Baker McKenzie.

CLINICAL TRIALS HANDBOOK
Americas

ARGENTINA

Argentina

Vanina Caniza | María Magdalena Podio | Guido Demarco

Introduction

On a federal level, clinical trials conducted in Argentina are regulated and supervised by the National Administration of Drugs, Food and Medical Technology (*Administración Nacional de Medicamentos, Alimentos y Tecnología Médica* or ANMAT), the application authority under the Argentine Ministry of Health (MH). In addition, and depending on the Argentine jurisdiction where the trial is to be conducted (e.g., province), other local regulators are likely to be involved.

Regulatory framework

On a federal level, clinical trials are primarily governed by the following regulations, as amended and supplemented from time to time:

- ANMAT Disposition No. 969/97 as amended by ANMAT Disposition No. 6550/08 (Applicable Regime to the Clinical Studies for Medical Devices)
- ANMAT Disposition No. 6677/10 (Good Clinical Practices Regime for Clinical Pharmacological Studies)
- MH Resolution No. 1480/11 (Good Practices Guide for Clinical Investigations on Human Beings)

The main regulations that have been listed above were inspired by the ethical guidelines for the conduct of clinical trials stipulated under several international declarations and principles, such as those issued by the World Health Organization (WHO) and by the Council for International Organizations of Medical Sciences (CIOMS).

The federal regulations in force have been modified in the last years, establishing regulatory distinctions between trials involving molecule-based Investigative Medical Products (IMPs) or study drugs of biological origin. This issue has been discussed within the scientific community and the pharmaceutical industry, and has finally impacted local Argentine regulations now that studies on biological drugs are specifically regulated within the framework of ANMAT Decision No. 6677/10.

Despite the fact that many Argentine jurisdictions have adhered to the regulations stipulated by ANMAT and by the MH at a federal level, a case-by-case analysis of the applicable legal framework is recommended to determine the application of specific local regulations to a given clinical trial.

In addition to the sanitary regulations outlined above, it is important to note that clinical trials conducted in Argentina will be subject to other federal regulations of vital importance, such as Data Protection Regulations and Law No. 26,529 (on patients' rights and informed consent), enacted in 2009.

The Personal Data Protection Law (PDPA), sets forth the legal framework for the protection of personal data entered in public or private files, registers, databases and other technical means for the treatment of data, meant to provide reports on such data. The purpose of the PDPA is to protect the honor and privacy of the individuals to whom such data refers ("Data Subjects") and to guarantee their access to all registered information about them.

Under the PDPA, information referring to the health of the Data Subjects is considered "sensitive data." As a general rule, the PDPA forbids the treatment, transfer and creation of databases containing sensitive data.

All the information included in this section are exclusively based on federal regulations in force.

Clinical trial agreements (CTAs)

ANMAT's prior authorization is required for any protocol in Phases I, II or III. Phase IV protocols require prior authorization only in certain specific cases (e.g., those using a placebo control group).

In general terms, and prior to submission for approval with ANMAT, clinical trials should be described in a clear and detailed protocol and approved by an independent ethics committee, which will ensure that the subjects' security, integrity and protection are respected. The ethics committee shall be independent from the investigators participating in the trial and must be integrated by individuals from different fields, including professionals of different disciplines and individuals or entities renowned for their commitment to ethics and the defense of human rights. The composition and work plan of the ethics committee must be reported to ANMAT, together with all other documents and information required for filing under the regulations in force. If the center where the trial is to be conducted has an internal ethics committee (*Comité de Docencia e Investigación*), approval by such committee is also necessary.

Other required notices and authorizations include: (a) an authorization issued by the highest authority within the institution or center where the study is to be conducted; (b) evidence that due notice of filings with ANMAT was given to the highest sanitary authority within the jurisdiction where the trial is to be conducted; and (c) approval of the informed consent forms by the Personal Data Protection Authority (*Dirección Nacional de Protección de Datos Personales* or DNPDP).

