Comisión Nacional de Bioética

Guía nacional para la integración y el funcionamiento de los Comités de Ética en Investigación

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National Bioethics Commission

National guide
for the integration and operation of
Research Ethics Committees

National guide for integration and operation
of Research Ethics Committees
Sixth edition, 2018

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presentation

On the international scene, Mexico has been characterized as a country that promotes scientific and technological progress in health, an area in which innovations are presented at an increasingly accelerated pace. Considering the importance of channeling this development within the framework of human rights, the common good and adherence to international ethical criteria, in recent years regulatory changes of great impact have been implemented in the National Health System; thus establishing fundamental provisions to promote a culture of Bioethics throughout the national territory, focused mainly on strengthening research with human beings, attached to the best international practices.

The Ministry of Health, through the National Bioethics Commission, consolidates the institutional mechanisms that guarantee the well-being and respect for the rights of subjects participating in health research, while emphasizing the essential role of review processes ethics for your protection.

The National Bioethics Commission promotes the study and observance of ethical principles and criteria in health research and includes among its functions promoting the integration and registration of Research Ethics Committees (CEI), as well as establishing the precise criteria for the adequate operation of these collegiate bodies, also supporting the training of their members.

The criteria for the integration and operation of the RECs are issued through the National Guide for the integration and operation of Research Ethics Committees, in its sixth edition. It has been revised in accordance with the new provisions in Mexico regarding health research with human beings and the updating of international guidelines, with the aim of strengthening the RECs.

This National Guide proposes new elements to facilitate its operation, gives greater clarity to the criteria for its integration, installation and operation; In addition, it includes the process of monitoring the Committees carried out by the National Bioethics Commission. Likewise, it establishes more efficient processes for the procedures associated with the registration, modifications and renewal of the CEI.

In short, the sixth edition of the National Guide for the integration and operation of Research Ethics Committees consolidates the commitment of the National Bioethics Commission to foster a culture of bioethics in Mexico, emphasizing the protection of integrity and human rights. of the people who participate as research subjects. With the establishment of Research Ethics, Mexico's position as a leader in world-class research is consolidated.

The updating of the Guide involved the participation of Research Ethics Committees, State Bioethics Commissions, health establishments, the pharmaceutical industry, contract research organizations, universities, researchers and other professionals interested in the subject.

Manuel H Ruiz de Chavez
National Bioethics Commissioner

1. Marco conceptual

Bioethics is currently a fundamental tool for establishing agreements in the face of scientific, social and legal challenges, in a framework of reflection and interdisciplinary, plural and secular analysis in societies where dissimilar points of view and values coexist; it is also important to contribute to the analysis of aspects not foreseen in the legal regulations that may arise around medical practice and health research with human beings.1 For the National Bioethics Commission, bioethics is: The branch of ethics Applied science that reflects, liberates and makes regulatory and public policy approaches, to regulate and resolve conflicts in social life in the life sciences, as well as in medical practice and research that affect life on the planet , both now and in future generations.2

1.1 Background of the ethical framework and importance of research ethics

Research ethics, as one of the branches of bioethics, arises in response to the need to protect people who participate in the development of science as research subjects. There were numerous cases of scientific malpractice that occurred throughout the 20th century, examples of which are: **1. Tuskegee Study (1932-1972):** Sponsored by the US Department of Health, it investigated the effects of untreated syphilis in 400 African-American men. The investigators did not provide the already known and available penicillin treatment for the treatment of syphilis. The subjects were not informed that they were part of an experimental study; **2. Willowbrook Experiment (1956-1980):** Hepatitis experiments were conducted on mentally handicapped children at Willowbrook School. They intentionally infected the participants and observed its natural progression.

The experiments were approved by the New York Department of Health; **3. Milgram Experiment (1961-1962):** Stanley Milgram conducts his obedience experiments, which showed that many people are willing to do things they consider to be ethically wrong when following orders from an authority, and **4. The Beecher article (1962):** Henry Beecher publishes an article in N. Engl. J. Med, denouncing 22 unethical studies in biomedicine, including the Tuskegee and Willowbrook study (Resnik, niehs.nih.gov). With these cases we can understand that not everything scientifically possible is ethically correct.

Although it is undeniable that research with human beings contributes to technological development and social welfare, the aforementioned facts are an example that ethical reflections are important to favor the protection of subjects and that they are not merely considered as a means to such end. Due to the above, they are considered unethical research and consequently unacceptable (Koepsell & Ruiz de Chávez 2015, 13-29).

