Liberty and
Order

MINISTRY OF SOCIAL PROTECTION
RESOLUTION NUMBER 2378 OF 2008
(June 27)

Whereby Good Clinical Practices are adopted for institutions that conduct research with drugs in human beings

THE MINISTER OF SOCIAL PROTECTION

In exercise of the powers granted by the law, in particular the powers conferred upon through Article 8 of Law No. 10 of the year 1990, Item 2 of Article 173 of Law No. 100 of the year 1993, Item 6 of Article 2 of Decree No. 205 of the year 2003, and

WHEREAS

Through official letter No. 28655 dated March 10, 2005, the Pan American Health Organization – PAHO sent the Good Clinical Practices document to this Ministry. Such document was prepared by the Work Technical Groups delegated by the countries that form the Pan American Network on Drug Regulatory Harmonization – PANDRHA, during the meeting held in the Dominican Republic from March 2 to March 4, 2005, where Colombia was represented by the Colombian Institute for Food and Drug Surveillance (INVIMA), and the PANDRHA, through the PAHO, undertook to officially deliver the document to the member countries, with the purpose of the ultimate adoption of the document.

In accordance with letter f) of Article 6 of Resolution 8430 of the year 1993, research conducted in human beings should be conducted by professionals who have the necessary knowledge and experience to protect the integrity of the human being under the responsibility of a health entity, supervised by health authorities, provided that they have the necessary materials and human resources to guarantee the well-being of the research subjects.

Clinical research with drugs conducted in human beings may cause undesired effects on the participants and the research subject may suffer damage as an immediate or late consequence of the study.

The right to life, physical integrity and health are fundamental rights of citizens.

In any research where a human being is the research subject, the criterion of respecting the person’s dignity and the protection of his/her rights and wellbeing should prevail.

Research involving drugs in clinical pharmacology comprise the studies sequence carried out from the first time they are administered to a human being until data are obtained on its therapeutic safety and efficacy on large population groups.

Through Resolution 3823 of the year 1997, it was established that drugs research projects will be evaluated by the Colombian Institute for Food and Drug Surveillance (INVIMA), which must issue a quarterly report to the Ministry of Social Protection, with a copy of the result of such studies, once completed.

By virtue of the aforesaid,

HEREBY RESOLVES:

ARTICLE 1.- PURPOSE.- To officially and mandatorily adopt the Good Clinical Practices for institutions that conduct research with drugs in human beings contained in the Technical Schedule which is made part of this resolution.

ARTICLE 2.- GOOD CLINICAL PRACTICES.- The implementation of the Good Clinical Practices and their strict compliance will be the responsibility of the research area of the research institution, or the one acting in its stead.

PARAGRAPH.- Clinical trials may only be started to demonstrate the efficacy and safety of a drug, provided always that there is a justification.

ARTICLE 3.- GOOD CLINICAL PRACTICES CERTIFICATE.- The Colombian Institute for Food and Drug Surveillance (INVIMA) should verify that the institutions that conduct research with drugs in human beings comply with the Good Clinical Practices adopted through this resolution, in development of which, a certificate should be issued.

PARAGRAPH.- The Good Clinical Practices Certificate issued by the Colombian institute for Food and Drug Surveillance (INVIMA) should be valid for five (5) years.

ARTICLE 4.- REGISTRY OF RESEARCH PROJECTS WITH DRUGS IN HUMAN BEINGS.- All research projects with drugs in human beings should be registered before the Colombian Institute for Food and Drug Surveillance (INVIMA).

FIRST PARAGRAPH.- The Colombian Institute for Food and Drug Surveillance (INVIMA) will verify the investigations in the facilities of the Research institutions whenever it deems it convenient.
SECOND PARAGRAPH.- The institutions where research in human beings is conducted through the application and use of drugs should have the certification of conditions of the Single Authorization System (*Sistema Único de Habilitación*).

THIRD PARAGRAPH.- The research projects should have a copy of the project registration before the Colombian Institute for Food and Drug Surveillance (INVIMA) attached, when requesting its approval.

ARTICLE 5.- PROJECTS APPROVAL.- Clinical research projects with drugs in human beings must not commence unless the Colombian Institute for Food and Drug Surveillance (INVIMA) previously approves the project or issues a favorable opinion in connection with the project.

ARTICLE 6.- INTERRUPTION OF RESEARCH.- The Colombian Institute for Food and Drug Surveillance (INVIMA) may interrupt a clinical research at any time or demand that modifications be introduced to the project, in the following cases:

a) Modification of the authorization conditions.
b) Noncompliance with Good Clinical Practices
c) Protection of human beings subject to trials.
d) Defense of public health.

PARAGRAPH.- The favorable or unfavorable results of each clinical research, whether it is completed or abandoned, should be informed to the Colombian Institute for Food and Drug Surveillance (INVIMA).

ARTICLE 7.- INSTITUTIONAL ETHICS COMMITTEE.- The research institutions should have an Institutional Ethics Committee complying with what has been established in the Technical Schedule, which is made an integral part to this resolution.

FIRST PARAGRAPH.- Any research project in human beings must be evaluated and approved by the Institutional Ethics Committee. The committee must evaluate the research project, the informed consent form (document explaining the purpose of the research, including the risks and benefits to the potential participants), the information known about the drug (including reports on unexpected adverse events) and any potential publicity planned to obtain participants.

SECOND PARAGRAPH.- Research projects conducted by institutions that do not have an Institutional Ethics Committee should be approved by the Institutional Ethics Committee of another institution which has a Good Clinical Practices compliance certificate issued by the Colombian Institute for Food and Drug Surveillance (INVIMA).

ARTICLE 8.- GRADUAL COMPLIANCE PLAN.- All institutions that conduct clinical research with drugs in human beings should submit, within six (6) months following the issuance of this resolution, a gradual compliance plan that permits the implementation, development and application of Good Clinical Practices. The schedule should include compliance control annual deadlines, which will be

subject to verification by the Colombian Institute for Food and Drug Surveillance (INVIMA) and should be attached to all research projects.

ARTICLE 9.- SANCTIONS.- The non-compliance with the provisions established in this resolution will be punishable by the sanctions set forth in Article 577 of Law No. 09 of the year 1979, or in the rules that amend, modify or replace such provision.

ARTICLE 10.- TEMPORARY.- The institutions that conduct clinical research with drugs in human beings will have a term of two (2) years to obtain the Good Clinical Practices certification issued by the Colombian Institute for Food and Drug Surveillance (INVIMA).

ARTICLE 11.- EFFECTIVENESS.- This resolution is effective as from its publication date.

THIS RESOLUTION SHOULD BE PUBLISHED AND ENFORCED

Issued in Bogotá, D.C., on

(Original signed by)
DIEGO PALACIO BETANCOURT
Minister of Social Protection

TECHNICAL SCHEDULE

CHAPTER I

GLOSSARY

Direct Access. Authorization to examine, analyze, verify, and reproduce any records and reports that are important to evaluate a clinical study. Any party (e.g., authorities, sponsor's auditors) with direct access should take all the reasonable precautions, within what has been set forth in the applicable regulatory requirements, to maintain the confidentiality of the subjects' identities and sponsor's proprietary information.

Quality Assurance. All planned and systematic actions that are established to guarantee that the study is being performed and the data are generated, documented (recorded), and reported in compliance with Good Clinical Practices (GCP) and the applicable legal requirements.

Randomization. The process of assigning trial subjects to treatment or control groups using an element of chance to determine the assignments in order to reduce bias.

Audit. A systematic and independent examination of trial-related activities and documents to determine whether the activities were evaluated and the data were recorded, analyzed and accurately reported according to the protocol, sponsor's

standard operating procedures (SOPs), Good Clinical Practice (GCP), and the applicable regulatory requirements.

Trial Data Audit. A comparison of the source data and records associated with the final or intermediate report, to determine whether the source data were accurately informed, whether the trials were conducted in accordance with the protocol and the applicable GCP, to obtain additional information not included in the report and to establish if in obtaining the data, procedures that may invalidate such data were used.

Biosafety in the clinical laboratory. The rules and procedures that guarantee the control of physical, chemical, biological and ergonomical risk factors that might affect the personnel related to the clinical laboratory or the members of the community.

Good Clinical Practice (GCP): A standard for the design, conduct, performance, monitoring, auditing, recording, analysis, and reporting of clinical trials, which provides assurance that the data and reported results are credible and accurate, and that the rights, integrity, and confidentiality of research subjects are protected.

Well-being (of the research subjects). The physical and mental integrity of the subjects participating in a clinical trial.

Blinding.- A procedure in which one or more parties to the trial are kept unaware of the treatment assignment(s). Single blinding usually refers to subject(s) being unaware of the assignment and double blinding usually refers to the subject(s), investigator(s), monitor, and, in some cases, the analyst being unaware of the assignment to the investigational product.
Trial Site. The location(s) where trial-related activities are actually conducted.

Audit Certificate. The minutes signed by the parties involved in the audit, in which the auditor confirms that an audit has taken place.

Subject Identification Code. A unique identifier assigned by the investigator to each research subject to protect the subject's identity and used in lieu of the subject's name when the investigator reports adverse events and/or other trial-related data.

Coordinating Committee. A committee that may be organized by the sponsor to coordinate the performance of a multicenter trial.

Institutional Ethics Committee (IEC). An independent body constituted of medical, scientific and non-scientific members whose responsibility is to ensure the protection of the rights, safety and well-being of the human beings involved in a trial through, among other means, the review, approval, and permanent

revision of the study project, and the modifications to the documentation and the informed consent of the research subjects.

Independent Ethics Committee. An independent body (a review board or a committee, institutional, regional, national, or supranational), constituted of medical professionals and non-medical members, whose responsibility it is to ensure the protection of the rights, safety and well-being of human subjects involved in a trial and to provide public assurance of that protection, by, among other things, reviewing and approving/providing favorable opinion on the trial protocol, the suitability of the investigator(s), facilities, and the methods and material to be used in obtaining and documenting the informed consent of the research subjects.

Confidentiality. It is applicable to information, reports or communications which are the sponsor's proprietary information or to the identity of a subject, which may only be disclosed to other authorized parties or to the relevant health entity.

Comparator. An investigational or marketed product (i.e., active control), or placebo, used as a reference in a clinical trial.

Informed Consent. A process by which a subject voluntarily confirms his or her willingness to participate in a particular trial, after having been informed of all aspects of the trial that are relevant to and may affect the subject's decision to participate. Informed consent is documented by means of the informed consent form, which must be signed and dated by the participant, two witnesses and the investigator medical doctor.

Quality Control (QC). The operational techniques and activities undertaken within the quality assurance system to verify that quality requirements of the trial-related activities have been fulfilled.

Essential Documents. Documents which individually and collectively permit the evaluation of the conduct of a study and the quality of the general data.

Source Documents. Original documents, data, and records (e.g., hospital records, clinical charts, laboratory notes, memoranda, subjects' diaries or evaluation checklists, pharmacy dispensing records, recorded data from automated instruments, copies or transcriptions certified after verification as being accurate copies, microfiches, photographic negatives, microfilm or magnetic media, x-rays, subject files and records kept at the pharmacy, the laboratories, and at medico-technical departments involved in the clinical trial).

Protocol Amendment. A written description of a change(s) to or formal clarification of a protocol.

Financing Entity. An individual, company, institution or organization responsible for the financing of a clinical trial.

Biological Specimen/Sample. Tissue, liquids or substances derived from the human body with the purpose of analyzing and thus providing information for the diagnosis, prevention or treatment of any sickness, or the evaluation of a person's health.

Clinical trial. Any investigation in human subjects intended to discover or verify the clinical, pharmacological and/or other pharmacodynamic effects of investigational product(s), and/or to identify any adverse reactions to investigational product(s), and/or to study the absorption, distribution, metabolism and excretion of an investigational product with the object of ascertaining its safety and/or efficacy.

Non-clinical trial. Biomedical trials not conducted in human beings.

Multicenter Trial. A Clinical Trial conducted according to one single protocol but at more than one site and, therefore, carried out by more than one investigator.

Evaluator. Person appointed by the INVIMA or another entity in charge of executing the evaluation process, to be carried out in one or more institutions.

Adverse Event (AE). Any untoward medical occurrence in a patient or clinical investigation subject administered a pharmaceutical product and which does not necessarily have to have a causal relationship with this treatment. An adverse event (AE) can, therefore, be any unfavorable and unintended sign (including an abnormal laboratory finding), symptom, or disease temporally associated with the use of a medicinal (investigational) product, whether or not related to the medicinal (investigational) product.

Serious Adverse Event (SAE). Any untoward medical occurrence in a patient or clinical investigation subject administered a pharmaceutical product and which does not necessarily have to have a causal relationship with this treatment. A serious adverse event (SAE) can, therefore, be any unfavorable and unintended sign (including an abnormal laboratory finding), symptom, or disease temporally associated with the use of a medicinal (investigational) product, whether or not related to the medicinal (investigational) product, which at any dose:

a) Results in death,
b) Is life-threatening,
c) Requires the patient's hospitalization or the prolongation of existing hospitalization,
d) Results in persistent or significant disability/incapacity.

Case Report Form (CRF). A printed, optical, or electronic document designed to record all of the project-required information to be reported to the sponsor on each research subject.

Committee Operating Guidelines (COG). Detailed and written instructions to achieve uniformity in the execution of a specific function. Equivalent to the Standard Operating Procedures Manual (SOPM).

Inspection. The act by sanitary authority (ies) or the Ministry of Social Protection of conducting an official review of documents, facilities, records, and any other resources that are deemed by the authority(ies) to be related to the clinical trial and that may be located at the site of the trial, at the sponsor's and/or contract research organization's (CRO's) facilities, or in other sites deemed appropriate by the regulatory authority(ies).

Health care services institution. To the effect of this resolution, health care providers and professional practice groups that have the necessary means to render health services are deemed health care services institutions.

Investigator. A person responsible for the conduct of the clinical trial at the institution. If a trial is conducted by a group of individuals, the investigator is the responsible leader of the group and will be called the principal investigator.

Investigator's Brochure. A compilation of the clinical and nonclinical data on the investigational product(s), which is relevant to the study of the investigational product(s) on human subjects.

Standard Operating Procedures Manual (SOPM). Detailed, written instructions to achieve uniformity in the performance of a specific function. Equivalent to the Written Operating Guidelines (COG).

Monitoring. The act of overseeing the progress of a clinical trial, and of ensuring that it is conducted, recorded, and reported in accordance with the protocol, Standard Operating Procedures Manual (SOPMs), Good Clinical Practice (GCP), and the applicable regulatory requirement(s).

Contract Research Organization. A person or an organization (commercial, academic, or other) contracted by the sponsor to perform one or more of a sponsor's trial-related duties and functions.

Subject/Research subject. An individual who participates in a clinical trial, either as a recipient of the investigational product(s) or as a control.

Sponsor. An individual, company, institution, or an organization which takes responsibility for the initiation, management, and/or financing of a clinical trial.

This function may be performed by a corporation or agency external to the institution or by the investigator or hospital-related institution.
Sponsor-Investigator. An individual who both initiates and conducts, alone or with others, a clinical trial, and under whose immediate direction the investigational product is administered to, dispensed to, or used by a subject. The obligations of a sponsor-investigator include both those of a sponsor and those of an investigator.

Standard Operating Procedures (SOPs). Detailed, written instructions to achieve uniformity of the performance of a specific function.

Investigational Product/Drug. A pharmaceutical form of an active ingredient or placebo being tested or used as a reference in a clinical trial, including a product with a marketing authorization when used or assembled (formulated or packaged) in a way different from the approved form, or when used to gain further information about the approved use.

Protocol. A document that describes the objectives, design, methodology, statistical considerations, and organization of a trial. Usually, the protocol also gives the background and rationale for the trial, but these could be provided in other protocol referenced document. The term protocol includes protocol amendments.

Audit Report. A written evaluation by the sponsor's auditor of the results of the audit.

Subject/Research subject. An individual who participates in a clinical trial, either as a recipient of the investigational product(s) or as a control.

Quality System. It is defined as the group of actions and procedures aimed at assuring the quality of results in the long term, immediately identify changes in the results derived from failures in any of the components of the procedures, and monitor different factors that may alter the precision of results.

Impartial Witness. A person independent from the trial, who may not be influenced in bad faith by the personnel involved in the study and shall attend the procedure of obtaining the informed consent, in the event that the subject or the legally accepted subject representative is not able to read. This independent person shall be responsible for reading the informed consent and any other written information provided to or by the subject.

