

National Guidelines for integration and operation of the Research Ethics Committee (REC)

Research Ethics Committee (REC)

The Ethics Research Committees are part of the institutional commitment assumed by the establishments where research in humans is performed, with regulatory bodies, research participants and generally with the society as a whole. The inclusion of ethical issues in research protocols is a quality indicator comparable to the methodological rigor of scientific research, where the REC should be the guarantors that research responds, from the assessment of ethical aspects to the interests and the needs of citizens. Therefore, and according to the provisions of the General Health Law, the Research Ethics Committee must be established and must operate, in all institutions, and in public and private establishments, where humans participate in research.

Conceptualization of the Research Ethics Committee

The Research Ethics Committees are autonomous, institutional, interdisciplinary, plural and consultative, corporate bodies created to assess and determine the research protocols in humans:

- **Autonomous:** These must be free of political, religious and economic influence.
- **Institutional:** These belong to a National Health System institution grouping legal figures limited by the set of standards regulating such situations within the bioethics context.
- **Interdisciplinary:** They converge the knowledge from different disciplines of philosophical, scientific, social, anthropological, psychological, technical, legal kind as well as health care and health research, for analysis and possible solution of a problem.
- **Plural:** To recognize and promote diversity and try to reach reasonable agreements between different positions within a discussion that starts from a minimum of shared knowledge.
- **Consultative:** Looking for determining the values of social ethics and act as first instance courts to issue rulings, opinions or recommendations of a general nature.

The REC provide spaces for deliberation, in which the discussion and reflection in an atmosphere of freedom and tolerance is developed. Such groups have a social role with the researcher, supporting research in order to solve, so prudent and appropriate, ethical dilemmas posed by each of the related research. From the above, it can be said that the Ethics Research Committees represent:

- A guide and support from the researcher's awareness.

- Protection for the participants in such research.
- Public guarantee of respect and human dignity.
- An example to promote interdisciplinary and multi-region education.
- An essential part of institutional bioethics awareness.

Objectives

The objectives of the Research Ethics Committees are:

- a. Help safeguarding the dignity, rights, safety and wellbeing of all current or potential research participants and communities involved, taking into account national and international regulations on ethics in research.
- b. Providing advice to the owners of the establishments and institutions to support the decision on the authorization of research development within their responsibility units.
- c. Monitoring the implementation of the regulations and ethical content in research and other applicable provisions and assist researchers to perform optimal studies.
- d. Promoting that the benefits and disadvantages of research between groups and society classes are distributed, taking into account age, gender, economic status, cultural and ethnic considerations.

Functions

The functions of the Ethics Research Committees are:

- a. Developing guidelines and institutional ethical guides on research for health, compliant with the current valid regulations.
- b. To evaluate and determine the ethical content in research protocols involving human subjects.
- c. To follow-up ethical recommendations that apply to research protocols and to support the researcher for the ethical conduct of its protocols.
- d. To assist in the implementation of the General Health Law and Regulations in terms of Research and other regulations applicable to health research.
- e. To establish mechanisms for cooperation with other Committees, and for joint evaluation of research protocols when necessary.

f. To prepare the reports according to the standards established and submit them to the appropriate authorities.

From the above, the general functions of the committees are:

Decisive function: Provides the responsibility of the Ethics Research Committees for:

- Analyzing and reviewing research protocols for its consideration, as well as supporting the Research Committee in the decisions making on bioethical issues or dilemmas that arise from the research.
- Evaluating and determining, from the ethical point of view, the contents that are presented in the research in a transparent, independent, competent, timely, quality, free from political influence, institutional, professional and commercial manner.
- Advising the interruption or suspension of any research.

Control and monitoring function: Provides continuity to the resolutions issued by the Committee, to do so, it is necessary to develop guidelines and institutional ethical guidelines and organizational manuals and procedures. When performing these functions, they should be able of:

- Monitoring the implementation of the current legislation, and the criteria established by the National Bioethics Commission in terms of bioethical research in humans.
- To inform the competent authorities the conduct that should be punished.
- Monitoring the implementation of the guidelines and other applicable provisions.

Educational function: Consists of promoting research ethical training among its members and the health facility staff in the head-quarter, permanently. This can be performed in three levels: 1. Within the Committee, 2. To the facilities' staff, and 3. To the general population.

