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CLINICAL TRIALS HANDBOOK
Americas

VENEZUELA

Venezuela

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Introduction

The regulator of clinical trials in Venezuela is the Rafael Rangel National Institute of Hygiene (**RRNIH**), which is part of the People's Ministry of Health.

Regulatory framework

The regulatory framework governing clinical trials is found mainly in the Investigation Regulations on Clinical Pharmacology, which are part of the Rules of the Pharmaceutical Products Review Board ("**Regulations**"). There are different legal bodies that contain dispositions regulating clinical trials (i.e., the Law on the Exercise of Medicine); however, most ratify what is established in the Regulations.

With respect to clinical trials regarding the transplant of organs, tissues and cells, the Law on Organs and Anatomic Material Transplants in Humans prohibits carrying out such investigations, diagnostic tests and clinical trials on children and teenagers.

In addition, from a practical standpoint, the Ministry applies certain procedures that are not written in regulations, rules or laws but have arisen out of practice. It is therefore important that the pharmacist or doctor handling the clinical trials verify with the Ministry any new procedures or requirements.

With respect to biological products, as set out in the Regulations, the investigator must provide details of the product's origin, the means of obtaining it, the elaboration method, the purification method, controls during the process (from raw material up to the finished product), analytical methods and specifications, impurity profile, and stability and conservation conditions for the active ingredient as well as for the finished product.

Where the product originates from a human being (such as products with hemoderivatives and similar products), the information must include evidence that there are no infective agents.

On November 2013, the RRNIH initiated a public consultation on the draft for the "Best Clinical Practice Rules for Clinical Trials." So far, the corresponding law has not been published.

Clinical trial agreements (CTAs)

Pursuant to Article 13 of the Regulations, clinical studies must be approved by health authorities through the RRNIH. Article 14 of the Regulations further sets out extensive legal and technical requirements, as well as documents that must be filed with the RRNIH when requesting approval.

A Venezuelan pharmacist or medical doctor with a degree from a Venezuelan university must handle the approval request. He or she will represent the public or private institution where the study will be carried out ("**Investigation Institution**").

Pursuant to Article 7 of the Regulations, the sponsor must bear the costs of the investigation, including those covering damages that may be suffered by the subjects of the study as a result of the active ingredients, medicines and/or methods used in the study, as well as the costs of professional liability insurance covering the doctor(s) responsible for carrying out the Phase 1 and early Phase 2 studies, and the investigators associated with those studies.

Pursuant to Article 19, No. 4 of the Regulations, one of the documents required for the approval of a clinical study is either an original declaration by the sponsor that he or she assumes the responsibilities and costs of any damages that may be suffered by the subjects involved in the study as a result of the active ingredients, medicines and/or methods used in the study, or a copy of the insurance policy covering the medical expenses, disabilities or death of study participants.

In Phase 1 and early Phase 2 studies, the doctor leading the study as well as the associated investigators should be protected by a professional liability insurance policy covering the risks that could arise out of the study.

Sponsor and contract research organizations (CROs)

The sponsor is responsible for all costs related to the clinical study, as well as any damages that may be suffered by the subjects as a result of their participation in the study.

The following are certain legal functions of the sponsor:

- Filing the preliminary research project with the RRNIH, validated by the scientific department of the sponsoring institute or by a medical consultant
- Executing a declaration regarding the availability of resources, equipment and other means needed to carry out the proposed clinical study and to avoid risks or treat injuries that study subjects may suffer
- Executing a declaration regarding the number of patients to be evaluated in Venezuela and the amount of the active ingredient to be imported; if the study deals with psychotropic drugs or drugs that are potentially habit-forming, executing a sworn affidavit
- For Phase 1 and early Phase 2 studies, providing a copy of the insurance policy covering medical expenses and disabilities, as well as life insurance that protects the subjects of the study
- Providing a copy of the professional liability insurance policy covering the doctor responsible for Phase 1 and Early Phase 2 studies, as well as the associated researches, if relevant
- For all clinical studies, executing a declaration assuming responsibility and expenses for damages to the subjects of the study as a result of active ingredients, placebos, medicines and/or methods used during the study; or providing a copy of the insurance policy covering medical expenses and disabilities as well as life insurance of the subjects.
- For long-term studies, forwarding a report every six months, with a written evaluation of the progress of the study (If the study deals with psychotropic drugs or drugs that are potentially habit- forming, the report must be forwarded every three months and should indicate the number of participating patients, the amount of medicine that has been administered and the length of time the patient has been under.)
- Within a year of the end of the study, filing a report of the results of the clinical (This term may be extended at the discretion of the Review Board.)