CHAPTER II

REQUIREMENTS TO BE COMPLIED WITH BY INSTITUTIONS PERFORMING CLINICAL RESEARCH IN HUMAN BEINGS

I. INSTITUTIONAL EVALUATION PROCESS

Evaluation consists in a process that involves the management of an institution or its representatives, the chairperson or coordinator of the Independent Ethics Committee (IEC), the institution's active investigators, research coordinators and the person appointed by the government authority, referred to as the *Evaluator.* For this process to be effective, the management of the evaluated institution must know in advance the aspects and requirements applicable to the evaluation, as specified in this regulation. The "Institutional Evaluation" process will comprise two key stages: firstly, the evaluated institution gathers the information required, while at the second stage, the evaluator performs one or various visits to the institution and verifies compliance with each aspect. The paragraphs below thoroughly describe the steps to be followed during these two (2) stages:

1. NOTICE TO THE INSTITUTION ON COMMENCEMENT OF THE EVALUATION

INVIMA or the government authority in charge of evaluation notifies the institution of the commencement of the evaluation process. Such notice is delivered to the institution upon evaluating this technical document. Moreover, the evaluated institution must appoint a representative to assist in the evaluation process, coordinate evaluator's visits and contact the members of the institution who will take part in the evaluation.

1.1 Evaluator's visit

At this visit, the *Evaluator* will meet with the representative of the institution in charge of assisting in the evaluation process. During such visit, the evaluator must:

a) Review the log for research projects finished and in-progress for the last year (last twelve (12) months prior to the date of the visit).

b) Perform a randomized selection of the projects that will compose the evaluation process; a randomized selection of 10% or at least two (2) of the projects finished or in-progress for the last year is deemed a fair sample of the projects carried out at the institution.

c) Schedule subsequent visits, within a term no greater than ten (10) business days to:

1) evaluate the IEC;
2) evaluate the investigators of the selected projects; and
3) evaluate the sponsors for the selected studies (this evaluation will be carried out simultaneously with the evaluation of the investigator).

1.2 Subsequent visits

In accordance with the agreed-upon plan, the evaluator will perform any visits necessary to gather the information required in the “Data Sheets for Institutional Evaluation”. The information will be gathered through interviews with the people involved (IEC chairperson, investigators, research coordinators and head of the research area of the institution, if any, etc.) and verified through reviews of manuals, IEC's files and in-progress projects.

2. EVALUATION BY THE INVESTIGATIONAL ETHICS COMMITTEE (IEC)

2.1. Institutional Evaluation Process

To evaluate the IEC, the evaluator will hold an interview with its chairperson and/or secretary. Upon such interview, the IEC must make available to the evaluator the manuals, guidelines or documents describing the duties, responsibilities and procedures of the IEC for review thereof. Furthermore, the evaluator must verify compliance with such requirements by reviewing the records, communications and other files of the Committee. Based on these reviews, the evaluator may gather the required information to establish if the IEC involved effectively complies with the duties, responsibilities and guidelines set forth in writing. The key aspects to be complied with by the IEC are shown in Tables 1 to 3 of this schedule. The evaluator must consider that in certain institutions, the IEC engages exclusively in evaluating the ethical aspects of research projects, delegating the methodological review upon technical committees, while in some other cases the IEC reviews both ethical and scientific aspects. Moreover, in some institutions, the IEC may delegate certain operative aspects to a research area. Therefore, the evaluator should possibly verify compliance with said aspects, reviewing files from other committees or the research area.

If the IEC has Committee Operating Guidelines (COG) or a Standard Operating Procedures Manual or Rules, the initial task of the evaluator during the visit will consist in identifying which of the aspects described as "requirements" are included in those documents, in the additional documents provided by the Committee and which aspects have apparently not been previously contemplated in those documents. After conclusion of the initial review, the evaluator must verify or confirm compliance with such operating guidelines, the aspects to be complied with by the Committee through review of other documents such as minutes of meetings, letters to investigators and documents for specific projects. In other words, the fact that certain procedures are part of the COG should not lead to the assumption that such operating guidelines are effectively complied with. Lastly, the information gathered by the evaluator should be logged in Schedule 1: Evaluation of the Investigational ethics committee" of the "Data Sheets for Institutional Evaluation”. If the IEC does not have a COG, the need to

submit such document upon the following evaluation will be specified. However, the evaluator will continue with such evaluation trying to assess compliance with the aforementioned aspects by reviewing other documents.

2.2. Aspects to be complied with by the Investigational ethics committee

The key aspects to be complied with by a IEC include elements that guarantee fulfillment of its duties towards individuals and society in general, as well as aspects to guarantee that the processes and duties performed by the IEC safeguard the constitutional rights of the individuals who participate in research works carried out by the institution. These aspects have been grouped in three categories:

a) Duties (Table 1)
b) Structure (Table 2)
c) Procedures (Table 3)

TABLE 1. DUTIES OF THE INVESTIGATIONAL ETHICS COMMITTEE (IEC)

Key requirement - Aspect	Evaluation Method	Comments
1. Safeguarding the rights of research participants	Reviewing: Committee operating guidelines (COG)	
2. Evaluating and approving or rejecting proposed research projects before commencement thereof	Reviewing: COG Minutes of meetings by the IEC IEC's communications	
3. Obtaining and maintaining the documents required for each study considered	Reviewing: COG Committee files Proposals evaluated during the last year Study files	
4. Considering investigators' skills and capabilities	Reviewing: COG Study files (CVs)	
5. Evaluating, from time to time, the progress made regarding studies approved and in-progress	Reviewing: COG Minutes of meetings of the IEC. Study files	

TABLE 2. STRUCTURE OF THE INVESTIGATIONAL ETHICS COMMITTEE (IEC)

Key requirement - Aspect	Evaluation Method	Comments
1. The Committee must be composed of at least 5 members	Reviewing: Committee operating guidelines (COG) Minutes of the meeting of the IEC List of members of the Committee	
2. There must be a balance as regards gender and age of the members of the Committee.	Reviewing: COG List of members of the IEC	
3. The Committee must be multi-disciplinary in nature a) There must be at least one member whose primary interest does not fall under a scientific area. b) There must be at least one physician. c) There must be at least one independent member not reporting to the institution / site where the study will be performed.	Reviewing: COG Minutes of meetings by the IEC List of IEC's members	
4. The regulation on consultants' participation is followed, when applicable.	Reviewing: Committee operating guidelines (COG) Minutes of meetings of the IEC List of members of the IEC	

5. The requirements and processes for selecting members as to the following aspects must be expressly set forth: a) Individual(s) in charge of selecting the members of the Committee, b) Procedures for selecting the members of the Committee (appointment, consensus, voting, other), c) Method of evaluation of possible conflicts of interest of candidates, d) Aspects considered as "Unsuitability" of individuals to be members of the Committee.	Reviewing: Committee operating guidelines (COG) Record of IEC structure
6. The conditions for appointment of the members of the Committee must include: a) Willingness / acceptance by members to disclose certain personal information (name, occupation, affiliation), b) Willingness of members to record and make available information regarding payments and reimbursements received for their work as members of the Committee (if any), c) Written confidentiality agreement, duly signed, regarding the topics discussed by the Committee	Reviewing: Committee operating guidelines (COG) Record of appointment Record of IEC structure

7. The conditions of membership must include: a) Duration of the appointment b) Policy on renewal of appointment c) Policy on disqualification d) Policy on resignation e) Policy on replacement f) Name of position (chairperson, secretary, members) g) Responsibilities for the position	Reviewing: Committee operating guidelines (COG) Minutes of meetings of the IEC
8. The quorum requirements to hold meetings and deliberate must include: a) Minimum number of members required; b) Qualifications and discipline of members to reach the quorum for appointment meetings.	Reviewing: COG Minutes of IEC meetings
9. The conditions for participation of independent guest consultants should be clearly specified.	Reviewing: Committee operating guidelines (COG) Minutes of meetings of the IEC
10. There must be a description of the training or coaching to be complied with by the members of the Committee.	Reviewing: COG Minutes of meetings of the IEC Additional documentation (certificates of course material) Review of IEC's library

TABLE 3. PROCEDURES OF THE INVESTIGATIONAL ETHICS COMMITTEE (IEC)

Key requirement - Aspect	Evaluation Method
1. The Committee must specify: a) The institutional authority to which it reports; b) If it is not under direct subordination by such authority to deliberate and adopt decisions.	Reviewing: COG

2. The method followed by the Committee to evaluate the proposals submitted must be set forth in writing and specify: a) The number of members evaluating the documentation for each proposal (all members or certain representatives). b) The minimum documentation requiring evaluation by all members. c) The minimum time required to evaluate proposals (delivery of documentation).	Reviewing: COG
3. The requirements to adopt decisions after evaluating proposals submitted during the meetings of the Committee must be thoroughly described and include: a) The predefined method to reach a decision (by agreement, voting) b) As long as possible, decisions must be made by agreement c) Decision-making methods when no agreement is reached d) Restriction policies to participate in the evaluation of proposals, where one or more Committee members have a conflict of interests	Reviewing: Committee operating guidelines (COG) Minutes of meetings
4. The Committee must establish the requirements and mechanisms for prompt/special approval, including: a) The type of eligible study for this type of approval. b) This procedure is only admissible for minimum risk studies. c) The procedure to be followed for review. d) The method for ratification by the Committee of decisions made promptly.	Reviewing: Committee operating guidelines (COG) Minutes of meeting Records of Committee's communications
5. The Committee must specify the documents to be submitted by investigators with each request for evaluation of research proposals. These documents must include, at least: a) CV of investigator b) Study project c) Informed consent d) Documents that try to attract e) Potential participants in the study f) Project budget	Reviewing: Committee operating guidelines (COG) Information documents for investigator Study files

6. The Committee must describe in writing the aspects to be considered during the evaluation of each proposal submitted for approval. These aspects must include: a) Suitability of investigator to develop the study (expertise, qualification, support group), b) Information available on the product (drug, device) under research, c) Scientific background of proposal, d) Technical quality of research, e) Feasibility of the research project (possibility to reach expected conclusions, balance of benefits, risks and inconveniences for participants, necessary financing and resources), f) Suitability and adequacy of information to be delivered to participants, g) Content of informed consent, h) Ethical aspects related to the inclusion of vulnerable populations, i) Compensation and redress in the event of injury or death attributable to study therapy, j) Scope to compensate or reward participation by individuals, k) Characteristics of sponsor (relation to investigator, conflict of interests).	Reviewing: Committee operating guidelines (COG) Minutes of meetings

7. The Committee must give written notice to the investigator of any decisions made regarding the project under evaluation within a period of two weeks after the meeting. This notice must include, at least: a) Study identification; b) Studied documents; c) Date of evaluation and number of the related minutes of meeting d) Decisions or opinions related to the study e) Grounds for the decisions, particularly in the event of rejection f) Procedures to be followed by the investigator to submit the project to reconsideration	Reviewing: Committee operating guidelines (COG) Committee records and schedule Record of Committee's communications
8. The Committee must implement measures aimed at guaranteeing successful meetings. These measures include: a) Schedule Committee meetings duly in advance b) Give timely notice to members c) Previously deliver any documents necessary for the meeting to each member d) Reflect the discussion and agreement in the minutes e) Keep a record of minutes f) Keep records of communications sent to the members of the Committee	Reviewing: COG Schedule and minutes of the Committee Records of Committee communications
9. The procedures established by the Committee to follow the progress of studies from approval to termination must be in writing. These procedures must include: a) Criteria to define periodicity of follow-up (at least once a year). b) Method to follow up each project, including an annual review based on the number of recruited individuals, the last project version, summary of adverse events, summary of non-anticipated problems, summary of new information available, copy of the current consent form.	Reviewing: Committee operating guidelines (COG) Records of Committee communications Record of in-progress studies

10. The Committee must define procedures to: a) Avoid the inclusion of individuals in a study before the Committee grants its approval in writing b) Avoid implementation of changes – project amendments without prior notice c) Avoid non-compliance upon submission of reports for project follow-up d) Guarantee that the investigator notifies project deviations e) Guarantee that the investigator notifies adverse events or reactions f) Guarantee that the investigator notifies on any new information that may adversely affect the security and safety of the individuals or study development g) Report investigators on any penalties resulting from failure to comply with these provisions	Reviewing: COG Record of Committee communications Record of in-progress studies
11. The type of documents and project-related communications must be specified in writing, which must be kept on file by the Committee, specifying also the minimum time these documents must be kept on file.	Reviewing: COG Record of in-progress and finished studies

2.3 Documentation and records to be kept by the IEC

Documents play an important role in processes to evaluate and guarantee compliance with ethical principles applicable to research in human beings, which become the “evidence” available to the IEC of fulfillment of its various responsibilities for the purposes of institutional research. The availability of guidelines or rules to direct internal processes and activities, and minutes of meetings and communications exchanged with investigators are considered “evidence” reflecting performance by the IEC and compliance or non-compliance with the various aspects specified above. Keeping and filing theses documents also facilitate external and internal audit procedures to be carried out by the institution as part of its quality improvement mechanisms. Table 4 gathers a list of documents to be held by the IEC. Upon verifying these documents, the evaluator must again consider that in certain institutions these documents may form part of the records of the IEC, research committees and/or research areas.

TABLE 4. DOCUMENTATION AND FILING OF RECORDS FROM THE RESEARCH COMMITTEE (IEC)

Type of record	Document
Committee's OPERATION FILE	Standard Operating Procedures Manual
	List of members
	Members' CVs
	Financial records: income, expenses and payments to members
	Applicable forms for proposal review
	Schedule of meetings
	Minutes of meetings, including an annual report on the Committee's performance.
	Copy of communications not related to project performance.
	Rules applicable to investigators.
	Copy of all documents for proposals reviewed but NOT approved.
STUDY FILES (these documents must be kept for each study in progress)	Investigator's brochure (all versions)
	CV of principal investigator
	CVs of co-investigators
	Full project initially approved
	Approval of initial project
	Letters for request of approval of project amendments
	Approval of project amendments
	Informed consent form (all versions)
	Approval of initial informed consent
	Letters for request of approval of informed consent amendment
	Approval of subsequent informed consent versions
	Information for delivery to participants
	Approval of material delivered to participants
	Financial aspects: budget
	Insurance policy for participants
	Sponsor- Institution/Investigator contract
	Copy of communications on decisions and recommendations made by the IEC to investigators.
	Approval of incentives and compensations to participants not considered in prior reviews
	Approval of annual project report

Notice of adverse events
Notice of project deviations/infringements
Final project report

3. EVALUATION OF ACTIVE INVESTIGATORS WITHIN THE INSTITUTION

3.1 Evaluation process

Tables 5 to 7 have been designed for the institutional investigator evaluation process, which allows evidencing the performance of investigators in projects. This evaluation includes an interview to investigators and/or study coordinators, and a review of projects and procedure manuals, and other documents for each project. Thus, it is possible to define with adequate reliability whether investigators respect the rights of the individuals who participate in their researches and comply with the responsibilities and duties established by Good Clinical Practices.

In order to facilitate the investigators' evaluation process, a list of aspects to be considered during the evaluation has been drafted, as shown in Tables 5 and 6 of this document, together with the respective compliance evaluation form. Table 7, particularly, includes the list of documents that investigators must have; the *evaluator* must verify their availability and filing. Tables 8 to 17 allow to evaluate the principal investigator and Table 18 the study sponsor.

Pursuant to the evaluation process described above, at the first visit to the evaluated institution, the individual in charge of the institution to assist in the evaluation will report to the evaluator the names of any drug research studies pending at the institution at that point. Based on that, the evaluator will perform a randomized selection of study-investigators to support its evaluation (10% of total in-progress studies or at least two studies). The investigators for these studies will be called for an evaluation at a second visit to be carried out by the evaluator on an agreed-upon date and within a term no greater than 10 business days. In the event that the institution has no studies in progress, based on the procedure described above, the projects concluded in the last year will be selected for evaluation.

During the visit, the evaluator will interview each study coordinator and/or investigator, and will verify proper operation thereof by reviewing the methods to gather information on participants, monitoring and coordination forms, and other documentation. The evaluator will select the files corresponding to some participants included in the study. The number of files for patients to evaluate

depends on the total number of patients included in the study at the time of evaluation (Chart 1).

***Chart 1*. Number of files for participants to be evaluated per selected study**

Number of participants included in the study	Number of files to evaluate
1 to 20	*2*
From 21 to 50	*4*
51 and more	*6*

To verify the requirements for compliance related to the "Informed Consent" it is necessary to review a larger number of participants' files. The evaluator will determine the number of files to evaluate pursuant to the number of participants recruited at the time of evaluation, pursuant to the instructions given in Chart 2.