ANMAT has been empowered with broad control authority, which survives even after the termination of the trials, to protect the safety of the research subjects. At all times, ANMAT can access and inspect the medical centers where the trial is being conducted in order to: ensure that the Good Clinical Practices are met; analyze and keep the reports submitted by the principal investigators; meet and interview the subjects participating in the trial; and even interrupt the trial if deemed appropriate (i.e., subject injuries, breach of protocol or informed consent).

All CTAs must reflect the obligations, rights and guarantees by which the parties to the agreement (typically the sponsor and/or the principal investigator and/or the center where the trial shall be conducted) shall abide and the economic arrangement between them, all in accordance with the regulations in force.

The CTAs shall be submitted for review by the ethics committee and evidence of such submission must be filed with ANMAT.

The party responsible for filing for authorization with ANMAT is, in principle, the sponsor.

Both the sponsor and the principal investigator share certain obligations regarding reporting duties (e.g., periodic reporting duties, reports on Serious Adverse Events and Reactions) toward ANMAT and the ethics committee.

The sponsor shall ensure that all drugs, products and procedures related to the trial are provided for free to the research subject. In addition, and according to Resolution MH 1480/11, the sponsor must ensure that adequate insurance or other coverage is taken in order to cover for all costs and expenses involved in the trial and to cover for any risk or potential damage suffered by the research subjects.

As anticipated, only some Phase IV studies require ANMAT's prior approval (e.g., those using a placebo control group). In general terms, CTAs for Phase IV protocols requiring ANMAT's prior approval should not substantially vary from those for Phase I, II or III studies.

CTAs for Phase IV studies that do not require ANMAT's approval could be simpler, in the understanding that there are less regulatory requirements related to the submission to ANMAT of documents and information. This tends to give more freedom for the parties to negotiate the terms of agreement.

The Phase IV studies that do not require ANMAT's prior authorization should nonetheless be previously authorized by an independent ethics committee and by the center's Investigational Ethics Committee (Comité de Docencia e Investigación), as applicable. In these cases, only the notice of the initiation of the study must be given to ANMAT. This notice shall be deemed to constitute a sworn statement.

Sponsor and contract research organizations (CROs)

In principle, the sponsor is responsible for the initiation, management, supervision and financing of the clinical trial.

The sponsor is also responsible for the following, among others:

- Obtaining approval for the conduct of the trial from the intervening centers, the ethics committee/s and the regulatory authority
- Appointing the appropriate investigator and center/s
- Supplying all trial materials and necessary funding for the conduct of the trial
- Hiring adequate insurance to cover all costs involved in the study and any damage that ma be suffered by the research subjects
- Monitoring the development of the trial and compliance with the protocol
- Suspending the trial in case of deviations from the protocol that may endanger the safety of the subjects
- Ensuring adequate registration of all data related to the trial, compliance with data protection regulations, as well as keeping and making available the trial data

Some of the obligations imposed on the sponsor by the regulations in force may be undertaken jointly with and/or delegated to other parties (e.g., CRO, investigator, monitoring committee).

Despite the fact that there is no express stipulation in this respect, and considering that the sponsor is commonly a foreign pharmaceutical company or medical device manufacturer, it has become a fairly widespread practice for the foreign sponsor to appoint another party to act as its local representative vis-à-vis the sanitary authority (the principal investigator or a CRO). In these cases, ANMAT performs a very strict review of the information provided to the research subjects in the informed consent forms to make sure, among other things, that the following are clear: (a) all drugs, products and procedures involved in the trial will be provided free of charge to the research subject; (b) the party responsible for the trial and for supplying all necessary materials and procedures; (c) contact person in case of an adverse event/effect or in case of damage suffered by the research subject; (d) compensation and treatments are available in case of damage or injury suffered in connection with the trial; and (e) adequate insurance will cover any damage caused to the research subject.

In principle, whoever acts as local sponsor vis-à-vis the sanitary authority will ultimately undertake joint and several liability for the conduct of the trial, together with the actual sponsor.

