Baker McKenzie.

CLINICAL TRIALS HANDBOOK
Americas

COLOMBIA

Colombia

Diana Bohórquez | Alejandrina Adrián

Introduction

Clinical trials in Colombia are regulated by Instituto Nacional de Vigilancia de Alimentos y Medicamentos (INVIMA).

Regulatory framework

The current Colombian provisions regarding clinical trials are the following: Resolution 2378 of 2008; Resolution 8430 of 1993; Resolution 2011020764 of 2011; Minutes 5 of 2008 issued by INVIMA; and the Declaration of Helsinki with all the amendments.

Additionally, INVIMA published in April 2015 a set of guidelines related to the different stages of evaluation and implementation of clinical studies. Compliance to these guidelines is mandatory for all parties involved:

- Guideline for Ethics Committees of Investigation
- Guideline for Evaluation of Research Protocols
- Guideline for Medicines and Supplies in Clinical Research
- Guideline for Selection of the Investigator

In October 2018, INVIMA published a database of clinical studies of medicines made in the country since 2014. This database allows the analysis, consultation, follow-up, approval, denial or suspension of each of the studies that are ongoing in Colombia.

Currently, the average total evaluation time of a clinical study in Colombia is 124 days.

Clinical trial agreements (CTAs)

Under current regulations, prior authorization from the Ethics Committee (CEI) of the institution where the investigation will be performed and authorization to proceed with the clinical trial from INVIMA are required to carry out a clinical trial in Colombia.

Likewise, any change in the protocol or interruption of the study must be reported appropriately to both INVIMA and the CEI.

There are no specific requirements in obtaining a CTA. However, to carry out the CTA according to Colombian provisions, the following must be considered:

- The protocol of the investigation approved by INVIMA, as well as the curriculum vitae of the physician investigator and a letter guaranteeing fulfillment of the commitments under the Helsinki Declaration
- The informed consent, with prior authorization from the Ethics Committee, of the institution where the investigation will be performed, as well as from INVIMA

The above approval or consent must include information on the pharmaceutical product; the known or expected adverse events; any relevant information that may affect the decision of the subject to participate in the study; the

right of the subject to be given answers to any questions or queries he or she may have in connection with the clinical trial; the freedom of the subject to withdraw his or her consent any moment and to stop participating in the study, without prejudice to continuing any applicable treatment or follow-up; the assurance that the identity of the subject will not be revealed and that all information will be treated as confidential; and the right of the subject to information on any and all results obtained during the performance of the study, and to any indemnification payments to which he or she is entitled.

- Resolution No. 2378 of 2008, which states that it is advisable to include a liability and indemnification clause in the CTA

Provisions regarding this matter establish that one of the sponsor's functions is to take the necessary measures guaranteeing the protection and safety of the participant in a clinical trial. Taking into account this obligation, the sponsor may take out an insurance policy for adverse events associated with the study drug, with the value of the policy based on international standards.

In case the insurance does not fully cover damages, the sponsor, the principal investigator and the institution where the clinical trial was performed would be jointly liable for the damages.

There are no specific additional requirements affecting the different trial phases.

Sponsor and contract research organizations (CROs)

The sponsor has the following obligations:

- Guarantee the confidentiality and protect the data and information of the participants in a clinical trial
- Record the responsibilities of the investigator and the personnel involved in the trial
- Ensure that the investigator and the personnel involved in the study have received the instructions and training necessary to carry out the trial
- Supply the conditions for archiving the essential documents of the clinical trial for at least two years
- Guarantee a monitoring system during the study, and report the findings
- Execute an agreement with the investigator or institution in order to fulfill the terms and payments agreed in the contract
- Comply with the timely report of adverse events pursuant to the requirements set forth in Resolution 2011020764 of 2011
- Monitor the clinical trial, which involves verifying compliance with the relevant provisions (e.g., making sure the participants have duly signed the informed consent) and establishing sanctions in case of non-fulfillment of the clinical trial protocol
- Inform INVIMA and the Ethics Committee of the reasons for prematurely concluding or suspending a clinical trial

The obligation of the sponsor may not be transferred or delegated to the institution.

There is no requirement for the sponsor to be located in the country where the clinical trial is taking place.

The sponsor may be represented by a local representative, which has responsibilities similar to those of the sponsor and has to comply with the sponsor's obligations.

To begin a clinical trial, it is compulsory to file and obtain an authorization from INVIMA for the protocol of the clinical trial but not for the agreements.

Investigator

The principal investigator plays a special role in the development (mainly the planning, conduct and termination) of the clinical trial.

Its functions are as follows:

- Ensure the availability during the study of sufficient qualified personnel who will handle the budget of the trial; verify whether the research personnel were informed of their duties and responsibilities, the study objective, and the pharmaceutical product in investigation; and guarantee compliance with ethical principles and Good Clinical Practices
- Make sure that the Ethics Committee has approved the protocol of the study and the informed consent with the amendments, and has notified the clinical trial participants of pharmacological and other known information on the product under research
- Verify compliance of the clinical research protocol; jointly agree with the sponsor in case of changes in the protocol, then amend the protocol and file an application for a new authorization before INVIMA; and notify the sponsor and the Ethics Committee of the changes and the reasons for them
- Make sure that the number of participants in the trial is the number specified in the protocol, in compliance with eligibility or qualification criteria; maintain the privacy and confidentiality of the participants; organize the information on the clinical trial concerning the causes of voluntary retirement; measure the final outcome of the participants that did not finish the clinical trial; and establish the required amendments to avoid new losses in the trial
- Verify whether the informed consent has been signed by the participants or their legal representatives in the trial, as well as by two witnesses and the physician responsible for informing the participants about the trial
- Verify that the informed consent was executed by a legal representative of the participant in case the clinical trial includes vulnerable population, and inform said participants of the objectives of the trial accordingly
- Handle the pharmaceutical product under investigation in the clinical trial and verify that the participants received adequate instructions concerning the use of said product