Chart 2. Number of files to be selected to evaluate the informed consent

Number of participants included in the study	Number of Informed Consents to evaluate
1 to 50	All
More than 50	50 selected randomly

During this process, it is necessary for the investigator or a representative appointed by the latter to be always present to guide the *evaluator* in locating certain key documents and, thus, optimize the evaluation.

The information gathered by the evaluator during this process will be specified in Section 2, Data Sheet for Institutional Evaluation. The evaluator must specify the information for each evaluation independently, submitting a copy of Section 2 for each investigator.

If a large number of research studies involving drugs is being carried out at the evaluated institution, it will be necessary for the evaluator to perform visits until completing the evaluation of all investigators.

TABLE 5. INVESTIGATORS' SKILLS

Key requirement - Aspect	Evaluation Method
1. The investigator must have adequate information to conduct the study: a) Academic training b) Experience c) Training	CV of investigator and other relevant documents
2. The investigator must be familiar with the adequate use of the product under research	Pre-study training certificates Investigator Project Manual
3. The investigator must have knowledge of: a) Good clinical practices b) Ethical principles for research in human beings c) Colombian regulations	Certificates for training or attendance at Good Clinical Practices courses. Knowledge of the Declaration of Helsinki, CIOMS Ethical Guidelines and Resolution 8430 of 1993, and other amending or supplementary rules
4. The investigator must disclose any conflict of interest upon conducting the study.	Review of the disclosure of the conflict of interest in the project or letter to the IEC

3.2 Duties and responsibilities of the investigator

The principal investigator (PI) plays a key role in planning, conducting and concluding a research. For easier identification, understanding and evaluation of the aspects related to the responsibilities and duties to be complied with by the PI, they have been divided based on each process.

TABLE 6. DUTIES OF THE PRINCIPAL INVESTIGATOR REGARDING PROCEDURE STANDARIZATION

Key requirement - Aspect	Evaluation Method
The investigator, or a designee (study coordinator), must design and make available for consultation the Standard Operating Procedures Manual for research	Review of project file

TABLE 7. DUTIES OF THE PRINCIPAL INVESTIGATOR REGARDING STUDY PERSONNEL

Key requirement - Aspect	Evaluation Method

1. The investigator must make available sufficient qualified personnel for the expected duration of the study	Participant's CV
2. The investigator is responsible for managing the study budget	Form of responsibilities
3. A list with all qualified individuals who have been delegated tasks related to the study must be kept	List of organizational chart of study personnel.
4. The investigator must guarantee that the personnel participating in the study is properly informed regarding: a) Study project b) Product under research c) Duties and responsibilities related to the study d) Ethical principles and Good Clinical Practices	Pre-study training certificates. Form of responsibilities for each individual involved in the study. Evidence of informational workshops

TABLE 8. DUTIES OF PRINCIPAL INVESTIGATOR REGARDING COMPLICANCE WITH ETHICAL REGULATIONS

Key requirement - Aspect	Evaluation Method
1. Before commencing the study, the investigator must obtain written approval from the IEC of the following documents: a) Study project; b) Informed consent form; c) Inform consent form updates; d) Information on study participants (individuals subject to the research study)	Reviewing: Approval letters from the IEC on: Research project Informed consent Recruiting material and procedure updates.
2. The investigator must provide the IEC with a valid copy of the Researchers' Manual and information previously obtained on clinical pharmacology for the drug	Verify availability of the Investigator's Brochure in the IEC's files.

3. The investigator must make available for review and audit all required study-related contracts and records, and allow inspection thereof by competent authorities and the IEC	Reviewing: Contract Approval by the IEC Approval by the INVIMA for the drug under investigation

TABLE 9. DUTIES OF THE PRINCIPAL INVESTIGATOR REGARDING ADHERENCE TO THE PROJECT DURING THE STUDY

Key requirement - Aspect	Evaluation Method
1. The investigator must guarantee that the study is carried out pursuant to the agreed-upon project, as approved by the IEC.	Reviewing: Project or manuals Verification of availability of a thorough study-monitoring and performance plan. Training certificates for those involved
2. In the event that changes to the project are required, the investigator must: a) Agree the change in advance with the sponsor. b) Request a new project approval and amendment to the IEC	Reviewing: Communications to the sponsor Letters to the IEC for approval of project amendments
3. The investigator must notify any deviation from or unexpected change in the project to the sponsor and the IEC, explaining the reasons therefore and, if applicable, explaining any proposed amendment to the project	Reviewing: Notice to the sponsor and the IEC of project deviations Letters to the IEC for approval
4. The investigator must guarantee that the randomization procedures are complied with (if applicable).	Reviewing: Randomized procedure described in the project Verification of the randomized participants list
5. The investigator must document and immediately explain to the sponsor any anticipated breaking of the blind.	Reviewing: Reports of deviations from the project Review of notices to sponsor

6. The investigator is liable to the sponsor and the Ethics Committee for adherence to the project during the study	Verification of: Compliance with data records, follow-up of participants, reports of adverse events and reports on project deviations

TABLE 10. DUTIES OF PRINCIPAL INVESTIGATOR REGARDING INFORMATION MANAGEMENT

Key requirement - Aspect	Evaluation Method
1. The Investigator must guarantee that the information reported in the "case report forms" and in all required reports is accurate, legible and is complete and updated.	Review of case report forms
2. The investigator must guarantee that the information reported through the case report forms deriving from the source documents is consistent therewith. Otherwise, notice of any inconsistency must be given.	Reviewing: Case report forms Discrepancy reports
3. All case report forms must be signed by the investigator. If corrections are necessary, the investigator must: a) Sign and date the amended information b) Guarantee that the information has been adequately corrected (erroneous information must be crossed out with an horizontal line only in order not to obstruct the original entry)	Reviewing: Case report forms Corrections in case report forms
4. The investigator must guarantee that study documents are kept in a safe, private and locked place.	Reviewing: Records of study-related documents
5. The investigator, upon agreement with the sponsor, must keep key documents for at least 2 years after the last approval of a trade request or for at least 2 years following formal suspension of the clinical development of the product under research.	Project or study file

TABLE 11. RESPONSIBILITIES AND DUTIES OF THE PRINCIPAL INVESTIGATOR REGARDING ADVERSE EVENTS INVOLVING

PARTICIPANTS

Key requirement - Aspect	Evaluation Method
1. The investigator must report to the sponsor any adverse event and/or lab irregularity detected, pursuant to the reporting requirements and within the time periods specified in the project.	Reviewing: Reports of adverse events Reports of lab irregularities
2. The investigator must report to the sponsor any serious adverse event, as follows: a) no later than 24 hours after occurrence; b) after immediate reporting, send a detailed notice of the event; c) preserve confidentiality of the information (do not include personal information identifying the participant); d) draft a report pursuant to the reporting requirements set forth in the project	Reviewing: Procedure for reporting serious adverse events as described in the project or manuals. Report of adverse events (date and time) Reports of described lab irregularities. Verification of the described delivery system implementation. Verification of delivered reports. Reports of adverse event follow-up.
3. The investigator must provide the sponsor and the IEC with additional information as requested in cases of reported deaths.	Review of reports to the IEC and sponsor Verification of reported deaths

TABLE 12. FUNCTIONS OF THE PRINCIPAL INVESTIGATOR CONCERNING INCLUSION AND FOLLOW UP OF STUDY PARTICIPANTS

Item – Key requirement	**Evaluation method**

1. Investigator must ensure that the number of participants included in the study is the number specified by the project or sponsor.	Revision of: The project The list of participants
2. Investigator must ensure that the privacy and confidentiality of the research participants are kept.	Revision of: Study manual Study personnel functions
3. Investigator must ensure that all participants meet the eligibility requirements listed in the project.	Revision of: List of inclusion/exclusion criteria Participants (inclusion) case report forms
4. Investigator must ensure that all medical decisions related to study participants are in charge of a qualified physician (investigator or co-investigator).	Revision of: Study manual Study personnel functions
5. Investigator must ensure that medical care provided to a participant in case of an adverse event or of need because of any reason is the most appropriate.	Revision of: Participant handling specifications according to the project Participants medical history Information given to participant Informed Consent
6. Investigator must make the biggest possible effort in order to obtain the complete information and to maintain follow-up of all participants entering the study by: a) Identifying participants who were lost at follow-up. b) Documenting causes of voluntary withdrawal. c) Trying to measure the final outcome in participants who do not complete follow-up. d) Establishing corrective measures to prevent new lost at follow-up.	Revision of: List of participants who entered the study Follow-up compliance forms Follow up control register and agendas

TABLE 13. RESPONSIBILITIES / FUNCTIONS OF THE PRINCIPAL INVESTIGATOR CONCERNING THE INFORMED CONSENT APPLICATION

Item – Key requirement	**Evaluation method**
1. Investigator must make sure that all participants included in the study	Revision of: Informed consents of participants

have given the informed consent pursuant to the Colombian legal provisions: a) Signature and identification document of participant. b) Signatures and identification documents of two witnesses. c) Signature of the physician responsible for the research who informed the patient on the study.	included in the study
2. In cases of studies including vulnerable populations (for example, minors, subordinates, or participants with mental impairments), investigator must ensure that: a) The person giving consent to participate in the study is suitable (for example, the legal representative). b) The participant has been informed of the study to the extent of his understanding. Participant must sign and date the informed consent by himself if he has the ability to do so.	Revision of: Informed consent application standardized procedure Informed consents
3. Investigator must ensure that the study participant has a copy of the signed and dated informed consent.	Revision of: Informed consent forms
4. Investigator must ensure that the participant's medical history includes a note specifying his participation in the study.	Revision of: Participants' medical history
5. Investigator must update the informed consent form and inform the participants or their legal representatives of any new information that could be relevant for their intention to continue study participation, and document that such notification was made.	Revision of: Informed consent Letters informing changes to the consent

TABLE 14. RESPONSIBILITIES OF THE PRINCIPAL INVESTIGATOR CONCERNING THE HANDLING OF THE INVESTIGATIONAL PRODUCT (DRUG)

Item – Key requirement	**Evaluation method**
1. Investigator is responsible for the accounting of the investigational product, however, he may appoint this task to a suitable supervised person.	Revision of: Study personnel functions in the project.
2. Regarding the handling of the investigational product, investigator must ensure that: a) Drug receipt and delivery registries are being prepared appropriately. b) There is an existing product inventory in the institution. c) There is an existing drug delivery registry for each participant, specifying delivered amount, dose, delivery date and scheduled date for adherence control. d) All registries of the drug under study specify: lot/serial number, expiration date, code number assigned to the investigational product, randomization number or participant's identification number.	Revision of: Investigational product's accountability records Drug delivery registry for each participant
3. Investigator must make sure that the investigational product is stored according to Manufacturer's specifications.	Revision of: Storage conditions specified by the sponsor or the Manufacturer in the project or in the study manual
4. Investigator must make sure that the investigational product is used only within the project approved by the IEC.	Revision of: Investigational product's accountability records Study file Drug delivery forms
5. Investigator must ensure that participants receive appropriate instructions for the use of the drug	Revision of: Information for participants Suitability of the person in charge of

under study (control and experimental therapies)	delivering the drug Each participant's drug record

TABLE 15. RESPONSIBILITIES OF THE PRINCIPAL INVESTIGATOR CONCERNING SAMPLE AND BIOLOGICAL SPECIMENS COLLECTION AND PROCESSING

Item – Key requirement	**Evaluation method**
1. In case it is necessary to analyze biological samples, investigator is responsible for: a) Ensuring the existence of written procedures on handling samples taken for the study. b) Identifying the suitable person / laboratory / institution to take, process, and handle samples. c) Having the certificate or document accrediting the person, laboratory, or institution available.	Revision of: Sample taking, storage, transport and processing manual Verification of the identification and qualification of the person or laboratory in charge of processing the samples
2. Investigator must ensure that the findings of tests on biological samples are valid and reliable, by: a) Available infrastructure and supplies required to perform the test (reagents, equipment, facilities, etc.) b) Test standardization according to the laboratory operating procedures manual.	Revision of: Study project Verification of supplies and infrastructure required according to the project and test type to be performed on participants.
3. Investigator must make sure that during the samples and biological specimens report and processing the participant's right to confidentiality is respected.	Revision of: Laboratory study file Laboratory documents
4. Investigator must ensure the correct interpretation of the findings of laboratory tests, knowing and having the normal values in the study file.	Revision of: Study file Laboratory documents

5. In case samples must be sent to other laboratories or institutions, investigator must ensure the adequate conservation and handling of samples by: a) Formulating indications on the samples storage and shipping. b) Hiring trained and qualified personnel to handle the samples conservation and shipping. c) Verifying that the institution counts with the supplies and facilities necessary for conservation and shipping. d) Preparing the shipping registers for taken and shipped biological samples.	Revision of: Research project Sample handling manuals IATA certificates for the bacteriologist or laboratory in charge of shipping the samples Samples taking and shipping registers Verification of existence of necessary infrastructure

TABLE 16. RESPONSIBILITIES AND FUNCTIONS OF THE PRINCIPAL INVESTIGATOR CONCERNING THE DISCLOSURE OF THE RESEARCH OUTCOMES

Item – Key requirement	**Evaluation method**
1. Investigator must submit to the IEC written summaries of the state of the study at least once a year, or more frequently if required by the IEC.	Documents submitted to the IEC for the follow-up process
2. Investigator must notify any significant change that affects the study condition: a) Transfers / resignations within the investigator group b) Vacations / changes in the contracts with Health Promoting Companies	Interview with investigator Revision of letters sent to the IEC
3. Upon completion of the study, investigator must submit to the IEC a summary of the study, including	Revision of letters sent to the IEC

the number of randomized participants and the number of participants who completed the study.	
4. Investigator is responsible for ensuring that the study data are disclosed within the scientific community, whether they are favorable for the therapies under study or not.	Revision of clauses on contract publication.

3.3 Documents and records that the principal investigator must keep in file

Documents are an important part of research processes, turning into the "record" of the research's development in its different phases. The study project is considered "the contract" entered into between the investigator and the IEC, the participant subjects and the sponsor. The manuals, letters and communications exchanged with the other parties involved in the research are considered "the evidence" that reflects the investigator's performance in several of the items presented above.

In addition, holding and recording these documents simplifies the internal and external auditing processes that the institution must perform as part of its quality improvement mechanisms. Table 17 gathers a list of documents that the IP must hold according to Good Clinical Practices (GCP) and national regulations.

TABLE 17. DOCUMENTS AND RECORDS THAT THE PRINCIPAL INVESTIGATOR MUST KEEP IN FILE

Type of file	Document	Comments
Study project	Initial project version; signature page. Letter of submission of project to IEC's approval. IEC's letter or approval of initial project.	
	Project revisions. Signature page. Letter of notification of project revision to the IEC.	

	Project amendments. Signature page. Letter of submission of amendments to the IEC.	
Informed Consent	Informed consent initial form. Letter of submission of initial informed consent to the IEC. IEC's letter of approval of initial informed consent.	
	In case of changes to the informed consent, letter of submission of informed consent update for IEC's approval Copy of informed consent receipt by participants. Advertisements for recruitment.	
	Letter of submission of advertisements for recruitment. Letter of approval of advertisements for recruitment. Material given to participants. Letter of submission. Letter of approval of material given to participants.	
Other Approved documents	Letter of submission of incentives proposed to the IEC. Letter of approval of incentives by the IEC.	
Administrative and financial items	Study budget.	
	Contract and agreements with financing entities.	
	Contract and agreements with sponsors	
	Accountability reports on the project's management.	
Reports	Half-yearly progress reports sent to the IEC.	
	Notifications on project deviations sent to the IEC and sponsor.	
	Final study report sent to the IEC.	
tional	Storage instructions for the	

	investigational product.	
	Accountability records for the investigational product: general (inventory) and for each participant.	
	Copy of Registers of approval of drug by INVIMA.	
Research Personnel	List of study personnel. Principal investigator's CV Co-investigator's and team member's CVs.	
	Investigator's, co-investigator's and other study personnel's training certificates.	
	Principal investigator's responsibilities form. Co-investigator's responsibilities form. Study personnel's responsibilities form. Investigator's signature page. Co-investigator's signature page. Study personnel's signature page.	
Clinical Laboratory	Registration in the special registry of health care providers before the relevant Department or District Institution.	
	Samples shipping (current regulations).	
	Laboratory normal values.	
	Laboratory manual.	
	Biological samples shipping register.	
	Inventory of taken and stored biological samples.	
Participants' Records (Forms)	Informed consent signed by each participant.	
	Original copy or photocopy of laboratory and paraclinical examinations records.	
	Case report form for each participant, discrepancy forms.	
	Adverse event reports from the	

	beginning of participants' recruitment up to date.	
	Death reports from the beginning of participants' recruitment up to date.	
	Participants' directory.	
Other Basic Documents	Investigator group statement of conflict of interests.	
	List of screened participants (verify selection criteria).	
	List of participants fit for the study (prescreened).	
	List of participants definitively included.	
	Research sites standardized procedures manual.	
	Investigator's brochure and letter sending a copy of the investigator's brochure to the IEC. Investigator's brochure updates.	
	Guidelines of Good Clinical Practices	
	Declaration of Helsinki.	
	Resolution 8430 of 1993.	
	Monitoring visits reports.	
	Regulatory entity's auditing reports (IEC or sponsor).	
	Study close-out visit reports Supplies registry.	