The benefit of research with human beings in the progress of medicine is unquestionable; however, as it is an activity that carries risks, in many unpredictable cases, it is necessary to provide researchers with a framework of action to ensure the protection of study subjects and guarantee ethically acceptable conditions in the production of knowledge and development of research. research (Emanuel, Grady & Crouch 2008). In this regard, bioethics, without being a code of immovable precepts, integrates analytical activity and is based on philosophical principles and scientific criteria to channel scientific development towards the common good.

All research involving human beings must be carried out in accordance with universally recognized ethical standards (Emanuel, Grady & Crouch 2008) -in order to minimize

[1] The term "bioethics", coined by Fritz Jahr in 1926, was defined for the first time as an ethics of the relationship between human beings. us with non-human animals and nature. Van Rensselaer Potter subsequently incorporated it into contemporary academic discourse and general culture with his article Bioethics, the science of survival, published in 1970, as well as in his book Bioethics: bridge to the future. (Gonzalez 2008).

[2] Notion, formulated at the XXXIX Ordinary Session of the Council of the National Bioethics Commission in December 2012.

the possibility of causing harm to a minimum - and reflected in national and international guides and guidelines. Consequently, in all research in which the human being is the subject of study, the criterion of respect for their dignity and the protection of their rights and well-being must prevail (Research Regulations, article 13).

1.2 Research with human beings and ethical principles

"Medical progress is based on research, which must ultimately include studies in humans. The main purpose of research with human beings is to understand the causes, evolution and effects of diseases and to improve preventive, diagnostic and therapeutic interventions (methods, procedures and treatments). Even the best proven interventions must be continuously evaluated through research, so that they are safe, efficient, effective, accessible and of quality" (Declaration of Helsinki, principles 5 and 6).

Research ethics promotes the observance of the ethical principles of autonomy, beneficence, non-maleficence, justice, equity, scientific integrity and responsibility in the research process, from its design to the publication of results, to ensure the protection of the persons in their integrity and rights, also contributing to individual and social well-being:

- **Respect for autonomy:** recognizes the capacity of people to make decisions; This principle materializes through the process of informed consent. It is important to emphasize that, unlike medical practice, in which the main benefit is the relief or cure of the patient, in research there is only the possibility of potential benefits for which it is essential that the subject is informed about the nature of the disease. nature of the research, clear description of the procedures, purpose, known risks, potential benefits and other known information, so that your decision to participate in the research is free and voluntary.

  Free and informed consent implies that there are no influences or coercion in the research subject's decision to participate. In the case of investigations in which individuals incapable of consent participate, this principle requires us to consider additional protection mechanisms that guarantee the non-violation of their human rights and human integrity.

- **Beneficence and non-maleficence:** These principles are contained in the ethical imperative of maximizing possible benefits and minimizing potential harm or risk. In research, the principle of beneficence requires ensuring scientific relevance, the competence of researchers and the protection of research participants. It must be considered that, although the investigations confer a potential risk, this should only be assumed when there is no other option with similar results.

  Proportionality between risks and benefits is fundamental in the ethics of health research involving human subjects and the research should only be approved if there are no unreasonable risks or harms in relation to the benefits, whether physical or psychological, even if the person consented to participate in said research.

- **Justice:** This principle implies that the research responds to the needs of a specific population, in addition to the equitable distribution of burdens and benefits among the research subjects, in order to ensure that it is science and not vulnerability that

that dictates who participates as a study subject. Selection can be considered equitable only when: **a.** the people recruited as subjects are in a position to benefit if the research provides a positive result, and **b.** the possibility of risks to the subjects is minimized, while the social and scientific benefits of the research are maximized.

- **Principle of responsibility:** This precept, developed by the German philosopher Hans Jonas, (Hans Jonas 1995), requires us to consider the dizzying advance of technology, especially in the field of biomedicine, the implications for future generations in the development of new technologies. The impact of the innovation and development process, in many cases, has an unpredictable scope; Therefore, it is essential to consider the prospective dimension of the research and establish preventive measures, in order to ensure the continuity of the species in favorable conditions.