The Ethics Research Committee

Integration

Health facilities where research is conducted in humans should create the Ethics Research Committee, which is responsible for the ethical review of research. This should be integrated by medical personnel from different specialties and professionals from different areas such as psychology, nursing, social work, sociology, anthropology, philosophy, law, etc., preferably with bioethics' training; and it should be considered that it is very important to have representatives of the core of people affected or users of health services; in order to reach the number agreed of its members, ensuring gender balance, including at least one member not assigned to the facility. It is up to the members according to their training fields and the accuracy of the theoretical and methodological aspects of such protocols.

For example:

- Professionals in research and clinical aspects, clarify the technical information protocols, such as the methodology, the relevance of research and the assessment of risks and benefits.
- Ethicists, contribute to the orderly discussion of ethical elements involved in the analysis.
- Lawyers will define the legal framework under which the case will be analyzed

The Committee will be integrated by:

- a. President.
- b. Members of the Council (four minimum).

During the performance of their duties, a secretary will assist, who shall be appointed by the President from among the members. The President in agreement with the members of the Committee may bring to the attention of the manager or owner of the Establishment, the extension of the REC integration. He also may invite and consult internal and external experts, whose intervention is deemed necessary for the decision making related to the issues under discussion in the sessions. The participation of the Committee's members, will be a honorific one, however, it must be considered that the representatives of the community may compensate the expenses that this activity will generate.

In the case of newly established Committees and when within the institution, no candidate obtains the right people, the operator according to the Regulations of the General Health Law in Health Research, along with the President's Committee may request support and advice of the committees constituted in the next level of their own department or from other institutions of the National Health System.

Members Requirements: The selection of the members must consider the following:

- I. Having a personal history that demonstrates competence and ethical behavior (job referrals, community and / or organization to which he/she belongs).
- II. Documenting professional excellence and recognition in the field of performance.
- III. Having some training or training in bioethics and/or research ethics.
- IV. Having experience in the evaluation of research protocols.
- V. Be committed to be continuously trained in the knowledge of ethics research.

VI. Being respectful, tolerant, open to dialogue, flexible, prudent, honest and having a conciliatory behavior.

VII. Representing the interests of the community, with the required capacity.

VIII. No conflicts of interest must arise regarding the duties assigned.

Selection: The Committee shall establish within its operating rules, the process to select its members. The selection of members should include curriculum evaluation, personal interview and the aspects considered as necessary for the integration and operation of such Committee. The President should not belong to the governing body of such establishment. The Secretary shall be appointed by the President from among the members, and his/her main function will be assisting the Committee in order to carry out its functions. The selection should include curriculum evaluation, personal interview and the aspects that are considered as necessary for proper integration and operation. The professionals that were assigned to form part of the committee shall have expertise in the area of health, and it is recommended that at least one of them has advanced knowledge in bioethics and research ethics, as well as qualitative and quantitative methodology. They must have a policy for reappointment. They shall determine the procedure for resignation and replacement of the members.

The REC may eventually resort or establish a list of external consultants who provide special expertise in some proposed research protocols, in case the Committee does not have the expertise on the knowledge or experience required to evaluate them. The invited consultants may be specialists in ethical or legal aspects in specific methodologies or disease or may be representatives of communities, patients or special interest groups. Independent consultants may participate personally in the sessions or post their comments. In any case, they only have the right to speak but not to vote, so they cannot participate in the deliberations.

Designation: In the case of a newly established committee, the owner of the establishment shall appoint the President. The President appointed shall have the power to appoint the other members. The term of office of the first Board shall be of three years. After the first run, the members of the Committee will propose a short list to designate the person to the office of President. Also, at the end of the three years, the members will nominate candidates for the renovation of the remaining members, seeking the stepped substitution. The consistency of designation awarded to members of the Committee shall include at least the following requirements:

I. Full name of the person designated and positions that will be held.

II. Duration of the assignment.

Besides, the record of each member of the Committee shall include the following documentation, accepted and signed:

- I. Commitment to ensure the interests of research participants.
- II. Commitment to confidentiality, protection and use of information.
- III. Acceptance and compliance with policies and regulations for the operation of such Committee.
- IV. Express signaling that the incorporation to the Committee will be honorific.
- V. Clause for policies and management of conflicts of interest.

In the case of external consultants, they must also sign a confidentiality agreement, protection and use of information, as well as a non-conflict of interest agreement according to their participation in the REC meetings.