4. SPONSOR'S EVALUATION OF RESEARCH

4.1 Evaluation Process

The sponsor's evaluation will be made on the same 10% of studies selected randomly for the investigator's evaluation. When choosing a certain study, it is necessary to identify whether the sponsor is the investigator or an external corporation or agency. According to this classification, the Evaluator shall gather the information pursuant to the relevant section of "Institutional Evaluation Data Sheet". In case the investigator is the sponsor, his

obligations and functions must be evaluated from the sponsor's point of view and the investigator's point of view independently.

4.2. Sponsor's Responsibilities and Functions

Tables 18 to 20 show the responsibilities and functions that the external sponsor of a research must fulfill with the investigator, the institution and the study participants. The institution must ensure that the external or internal sponsor complies with every item listed in said tables. Moreover, if the institution in the research's sponsor, it is its responsibility to demonstrate that it complies with said items.

In case the investigator or the institution under evaluation is the study sponsor, they should take the responsibilities described in table 18 and fulfill the functions described in Table 19. In addition, they will handle relations with the financing entity, complying with the items listed on Table 20.

TABLE 18. STUDY SPONSOR´S RESPONSIBILITIES

Item – Key Requirement	Evaluation Method
1. Investigator must ensure the protection and safety of the research participants, by: a) Implementing a safety monitoring system. b) Reporting adverse events at a global level (multicenter studies)	Revision of: Project Safety monitoring plan Project records
2. Investigator must ensure quality and quality control during research. These measures include: a) Ensuring that the study personnel is trained in the study procedures and handling. b) Ensuring that the conduction of studies and the generated data agree with the project and comply with GCP. c) Controlling data handling to ensure reliability. d) Keeping all agreements with investigator/institution in writing.	Revision of: Study record Pre-study training certificates
3. Sponsor must obtain and document	INVIMA'**s** Memorandum of approval of

the approval of use of the study product from INVIMA.	the project
4. Investigator must ensure the control of distribution and return of the investigational product during the study. These measures include: a) Supplying the investigational product. b) Keeping records that document the shipping, receipt, return and destruction of the product involved in the study.	Letters of delivery and return of investigational product.
5. Investigator must ensure that the study personnel knows and adequately handles the investigational product, by: a) Training personnel in charge of handling and dispensing the product. b) Handing out written procedures and instructions for handling and storing de drug under study: 1. Procedure for adequate and safe receipt of drugs. 2. Storage conditions. 3. Method of delivery to participants. 4. Final dispensing of the drug not used in the study.	Revision of accountability records of the investigational product.
6. Investigator must have the data on the safety and efficacy of the clinical or preclinical previous studies available to support the administration to humans. a) Route of administration b) Dose c) Period of time d) Study population e) Adverse reactions f) Contraindications	Investigator's brochure and project
7. Investigator must deliver the clinical study budget for the participating	Study budget

center, specifying: a) Investigators´ compensation b) Participants budget c) Equipment purchase d) Paraclinical and laboratory examinations	

TABLE 19. SPONSOR´S FUNCTIONS

Item – Key Requirement	Evaluation Method
1. Sponsor must ensure the protection of participants` confidentiality: a) Assigning identification codes b) Providing resources for the record of the identification page of each subject to be independent from the CRF	Revision of: Study project Randomization systems Participating subjects records
2. Sponsor must ensure that the responsibilities of the investigator, the coordinators and the other personnel required in the study are clearly documented and accepted by everyone involved.	Revision of COG
3. Sponsor must ensure that all study investigators and coordinators have received the instructions and training in the project follow-up, diligence of special reports and case report forms.	Registers
4. Sponsor must enable the necessary conditions to record the documents on studies in curse.	Revision of: Record facilities
5. Sponsor must ensure and enable the conservation of the record of essential documents for at least two years.	Project: Agreement with the sponsor. Letters exchanged with sponsor.

6. Sponsor must ensure a periodic monitoring system during the study, and report the findings of each visit in writing.	Monitoring reports.
7. Sponsor must establish an agreement or a contractual obligation with the investigator/Institution. a) Comply with the terms set in the contract. b) Make the payments and disbursements established in the contract.	Record of each study. Institution record.
8. Sponsor must ensure that the monitor complies with the following functions during the monitoring visits: a) Verifying the adherence to the project by the investigator group. b) Confirming that every patient who entered the study has given and signed the informed consent. c) Ensuring that the investigator receives the current investigator brochure. d) Verifying the processes of inclusion and randomization of eligible subjects. e) Reporting the recruitment rate of subjects. f) Verifying that investigator provides all reports, notifications and applications. g) Determining if all adverse events are reported appropriately within the required periods of time. h) Determining if the investigator keeps the essential documents for the conduction of the study. i) Communicating project deviations and taking appropriate measures to prevent recurrence of detected deviations. j) Giving a written report to	Monitoring reports

investigator on the monitoring visits and the corrective measures to any problems found.	
9. Sponsor must create mechanisms to audit the study and guarantee an independent auditing system.	Procedures and registries
10. Sponsor must establish the measures (sanctions) that he will take in case of persistent non compliance of the project by the investigator / institution, and inform investigator of them.	Each study's record Investigator's / sponsor's record.
11. Sponsor must inform investigators, the institution and the IEC on the reasons for the early termination or suspension of the study.	Each study's record Investigator's / sponsor's record.

TABLE 20. RELATIONS WITH FINANCING ENTITY

Item – Key Requirement	Suggested Evaluation Method
1. Financing entity must establish a contractual obligation or agreement with the investigator / institution that establishes: a) Terms for the entering into force and termination of the contract. b) Dates and methods of payment and disbursement. c) Products expected from the financed activity. d) Compliance clauses.	Revision of: Each study's individual file.
2. The investigator / institution sponsoring the study must allow auditing of the research process by the financing entity.	Revision of: Each study's individual file.

3. The investigator / institution sponsoring the study must prepare periodic progress reports of the study to be submitted to the financing entity in accordance with the terms established in the contract.	Revision of: Each study's individual file.

5. ANALYSIS OF THE INFORMATION OBTAINED DURING INSTITUTIONAL EVALUATION

The institution that performs clinical research with drugs must comply with all the items set forth in this document, thus guarantying that research processes are developed suitably and that both the safety of participant subjects and the validity of the outcomes obtained in the research are protected. Acknowledging that some of these items are more relevant than others, they are presented below, classified into three categories that have been defined taking into account the relationship that each evaluated item has with the safety and the rights of the subjects participating in the research.

The information obtained by evaluator during institutional evaluation will be analyzed according to this classification, so that the Sanitary Entity may choose different corrective measures in case the institution does not comply with some or several of the evaluated items. For this classification, evaluator has the evaluation criteria in section 5 "Institutional Evaluation Data Sheet" (Schedule 3).

5.1 Critical or Highly Important Items

The items that are considered highly important are those items whose non compliance implies a higher risk for subjects participating in the research or puts the validity of the research's outcomes in risk. Consequently, failure to comply with "highly important" items requires immediate attention and suspension of the research process, until corrective measures are taken. The lack of written standardized procedures is considered equally critical, even when procedures are actually followed in practice.

5.2 Non-Critical or Moderately Important Items

This category includes items that must be corrected in the institution within minimum time, given that they could otherwise impact the integrity of the research outcomes or the acceptance of the study's conclusions, but without directly affecting the safety or the rights of the subjects participating in the research.

CHAPTER III

INSTITUTIONAL EVALUATION DATA SHEET

I. APPLICATION INSTRUCTIONS

The Institutional Evaluation Data Sheet is the instrument that the evaluator will use to gather the necessary information regarding the items that must be complied with by the institutions that perform clinical research on human subjects, with reference to ethical principles and good clinical practices. For its correct application, he must know the technical document for the evaluation of institutions that perform clinical research on humans, which clearly describes the items considered in the evaluation and provides a guide on how to evaluate its compliance.

1. Institutional Evaluation Process. The institutional evaluation process seeks to obtain information on the following items:
a) The Investigational ethics committee (IEC).
b) The work of investigators, and, through them, the relevant items of the study coordination.
c) The work of study sponsors, verifying, through them, the compliance of study conduction supervision and monitoring activities.

2. Stages of Institutional Evaluation. Institutional evaluation is complied with in two basic stages: in the first stage, the institution to be evaluated gathers the required information, while in the second stage, the evaluators make one or more visits to the institution and verify compliance with each item. These two stages imply that the Evaluator follow the following steps:
a) Making contact with the institution to inform it on the evaluation and request the designation of an institution delegate to assist in the evaluation. The period between notification and evaluation must not exceed 10 business days.
b) Delivering to the institution the “Institutional Evaluation Technical Document” for institutions performing clinical research on humans. This will enable the institution to prepare the information required for the verification visits.
c) Requesting the list of active studies to date and of studies completed during the last calendar year to the institution.
d) Randomly selecting a number equivalent to 10% (at least two studies) from said list of active or recently completed research in order to use this sample to evaluate investigators, sponsors and certain procedure verification items of the Investigational ethics committee (IEC).
Once selected, the institution shall be informed of the selected studies.
e) Rescheduling the visit to make the IEC evaluation in an interview agreed upon with the president or his delegate.
f) Verifying during the visit whether the IEC complies with Good Clinical Practices (GCP) for research in humans, by revising:

1. Manuals, rules, memorandums or other documents describing IEC's functions, responsibilities and operating procedures.
2. Meeting minutes, mail records and other IEC records where it must be recorded that the Committee complies with the recommended principles regarding its responsibilities, composition and procedures (Tables 1 to 3 "Institutional Evaluation Technical Document"), and that it adequately keeps a register of its activities (Table 4 in the same document). In case the institution delegates the revision of methodological or operating items of the research projects to other research offices or committees, evaluator shall verify compliance of these items by revising the records from said research offices or committees.

g) Registering the gathered information on the IEC in item 2 of this sheet.

h) Scheduling an appointment with the principal investigator (PI) or coordinator of the selected studies to make the evaluation. This study evaluation visit may take place the same date of the IEC evaluation.

i) Verifying if the Principal Investigator (PI) of the selected studies complies with GCP for research in humans by revising:

1. The study operating manuals and project.
2. The records of the study and of the participating subjects. To guide this verification, evaluator may follow the description of Tables 5 to 16 in the institutional evaluation technical document. In order to review items related to the participating subjects' records, a random selection must be made, according to the number of participants included in the study at the time of the evaluation, as presented in Chart 1, Schedule 1.

j) Selecting participants records over which the evaluation of items related to the informed consent described in table 14, Schedule 1, will be made. This selection shall be made according to the number of participating subjects recruited at the time of the evaluation, as presented in chart 2, schedule 1.

k) Registering the information gathered on the evaluation of each investigator in Section 3 of this sheet.

l) Evaluating the items that the sponsor must comply with, described in tables 18 to 20 in Schedule 1, Institutional Evaluation Technical Document. This evaluation may be made simultaneously or immediately after the evaluation of each project's investigator, which enables verification work, since it is usually necessary to revise the same records of each project.

m) Registering the information on the study sponsor in Section 4 of the institutional evaluation data sheet.

n) Repeating this evaluation (on investigator and sponsor) as many times as necessary according to the number of selected studies.

ñ) Preparing a report with the evaluation outcomes.

II. DATA SHEET FOR INSTITUTIONAL EVALUATION OF ENTITIES PERFORMING CLINICAL RESEARCH WITH HUMAN BEINGS

1. GENERAL INFORMATION

	day	month	year		day	month	year
Date of Evaluation initiation				Date of Evaluation completion			

1.1. Identification of institution under evaluation

1. Name of institution		
2. Registration in the *registro especial de prestadores de servicios de salud* [Special registry of health services providers]		
3. Address		
4. Telephone numbers	Telephone No 1	Telephone No 2 (fax)
5. Name of person appointed to assist in the evaluation		Position

1.2. Identification of evaluator

1. Name of evaluator	
2. Entity represented by evaluator	
3. Position	

2. EVALUATION OF INVESTIGATIONAL ETHICS COMMITTEE (IEC)

In this section all the information referring to responsibilities, functions and procedures of the Investigational ethics committee (IEC) is compiled. For its evaluation, you must meet the committee chairperson and consult the Committee Operating Guidelines (COG) or Manuals. In addition, you must verify if the items contained in the Committee operating guidelines are being fulfilled by revising minutes of meetings and other records of the IEC.

In those questions about requirements for written procedures, you will find two possible answers and a space for "comments" to add any information you deem necessary. Mark:

YES □, *if the requirement IS included in the documents*
NO □, *if the requirement IS NOT included in the documents*

In those questions about verification, you will find three possible answers, mark:

YES □, *if the requirement HAS BEEN <u>complied with in all the cases that were reviewed</u>*
NO □, *if the requirement HAS NOT BEEN <u>complied with in any of the cases</u>*
S/C□, *if the requirement has been complied with <u>only in some cases</u>*

2.1 General Information about the Investigational ethics committee

1. Name of Committee	Name
2. Name of current chairperson	Name

2.2 Responsibilities of the Investigational ethics committee

For its evaluation you must consult the Standard Operating Procedures Manual (SOPM), Committee Operating Guidelines (COG) and/or minutes evidencing the formation of the committee and verify if the following items are described.

1. Is protecting the rights of those subjects participating in clinical research included in the Committee's responsibilities? YES □ NO □	Comments
2. Is evaluating, approving and disapproving the proposed research studies before conducting them included in the responsibilities of the Investigational ethics committee? YES □ NO □	Comments
3. Is obtaining and keeping the required documents related to each study under the Committee's	Comments

consideration included in its responsibilities? YES □ NO □	
4. Is evaluating the competence of investigators included in the Committee's responsibilities? YES □ NO □	Comments
5. Is conducting evaluations on a periodical basis of the studies approved and of those that are being conducted included in the Committee's responsibilities? YES □ NO □	Comments

2.3 Revision of written standard procedures

The following questions refer to the composition and procedures of the Institution's Investigational ethics committee. For its evaluation it is required to consult the Standard Operating Procedures Manual (SOPM), Committee Operating Guidelines (COG) and/or minutes evidencing the formation of the Committee and verify if these items are described.