Regarding the reporting of adverse events (including laboratory abnormalities during specific periods of the clinical trial), according to the requirements described in Resolution 2011020764 of 2011, the investigator has the following obligations:

- Report serious adverse events to the sponsor within 24 hours after the event; send the notification immediately with the details of the event; keep the events confidential; and prepare the report according to the requirements established in the protocol
- Provide the sponsor and the Ethics Committee with the required additional information in case of a participant's death
- Inform INVIMA of a serious adverse event within the next seven working days after the occurrence to allow INVIMA to decide on whether the study should be continued

- Ensure that the participant will receive immediate, adequate and appropriate medical attention in case of an adverse event
- File before the Ethics Committee a clinical trial summary once a year; when the trial is finished, this summary must include the number of all participants, specifying the participants who finished the study. The results of the trial would be relayed to the scientific community.

Study drugs

Authorization from INVIMA is necessary before administering the study drug to the participants. To obtain such authorization, it is necessary to include in the protocol, as well as in the informed consent, scientific known information on the product, including indications, contraindications, all known adverse effects of the medicine, safety, tolerability, efficacy, bioavailability, name, formulation, administration and dosage, among others. Additionally, the informed consent must describe the regulatory status of the drug (investigational or approved) and the indication that is being evaluated. If the drug is approved for a certain indication, this must be declared.

In cases involving the importation of study drugs not yet registered for sale in Colombia, it is necessary to obtain authorization from INVIMA only after the study protocol has been approved.

In Colombia, there are no express provisions regarding the financing of the study drug. Generally, the study drug is provided by the sponsor and may not be sold, since commercialization of the drug requires health registration at INVIMA. At this stage, no health registration is usually granted yet in Colombia for such product, except where the clinical trial is being developed to study a drug that already has a valid health registration in force.

Participants in a clinical trial in Colombia do not pay to be part of a clinical trial. Moreover, the cost of drugs is not reimbursable.

Costs concerning the medical procedures of the protocol are usually the responsibility of the sponsor and are included in the budget for the clinical trial.

Liability for the study pertains to the following:

- Compliance of what is established in the clinical trial protocol
- Informed consent signed by the participant, legal representative (if any), two witnesses and the physician investigator who explained the objective of the trial to the participant
- Inclusion of known pharmacological information in the clinical trial protocol and in the informed consent stating the adverse events reported, if any

It is advisable to include a liability and indemnification clause in the Clinical Trial Agreement. Provisions regarding this matter establish that one of the sponsor's functions is to guarantee the protection and safety of participants in a clinical trial. Taking into account this obligation, the sponsor may take out an insurance policy for adverse events associated with the study of the drug. The value of the policy must be based on international standards.

Provisions also indicate that in case the insurance does not fully cover the damages, the sponsor, the principal investigator and the institution where the clinical trial was performed would be jointly liable for the damages. They would not be released from their responsibility by arguing that the clinical trial was approved by INVIMA or by the Ethics Committee.

Relating to the publication of the study results, provisions establish specific requirements in order to ensure the confidentiality of participant information.

Collected data on the participant may include information that may be used to identify the participant, such as name, address, telephone number, photograph, date of birth, social security number, new and existing medical records, or types, dates, and results of various tests and procedures. The name of the participant will not be disclosed unless the results require his or her identification and the participant expressly provides authorization.

Aside from the participant's identification, personal information on his or her health and treatment in the study may be processed by or transferred to other parties in other countries for clinical research and safety reporting purposes. However, the sponsor must do all necessary efforts to keep the participant's personal information confidential.

The results of a clinical trial may be presented at meetings or in publications. However, the participant will not be personally identified in any presentation or publication unless there is authorization to do so.

In Colombia, pharmaceutical products may not be commercialized without a health registration, unless authorized by INVIMA (which is empowered to authorize the commercialization of a drug without a health registration, especially non-available vital drugs or drugs for donation purposes). Therefore, the study drug (non-available vital drugs or donation drugs) may be provided to the trial subject after termination of the clinical trial upon authorization from INVIMA, or when health registration has been granted to the drug.

Intellectual property (IP) and data

According to Decision 486 of 2000, IP rights resulting from a trial belong only to the inventor but may be transferred by the inventor to any natural or legal person through a written agreement.

Taking into account that pharmaceutical companies conceived and developed the study, and approached the institution and/or investigator to perform the study, we suggest including in the agreement a clause declaring the following:

"*Institution and investigator hereby each acknowledge that the sponsor shall own the exclusive right to any and all inventions or discoveries, patentable or not, which are conceived or reduced to practice during the course of the trial by investigator or institution, any sub- investigator or any of their respective employees or agents.*

Institution or investigator shall promptly notify the sponsor in writing of any such invention or discovery, and shall fully cooperate with the pharmaceutical company and the sponsor to vest rights therein and to obtain patents or other legal protections thereon."

Decision 486 of 2000 further establishes that authorities will grant patents of products or procedures in all technology fields if said inventions are new, involve an inventive step and have an industrial application.

If the results of a clinical trial are therapeutic or involve surgical methods for human or animal treatment, or diagnostic methods for application to humans or animals, these inventions are not patentable.

As mentioned, clinical trials are in most cases supported by pharmaceutical companies interested in demonstrating the effectiveness and safety of a new molecule in treating a disease, with the intention of registering it as a pharmaceutical product and then commercializing it. The pharmaceutical company approaches physicians and requests them to be the principal investigators who will coordinate the trial and fulfill all the requirements mentioned above before the Health Authority.

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