REC Members Functions

President

- I. Coordinating the Committee's activities as well as convene, organize, and attend chair meetings according to the criteria established in the Committee's guidelines.
- II. Implementing mechanisms for prevention and detection of interest conflict within the Committee.
- III. Implementing the process of assigning and renewing members under the rules of procedure within the Committee.
- IV. Promoting continuous training activities in the Committee internally and externally, including the population within the influence area.
- V. Reporting and signing the reports and resolutions issued by the Committee to the corresponding authorities.
- VI. Issuing the information of the activities to provide it to the instances that have legal and administrative power to require it.
- VII. Registering the Committee for the National Bioethics Commission, as well as the appropriate instances, and updating according to the established guidelines.
- VIII. To carry out all similar functions to those listed.

Member Secretary

- I. To summon the members, at the express request of the president to the meetings of the Committee.

II. Preparing and providing work agendas for meetings and to submit the members of the Committee the necessary documentation in advance, except for expedited sessions.

III. Coordinating the preparation of the normative and operating documents and instruments, for the integration and development of activities in the Committee.

IV. Setting the minutes of meetings, collecting participants signing for their confirmation and distribution where appropriate.

V. Receiving the proposed points to be discussed in the meetings of the Committee and to check that the information is appropriate and sufficient in order to include it in the agendas.

VI. Integrating the annual program of activities including advisory actions, training and monitoring requiring the input from the Committee members.

VII. Collaborating in training activities, bioethics' updating and dissemination among the establishment personnel.

VIII. Preparing assessment reports and opinions requested to the Committee in order to issue them with opportunity to those who apply.

IX. Integrating and delivering to appropriate instances the resolutions issued by the Committee in a timely and adequate manner.

X. Establishing information mechanisms for the president and members of the announcements received by the Committee.

XI. Perform the registration of the donations and values assigned to the Committee.

XII. Maintaining updated files of the Committee, by recording activities and evidential documentation.

XIII. Perform such other functions as may be assigned by the president.

Members

I. Systematically review of research protocols or any other information or documents that may be assigned by the President to comply with the functions and objectives of the Committee.

II. Participating in meetings for the analysis, evaluation and opinion of the research protocols, for the issuance of resolutions agreed by the Committee.

III. To follow up on agreements made and to identify issues that could be cause of deliberation by the Committee.

IV. Assisting in the selection and renewal of members of the Committee by checking compliance with the requirements for its designation.

V. Collaborating in training, updating in bioethics and other actions of the Committee with the staff and the population of the influence area within the establishment.

VI. Perform any other functions as assigned by the President.

External Consultants

I. To advise the committee on ethics in terms of research, as well as in the evaluation of research protocols at its request, either in person at meetings or by sending their technical comments.

II. Participating with integrity and oblivious to conflicts of interest in sessions as expressly summoned.

Implementation

The Committee shall be installed under the responsibility of the establishment's head officer according to the provisions of the General Health Law, being established in such formal act according to the circumstances within the implementation certificate (Annex 2). The Implementation Certificate will specify the following requirements:

I. Name and address of the establishment.

II. Address of the Committee and the institution to which the person belongs.

III. Purpose of the Committee.

IV. Features and functions of the Committee.

V. Integration of the Committee.

VI. Faculties of the members of the Committee.

VII. How to finance operating expenses of the Committee.

VIII. Legal basis containing the same faculties of the holder for the Committee's constitution.

IX. Manifestation of the owner of the establishment that is responsible for the Committee.

X. Signature of the party responsible for the establishment.

XI. Place, date and time of installation.

Operation

The RECs are spaces for protocols assessment and analytical discussion of their ethical content, which perform their duties in sessions prevailing in discussion and reflection, in an atmosphere of freedom and tolerance. In its organization and operation and activities technical and administrative processes are included, appropriate to the organizational structure of such establishment.

Operating Funding

Operating expenses for REC will be funded by the establishments' authorities, according to internal guidelines. The Committee may receive financial resources or in-kind contributions from external sources to evaluate protocols. Under no circumstances these may be delivered directly to any member. These contributions should not be translated into conflicts of interest between the funding source and the functions of the Committee. Whoever is submitted to a research protocol review must deposit the resources in a special fund provided by the establishment. The collected funds must be respected by both facilities' authorities and members, so these are not used for other purposes other than supporting the REC. These will be managed with full transparency and have been mainly designated for operation and training of its members. It is important that members of the Committee are supported by the authorities of the establishment, at least in the following aspects:

- I. Time to participate in regular and special sessions of the Committee.
- II. Academic or work acknowledgements for their performance in the Committee.
- III. Support for continuous activities of bioethics and ethics research inside and outside the institution.
- IV. Physical space for the headquarters of the Ethics Research Committee.
- V. Administrative support, as it requires a formal record of consults made to the Committee.
- VI. Necessary support of material in order to provide the proper performance.
- VII. In the case of the community representative, the user of services or temporary external consultants, if necessary, should consider the payment of expenses for transportation and additional reward for their performance in the committee.