1. Does the Committee have Committee Operating Guidelines (GOC) or manual? YES □ NO □	Comments
2. Is the required minimum number of members of the Committee clearly established? YES □ NO □	Comments
3. Is the percentage of men/women that must form the committee established? YES □ NO □	Comments
4. Is it stipulated that the members of the Committee must represent different age groups? YES □ NO □	Comments
5. Is it established that the Committee must be formed by multidisciplinary members?	Comments

YES □ NO □	
6. Are the minimum qualitative characteristics (i.e. basic disciplines) required for members of the Committee described? YES □ NO □	Comments
7. Is there a description of the role of alternate members, their functions and rights? YES □ NO □	Comments
8. Are there written procedures governing the selection and appointment of the members of the Committee? YES □ NO □ If your answer is NO, go to question 10	Comments
9. Verify if the following items are specified in the members written selection procedures: a) Person(s) in charge of selecting the members of the Committee b) Procedures for selecting the members of the Committee (appointment, agreement, vote or others). c) Method for evaluating possible conflict of interests of the candidates.	 YES □ NO □ YES □ NO □ YES □ NO □
10. Are those requirements that must be met by elected members clearly established? YES □ NO □ If your answer is NO, go to question 12	
11. Verify if the following items are included in the requirements that must be met by the members of the Committee:	

a) Predisposition/acceptance by members to disclose information about their academic background and professional experience b) Predisposition by the members to make available any information on payments and reimbursements they received in exchange for working as members of the Committee c) That the confidentiality agreement, as well as all the matters discussed by the Committee, must be signed by all the members.	YES □ NO □ YES □ NO □ YES □ NO □
12. Are the following items on membership conditions clearly described? a) Position title (chairperson, secretary and members) b) Selection process for each position c) Length of membership-position. d) Responsibilities. e) Conditions for replacement/removal or resignation. f) Disqualification due to a conflict of interests	YES □ NO □ YES □ NO □ YES □ NO □ YES □ NO □ YES □ NO □ YES □ NO □
13. Is the minimum number of members required to transact business specified? YES □ NO □	Comments
14. Is there a description of the qualitative characteristics (disciplines) that must be met by members attending the meeting to constitute a quorum for such meeting? YES □ NO □	Comments
15. Is participation of consultants external to the Committee mentioned? YES □ NO □	Comments

If your answer is NO, go to question 17	
16. Are the requirements for the participation of such consultants specified? YES □ NO □	Comments
17. Is there a description of the processes/mechanisms for initial and continuing training of the Committee members? YES □ NO □	Comments
18. Do the COG or the minutes evidencing the formation of the Committee mention the institutional authorities to which the IEC is subordinated? YES □ NO □ If your answer is NO, go to question 20	Comments
19. Do the SOPM or COG mention if the Committee is under no direct subordination of such authorities to deliberate and take decisions? YES □ NO □	Comments
20. Are the methodologies followed by the Committee to evaluate proposals established in writing? YES □ NO □ If your answer is NO, go to question 22	Comments
21. Verify if in the methodologies for the evaluation of specific proposals it is required to indicate: a) The number of members required	YES □ NO □

to evaluate the proposal to present it to the Committee. b) A list of the basic documents that must be evaluated by all the members. c) The time required to evaluate a proposal.	YES □ NO □ YES □ NO □
22. Are the requirements for taking decisions after the evaluation of proposals described? YES □ NO □ If you answer is NO, go to question 24	Comments
23. Verify if the requirements described for taking decisions include: a) The predefined method to reach a decision (by agreement, vote, others). b) That as long as it is possible decisions must be taken by agreement. c) The mechanisms used to take decisions when an agreement cannot be reached. d) Policies restricting the participation in the evaluation of proposals by one or more Committee members having a conflict of interests regarding such proposals.	YES □ NO □ YES □ NO □ YES □ NO □ YES □ NO □
24. Are the items considered by the Committee in evaluating each research proposal described? YES □ NO □	Comments
25. Are the mechanisms and requirements for an expedited/extraordinary procedure of approval of research proposals established? YES □ NO □	Comments

26. Are the documents required by the Committee to submit a proposal to consideration established in writing? YES □ NO □	Comments
27. Are the items that must be included in the notices that the Committee will send to the investigators about the evaluated proposals established in writing? YES □ NO □	Comments
28. Are the follow-up strategies for ongoing research projects established in writing? YES □ NO □	Comments
29. Is there any written specification regarding which measures or sanctions will be taken by the Committee if: a) Participating subjects are included in studies before the Committee issues its approval and opinion in writing? b) Changes to a project are implemented without prior approval? c) Required information for projects follow-up is not provided? d) Any deviation from the project is not informed to the IEC? e) No notice is given to the IEC about any reaction or adverse event to drugs? f) IEC is not notified of new information that could adversely affect the safety of the subjects participating in the study?	YES □ NO □ YES □ NO □ YES □ NO □ YES □ NO □ YES □ NO □ YES □ NO □
30. Is there a description of those documents related to projects that must be kept by the Committee?	Comments

YES □ NO □	
31. Is the length of time during which the Committee must keep such documents specified? YES □ NO □	Comments
32. Has the IEC established the regularity for the presentation of progress reports of each project? YES □ NO □	Comments

2.4 VERIFICATION OF COMPLIANCE IN IEC PROCESSES AND PROCEDURES

The following questions are intended to confirm if those matters regarding composition and procedures described above are being fulfilled. For their evaluation, you must revise IEC's records, minutes, and those records related to the projects selected for review at the beginning of the evaluation process.

1. What is the number of members forming the IEC at present?	Number of members	
2. What is the number of men and women forming the Committee?	Number of men	Number of women
3. At present, the Committee is formed by at least: a) One member whose primary interest area is not related to science. b) One doctor. c) One member that is not related to the institution.	 YES □ NO □ YES □ NO □ YES □ NO □	
4. Verify if the following items regarding membership are mentioned in the Committee's records or minutes documenting the appointment of members:		

a) Title of designated position. b) Description of the selection process of members. c) Term of membership-position. d) Responsibilities. e) Statement of conflict of interests	YES □ NO □ YES □ NO □ YES □ NO □ YES □ NO □ YES □ NO □
5. Verify if there is any supporting documentation or certificate evidencing that education activities for the members of the Committee have been conducted. YES □ NO □	Comments
6. Does the Committee have a library where the members can consult reference documents? YES □ NO □	Comments
7. Verify if the minutes of Committee's meetings evidence that the Committee has taken into account any possible conflict of interests of the participating members when deliberating and taking decisions about research projects (*restriction policies for deliberating or voting in case of conflict of interest*) YES □ NO □	Comments
8. Verify if the minutes of Committee's meetings or the selected studies records (written report of evaluators, checklists) evidence that the items described below have been taken into account in the evaluation process: a) Eligibility of the investigator to conduct the proposed study (experience, qualification, support group) b) Available information about the product (drug) under investigation.	YES □ NO □ S/C □ YES □ NO □ S/C □ YES □ NO □ S/C □

c) Scientific background of the research proposal. d) Technical quality of the research project. e) Plausibility of the research project (possibility to reach the expected conclusions, balance of benefits, risks and problems for participating subjects, financing and required resources). f) Relevance and suitability of the information that will be given to possible participating subjects. g) Informed consent form h) Ethnic matters about inclusion of vulnerable populations (minors, students, subordinates, pregnant women, disabled persons). i) Compensation established for damage or death attributable to the therapy under study. j) Compensation or retribution to subjects for their participation. k) Expected recruitment rates. l) Characteristics of sponsor (relation with investigator and conflict of interest).	YES □ NO □ S/C □ YES □ NO □ S/C □ YES □ NO □ S/C □ YES □ NO □ S/C □ YES □ NO □ S/C □ YES □ NO □ S/C □ YES □ NO □ S/C □ YES □ NO □ S/C □
9. Verify if the minutes of Committee's meetings or records of studies that have not been approved include the items described below: a) The reasons for disapproval are specified. b) The procedures that must be followed by the investigator to submit the project for reconsideration.	YES □ NO □ S/C □ YES □ NO □ S/C □
10. Has the IEC made expedited approvals of clinical studies with drugs in the last year? YES □ NO □ If your answer is NO, go to question 12	Comments

11. Verify if the minutes of Committee's meetings or the notices sent to investigators evidence that the following items have been complied with: a) The type/s of study/studies that were approved in an expedited manner was/were suitable for this type of approval. b) The required revision by at least one member was made. c) Approval was ratified in the following Committee's ordinary meeting.	YES □ NO □ S/C □ YES □ NO □ S/C □ YES □ NO □ S/C □
12. Verify in the records of research proposals selected for evaluation if the following documents, at least, have been presented: a) Investigator's CV b) Study project c) Informed consent d) Documents intended to attract potential participating subjects to the study e) Budget	YES □ NO □ S/C □ YES □ NO □ S/C □ YES □ NO □ S/C □ YES □ NO □ S/C □ YES □ NO □ S/C □
13. Verify if the communications records evidence that the Committee does communicate its decisions in writing to the investigator. YES □ NO □ If your answers is NO, go to question 16	Comments
14. Verify if the following items were included in the notices sent to investigators of the selected studies: a) Study Identification. b) Studied documents. c) Date of evaluation and number of minutes of the corresponding meeting.	YES □ NO □ S/C □ YES □ NO □ S/C □ YES □ NO □ S/C □ YES □ NO □ S/C □

d) Decisions or opinions related to the study.		
15. Verify if the notices sent to investigators of selected studies were received within a reasonable period of time (10 to 20 days) after deliberation by the Committee YES □ NO □ S/C □	Comments	
16. Are the dates of Committee's ordinary meetings scheduled? YES □ NO □ S/C □ If your answer is NO, go to question 18	Comments	
17. Verify if the meetings schedule complies with the following items: a) The schedule of the Committee's meetings is available for research investigators and sponsors. b) There are copies of notices sent to the members of the Committee about meeting dates or notices to attend such meetings. c) There are copies of notices sent to the members of the Committee for submitting those documents that will be analyzed in the scheduled meeting. d) There are minutes of each Committee's meeting according to the schedule.	Comments	
18. Check the minutes of meetings and/or communication records of the selected projects to verify if the IEC takes into account the following aspects for the (annual) follow-up of ongoing research studies (if an evaluated project is deemed to be conducted for less than one year, inform about this in the comments box): a) Number of recruited subjects.	YES □ NO □ S/C □ YES □ NO □ S/C □	Comments

b) Last version of project. c) Summary of adverse events. d) Summary of unanticipated problems. e) Summary of new information available. f) Current copy of informed consent.	YES □ NO □ S/C □ YES □ NO □ S/C □ YES □ NO □ S/C □ YES □ NO □ S/C □	
19. Are there any information mechanisms by the IEC for investigators who want to request an evaluation of projects? YES □ NO □ If your answer is NO, go to item 2.5	Comments	
20. Verify if information given by the IEC to investigators or sponsors include the following items: a) Specification of the required documentation to evaluate a proposal b) Items considered by the Committee in evaluating a proposal. c) Conditions that must be met before recruitment starts. d) Steps and requirements that must be followed and met when there are amendments or changes to a project.	YES □ NO □ YES □ NO □ YES □ NO □ YES □ NO □	

2.5. REVISION AND VERIFICATION OF DOCUMENTATION AND RECORDS THAT MUST BE KEPT BY THE IEC.

Following, verify if the documents described in the following checklists are part of the Committee's records. To check the studies records revise the binders of the selected projects. If any of the documents cannot be found in ALL the studies under revision, mark the S/C (some cases) box. Nevertheless, you may find documents not applicable to the project under evaluation, such as amendments to the project or the informed consent form, if they have not been made. In such case, mark the N/A (not applicable) box.

2.5.1 Checklist for Committee's operating records

Document Type Records		**In the Committee's records**
COMMITTEE'S OPERATING RECORDS	Committee Operating Guidelines or Standard Operating Procedures Manual	YES □ NO □
	List of members	YES □ NO □
	Members' CVs	YES □ NO □
	Financial registers: money received and paid, payments to members.	YES □ NO □
	Forms of applications for proposals revision.	YES □ NO □
	Schedule of meetings	YES □ NO □
	Minutes of meetings, including an annual report about how the Committee is working.	YES □ NO □
	Copies of communications not related to conduction of projects.	YES □ NO □
	Rules and regulations for investigators	YES □ NO □
	Copy of all the documents related to those proposals that have been reviewed but have NOT been approved.	YES □ NO □
RECORDS OF SELECTED STUDIES	Investigator's brochure (all versions)	YES □ NO □
	Principal investigator's CV	YES □ NO □
	Co-investigators' CVs	YES □ NO □ S/C □
	Initially approved complete project	YES □ NO □ S/C □
	letter of approval of initial project	YES □ NO □ S/C □
	Letters presenting project amendments for approval	YES □ NO □ S/C □ N/A□
	Approval of amendments to the project	YES □ NO □ S/C □ N/A□
	Informed consent form (all versions)	YES □ NO □ S/C □

	Approval of initial informed consent	YES □ NO □ S/C □
	Letters presenting amendments to the informed consent for approval	YES □ NO □ S/C □
	Approval of subsequent versions of informed consent	YES □ NO □ S/C □
	Information to be provided to participating subjects	YES □ NO □ S/C □ N/A□
	Approval of materials provided to participating subjects	YES □ NO □ S/C □ N/A□
	Recruitment notices	YES □ NO □ S/C □ N/A□
	Approval of recruitment notices	YES □ NO □ S/C □ N/A□
	Financial matters: budget	YES □ NO □ S/C □
	Insurance policy for participating subjects	YES □ NO □ S/C □
	Agreement entered into between sponsor-institution/ investigator	YES □ NO □ S/C □
	Copy of communications regarding decisions and recommendations made by the IEC to investigators	YES □ NO □
	Approval of incentives and compensation to participating subjects not included in previous reviews	YES □ NO □ N/A□
	Project annual report	YES □ NO □ S/C □ N/A□
	Notice of adverse events	YES □ NO □ N/A□
	Notice of deviations from/ violations to the project	YES □ NO □ N/A□
	Projects final reports	YES □ NO □ N/A□

Once the information related to IEC's evaluation is collected, evaluate the investigators according to the steps described in item 3.

3. EVALUATION OF INVESTIGATORS

Note: reproduce this part of the guidelines the number of times needed in order to have one for each selected study for evaluation.

The following questions refer to the requirements that must be met by investigators of active projects or of those which have recently been finished in the institution.

A 10% of the total number of research studies performed in the institution under examination has been selected for this part of the evaluation. You must have an interview with the principal investigator of each of them. To facilitate collecting the information required in this section, you must count on the investigator's or his deputy's assistance throughout the evaluation. Questions related to verification of information must be answered according to revision of records of participating subjects included in the research and selected for the evaluation.

In those questions about requirements, you will find three (3) possible answers, mark:

YES □, *if the requirement IS complied with*
NO □, *if the requirement IS NOT complied with*
N/A □, when the requirement does not apply to the specific case under evaluation

In the questions about verification, you will find three possible answers, mark:

YES □, *if the requirement HAS BEEN complied with in all the cases that were reviewed*
NO □, *if the requirement HAS NOT BEEN complied with in any of the cases*
S/C□, *if the requirement has been complied with only in some cases*

3.1 General information about investigator

1. Name of investigator	
2. Name of the research project that is being performed by investigator	
3. Investigator's position in the institution	
4. Type of agreement entered into with the institution	

3.2 Competence of research team

1. Does the investigator's CV	Comments

evidence the investigator's academic qualifications? YES □ NO □	
2. Does the investigator's CV evidence that the investigator has experience in or knowledge about the research area? YES □ NO □	Comments
3. Is there any evidence (certificates, training meetings) showing that every person involved in handling participating subjects has adequate information about: a) The research project? b) Procedures for assignment and evaluation follow-up of subjects participating in the study? c) Handling of research product(s)? d) Good Clinical Practices? e) Ethical principles for research in human beings? f) National regulations on clinical research?	
4. Is the statement of conflict of interests signed by the investigator available? YES □ NO □	Comments

3.3 FUNCTIONS AND RESPONSIBILITIES OF INVESTIGATOR

Regarding organization and conduction of the study

1. Is there a manual that compiles all standard procedures of the research? YES □ NO □	Comments

2. Is there a flowchart about the working group involved in the study? YES □ NO □	Comments	
3. Is there a manual describing the functions of the different members of the working group involved in the study? YES □ NO □	Comments	
4. Does the manual describe who is responsible for all the medical decisions related to the subjects participating in the study? YES □ NO □	Comments	
5. Is the person handling subjects participating in the study a qualified doctor? (investigator or co-investigator of the study) YES □ NO □	Comments	
6. Does the study include a written and dated approval by the IEC regarding: a) A research project? b) Informed consent form? c) Information about subjects participating in the study? d) Updates of the informed consent form? e) Amendments to the project?	 YES □ NO □ YES □ NO □ YES □ NO □ N/A□ YES □ NO □ N/A□ YES □ NO □ N/A□	Date dd/mm/yy
7. Verify if approvals obtained for the study comply with the following requirements: a) The date of the letter of approval of the study project and of the informed consent is prior to the date of inclusion of the first *subject*	 YES □ NO □ YES □ NO □ N/A□	

participating in the study b) Amendments to the project were approved by the IEC before their implementation c) Updates of informed consent and recruitment procedures of participating subjects were approved by the IEC before their implementation	YES □ NO □ N/A□
8. Has the investigator presented to the IEC the annual report on the status of the study? YES □ NO □ N/A□ If your answer is NO or N/A, go to question 10	Comments
9. Verify if the reports include the following requirements: a) Number of randomized/included patients b) Summary of serious and non serious adverse events c) Summary of unanticipated problems d) Summary of new information available	YES □ NO □ YES □ NO □ N/A□ YES □ NO □ N/A□ YES □ NO □ N/A□
10. Does the investigator have the "investigator's brochure" available? YES □ NO □ N/A□	Comments
11. Does the study establish that assignment to treatments must be randomized? YES □ NO □ N/A□ If your answer is NO or N/A, go to question 13	Comments
12. Verify if: a) The procedure for randomized assignment to treatments is described in the project and/or SOPM	YES □ NO □ YES □ NO □

b) There is a list containing the randomization number of each participating subject?	
13. Has the recruitment period of the study finished? YES □ NO □ If your answer is NO, go to question 15	Comments
14. Verify if the number of recruited patients equals the sample size specified in the project. YES □ NO □ N/A□	Comments