1.3 International documents relevant to research involving human beings

In the international ethical framework, there are declarations, guidelines, guides or recommendations on research ethics, which constitute criteria to guide research involving human beings in accordance with the internationally accepted ethical principles indicated in the previous section. These documents emphasize that all research involving human beings must be evaluated by a **Research Ethics Committee (REC).** [3]
In this regard, the following are listed:

- Nuremberg Code, August 20, 1947.[4]
- Universal Declaration of Human Rights, UN, 1948.
- Declaration of Helsinki, AMM, 1964. Last amendment October 2013.
- Belmont Report, National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research, NIH USA, April 18, 1979.
- Universal Declaration of Human Rights of Future Generations, UNESCO, 1994.
- Good Clinical Practice Guideline (GCP), ICH E6 (R2) 1996. Last amendment November 9 bre 2016.
- Declaration on the Responsibilities of Current Generations towards Future Generations. UNESCO, 1997. • Convention for the Protection of Human Rights and the Dignity of the Human Being with respect to the Applications of Biology and Medicine “Oviedo Convention”, Council of Europe, 1997.
- Operational Guidelines for Committees of Ethics that evaluate Biomedical Research, WHO, 2000.
- International Ethical Guidelines for Health Related Research with Human Subjects, CIOMS, 2002. Last amended 2016. • International Declaration on Human Genetic Data, UNESCO, 2003.
- Universal Declaration on Bioethics and Human Rights, UNESCO, 2005.
- Handbook for Good Clinical Research Practice, WHO, 2005.
- Guide No. 1 Creation of Bioethics Committees, UNESCO, 2005.
- Guide No. 2 Functioning of Bioethics Committees: Procedures and Policies, UNES CO, 2006.

[3] Unlike the denomination adopted in other countries, such as the "Institutional Review Board" (which translates as "Institutional Review Council"), the term "Research Ethics Committee" distinguishes these from other instances of review and specifies the role they play in health research.

[4] You can consult each complete document in the respective link in the references section.

• International Ethical Guidelines for epidemiological studies, CIOMS, 2009. • Guidelines and operational guidance for the ethical review of health research with human beings. WHO, 2011. Translated into Spanish by PAHO, 2012. • Guide for members of Research Ethics Committees. Council of Europe Bioethics Steering Committee, January 2012.

In addition to these international documents, it is also important to mention the International Covenant on Civil and Political Rights (ICCPR), adopted by the United Nations General Assembly through Resolution 2200 A (XXI), on December 16, 1966, which establishes the prohibition of subjecting any person without their consent to medical or scientific experiments. It is very striking that this provision is found within the same article 7 that prohibits torture, cruel, inhuman or degrading treatment or punishment, when in the collective imagination, decades after the Second World War, it has been possible to disassociate the torture of scientific research. This should remind us as Humanity that degrading scientific research can never again be justified for the sake of a misunderstood "scientific progress" (Saruwatari 2015, 13).

Due to the foregoing, the ethical review of research projects by a CEI has been constituted nationally and internationally, as a mandatory rule, whose purpose is to guarantee the highest possible degree of protection to the subjects who participate in the investigation.

1.4 Institutionalization of bioethics in Mexico

The most recent health legislation is influencing with greater force in areas of bioethics such as: the protection of the rights of patients, the strengthening of the bioethical infrastructure, scientific integrity, the ethics of research and the protection of subjects of research. To face such responsibilities, National Bioethics Commissions or Committees have emerged in various countries, as bodies that advise political representatives and governments, promoting democratic and public debate, as well as the analysis and development of public policies in ethical fields. complex. Their function is not strictly normative, these Commissions define the problems, study them and expose points of view in order to explore possible solutions and formulate recommendations.

In Mexico, the repercussions of the institutionalization of bioethics have been reflected in different orders of social life. The Mexican State created in 1992, through the Ministry of Health, the National Bioethics Commission and in 2005 granted it, by presidential decree, the character of a decentralized body, granting it powers to help safeguard dignity and respect. to human rights in medical care and health research.

Currently, the national bioethics infrastructure is made up of the National Bioethics Commission, the State Bioethics Commissions, the Hospital Bioethics Committees and the Research Ethics Committees. In this way, bioethics is taken to the field of public and governmental action to support the formulation and evaluation of public policies. The application of knowledge and the development of bioethical culture are favorable to guarantee individual and social well-being.

2. Regulations in Mexico

"Research for health is a determining factor to improve actions aimed at protecting, promoting and restoring the health of the individual and of society in general; to develop Mexican technology in health services and to increase their productivity" (Regulation of Research), in accordance with the bases established in the General Health Law, as well as in its Regulations on Health Research. The development of research for health must address ethical aspects that guarantee the dignity and well-being of the person subject to research.

All health research that involves the participation of human beings must have the evaluation and, where appropriate, approval of a Research Ethics Committee; the requirement is mandatory both nationally and internationally.

Article 41 Bis, section II of the General Health Law, establishes the obligation to have Research Ethics Committees in establishments for medical care in the public, social or private sector of the national health system, which will be **subject to the criteria established by the National Bioethics Commission.** In this sense, the National Commission promotes the integration and operation of the RECs, with the powers granted by the applicable legal provisions, as well as support for the training of the members of these committees.