Sessions

The Committee shall meet in ordinary, extraordinary, joint, and expeditiously sessions:

- **Ordinaries:** These sessions are established through the annual work program, determining dates, times of sessions and terms of the call.
- **Extraordinary:** These sessions are held by express request and depending on situations related to the work of REC, researchers, participants or the institution. They are carried out by the call of the president.
- **Expedited:** Sessions held for urgent amendments to the approved projects or to increase security of the volunteers participating, as well as the approval of research projects with minimal risk.
- **Joint:** The REC may meet jointly with the Research Committee for the integral assessment of research protocols. In cases which by their nature it is required, as in the evaluation of multicenter studies, the REC's Committees may meet with other establishments, for evaluation and opinion of these protocols.

Decision-making

The decisions made by the REC, will only be valid when there is a quorum established, and also they will have to observe the following requirements:

- I. The Committee may request the responsible researcher to clarify doubts for the assessment of any protocol.
- II. Having all the necessary documentation and enough time to review it.
- III. Only the participating members can help in the decision making.
- IV. Make decisions by consensus, never by vote.
- V. Provide resolutions with solid arguments and substantiated.
- VI. Provide clear suggestions for further revision, in the case that decisions are conditioned.
- VII. Lay the foundations of negative decisions with clear and specific reasons, in addition to stating the procedure for submitting the application for review again.
- VIII. The decisions of the Committee shall be communicated in writing to the applicant, in a document of judgment according to the established procedures.

Results and results of the protocols' evaluation

- **Approved:** Meets the established requirements.
- **Pending approval:** a. Requires major changes, and should be evaluated by the complete Committee when making such changes, b. Requires minor modifications, and can be evaluated expeditiously, as settled in the chapter, and c. Postponed or assessment in process as the Committee requested further information or questions arose during the protocol review process.
- **Not approved:** Protocol rejected for ethical reasons meriting major restructuring and the beginning of the whole procedure as a new protocol, should be corrected, and then re-apply the review.

The REC must request favorable result and/or registration, as appropriate, before the National Bioethics Commission, according to General Provisions for Integration and Operation of Ethics Research Committees, which will allow the creation of a database containing information inherent in the integration and operation of the Committee, for statistical and monitoring compliance.

Assent and/or Record of the Ethics Research Committees

Pending: The request must be submitted electronically through the Commission's website, in the specified format, which contains the identification data of the establishment where the Committee will be installed, contact's data, and email in order to receive notifications, and the name and signature of the responsible person for such Committee. The information shall be auditable by the instances that correspond to such effect. The process involves self-assessment prior to the format developed for this purpose, which contains the basic integration and operation elements. The application shall contain the following information:

- I. Name, designation and address of the applicant.
- II. Name of legal representative, if applicable.
- III. Address, telephone and e-mail address to receive notifications.
- IV. Name of authorized persons to receive notifications.
- V. Identification Data of the Committee.
- VI. Name and address of the establishment which the Committee belongs to.
- VII. Committee's installation date.
- VIII. Name and position of members.

- IX. Name of persons with dialogue function.
- X. Postal address of the establishment.
- XI. E-mail.
- XII. Place and date of registration application issuance.
- XIII. Name and signature of the Committee's responsible.
- XIV. Other requirements considered in the Federal Law of the Administrative Procedure.

Also attached digitally:

- I. Implementation Certificate.
- II. Registration of designation for every integrant of such Committee.
- III. Required auto-evaluation format.
- IV. Document proving the legal status.

In case the applicant does not meet any of the requirements, he/she will be required electronically to do it, within a period of fifteen working days, noticed that otherwise his/her application will be deemed as not presented. The application will be entered for processing from 9:00 to 18:00 hours, from Monday to Friday.

Assent and/or registration: After meeting the requirements, the National Bioethics Commission will assent and/or registry, as appropriate, within a period of fifteen working days from the admissibility of the application or completing the request.