Regarding compliance with the project

15. Has there been any change or amendment to the project since the commencement of the study? YES □ NO □ If your answer is NO, go to question 17	Comments
16. Verify if the changes/amendments have complied with the following requirements: a) Approval by the IEC. b) Approval was prior to implementation of the change/amendment c) Approval by sponsor	 YES □ NO □ S/C □ YES □ NO □ S/C □ YES □ NO □ S/C □
17. Has there been any deviation from or violation to the project since the commencement of the study? YES □ NO □ If your answer is NO, go to question 19	Comments

18. Verify if the deviations/violations of the project have subsequently complied with the following requirements: a) Notify IEC as soon as possible b) Notify sponsor	YES □ NO □ S/C □ YES □ NO □ S/C □
19. From the commencement of the study it was required to make a premature breaking of the blinding or unmask the therapies under study YES □ NO □ N/A□ If your answer is NO or N/A, go to question 21	Comments
20. Verify if breaking the blinding complied with the following requirements: a) Immediate report including reasons for failure b) Inform to IEC	YES □ NO □ S/C □ YES □ NO □ S/C □

Regarding participating subjects and their records

21. Are the documents of information about participating subjects kept safely (in a private place, kept locked up)? YES □ NO □	Comments
22. Is a record kept regarding documents and "case report form" (CRF) for each participating subject included in the study? YES □ NO □	Comments
23. Verify if the "case report form" (CRF) of participating subjects screened for review complies with the following requirements: a) They are legible b) They are complete and updated	Comments

on the date of evaluation c) They are signed by investigator d) Corrections have been appropriately made and are signed and dated	
24. Does the registration method in the CRF assure that the participating subjects' privacy and confidentiality will be kept? YES □ NO □	Comments
25. Verify if all the participating subjects selected for review comply with all the screening criteria listed in the project. YES □ NO □ S/C □	Comments
26. Verify if regarding the participating subjects selected for review all the follow-up controls up to evaluation have been fulfilled according to the project YES □ NO □ S/C □	Comments
27. From the commencement of the study, has any subject withdrawn from the follow-up of the subjects participating in the study? YES □ NO □ S/C □ If your answer is NO, go to question 29	Comments
28. Verify if in withdrawal cases the following has been fulfilled: a) Identify participating subjects that have withdrawn b) Document the reasons for withdrawal c) Try to measure the final outcome in participating subjects that have not finished the follow-up d) Establish corrective measures to	 YES □ NO □ S/C □ YES □ NO □ S/C □ YES □ NO □ S/C □ YES □ NO □ S/C □

prevent any withdrawal in the follow-up	
29. Is there an investigator's note specifying the subject's participation in the study in the medical history of the participating subjects screened? YES □ NO □ S/C □	Comments

Regarding the Informed Consent Process

30. Verify if in the files of the study there is evidence that the participating subjects received a copy of the informed consent. Yes □ No □	Comment _____ _____

31. Review 50 of the informed consents given by the participating subjects of the study. In case of having less recruited subjects at the time of the evaluation, review all of them. Verify if the consents comply with the information requested in question 32 and record it in the table below.

32. Verify if the informed consent complies with the following requirements:

a) Signature of the participating subject with identification document
b) In case of inclusion of vulnerable populations, signature of the legal representative or guardian that has given consent.
c) Signature of two witnesses with identification document.
d) Signature of the physician responsible for the investigation that informed the participating subject about the study.
e) In case changes/updates have been made to the informed consent, it must be updated, signed and dated by the participating subjects under follow-up:

Admission Identification Number	Subject/Legal Representative Signature	Witness 1 Signature	Witness 2 Signature	Responsible Physician Signature	Updated/Existing Version Signature

	Yes No	Yes No	Yes No	Yes No	Yes No N/A
	□ □	□ □	□ □	□ □	□ □ □
	□ □	□ □	□ □	□ □	□ □ □
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	□ □	□ □	□ □	□ □	□ □ □
	□ □	□ □	□ □	□ □	□ □ □
	□ □	□ □	□ □	□ □	□ □ □

Regarding Adverse Events

33. Was there any adverse event and/or laboratory abnormality identified in the project from the initiation of the study? Yes □ No □ If the answer is NO go to question 34	Comment __________ __________
34. Verify if with the adverse events presented, the following requirements were complied with: a) Were reported to IEC b) Were reported to the sponsor c) The report was made within the agreed period in the project	 Yes □ No □ S/C □ Yes □ No □ S/C □ Yes □ No □ S/C □
35. Was there any serious adverse event (SAE) from the initiation of the study?	Comment __________ __________

Yes □ No □ If the answer is NO go to question 36	
36.Verify if with the SAE presented, the following requirements were complied with: a) Were reported to IEC b) Were reported to the sponsor c) The report was made within the first 24 hours as from the happening of the event d) A detailed notice of the event was additionally sent e) The confidentiality of the information of the participating *subject* was maintained f) A SAE follow-up was made	 Yes □ No □ S/C □ Yes □ No □ S/C □ Yes □ No □ S/C □ Yes □ No □ S/C □ Yes □ No □ S/C □ Yes □ No □ S/C □

Regarding the Investigational Product

37. Is there any specification specifying who is the person responsible for the accountability of the investigational product in the project or in the Standard Operating Procedures Manual (SOPM)? (The principal investigator or the representative) Yes □ No □	Comment _____ _____
38. Verify if regarding the handling of the investigational product, the following requirements were complied with: a) There are receipt and delivery records to the institution of the investigational product b) There is an inventory of the existing product in the institution c) There is a delivery record of the investigational product of each participating subject that specifies the amount delivered, doses, delivery date and scheduled date for the adherence control.	 Yes □ No □ S/C □ Yes □ No □ S/C □ Yes □ No □ S/C □

39. Verify if the following is specified in the records of the investigational product: a) Batch/series number b) Expiration date c) Single code number assigned to the investigational product d) Randomization number or participating subject ID.	Yes □ No □ S/C □ Yes □ No □ S/C □ Yes □ No □ S/C □ Yes □ No □ S/C □
40. Are the storage conditions of the investigational product specified in the project or in the Standard Operating Procedures Manual (SOPM)? Yes □ No □ If the answer is NO go to question 41	Comment _____ _____
41. Verify if the investigational product is stored according to what is specified by the manufacturer/project Yes □ No □	Comment _____ _____
42. Is there an informative document for the participating subjects with the adequate instructions about the usage of the investigational product (experimental and control therapies)? Yes □ No □	Comment _____ _____

Regarding samples and biological specimens collection

43. Does the study project include the taking of samples or biological specimens from the participating subjects? Yes □ No □ If the answer is NO go to item 3.4.	Comment _____ _____
44. Verify if, regarding the handling of biological samples, the following requirements are complied with:	Yes □ No □ S/C □
a) There are written procedures about the handling of biological samples.	Yes □ No □ S/C □
b) The person/ laboratory/ institution in charge of performing the taking, procedure and handling of samples is specified.	Yes □ No □ S/C □
c) There is a certificate or evidence authorizing such person, laboratory or institution.	Yes □ No □ S/C □
d) There is infrastructure and supplies required for performing the tests (reagents, machines, locative installations and others).	Yes □ No □ S/C □
e) It has the test standardization	Yes □ No □ S/C □
f) According to the laboratory operating procedure manual	
45. Verify if the responsible person for performing the collection, processing and handling of the samples is the institutional laboratory, and if this laboratory has already complied with the evaluation requirement of clinical laboratories registered in institutions that perform investigations with human subjects. Yes □ No □ N/A□	Comment _____ _____
46. Verify if measures have been taken for assuring that during the processing and report of samples and biological specimens the confidentiality right of the participating subject in the study is respected.	Comment _____ _____

Yes □ No □ S/C□	_____ _____
47. Is the correct interpretation way of the laboratory test results described in the project or in the SOPM? Yes □ No □	Comment _____ _____
48. Verify if the normal values of the laboratory tests are in the file or in the study manual Yes □ No □	Comment _____ _____
49. Is the need for sending samples to other laboratories or institutions described in the project or in the study manual Yes □ No □ If the answer is NO go to item 3.4.	
50. Verify if regarding the shipment of biological samples the following requirements are complied with:	Yes □ No □
a) In the project or in the manual there are written specifications about the shipment and storage of samples.	Yes □ No □ N/A□
b) The personnel in charge of preparing and performing the shipment is qualified and trained for performing the conservation and shipment of samples by air transport	Yes □ No □
c) The institution has the supplies and installations needed for the conservation of the samples	Yes □ No □
d) The consumables needed for performing the shipment according to the specifications are available	
e) Biological sample shipment records are kept	

3.4 Documentation and files that the principal investigator must have

Verify if in the files of the study documents described in the checklist appearing below are present. You may find documents that do not apply to the project being evaluated, as for example, amendments to the project or to the informed consent form, if they were not made. In such case, mark the N/A box, not applicable.

Checklist about the file documents that the investigator must have

Document	Present in the file
Initial version of the project	Yes □ No □
Signature page	Yes □ No □ N/A □
Letter of submission of the project for approval of the Institutional Ethics Committee (IEC)	
Approving letter of the initial project by the IEC	Yes □ No □
Project revisions	Yes □ No □ N/A □
Signature page	Yes □ No □ N/A □
Notice letter of revisions of the project to IEC	Yes □ No □ N/A □
Amendment to the project	Yes □ No □ N/A □
Signature page	Yes □ No □ N/A □
Letter of submission of amendments to the IEC	Yes □ No □ N/A □
Approving letter of amendments by the IEC	Yes □ No □ N/A □
Initial informed consent form	Yes □ No □
Letter of submission of the initial informed consent to the IEC	Yes □ No □

Approving letter of initial informed consent by the IEC	Yes □ No □
Letter of submission for approval of the update of the informed consent to IEC	Yes □ No □ N/A □
Approving letter of the update of the informed consent by the IEC	Yes □ No □ N/A □
Receipt-copy form of the informed consent by the participating subjects	Yes □ No □
Advertisements for recruitment	Yes □ No □ N/A □
Advertisements submission letter for recruitment	Yes □ No □ N/A □
Advertisements Approving letter for recruitment	Yes □ No □ N/A □
Materials delivered to the participating subjects	Yes □ No □ N/A □
Material submission letter delivered to the participating subjects	Yes □ No □ N/A □
Approving letter of materials delivered to the participating subjects	Yes □ No □ N/A □
Submission letter of incentives proposed to IEC	Yes □ No □ N/A □
Approving letter of incentives by IEC	Yes □ No □ N/A □

Document	**Present in the file**
Budget of the study	Yes □ No □
Contract and agreement with financing entity	Yes □ No □ N/A □
Contract and agreement with sponsors	Yes □ No □ N/A □
Accountability reports about the handing of the project	Yes □ No □ N/A □
Annual reports about the progresses of the study sent to the Institutional Ethics Committee (IEC)	
Notices, deviations and infringements to the IEC	
Final report of the study to the IEC	Yes □ No □ N/A □
Storage instructions of the investigational product	Yes □ No □
Accountability record of the investigational product	Yes □ No □

Study personnel list	Yes □ No □
Principal investigator CV	Yes □ No □
Co-investigators CV	Yes □ No □ N/A □
Other study personnel CV	Yes □ No □ N/A □
Investigator, co-investigator and other study personnel training certificates	Yes □ No □
Principal investigator's responsibilities form.	Yes □ No □
Co-investigator's responsibilities form.	Yes □ No □
Study personnel's responsibilities form.	Yes □ No □
Signature page of the investigator	Yes □ No □ N/A □
Signature page of the co-investigators	Yes □ No □ N/A □
Signature page of the other study personnel	Yes □ No □ N/A □
Survey of the investigator	Yes □ No □ N/A □
Statement of conflict of interests	Yes □ No □
Inclusion/exclusion criteria list	Yes □ No □
List of the pre-screened participating subjects	Yes □ No □
List of the included participating subjects	Yes □ No □
Study procedure brochure	Yes □ No □
List of IEC members	Yes □ No □
Investigator's brochure	Yes □ No □ N/A □
Letter for the sending of a copy of the Investigator's brochure to IEC	Yes □ No □ N/A □
Updates to the Investigator's brochure	Yes □ No □ N/A □
Approving letter of the initial project by INVIMA	Yes □ No □
Approving letter of the amendments to the project by INVIMA	Yes □ No □
Guide of the Good Clinical Practices	Yes □ No □
Declaration of Helsinki	Yes □ No □
Resolution 8430 of 1993	Yes □ No □
Laboratory accreditation certificate	Yes □ No □ N/A □
Certificates issued by an acknowledged entity, wherein there is proof that personnel is trained for performing the shipment processes	Yes □ No □
Laboratory normal values	Yes □ No □

Document	Present in the file
Laboratory manual	Yes □ No □
Biological sample shipment records	Yes □ No □ N/A □
Inventory of biological samples taken and stored	Yes □ No □ N/A □
Initial informed consent signed by each participating subject and updates	Yes □ No □
Original laboratory or other examinations reports	Yes □ No □ N/A □
Case Report Form (CRF) of each participating subject CRF discrepancy forms	Yes □ No □ Yes □ No □ N/A □
Medical history of each participating subject	Yes □ No □ N/A □
Death report	Yes □ No □ N/A □
Mailing with each participating subject	Yes □ No □ N/A □
Telephone contact with each participating subject	Yes □ No □ N/A □
Mailing with the sponsor	Yes □ No □ N/A □
Telephone contact with the sponsor	Yes □ No □ N/A □
Monitoring visit reports	Yes □ No □
Study closing visit report	Yes □ No □ N/A □

All the information corresponding to the principal Investigator evaluation of the first selected study has been gathered. On this same study the sponsor information must be filled in, before evaluating the investigators of the other studies.

4. EVALUATION OF THE SPONSOR OF THE STUDY

NOTE: Reproduce this section of the guide as many times as it is needed so as to have one per selected study for the evaluation

The questions below make reference to the requirements that the active project sponsors must comply with regarding the participating subjects and the institution where research takes place.

This part of the evaluation is also based on the previously selected studies from all the investigations performed in the institution being evaluated. The principal investigator of each of them must be interviewed. To facilitate the gathering of information requested in this section, the investigator or his representative must be present during all the evaluation.

The information verification questions must be answered based on the revision of the study files and on the participating subjects included in the investigation.

In the questions about requirements, you will find three possible answers, mark:

YES □, *if the requirement IS complied with*
NO □, *if the requirement IS NOT complied with*
N/A □, when the requirement does not apply to the specific case under evaluation

In the questions about verification, you will find again three possible answers, mark:

YES □, *if the requirement HAS BEEN complied with in all the cases that were reviewed*
NO □, *if the requirement HAS NOT BEEN complied with in any of the cases*
S/C□, *if the requirement has been complied with only in some cases*

When the investigator or the institution are the same sponsors of the study being reviewed, the same question described for the external sponsor must be applied, and additionally, questions of item 4.4 must be answered.

