable opinion of the research protocol from the ethics committee of the healthcare institution where the trial is to be conducted, which according to the ethics committee must be decided within 30 business days from filing
- Approval of the research protocol from the director of the healthcare institution where the trial is to be conducted, which must take place under its relevant internal rules
- Authorization of the research protocol from COFEPRIS, which according to the Federal Law on Administrative Proceedings must be decided within three months of filing

General requirements for authorization from COFEPRIS include the following: (i) information from the sponsor, including the clinical trial agreement (CTA) if a contract research organization (CRO); (ii) information on the site, including its notice of operation, the authorization from the director of the healthcare institution, the available resources for conducting the research, and the resources for attending to any emergency during the research; (iii) information from the ethics committee, including its certificate of registration, the list of members and its favorable

opinion of the protocol; (iv) research protocol, including a complete analysis of the risks for the human subjects; (v) informed consent forms; (vi) investigators' manual, including a summary of pre-clinical and a full description of the experimental product; (vii) information from the principal investigator, including his curriculum vitae, his license to practice medicine, his acceptance letter and his commitment to report adverse events; (viii) information of the research team, including their curricula vitae and their licenses to practice; (ix) schedule of activities; and (x) information of all related health inputs, including descriptions and quantities of drugs and medical devices to be used.

Conduct and results

After protocols have been authorized by COFEPRIS, all trials are recorded in the National Registry of Clinical Trials (RNEC). The information contained in the RNEC is collected by COFEPRIS in collaboration with those responsible for conducting the clinical trial (the sponsor, CRO or healthcare institution). The RNEC publishes an electronic database that only includes general information from the clinical trials. Confidential information is not included in the RNEC, nor are the personal health data of patients, which will be regarded as sensitive personal information under privacy laws and will be protected accordingly.

There is no binding provision to disclose or publish the results of clinical trials, but the Code of Ethics of the Council for Ethics and Transparency of the Pharmaceutical Industry (CETIFARMA) does contain a specific obligation for sponsors to disseminate the positive and negative results of the trials, particularly any adverse events.

Clinical trial agreements

To initiate any research with human subjects, there must be prior informed consent, elaborated by the principal investigator and approved by the ethics committee of the institution where the research will take place.

In the case of research with minimum risk, the ethics committee, for justified reasons, may authorize that the prior informed consent not be written, and in the case of research without risk, may even exempt the need of prior informed consent.

The GHL establishes that the sponsors and the research institution are responsible for the medical treatment that may be required for the damage caused by the clinical trials, as well as the indemnification that legally corresponds from any harmful consequences of the research.

The guaranty may be a bond, insurance or any other means that the competent health authorities consider valid and sufficient for covering potential costs.

There are no special requirements regarding the effects of authorizations corresponding to different trial phases, except that the clinical data produced in one phase is submitted on the next one.

Sponsor and contract research organizations

The operation of CROs is not fully regulated in Mexico. There are only explicit references found in the Clinical Trial Guidelines. However, there is no restriction with regard to delegating responsibilities of the sponsors to these entities.

There is no requirement for the sponsor to be located in the country and/or region where the clinical trial is taking place. The sponsor may be represented locally by a third party.

The liability of such third party shall be determined in the respective agreement, which is not subject to approval as such of the health authorities.

Investigator

The principal investigator will be in charge of the research. He or she must: (i) be a health professional; (ii) have adequate academic training and experience to supervise the corresponding research; and (iii) be affiliated with the health institution in which the investigation will be performed.

The principal investigator will be in charge of all technical aspects of the project and will have the following functions:

- Preparing the investigation protocol
- Complying with the procedures indicated in the protocol and requesting authorization for amendments in necessary cases regarding ethical and biosafety aspects
- Documenting and registering data generated during the investigation
- Creating an investigation file, which shall contain the protocol, amendments to it, data generated by the authorities, the final report, and all documental and biological material to be saved and related to the investigation
- Selecting the personnel who shall participate in the investigation and providing them with the information and training required to be able to develop their functions, and keeping them updated on the generated data and its results
- Preparing and presenting the partial and final reports of the investigation
- Taking other similar actions that may be necessary to comply with technical requirements

In case of adverse health effects in the course of the investigation, the principal investigator shall inform the ethics committee of all possible adverse effects or those directly related to the investigation.