Validity of assent and/or registration: It will be for three years; once this time has expired the information of the Committee shall be updated to remain current. The Committee shall apply electronically within one month before the expiration of the validity, which must be attached to the application and self-assessment format. The completion of these procedures does not require payment of any kind.

Control and monitoring

Integration and operation of REC are elements, which allow setting the quality level the services provided by a Committee, so it is important to maintain a control and monitoring system in order to identify areas of improvement and opportunity, that must be adequate to ensure better performance of their activities. In this regard, the National Bioethics Committee and/or the State Bioethics Commissions can inquire the establishment so the REC participates in such monitoring and control mechanism, when required. The process control and monitoring for Research Ethics Committees will be conducted through

supervisions and evaluations randomly determined by the National Bioethics Commission, in cooperation with the State Commission of Bioethics and the corresponding State Health Secretariat. The assessment elements are listed in this guide, in the requirements referred to forming, installation and operation paragraphs.

Information and files

The files resulting from the activities of the Committee, as well as personal information should be preserved in the REC's office, according to its operating rules and to the provisions of the current regulations. The access to them is subject to the approvals of the full committee and shall belong exclusively to the conditions that the same regulation authorizes.

Addendum: Procedures and operational activities

Requirements of sessions

The Operating Rules of the Committee must contain the conditions, characteristics of sessions and schedules, and must meet the following conditions:

- I. The REC shall meet at least six times a year.
- II. The scheduled dates will be announced in advance to interested people. The annual calendar will be released in January.
- III. The agenda and papers for each session will be provided at least seven days before the session. In the case of special sessions, they will be presented with three days' notice.
- IV. The minimum number of members required to complete a quorum shall be greater than 50% of the members.
- V. The president and/or secretary must be present as one of the minimum required to form a quorum. Without their presence the sessions of the Committee cannot begin.
- VI. Under the consideration of the Committee the researcher may be invited to present the proposal or delve into specific issues of the same, and this practice is desirable in order to reduce schedules and to optimize communication between REC and researcher.
- VII. They can be invited to the sessions or submit written comments, a representative of the community involved in a specific study to assess, as well as external consultants who must adhere to confidential criteria applicable to the rest of REC members. In this case, they will have the opportunity to comment but not the right to vote.
- VIII. Extraordinary sessions shall be convened by the President of the Committee and by written request.

IX. The REC may meet jointly with the Research Committee for integral evaluation of research protocols.

X. In cases that due to its nature it is required, as in the evaluation of multicenter studies, the REC may meet jointly with Committees which belong to other establishments, for the assessment and opinion for these protocols.

XI. In the event of any interest conflict of one REC member, he/she shall be declared disqualified for that particular deliberation, and not be considered to complete the quorum. This condition must be stated in the correspondent minutes.

XII. The expedited reviews will be made by the president and/or secretary, and/or any of the members who have reviewed the protocol and have issued their comments. The responsible for expedited evaluations must submit in the next meeting, these approvals to the Committee, so that they are endorsed, the approval shall be subject to confirmation by the Committee.

XIII. For legal and administrative purposes in meetings, minutes must be made, as well as establishing in the internal regulation of the Committee, the approval procedure, its protection and the file.

Evaluation of Protocols

This is the system of analysis by which the ethical content of information presented in the research protocol is valued. The Research Ethics Committees must value, at least:

I. Social pertinence to contemplate whether the research questions address the priorities in health, sanitary needs, and if they meet the scientific, regional, local or institutional, interests among others.

II. Validity and methodological design of such research.

III. Proportionality of risks and benefits of research, where the benefits should always be greater.

Selection criteria for potential participants, the site and the community:

a. Distribution of the potential risks, the equal benefit regardless of age, gender, socio-economic group, culture and ethnic considerations.

b. In case of vulnerable populations or individuals, they should seek protection and removal of coercion and intimidation elements. Reflection is essential in terms of the dependence of the patient-participant to the researcher (especially when it relates to your doctor) and related to the consideration of such research, in many cases, it is the only alternative to access diagnosis and treatments, and

c. To avoid the double standard, that is to say, the differential application of ethical criteria with diverse populations, whether or not they are multi-central researches, which are nationally or internationally financed.