4.1 General information of the Sponsor

1. Name of the Sponsor
2. Sponsored investigational project title

3. Research Sponsor Type *(mark X as applicable)*:

a) Pharmaceutical Industry	□
b) Academic Institution	□
c) Health Care Provider Institution	□
d) Governmental Institutions	□
e) Foundation or Organizations that provide support to research	□
f) The investigator	□

4.2 Responsibility of the Sponsor of the Study

1. Is the information regarding the safety and efficiency of the investigational product that was	*Comment* _____

obtained in the previous clinical or non clinical studies to support its administration in human beings available? Yes □ No □	
2. Is there an approval document for the use of the investigational product by the INVIMA? Yes □ No □	*Comment* _____
3. Did the sponsor take the following measures to guarantee the protection and safety of the subjects participating in the study? a) Implementation of a security monitoring system b) Implementation of an adverse event report and follow-up system with all the institutions participating in the study (multicenter studies) c) Supply of a contractual and extra-contractual policy for related adverse events attributed to the investigational product, whose amount shall agree with international standards	 Yes □ No □ Yes □ No □ Yes □ No □

4. Did the sponsor organize training courses to ensure the competence of the persons involved in the investigation regarding the following aspects?	
	Yes □ No □
a) The research project?	Yes □ No □
b) Assignment, follow-up and review procedures?	Yes □ No □
c) Assignment, follow-up and review procedures of subjects participating in the study?	Yes □ No □
d) Handling of the investigational product(s)?	Yes □ No □
e) Good Clinical Practices?	Yes □ No □
f) Ethical principles for research in human beings?	Yes □ No □
g) National Regulations about clinical research?	
5. Does the sponsor supply the investigational product (medication) to the study? Yes □ No □ *If the answer is NO go to question 7*	*Comment* _____
6. Verify if the sponsor meets the following requirements regarding investigational product handling:	
a) He/she controls the distribution and return of investigational products.	Yes □ No □
b) He/she provides the records to register information about shipping, reception, return and destruction of the investigational product	Yes □ No □
c) He/she provides the supplies required to store and preserve the product	Yes □ No □
d) He/she delivers a copy of the records regarding investigational product handling	

7. Verify if the instructions for investigational product handling include the following aspects: a) Suitable and safe reception procedure. b) Storage conditions. c) Way of delivery to participating subjects. d) Removal of the investigational product that wasn't used in the study.	 Yes □ No □ N/A □ Yes □ No □ N/A □ Yes □ No □ N/A □ Yes □ No □ N/A □
8. Is there a copy of the clinical study budget for the participating site delivered by the study sponsor? Yes □ No □ If the answer is NO go to item 4.3.4	*Comment* _____

9. Verify if the budget given by the sponsor specifies the following areas: a) Compensation for the investigators. b) Budget intended for participating subjects. c) Equipment purchase. d) Paraclinical and laboratory examinations. e) Participant subjects insurance whose amount shall agree with international standards. **Note:** if by any case or circumstance the Insurance doesn't cover the damages completely, the trial promoter, the study principal investigator and the Director of the institution or site in which the study was carried out will be jointly and severally liable, although there is no guilt. The administrative authorization or the Ethics Committee report shall not exempt them from the responsibility.	 Yes □ No □ Yes □ No □ Yes □ No □ Yes □ No □ Yes □ No □
4.3. Functions of the Study Sponsor	
1. Verify if the sponsor has met the following requirements to ensure the protection and confidentiality of participating subjects: a) Assign identification codes. b) Facilitate the filing of the "identification page" record of each participating subject independently from the Case Report Form (CRF) 2. Do the study documents specify the responsibilities of the investigator, the coordinators and the rest of the personnel required for the study?	 Yes □ No □ Yes □ No □ *Comment* _____

Yes □ No □ If the answer is NO go to question 4	

3. Are there any commitment or acceptance letters of the functions and responsibilities of the persons involved in the study? Yes □ No □	*Comment* _____
4. Did the sponsor make sure that the investigators and coordinators receive suitable training in the project before initiating the study? Yes □ No □ If the answer is NO go to question 6	*Comment* _____
5. Verify if the training provided to study investigators and coordinators included the following aspects: a) Randomization procedure b) Fill in case report forms c) Adverse event reports d) Project deviation report	 Yes □ No □ N/A □ Yes □ No □ N/A □ Yes □ No □ N/A □ Yes □ No □ N/A □
6. Did the sponsor provide the institution with the necessary conditions to meet the following requirements regarding the study documents? a) Securely store study documents. b) Preservation of the record of essential documents for at least five years after the end of the	 Yes □ No □ Yes □ No □ N/A □

study.	
7. Does the sponsor provide a monitoring system during the conduction of the study? Yes □ No □ If the answer is NO go to question 10	*Comment* _____

8.Verify if the monitoring process meets the following requirements:	
a) Monitoring visits shall be periodic and according to the recruitment rate of participating subjects.	Yes □ No □ S/C □
b) Visits are scheduled with the study investigator and coordinator.	Yes □ No □ S/C □
c) A written report must be made of the findings of every visit.	Yes □ No □ S/C □
9. Read the monitoring visit reports to verify if during the visits the following aspects have been evaluated:	
Adherence to the project on the part of the investigator group.	Yes □ No □ S/C □
a) Certainty that every participating subject has given and signed informed consent.	Yes □ No □ S/C □
b) Verification of the fulfillment of inclusion and randomization processes of eligible participating subjects.	Yes □ No □ S/C □
c) Report on the recruiting rate of participating subjects.	Yes □ No □ S/C □
d) Verification of the fulfillment of reports and notices by the principal investigator.	Yes □ No □ S/C □
e) Review and verification of adverse event reports.	Yes □ No □ S/C □
f) Verify if the essential documents for conducting the study are kept under certain conditions which guarantee the integrity of the data contained therein.	Yes □ No □ S/C □
g) Communication about project deviations.	Yes □ No □ S/C □
h) Definition of corrective measures to prevent recurrence of detected deviations.	

10. In case there is an external sponsor, has any contractual obligation or agreement been established with the investigator or institution? Yes □ No □ If the answer is NO go to item 4.4	*Comment* _____

11. Verify if the contract or agreement meets the following requirements: a) Establishes the terms set for initiation and termination of the contract. b) Establishes the form of payment and expenditures on the part of the sponsor. c) Products expected for the sponsorship that was granted. d) Establishes the measures (sanctions) taken by the sponsor in case of persistent non-fulfillment of the project by the investigator/institution. e) Specifies that the sponsor must inform the investigators and the institution and the IEC (Independent Ethics Committee) about the reasons for terminating or suspending a study prematurely.	Yes □ No □ S/C □ Yes □ No □ S/C □ Yes □ No □ S/C □ Yes □ No □ S/C □ Yes □ No □ S/C □
4.4 Relations with the Study Financing Entity When the Investigator is the Sponsor The questions below must be made only when the investigator or institution is the sponsor of the study and there is external funding to carry out clinical research. Otherwise, write N/A and continue with the evaluation of the sponsors of the other studies	
1. Has the financing entity established a contractual obligation or agreement with the investigator/institution? Yes □ No □ N/A □ If the answer is NO or N/A go to question 3	*Comment* _____

2. Verify if the contract specifies the following aspects: a) Initiation and termination terms of the contract. b) Funding amount according to the budget of the study. c) Payment and expenditure dates. d) Products expected from the financial relation or activity. e) Obligations of the investigator/institution.	 Yes □ No □ N/A □ Yes □ No □ N/A □ Yes □ No □ N/A □ Yes □ No □ N/A □ Yes □ No □ N/A □
3. Verify if the investigator/institution fulfills budget handling in the following aspects: a) Payment to the work group. b) Follow-up of income and expenses of the study (accounting reports). c) Obligations of the investigator/institution regarding equipment and supply purchase for the study. d) Payment to participating subjects according to the budget.	 Yes □ No □ N/A □ Yes □ No □ N/A □ Yes □ No □ N/A □ Yes □ No □ N/A □
4. Is there a written document establishing that the financing entity will carry out an audit of the research process? Yes □ No □ N/A □ If the answer is NO or N/A you have finished the sponsor evaluation	*Comment* _____
5. Verify if the following aspects regarding the audit have been fulfilled: a) Visits of the auditor in charge. b) The investigator/institution has made periodic reports on the advances of the study.	 Yes □ No □ N/A □ Yes □ No □ N/A □

5. EVALUATION CRITERIA ACCORDING TO THE RELEVANCE

Critical aspects: non compliance with critical aspects has a high impact on research quality and may endanger the safety of the patients. The following aspects are considered critical:

1) Number of members (men and women)
2) Memorandum of the Committee
3) Approval of the project by INVIMA or the delegated Sanitary Entity
4) Records
5) Records regarding investigator evaluations
6) CV of the investigators
7) Records and certificates regarding the training of the whole personnel
8) Conflict statements signed by the investigator
9) Procedure Manuals
10) Handling and procedure of amendments
11) Case report form
12) Written procedures and records
13) Participant selection
14) Control and follow-up of each and every participant screened for the study
15) Adverse event reports
16) Handling of biological samples
17) Handling instructions of the investigational product
18) Informed consent
19) Project record in a public or private net of clinical trials

Non-critical: non compliance with this item has a medium impact on research quality and does not endanger the safety of the patients. The following aspects are considered non-critical:

1) Committee Manual or Operating Guideline

2) Manual and/or form for making reports
3) Specification in the Manual of the number of members required to reach quorum.
4) Coincidence in the number of recruited patients and the sample size specified in the project.
   a) Verification if the patient has his own copy of the informed consent.
   b) Copy of the memorandum or certification in which INVIMA approved the use of the product for research.

CHAPTER IV

VERIFICATION OF THE REQUIREMENTS THAT MUST BE MET BY THE CLINICAL LABORATORIES OF THE INSTITUTIONS THAT CONDUCT CLINICAL RESEARCH IN HUMAN BEINGS

INTRODUCTION

The evaluation of clinical laboratories of the institutions which carry out clinical studies has the purpose of verifying if the laboratory has the necessary infrastructure and suitable organization to participate in clinical research, according to the ethical and technical universal principles related to research in human beings. As a consequence, the present evaluation is specifically focused on the fulfillment of national criteria and standards for research, and includes the review of aspects related to minimum required infrastructure for the taking, processing, preservation, security and transport of biological specimens necessary in the investigation, as well as the review of processes related to the investigation.

According to the principles of the Good Clinical Practices in human research, this evaluation process must achieve the following basic objectives:

a) Establish if during the collection, analysis and result report processes the rights of the research participants are respected.
b) Determine if the evaluated laboratory meets the quality standards and criteria that guarantee the safety of the biological samples taken from the subjects participating in clinical research, as well as the value of the results of the analysis made.

1. Requirements that Clinical Laboratories Must Meet

Every laboratory which makes, in Colombia, the analysis of biological specimens as part of clinical research must previously meet the following requirements which authorize it to work as a clinical laboratory within the General System of Social Security in Health.

a) To be registered in the Health Care Providers Special Registry.

b) To meet the quality standards defined in the current standards.
c) To comply with the current regulations for clinical laboratories, in Colombia, at the moment of the evaluation.

TABLE 2. COMPULSORY REQUIREMENTS THAT EVERY CLINICAL LABORATORY MUST MEET

Requirements	***Way of suggested evaluation***
1. The laboratory must be registered in the Special Registry of Health Care Providers, according to what was indicated in current health regulations.	Review of: Registration Certificate to the Special Registry of Health Care Providers
2. The laboratory must meet the quality standards defined in the Mandatory System of Guaranty of Health Care Quality of the General System of Social Security in Health.	Authorizing conditions fulfillment certificate

The following sections of this document compile the aspects additional to those defined in the single authorizing system that must be met by clinical laboratories willing to participate in clinical research with subjects.

2. Additional Requirements that Must be Met by Every Clinical Laboratory Participating in Clinical Research

The evaluation of the laboratories participating in clinical research is based on specific requirements that they must meet regarding clinical research processes, expecting the following:

a) Determine if the evaluated laboratory meets the quality standards that guarantee the safety of biological samples taken from subjects participating in clinical research and the validity of the results in the analysis that are made.

b) Establish if during the analysis and result report process the rights of the subjects participating in clinical research are respected.

2.1 Laboratory Personnel

Within the personnel that a clinical laboratory must have, three persons are identified whose responsibilities and functions are directly related to clinical research: the laboratory director, a person designated by the director as the person in charge of the study in the laboratory and the person(s) who directly make the tests or analyses required by the investigation. Tables 2 to 6 present the requirements defined as the obligations and responsibilities that each of those persons must assume in order to participate in clinical research with drugs.

CHART 1. MANDATORY REQUIREMENTS THAT MUST BE COMPLIED WITH BY ALL CLINICAL LABORATORIES

Requirements	Suggested Evaluation Method
1. The laboratory must be registered with the Special Register of Health Services Providers, pursuant to the rules of health and regulations in full force and effect.	Revision of: Certificate of registration with the Special Register of Health Service Providers.
2. The laboratory must comply with quality standards defined in the mandatory System of Guaranty of Health Service Quality of the General System of Social Security in Health.	Certificate of compliance with authorization conditions.

In the following sections of this document, there is a compilation of the additional aspects to those defined in the Single Authorization System which must be complied with by those clinical laboratories willing to participate in clinical research with subjects.

2. Additional requirements which must be complied with by every clinical laboratory participating in the research.

The evaluation of the laboratories participating in the clinical research is based on specific requirements which must be complied with in reference to the clinical research processes, the aim of which is to:
a) Determine if the evaluated laboratory complies with the quality standards that guarantee the safety of the biological samples taken from the subjects participating in the research and the validity of the results in the analysis made.
b) Establish if the rights of those subjects participating in the research are respected during the analysis process and report of results.

2.1 Laboratory personnel

Within the personnel every clinical laboratory must have, three actors are identified with functions and responsibilities directly related to the clinical research: the director of the laboratory, a person appointed by the director to be in charge of the study in the laboratory and the person(s) directly conducting the trials or analysis requested by the research. Tables 2 to 6 show the defined requirements as obligations and responsibilities which must be complied with by these persons in order to participate in the clinical research with drug.

TABLE 2. REQUIREMENTS FOR THE DIRECTOR OF THE LABORATORY

Requirements	Evaluation Method
1. Be aware of the fact and make sure that laboratory personnel knows and complies with: a) Ethical principles for research in human beings b) National regulations c) Guidelines for Good Clinical Practices d) The Laboratory Manual and Quality System	Revision of: Certificates of personnel training in these topics
2. Pursuant to the trials and sample analysis requested by the studies, the director must assure the following aspects: a) The professional profile and the experience of the personnel appointed for the trials and analysis. b) The facility. c) The equipment. d) The availability of necessary supplies. e) The availability of an appropriate technical guide. f) The number of required	

professionals.	
3. Make sure of the existence of and the compliance with a *quality system assurance* which guarantees the validity of the results of the trials and analysis conducted in the laboratory.	Revision of the Manual of Quality, Quality system Registers. Verification with offered trial.
4 For each study, appoint a person to be in charge of the handling of biological specimens of each participant. This person must have the following characteristics: a) Appropriate qualification. b) At least, 2 years of training and professional experience previous to the beginning of the study. c) Knowledge of Guidelines for Good Clinical Practices (GGCP).	Revision of: CV of professionals in charge of researches carried out in the laboratory. Certificate of training in GCP
5. Make sure that the biosafety rules are of common knowledge and complied with in the laboratory.	Revision of: Manuals y registers of biosafety courses. Manuals of collection, transport and conservation of samples.
6) Make sure that the laboratory complies with national and international regulations for collection, transport and shipping of biological samples.	Revision of: Certificate issued by a renowned Entity evidencing that personnel is trained to carry out the shipping process. SOP manuals about conservation and transport of samples.
7) Make sure that the laboratory respects the participating subjects' rights in the research during the collection and process of samples and the report of results by adopting strategies that permit: a) Maintaining the privacy of the patient during the collection of samples or trial (provision of dresses, robes, etc., when appropriate). b) Maintaining the confidentiality of the information and the results of the patients during all the phases of	Revision of: Registers of patients' trial of the study. Revision of the study manual. This verification is supplemented by the revision of the aspects related to procedures.
the analytical process by using a system of codification that only allows those in charge of the study to relate	Revision of: Register of patients' trials of the study. Revision of the study manual.

the participant in the research to the results of the trial (code identification). c) Guarantee a mechanism of information to the participating subject in case of damage or loss of the specimen or the sample. (leaflet or instructions manual) d) Make sure that the participant has given his consent (by signing the informed consent form) for the collection of a sample or specimen.	This verification complemented with the revision of the aspects related to procedures.
5) Define a calibration and maintenance program of the laboratory equipment and keep a register.	Revision of the program and the registers.