The sponsor may delegate some of its obligations to a CRO, provided that the scope of such delegations is detailed in writing. If the sponsor's obligations are delegated to a foreign CRO, the regulations in force require that the CRO has a local representation in Argentina in accordance with Argentine laws.

The sponsor will retain ultimate liability for the obligations it has delegated to the CRO. In turn, the CRO will undertake the sponsor's obligations under the regulations in force, and could thus become jointly and severally liable with the sponsor for the conduct of the trial vis-à-vis the competent authorities and the research subjects.

Notwithstanding the foregoing, it is common for the sponsor and the CRO to insert indemnity clauses in the CTAs to govern the procedures for the reciprocal reimbursement of any expenditures they have been obliged to make as a result of their joint and several liability vis-à-vis the authorities and the research subjects.

The agreements signed between the sponsor and/or the investigator and/or the institution (including economic arrangements) must be submitted for review by the ethics committee in order to obtain approval for the trial.

Although the submission of the CTA to the regulatory authority is not expressly required, the agreements and financial aspects of the trial between the sponsor, the investigator and the institution/center shall be made in writing and will be part of the trial documentation. The sanitary authority has broad powers to request their submission at any time if it deems necessary.

Investigator

Under Argentine law, the investigator is responsible for conducting the clinical trial. Some of the duties and obligations of the investigator are: (i) to conduct the clinical trial in accordance with the protocol; (ii) to inform the trial subjects of all relevant aspects of the study and to obtain their informed consent; (iii) to store and safeguard all the materials involved in the clinical trial; (iv) to perform record keeping and reporting obligations; and (v) to make a study completion filing with the institution, the sponsor, the ethics committee and ANMAT upon conclusion of the trial.

The investigator shall not implement any deviation from, or changes to, the protocol without agreement of the sponsor and prior review and documented favorable opinion from the ethics committee and ANMAT.

The investigator should immediately report serious adverse events to the ethics committee, the sponsor and ANMAT, except for those serious adverse events that the protocol or other documents identify as not requiring immediate report. The immediate report should be followed by detailed written reports. During and following a subject's participation in a trial, the investigator/institution should ensure that adequate medical care is provided to a subject for any adverse event, including clinically-significant laboratory results, related to the trial.

When the investigator is a public official (i.e. physician employed by a public hospital) and the study is to be conducted in public facilities, authorization from the public institution must also be obtained, and special requirements will apply to the agreement depending on the jurisdictions involved.

Study drugs

As indicated in the beginning of this Chapter, ANMAT is in charge, among other things, of approving and supervising clinical trials carried out in Argentina. The sub-agency specifically in charge of clinical trials is the Clinical Trials Commission of the Direction of Evaluation of Medicines and Similar Products (*Comisión de Ensayos Clínicos de la Dirección de Evaluación de Medicamentos y Afines*).

As explained, ANMAT's prior authorization is required for any protocol in Phases I, II or III. Phase IV protocols require prior authorization only in certain specific cases (e.g., those using a placebo control group).

In addition, and as previously explained in this chapter, the sponsor undertakes the responsibility of financing the trial and is required to provide study drugs for free and to finance medical procedures provided for in the protocol.

Under the Argentine Civil Liability Regime, whoever causes damage to another must repair such damage. The extension of the obligation to indemnify will vary, not only depending on whether the damage was caused in the context of a contractual relationship or arising from liability in tort, but also on whether the obligation to repair the

damage depends on subjective factors (i.e., willful misconduct or negligence) or objective factors (such as the liability placed on the principal for the actions of its dependents, or for damages caused with perilous objects). Moreover, the diligence (which serves as parameter to determine a negligent conduct) expected from the damaging party will vary according to particular circumstances, such as profession and nature of the services rendered under a contract.