IV. If informed consent complies with national and international ethical standards.

V. Training for researchers and the entire team.

It is important to establish mechanisms previous for the review of the documentation provided in order to verify that they have all the information, so the committee may properly assess the protocol that has been submitted for its consideration. The REC will set the number of copies required for the documentation to be delivered, and if they have other delivery formats such as electronic media or electronic systems that need to register this information. The reception of the documentation shall take place in the Secretariat of the REC, where the record of the reception will be made in a book, with the stamp and date of the reception and in the requesting letter. The reception of the complete documentation will be done in a format and must be signed and stamped by the receiving and delivering person.

Requirements for the evaluation of protocols

I. Original protocol, which should include a section on ethical considerations, and in case it is in another language, translated into Spanish with edition date, supporting documents and annexes.

II. Summary of protocol in the original language and in case it is in another language, translated into Spanish.

III. Summary of previous studies on the subject, including unpublished studies but known by the researchers. The information about the research on the subject that has been previously published should include the nature, extent and relevance of animal studies and other preclinical and clinical studies.

IV. In the case of a therapeutic product research, this must have an adequate summary, available safety data, product's pharmacology and toxicology, a summary of the clinical experience for the product on the date of the presentation of the protocol (recent notes of the researcher, published data, and a summary of the characteristics for the drug or device).

V. Complete study schedule.

VI. Document setting out which are the commitments acquired by research subjects, the researcher, the establishment and if applicable the sponsor, where the potential benefits are defined as: continuity of subject's clinical follow up once the study is completed, as well as dispositions in order to continue the access of subjects to such treatment, indicating its modalities, the individual, establishment, organization or company that will be responsible for financing and the validity of the access.

VII. In research from highest to lowest risk for participants, a report should be submitted containing the details of the maintenance measures and life support, as well as agreements on insurance policies specifying their funding (with a copy translated into Spanish, in case it is in another language, with the signature and name of the authorized official translator), to provide treatment in case of damage caused by participation in such research, and to compensate for disabilities or death related to it.

VIII. Report for procedures and responsible persons of communicating the participant subjects the information generated during the study (for example: damages or benefits) or the information resulting from other research about the same topic that could affect subjects availability to continue in the study.

IX. Researcher's resume (updated, signed and dated), names and addresses of the institutions to which they belong (if not all of them are from the same institution or country). An executive summary will be provided in order to specify and support the researcher's experience and expertise for the research in question.

X. In case there is an external funding source, a statement containing the approximate amounts thereof must be submitted, as well as the commitments and financial or material benefits that such establishment, researcher, and work team will receive in order to reveal possible conflicts of interests.

XI. In cases where there is no external funding source, it is required approximately financial breakdown including costs and expenses that this research will represent for the establishment.

XII. Sponsor Data Report containing the sources and amounts in order to fund this research, the sponsoring organization and a report of benefits and financial commitments for the establishment thereof, researchers, research subjects and, where appropriate, with the community .

XIII. Report for supporting material that will be used (including announcements) for the recruitment of potential research participants.

XIV. Mechanism that will continue protecting the privacy of individuals and the confidentiality of information during the research process.

XV. Informed consent in its original version and dated.

XVI. Methodology to obtain informed consent, including the process description, as well as reporting procedures to the subjects involved in such research, name and position of the responsible person for obtaining it.

XVII. Mechanism and procedure for communication of results to research participants.

XVIII. In case of protocols previously rejected or with history of rejection of other Committees that pretend to submit of previous studies and significant evaluations which allowed a negative decision, as well as suggestions and modifications to the protocol to address the reason for such previous rejection.

Communication of the Decision

The Committee's decisions shall be communicated in writing to the applicant according to the established procedures, within a period not exceeding thirty days after the execution of the application. This communication of the decision must include the following:

- I. The exact title of reviewed research proposal.
- II. Clear identification of proposed research protocol or amendment.
- III. Date and version number (if any), on which the decision was based.
- IV. The names and, if possible, the specific identification numbers (version number/dates) of the reviewed documents.
- V. Data sheet for the research participant.
- VI. Name and academic level of the applicant.
- VII. Name of the institution and research headquarters.
- VIII. Date and place of decision. Date and place of resolution's issuance.
- IX. Name of the Committee that made the decision and registration code from the National Bioethics Commission.
- X. Clear statement of the decision made.
- XI. Reasons and requirements of the Committee, suggestions for revision and the procedure to review the application again, in case of a pending decision.
- XII. Reasons for the decision, in case of a negative decision.
- XIII. Statement of applicant's responsibilities (for example: confirmation of acceptance of any of the requirements set forth by the Committee) in case of a positive decision.
- XIV. Date and Committee's president or secretary signature.
- XV. Signature of the members of the Committee