CHART 3. REQUIREMENTS FOR THE PROFESSIONAL IN CHARGE OF THE STUDY IN THE CLINICAL LABORATORY

Requirements	**Evaluation Method**
1) The professional appointed as "person in charge of the research in the laboratory" must hold a degree of academic education in any of the following professions and must have professional experience in clinical laboratory of, at least, two (2) years: a) Bacteriology b) Microbiology c) Chemistry or pharmaceutical chemistry with academic education in one of the technical areas of clinical laboratory. d) Medicine with specialization in clinical pathology or in one of the technical areas of the clinical laboratory.	Revision of: CV of the professional. Documents and y training certificates.
2) The professional appointed as "person in charge of the research in the laboratory" must have knowledge and experience of application of GCP, adopted by the Ministry of Social Protection.	Revision of Certificates and CV.
3) Know the project, procedures and techniques described in the study	Revision of: Study manual.

manual as regards the handling of the participants' samples and biological specimens.	Verify that he knows the study manual.
4) Adhere strictly to the project and to the procedures described in the study manual as regards the handling and processing of biological specimens and timely notify any deviation to the investigator group.	Study manual Report forms of deviations from project / SOPM
5) Assign the distribution of the work related to the study pursuant to the needs of the research, considering each member of the personnel's training and experience.	List of responsibilities of the study's personnel in the laboratories.
6) Know and make sure that the SOP are complied with for collection, transport and shipping of biological samples.	Revision of: SOPM and verification with Registers of handling / shipping of samples.
7) Make sure that every result is documented, reported and filed according to the description in the study manual.	Revision of: Laboratory personnel's responsibilities with the study. Reports handed to the study investigator/ patients' files.
8) Make sure that privacy and confidentiality of the identification data are kept in the report and file of the results of the trials made to participants in the research.	Verification of results' registers identified by an identification document.
6) Sign and date the reports of the results submitted to indicate that the professional in charge of the study in the laboratory assumes responsibility for the validity of the result.	Revision of: Reports of the results
7) Make sure that the laboratory keeps a copy of the results of the trials conducted on patients of the study.	Revision of: Study files documents
8) Make sure that the file of the results is kept for at least two (2) years as from the end of the study.	Revision of: Files and registers of trials in previous studies
9) Keep a file of documents of the research study in the laboratory which facilitates auditing and which includes: a) A study project b) A list of the officials of the laboratory appointed for the research.	Revision of: Study file folder in the laboratory

c) CV of those officials appointed for the research study Project. d) Knowledge of good clinical practices of all participants of the research. e) Responsibilities of the laboratory personnel with the study. f) Copy of the investigator operating procedures of all trials that require the study and/ or research. g) List of the participating subjects treated in the laboratory. h) Relation of shipping of results to the coordinator of the study.	

CHART 4. REQUIREMENTS THAT MUST BE COMPLIED WITH BY THE PERSONNEL INVOLVED IN THE COLLECTION, PROCESSING, CONSERVATION AND TRANSPORT OF BIOLOGICAL SPECIMENS OF THOSE SUBJECTS PARTICIPATING IN THE RESEARCH.

Responsibilities	**Evaluation Method**
1) The technical personnel involved in the collection, processing and report of trials conducted on subjects participating in the research must hold a degree in any of the following professions and must have, at least, two (2) years of professional experience in clinical laboratory: a) Bacteriology b) Microbiology c) Chemistry with specialization in one of the technical areas of the clinical laboratory.	Revision of: CV, Certification and / or professional card of people involved according to description in the list of people involved and functions of the study file in the laboratory.
2. Know the Guidelines for Good Clinical Practices and the study manuals related to the work within the laboratory / study.	Revision of: Verify knowledge of the study manual.
3. Know and apply the quality system of the laboratory in all procedures carried out.	Verification of knowledge of the quality system of the laboratory described in the manual of quality of the laboratory.
4. Conduct the trials of quality control of the requested analysis for the study.	Revision of: Registers of the quality control program (graphic, etc.) in the last 6 to

	12-month period)
5. Guide participants of the study on the sample collection requirements.	Revision of: Instructions of sample collection in SOPM and study manual Information mechanism to participants in the studio
6. Know and implement the described SOP for the procedures in which he participates or which he conducts according to his responsibilities in the research.	Verify knowledge of the procedures of studies he is in charge of.
7. Communicate in a timely manner any deviation or inconsistency in the SOP to the professional “in charge” of the laboratory.	Revision of project deviations.
8. Register results in an accurate and timely manner according to the Good Clinical Practice principles.	Revision of: Reports of results. Forms of register of results of the study. Forms of patients’ follow-up in the laboratory.
9. Take prevention measures to minimize health risks, complying with biosafety rules.	Verify: Registers Knowledge of biosafety rules Knowledge of the Laboratory biosafety manual Certificate of biosafety courses.

2.2 Quality Guarantee.

a) Quality control program
b) Quality guarantee program (equipment and facility maintenance, safety and biosafety)
c) Evaluation of abilities and personnel competence (training, education, updating)
d) Aptitude trials (comparison with external laboratories)

Considering that the aim of Good Clinical Practices is to guarantee the safety of participating subjects and assure accuracy and validity of research results, the quality system constitutes one of the most important pillars of those laboratories conducting trials and sample analysis of subjects participating in the research.
Chart 5 summarizes the most important aspects that must be present in a quality system of a clinical laboratory processing samples for a clinical study.

TABLE 5: QUALITY SYSTEM

Requirement	Evaluation Method
1. The laboratory must have a quality system at least involving the following: a) A Quality Control Program b) A Quality Guarantee Program c) Ability and Competence Evaluation d) Aptitude Trials (external control)	Revision of: Manual of quality system. Registers of quality system implementation
2. The laboratory must have a Laboratory Quality Manual (LQM) which defines the quality system and describes its policies, components, as well as the different functions and responsibilities of the laboratory officials, required for the correct implementation of the quality system.	Revision of: Manual of quality system.
3. The LQM must establish the kind and frequency of the quality control activities in order to: a) Immediately detect alterations in the results due to failures in the equipment, environmental conditions or operator's mistakes. b) Monitor during a period of time the different factors that may alter the accuracy of the results (through internal and external control)	Revision of: Manual of quality system. Registers and quality control graphics in the last 6 to 12-month period.
4. The quality system must be carried out by one or more assessors appointed by the director of the laboratory.	Revision of: Manual of quality system Registers and methods of evaluation and follow-up.
5. The laboratory must have all the documentation which allows for the verification of the application of the different components of the quality system in the last year (according to the laboratory evaluation trial): a) Register-Graphics with quality control results of each of the trials/ analysis conducted in the laboratory. b) Maintenance registers, guarantee from the providers, history of the equipment and technology used in the laboratory. c) Register or certificate of training of laboratory technicians and professionals in the use of technology.	

Training certificates of the laboratory technicians who are members of the personnel as regards continuous education courses. d) Register of adverse events associated to the use of equipment and technology used in the laboratory. e) Certifications of certifications of the technicians who are members of the personnel, as regards continuous education courses. f) Register of the evaluation process of Performance evaluation (Ability and competence) of laboratory technicians and professionals. g) Registers of the results of activities of external control (evaluations, comparisons with others...)	

2.3 Audit for improvement

Clinical laboratories which conduct analysis of biological specimens as contribution to the research of drugs in human beings must establish and comply with an internal auditing program based on quality standards that serve as a guidance to the different activities carried out in the laboratory, so that a continuous quality improvement is guaranteed pursuant to the sanitary regulations in force. Auditing is a required means of achieving a continuous improvement in the quality of health care. Auditing for quality improvement is the systematic and continuous mechanism of evaluation of compliance with the quality standards which supplement those determined as basic in the Single Authorization System, the internal audit, as the self-control process and the external audit as components of an integral auditing program.

CHART 6: INTERNAL AUDITING PROGRAM

Requirement	Evaluation Method
1. The director of the laboratory is in charge of the following: a) Making sure of the existence of an internal auditing program. b) Assigning and assuring the training of the internal auditors. c) Preparing the internal auditing agendas.	Revision of: Documents of the auditing program. This revision complements the verification of the other aspects described in this chart.
2. The laboratory (or entity) must have a written auditing program which must	Revision of: Manual of quality of the entity or the

include: a) The aim (auditing the system, not the persons) b) Structure c) Procedures d) Implementation mechanisms e) A person in charge of the auditing program f) Auditors g) Contents of the audit report	laboratory
3. The auditing program must be carried out by one or more auditors appointed by the director of the laboratory (or entity director), whose responsibilities must be described in the laboratory manual of quality.	Revise the entity or laboratory manual of quality
4. Auditors can be employed by the laboratory or can be external consultants and must be qualified for auditing processes	Revision of: Auditors' CV Certificates of training in auditing
5. Internal auditors must prove that: a) They are aware of the previous audit reports. b) They are aware of the local requirements and standards (manual of quality, SOPMs, working instructions, etc.) c) They are aware of the auditing program. d) They have a standardized list of control for the auditing of each area and / or auditing procedure.	Verification of: Audit registers and /or reports. Verification on knowledge of Quality Rules. Audit agendas Register documents of findings during audits
6. The internal auditing program must show that it designs and plans to carry out frequent controls to make sure that: a) The documents of the quality system answer the needs of the laboratory and, therefore, the needs of the research. b) The documented procedures and instructions are practicable, understandable and implementable. c) Employees training conforms the needs of their functions and responsibilities.	Revision of: Auditing program and its components. Training registers

7. The internal audit agenda must cover the evaluation of all aspects of the quality system, at least, once a year. However, specific activities may be audited more frequently, depending on its importance.	Revision of: Audit agendas Audit plan
8. The internal audit agenda must include the possibility of conducting extraordinary audits due to: a) Not anticipated problems. b) Problems identified in previous audits. c) Requests by the director of the laboratory or regulatory entities.	Revision of: Audit agendas Description of the program.
9. There must be a plan of internal audits. The plan of each audit must specify the following: a) The auditor b) The object of the audit c) The date on which the audit is to be conducted (In the planning, it is enough with mentioning the month scheduled for conducting the audit).	Revision of: Audit plan Verification of the auditors' performance in the registers of audit reports.
10. The laboratory must hold the documents which allow for the verification of the existence, operation and effectiveness of each audit. The documents about each audit must include: a) A standardized card of the collection of information about each audited process area. b) Evidence collected with or without reference to the audited process. c) An audit report, which must include: 1. A description of the findings (good and bad aspects) 2. Constructive suggestions for the improvement of the processes in each area. 3. A clear identification of those areas which require corrective actions. 4. A definition of corrective measures and the person in charge of them. 5. The name of the auditor, the audited areas, persons and the place	

and date of the audit.	
11. The description of the findings reported by the audit must satisfy the following classification criteria: a) Acceptable: satisfies the GCP requirements and the requirements of the laboratory according to the manual of quality, SOPM, etc. b) Serious failure: Failure in the satisfaction of the GCP c) Slight failure: Satisfies the GCP requirements, but fails to satisfy the laboratory requirements (described in the manual of quality, SOPM) d) Requires attention: a certain area can be improved.	Revision of: Auditing program Report of the audits made
12. The laboratory must assure that self-control and follow-up actions proposed in the internal auditing program have been complied with. a) Implement an action plan in response to the audit findings. b) Keep a register (for verification purposes) of the actions taken as corrective measures that include the following: 1. Adopted measure 2. Objective 3. Implemented measure 4. Persons involved / participants 5. Date of implementation 6. Follow-up for evaluation of effectiveness.	Requirements Revision of: Registers and documents of the auditing program Verification of the action plan vs. reports of compliance
13. The auditor is responsible for the control and follow-up of the adopted corrective actions: a) He must make sure that the measures or actions have been correctly implemented. b) He must register in the “audit report” the follow-up made of the adoption of the corrective actions. c) He must register the follow-up closing when the corrective actions have been completed in the audit	Revision of: Audit reports Follow-up reports

report.	

3.4. Equipment for biological specimens' analysis and procedures

This section describes the aspects that the clinical laboratory must comply with as regards the procedures and use of equipment or necessary technology for the collection, process, analysis and conservation of samples, so that the quality is guaranteed in these processes (Table 7 and 8). Additionally, minimum aspects that must be considered are included in the different manuals of standardized operating procedures in the laboratory (Table 9), which, in the case of the laboratory, turns into an essential tool for the definition of processes tested in the programs of quality guarantee.

TABLE 7. HANDLING OF THE SAMPLES OF PARTICIPANTS OF THE RESEARCH

Requirement	**Evaluation Method**
1. The laboratory must have a register system that guarantees the confidentiality of the information of the patient through: a) Codes for the identification of participants of the research. b) Registers of patients of the study which are kept in a safe place and to which only the person in charge of the study in the laboratory may have access.	Revision of: Registers of patients (codes) Place where registers are kept
2. The laboratory must have the appropriate facilities to take, manipulate, transport and conserve the biological specimens of those persons participating in the research in the best way: a) The facilities must comply with all the aspects described as necessary in the specific SOP for the collection, manipulation, transport and conservation of each specimen according to each trial/ analysis to be conducted. b) The person in charge of the research must appoint the persons who will be in charge of taking, manipulating and conserving the specimens, and must comply with the	Revision of specific SOP Revision of registers of sample collection Revision of the facilities

functions and responsibilities established in chart 4.	
3. The laboratory must make sure that it has a transport system of samples that guarantees the appropriate conservation and safety of the samples taken from research participants: a) There must be written standardized operating procedures (SOP) based on good practices to guarantee sample safety and conservation. b) It must have the necessary facilities and technology for the shipping in order to comply with international regulations of collection, handling and transport of biological samples. c) It must have trained officials certified by renowned entities that prepare and carry out the shipping process. d) It must assure that only those officials who have been trained carry out the transport of specimens of the participants of the research.	Revision of: Specific SOPM Register of shipping Revision of certificates and proof of studies.

CHART 8. EQUIPMENT, MATERIALS AND REAGENTS

Requirement	**Evaluation Method**
1. The equipment and materials used in the process of sample analysis must be appropriate, according to the description in the SOP of the trials that the laboratory offers to the research.	Revision of: Documented inventory of physical equipment and material.
2. The laboratory must make sure that the equipment/ technology used for the trials and analysis work correctly: a) Each piece of equipment must be maintained periodically (according to the manufacturer) b) Every piece of equipment must be calibrated according to the manual of operation and the Quality Guarantee Program. c) The records of the calibration activities must be available.	Revision of: History of the instrument or equipment Maintenance records, calibration, inspection and equipment repair.

3. The laboratory must guarantee the integrity and the adequate use of reagents and chemicals: a) Reagents and chemicals must be those requested for the trials / analysis b) Storage of reagents and chemicals must comply with the requirements demanded by health regulations in full force and effect and with the conditions which have been specified by the manufacturer.	Revision of: Documented and current inventory of the reagents Consistency between SOP and the registers of reactives Registers of INVIMA (Colombian Institute for Food and Drug Surveillance) Expiration dates

TABLA 9. STANDARDIZED OPERATING PROCEDURES

Requirement	**Evaluation Method**
1. The laboratory must guarantee that the process of analysis of samples taken from subjects participating in the study is conducted in an accurate and standardized way: a) It must have written standardized operating procedures (SOP) for each procedure conducted in the laboratory. b) The SOP must be based on good practice standards and must be approved by the administration. c) The SOP must be written in a clear language, so that its execution and audit are permitted. d) Every SOP must be part of the MSOP of the laboratory. e) The officials in charge of conducting the analysis must know and strictly follow the described SOP which has been approved by the laboratory. f) The updating and amendments of SOP must be documented (date, change or inclusion) and must be based on scientific evidence duly referenced.	Revision of: SOPM Specific SOP Updating dates and references supporting the amendments. Revision of: SOPM Specific SOP Updating dates and references supporting the amendments
2. There must be written standardized procedures for the attention to the patient and they must include:	Revision of: Standardized Operating Procedures (SOP) Attention to the patient

a) Instructions for the preparation of the patient. b) Rules for the attention to the patient. c) Collection of data of identification of the patient. d) Record and conservation of the information of the patient, which assures confidentiality.	
3. There must be written standardized procedures for the handling of the sample / sample / biological specimen and it must include the following, with respect to each trial and analysis: a) Collection instructions b) Criteria of acceptance and denial of the specimen c) Transport, preparation, stability and preservation. d) Decontamination and disposal	Revision of: Handling of samples SOP
4. There must be written standardized procedures for the analytical procedure which include the following: a) Analysis procedure. b) Specific Quality controls for each test. c) Reference values d) Interferences in the technique	Revision of: Analytical procedure SOP
5. There must be written standardized procedures about the equipment which includes: a) Operation procedures b) Preventive maintenance c) Cleaning d) Calibration of measuring equipment e) Alarm signs f) Safety measures in the use.	Revision of: Equipment SOP
6. There must be written standardized procedures about the management of files which specify the following: a) Report of results b) Organization of documents c) Storage d) Recovery of registers and results	Revision of: Files SOP
7. There must be written standardized procedures about the management of	

files that specify: a) Report of results b) Organization of documents c) Storage d) Recovery of registers and results	
8. The deviations in the established procedures must be registered, reported and saved in the files of the laboratory.	Revision of: Register of SOP deviations