In a hypothetical scenario whereby a trial subject suffered damage while undergoing a particular clinical trial, any limitations of liability included in the CTA or in the informed consent forms might be subject to judicial scrutiny. In principle, and although the sponsor/investigator could eventually attempt a defense based on its diligence throughout the development of the study, or could prove that the alleged damage was caused by the actions of the study subject himself or herself, a third party for whom the sponsor/investigator is not responsible, or is an act of God or force majeure event, the court could still interpret that the sponsor/investigator has profited from the conduct of the trial in which the aggrieved trial subject was enrolled, and is therefore liable.

Argentine courts tend to grant sentences that include the obligation to compensate items, such as loss of profit and moral damage.

The limitation of liability provisions are generally not included in the informed consent forms because they are usually objected to by ANMAT and/or the ethics committee.

Investigators are required to make a study completion filing with the institution, the sponsor, the ethics committee and ANMAT upon conclusion of the clinical trial. The Registry of Clinical Trials on Human Beings has been created with the purpose of consolidating the information related to clinical trials, and to make it available to all biomedical areas, to health care personnel and to the scientific community in general. The incorporation of information to the registry is mandatory for health institutions and sponsors. The confidentiality of the records identifying the subject shall remain inviolate, and they shall not be made public. If the results of the study are published, the subject's identity shall remain protected and confidential.

The publication of the results of the investigations, both positive and negative, is highly recommended as they: (i) facilitate transparency; (ii) avoid the repetition of studies already carried out; and (iii) prevent new participants from taking unnecessary risks. To ensure the integrity of scientific information and promote the highest standards of professional conduct, investigators should present their results in publications or peer-reviewed scientific conferences before communicating them to public media or patient associations.

The investigator should, through prior agreements with the sponsor, ensure continuity of treatment for the trial subjects once their involvement in the study has ended, if its interruption endangers their well-being. The continuity of the treatment or the supply of products to be used should be expressly authorized by ANMAT. In turn, the ethics committee should verify compliance thereof.

Specifically, Resolution MH 1480/11 states that at the end of the investigation, all participants should share the benefits that have arisen from it, such as by continuing to receive the treatment that has been identified as the most beneficial. If it is not possible to ensure that treatment, they must be guaranteed access to appropriate treatments or other suitable alternative benefit approved by the ethics committee and for a determined period of time, or until their access is guaranteed by other means.

Although debatable, it could also be argued that the sponsor has to continue delivering the study drug to trial subjects until such drug becomes available and authorized in Argentina.

Intellectual property (IP) and data

Pursuant to Section 82 of the Employment Contract Law (**ECL**), the employee is the owner of all inventions or discoveries made by him or her, even when he or she had made use of instruments not belonging to him or her.

Nevertheless, according to the second paragraph of Section 82 of the ECL, the employer is the owner of all the inventions and discoveries deriving from industrial or manufacturing processes, methods or facilities of the establishment, or from experiments, research, improvements or betterment of those already existing, as well as of all inventions, discoveries, formulae, designs, materials and combinations that may be obtained, should the employee be hired for such purpose.

Ownership over inventions developed by the employee has to be analyzed on a case-by-case basis.

The employee may not waive in advance his or her rights to the invention and to a fair compensation, and all terms setting forth said waivers are deemed null and void (Section 10, subsection f of Law 24,481). Therefore, agreements on this issue shall be valid when they provide for a fair compensation, suitable for each case.

The existence of agreements related to compensations corresponding to the ownership of inventions is unusual, mainly because the compensation owed to the owner of the invention must be set in each particular case and because agreements in which employees waive their ownership on inventions in advance are null and void.

Investigator-initiated trials

Investigator-initiated trials are permitted in Argentina. Pharmaceutical companies may finance such trials (but would consequently undertake the corresponding liability of such financing). However, when the investigator initiates and conducts a trial without any other sponsorship, he or she undertakes the responsibilities of the sponsor under the regulations in force.

Baker McKenzie helps clients overcome the challenges of competing in the global economy.

We solve complex legal problems across borders and practice areas. Our unique culture, developed over 65 years, enables our 13,000 people to understand local markets and navigate multiple jurisdictions, working together as trusted colleagues and friends to instill confidence in our clients.

www.bakermckenzie.com