The board of the institution in which the investigation is being undertaken will also give notice to the health authorities about the existence of any adverse effect, no later than 15 business days from the time of occurrence.

Study drugs

In general, an authorization for the experimental use of medical products is required from COFEPRIS. However, as an exception, in case of an emergency in the treatment of a sick person, a physician may use a new therapeutic or diagnostic resource if there exists a justified possibility of saving a patient's life, restoring his or her health, or lessening, if not removing, his or her pain. The conditions to be met are as follows: (i) to have written consent from the patient or his or her representative/relatives; and (ii) to obtain subsequently the approval of the research and/or ethics committees.

There are no binding provisions requiring the publication of the study results. The CRSR establishes only that the principal investigator may publish partial and final reports of the investigation and disclose its discoveries. In contrast, the Code of Ethics of CETIFARMA does contain a specific obligation for sponsors to disseminate the positive and negative results of the trials, particularly any adverse events. In any case, any publication would have to respect the privacy/confidentiality of the patient's personal information.

Likewise, the CRSR sets forth that besides giving credit to the associated investigators and the technical personnel that participate in the investigation, a copy of these publications must be provided to the administration of the institution in which the investigation was carried out.

Intellectual property

There could be several Intellectual Property Rights (IPRs) involved in clinical trials. This could include: (i) existing patents over the active substance; (ii) existing patents over the manufacturing process; (iii) existing trademarks over the experimental drug; (iv) new copyright over the research protocol; (v) new copyright over the databases to be compiled; and/or (vi) new protection over the resulting clinical data, also known as data exclusivity. For that reason, IPRs are typically an important section of a CTA.

In Mexico, data exclusivity has been granted until very recently. Although the North American Free Trade Agreement (NAFTA) contained specific obligations in this regard, the Ministry of Health had traditionally opposed this form of protection. This started to change in 2012, when it issued internal guidelines that recognized limited forms of data exclusivity. COFEPRIS currently recognizes data exclusivity for clinical data relating to chemical drugs only, for a period of five years from the date of the marketing authorization. Although it can be obtained through litigation, the internal guidelines currently exclude biologics, biotech and orphan drugs. This, however, will change eventually with the Trans Pacific Partnership (TPP), which contains specific obligations for biologics/biotech drugs.

Privacy and data protection

Patient information is considered as personal data; specifically, any information that may reveal the present or future health condition of an individual would also be considered personal sensitive data. There are at least two sets of laws governing the processing of health-related information in Mexico: one for private entities and one for public entities. The first encompasses the processing of personal data held by private entities, such as companies, non-profit organizations and individual professionals, such as physicians working in the private sector. The second covers the processing of personal data held by public entities, such as agencies pertaining to the public administration, government-owned hospitals and research institutions, and physicians working in the public sector. While the first domain is regulated at the federal level by the FDPL, the second domain is regulated both at the federal and local level, and privacy-related provisions exist both in local privacy laws and public access laws. In view of the above, rules applicable to the processing of a patient's data in the context of clinical trials may vary significantly, depending on the nature of the host institution, the sponsors, the CROs and the patient. It is therefore in the best interest of all parties involved in the clinical trial to map at the outset the types of privacy laws that will apply to the trial and onward processing, and to design, implement and maintain the appropriate controls, measures and safeguards to allow for the appropriate collection, transfer and storage of sensitive data. In general, consent from the data subject is required for the processing of personal data, including the cross-border transfers of personal data or sensitive personal data. The transfer of such data is permitted as long as the proper disclosure of information has been made through a privacy notice, and certain contractual, security and technical measures and controls are in place.

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