Pursuant to Venezuelan rules, the sponsor does not have to be located in Venezuela or have a branch in Venezuela.

A Venezuelan pharmacist or doctor may represent the sponsor before Venezuelan authorities. If the sponsor has a local representative, that representative may act before Venezuelan authorities and represent the sponsor in matters relating to the public or private institution that will carry out the study.

Venezuelan legislation does not provide for CROs. However, since the sponsor does not directly carry out the study but finances the activities to be carried out by a Venezuelan private or public institution, it may be understood that

the institution acts as a CRO. It is important to bear in mind, however, that the sponsor is responsible for compliance with the CTA.

Finally, there is no express legal provision that requires the review of CTAs by regulatory authorities.

Investigator

The investigator is in charge of managing and directing the study. The following are certain functions of the investigator:

- Informing the study subjects of the conditions, effects, responsibility for damages, and all information the may be of interest to the subjects before, during and after the study
- Notifying the RRNIH if the study has been suspended and why
- Providing a signed declaration acknowledging his or her participation in the study, including his or her name, personal data and legible signature
- Obtaining approval of the investigation from the Ethics Committee of the hospital or institution where the study will be carried out
- Providing a document showing approval of the study by the hospital or institution where the study will take place (This must be an original document written on an official letterhead, stamped by hospital authorities and executed by the highest authority of the institution, and must contain the personal data as well as legible signature of said authorities.)

According to the Regulations, the investigator's legal functions vary according to the type and phase of the study. However, in all studies, the investigator is responsible for reporting any adverse effects to the Clinical Protocol Evaluation Office of the RRNIH. The time frame for filing the reports depends on the severity of the adverse effect.

Study drugs

An authorization from RRNIH is necessary in carrying out clinical pharmacological studies on human beings, including those using study drugs. In addition, study subjects (or their representative if they are not legally, mentally or physically fit) must sign a consent form. When requesting consent, investigators must inform the subjects of the risks and benefits associated with the study. In studies with vulnerable subjects, they need to comply with additional formalities in obtaining the subjects' consent.

There are no express provisions regarding the financing of drugs necessary for the study, nor are there provisions regarding who must pay for the drugs, whether or not the costs will be reimbursed, or if the sponsor is obliged to provide the study drugs or the medical procedures stipulated in the study protocol. However, as we have mentioned above, the sponsor, pursuant to Article 7 of the Regulations, must pay for all study costs, provide the study drugs to the subjects, and finance the medical procedures established in the investigation protocol.

Pursuant to Article 43 of the Regulations, promotion and advertising of clinical investigations must first be submitted to the Review Board for approval. In this regard, the material must comply with the ethical and scientific requirements set out in Chapter VI of the Regulations.

Pursuant to Article 55 of the Regulations, once the study has been completed, any unused pharmaceutical substance must be disposed of pursuant to Decree No. 2635, which contains the Partial Reform of the Rules for the Control,

Recovery and Handling of Dangerous Materials. However, there is no express legal provision prohibiting the use of pharmaceutical substances once the study has been concluded.

Intellectual property (IP) and data

Insofar as works protected under copyright are concerned, Venezuelan copyright law presumes that the right to works for hire or works created by an employee belongs to the person who ordered the work or the employer. If the sponsor is financing the study to be carried out by researchers in a Venezuelan medical institution, it may be argued that there is an employer-employee relationship and that the sponsor owns the rights to any copyrightable work arising out of the study.

In addition, Article 28 of the Regulations to Venezuelan Organic Labor Law states that if an employee's contribution to an invention has been decisive and his or her benefit as a result of the invention is notably disproportionate to the employer's benefit as a result of the invention, the employee will be entitled to a share of the profits resulting from the invention or improvement.

There is no express legal provision that prohibits investigator-initiated trials, as long as these trials are carried out in private or public medical institutions and comply with the Regulations. Finally, there is no express provision prohibiting pharmaceutical companies from supporting such trials.

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