The decisions shall be notified personally in writing to the applicant in the indicated period in the internal regulation of the REC, and shall not exceed thirty working days. The approvals are valid for one year. Within one year, the researcher will present a report and a format specifically designed for this purposes where he/she will indicate the stage of the project and the most relevant information (summary of established requirements for the initial evaluation). Changes in the technical or ethical matters will be emphasized (which must have been previously approved by the Committee). Failure to find any reason so the protocol is reassessed, and having complete the documentation, the endorsement or renewal of the validity will proceed.

The researcher may object, one-time, the decision issued by the REC, within seven working days after the notification of the decision. The researcher should provide the necessary elements to support his/her disagreement. In case such elements are not provided his/her request will be rejected. If the nonconformity request is accepted, the REC will review the application during the next regular meeting. After the ordinary session, the REC will reply to the grievance presented by the researcher within a 7 working days period. The decision issued by the REC to a request for nonconformity admits no appeal.

At the moment of receiving the resolution document, the researcher will submit the Committee a commitment letter, dated and signed which must contain at least the following sections:

- I. Mechanism for delivery of report(s) of progress or, if applicable, the termination or cancellation of such protocol.
- II. Mechanism to notify the Committee in case of protocol amendments (amendments not involving only logistical or administrative aspects of the study).
- III. Mechanism to notify the Committee in case of amendments to the recruitment material, information for potential research participants or the informed consent form.
- IV. Mechanism to report serious and unexpected adverse events related to the conduction of the study or non-expected circumstances.

Monitoring of the Protocols

The REC should establish procedures to monitor the progress of all studies resolved with a positive decision, from the moment the decision was made, until the completion of the research. The monitoring process should consider the following:

- I. The quorum requirements, the procedure's review, and the procedure of communication for monitoring reviews did not differ from the requirements for the initial evaluation.
- II. The range of follow-up reviews should be determined by the nature and by the events of various research projects, although each protocol should be submitted to a monitoring review, at least once a year.

III. Any amendment to the protocol, which eventually could affect or that clearly affects the rights, safety and/or welfare of participants in the research or while conducting the study.

IV. The serious and unexpected adverse events related to the conduct of the study or the product or study device, and the consequent answer of researchers, sponsors and regulatory agencies.

V. Any event or new information that may affect the benefit/risk magnitude of the study.

VI. The decision resulting from the monitoring review should be issued and communicated to the applicant, where the amendment, suspension or revocation of the original decision of the REC is indicated, or the confirmation that the decision is still valid.

VII. The researcher must notify the REC, for withdrawal/premature termination of such study, the reasons for suspension/termination, and must provide a summary of the results obtained in the study.

VIII. The REC must be notified by the researcher at the moment of completing a research study.

IX. The REC must receive a copy of the final summary or the final report of a study.

Information and files

The files must be preserved in the REC's office, as stated in the Federal Law of Transparency and Access to Public Government Information, and what is determined in the federal entities, as well as in the Federal Law on Protection of Personal Data Held by Individuals, and other applicable provisions in this area.

After the execution period of such study, the documents should be transferred to the central archives in the institution, with a backup and recording this event in the REC's database. All documentation and communication of a REC must be dated, numbered and filed according to written procedures. It requires a definition of the access procedure and retrieval of documents, records and files, specifying the persons authorized. It is responsibility of the president in turn of the REC, to protect the files research protocols for five years since the end of such period. After completed the implementation period, these will be transferred to the central file direction of the institution, registering it in the corresponding database. The classification of information contained in the file of information Committees for the purpose of access to government information, shall be according to the prescribed in the applicable regulations. In the REC's internal files it should be included:

I. Implementation Certificate of the Committee.

II. Regulations of REC

III. Manual of procedures for REC.

IV. Operational guidelines, manuals, national standards, international standards, technical documents, applicable regulatory texts.

V. Sessions schedules of REC.

VI. Copy of the appointments of the members.

VII. Identification list and updated resume of REC members.

VIII. Protocols evaluated with all the documentation analyzed, approval's record, copy of monitoring reports, reports and amendments. This must be kept in the office of REC.

IX. Reports of decisions, approval records and reports of rejection and suspension (ordered consecutively and foliated per year).

X. Reports of serious adverse events in each research or clinical trial.

XI. Minutes of the meetings listed, correspondingly per year. A copy of all the material submitted by the applicant.

XII. Periodic reports on the study and the final report, leaving a copy in the file for the protocol where all documentation related to the study must be set; protocol in its different versions, researcher's brochure, informed consent, researcher's curriculum, record of approval or rejection, reports and correspondence ordered by correlative date (it is required that each protocol is stored in a file identified with the title, code, name of the sponsoring institution, researcher's name and place or center where research takes place, as well as the starting and termination date).

XIII. Correspondence received. The documentation provided by the researchers, the correspondence exchanged with them and other people involved.

XIV. Records of expenses and/or use of the funds received according to the principles expressed in this guide and the guidelines of such institution and the correspondence that has been dispatched.

XV. Documents submitted by the project sponsor.

Support for researchers

Addressing national and international recommendations in the field of bioethics and research ethics, it is considered that the elements highlighting that research must be proposed, designed and conducted by persons qualified in scientific and clinical methods appropriate for the development of protocols, which should know the applicable regulations. The researchers will submit applications for review and evaluation, if they are

approved and there is viability in order to carry out the research, they should conduct it according to established ethical requirements.

Submission of applications

- The request for assessment of biomedical research in its ethical terms, must be submitted by a qualified researcher, who is directly responsible for the scientific and ethical conduct of such research. Under certain conditions, the sponsor of a clinical trial is responsible for submitting the research proposal.
- The proposed study must be submitted under the responsibility of a qualified counselor and member of the faculty or school involved in supervising the work, or the application is made on behalf of the student, jointly signed by the counselor.
- All the required documentation must be presented for a complete review of the ethical aspects of the proposed research, as specified in the standard operating procedures of the Committee.

Conducting research

- The research should be carried out according to the proposal approved by the REC.
- No deviations or changes shall be made without prior REC approval, except where immediate action is required to prevent damage to the participant(s) in the research. In such cases, this must be reported immediately to the REC for changes and/or deviations made and the correspondent justification.
- The REC should be informed about changes in the research site significantly affecting the performance of the test and/or raise the risk of harm to the participants, for example, the closure of the health care facilities in the research site or other impediments to access to the health care which was originally available, which was foreseen as an adequate condition.

Security Reports

- Adverse events should be reported immediately, as describe in the proposal, and according to the established procedures.
- The recommendations made by the Committee shall be conducted immediately.

Continuous reports and monitoring

- In case of suspension or early termination of a study, the applicant shall notify the reasons, shall submit a summary of the results obtained during the study, and shall describe the manner in which the registered participants will be notified, as well as care plans and subsequent consequent monitoring of the participants.
- If a study is completed or canceled, researchers should report it.
- When the Committee withdraws or suspends the approval, the investigator should inform the institution which is helping to conduct the research, the sponsor of the research and any other applicable instance.

- Researchers have an obligation to keep the research participants and their communities informed about the progress of the research and at appropriate intervals. The notice shall be in simple language, this notice is particularly important when: the research study is amended, suspended, is terminated or canceled, any changes occurring in the context of the research study that alter the potential benefits or risks, or to complete and conclude the research process, it is to say, its clinical trials.

Annex 1 (Op cit)

Annex 2

General Provisions of Ethics Research Committees

Since the publication of the aforementioned Decree, the National Bioethics Commission developed several actions:

- In December 2011, the State Health Secretaries made public of the Decree adding the Article 41 Bis and amends the Article 98 of the General Health Law, spreading at the same time the website of the National Bioethics Commission. CONBIOÉTICA subsequently developed working papers of the General Provisions for Integration and Operation of Hospital Bioethics Committee and Research Ethics in adherence to legal process for the approval of the General Provisions, the documents were sent to Labor General Directorate Legal Affairs and Human Rights of the Secretariat of Health.
- There was an electronic consultation nationwide, to collect opinions on the working papers, of people from various public and private health sector institutions, as well as academic and research bodies.
- As final document was obtained the "Agreement through which General Provisions for Integration and Operation of Research Ethics Committees, and the hospital units that include them, according to the criteria established by the National Bioethics Commission, "which is meant to identify the criteria for the integration and operation of the Committees that evaluate and research protocols in humans. The provisions shall be mandatory for the establishments referred in this document.