2.1. Legal framework for Research Ethics Committees

The National Bioethics Commission participates in the generation, promotion and dissemination of national legal and regulatory instruments, which allow compliance with its Creation Decree, published in the Official Gazette of the Federation on September 7, 2005 and modified on September 16 February 2017. These actions are reflected in various reforms to the national legal framework regarding research with human beings and CIS, consistent with the functions of the National Commission. Although the collaboration of the National Commission with various government agencies and research and higher education institutions has made it possible to channel the modernization of the national regulatory framework of the RECs, it has also helped to prevent their over-regulation (Ruiz de Chávez, Orozco, and Olaiz , S32).

Mexico has modernized its legal framework for health research in the period 2011 to 2016, among other things, with the purpose of strengthening the operation of the RECs, in order to

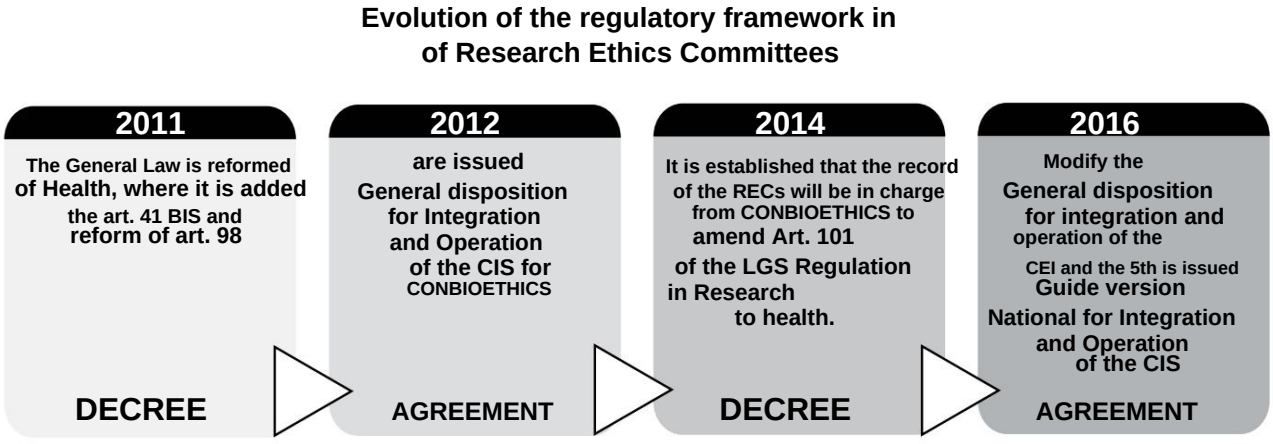

Figure 1.0 Timeline that represents the modifications to the legal and regulatory framework regarding of Research Ethics Committees, which has made it possible to strengthen their operation, going from a "operation notice" to the formality of a "CEI registration" issued by CONBIOÉTICA.

guarantee the protection of research subjects and contribute to the development of world-class health research in the country. This resulted in the registration of RECs, for the first time before the National Bioethics Commission, as of January 11, 2016. Figure 1.0 summarizes the evolution of the regulatory framework with respect to RECs.

On December 14, 2011, **the Decree amending the General Health Law was published in the Official Gazette of the Federation, by which article 41 Bis is added and article 98** of the aforementioned Law is amended, which stipulates the obligation health establishments in the public, social and private sectors to have Hospital Bioethics Committees and Research Ethics Committees, under the criteria established by the National Bioethics Commission (LGS 2011, articles 41 Bis

On October 31, 2012, the Agreement by which the **General Provisions for the Integration and Functioning of Research Ethics Committees** are issued and the hospital units that must have them, are published in the Official Gazette of the Federation. in accordance with the criteria established by the National Bioethics Commission. The aforementioned Provisions were **amended on January 11, 2016** and published in the Official Gazette of the Federation. The Provisions are indicative but not limiting, so the specifications regarding the creation and operation of the committee must be in accordance with current regulations and this Guide. In cases not provided for in the Agreement, the provisions of the Law, its regulations, the Guide and other applicable provisions shall apply. The National Bioethics Commission will disseminate the Guide and its updates on its website (General Provision of CEI 2012, THIRD).

The purpose of the Secretarial Agreement referred to in the previous paragraph is to indicate the criteria for the integration and operation of the committees that evaluate and rule on research protocols with human beings, and **its provisions are mandatory** for the establishments referred to . that instrument.

On April 2, 2014, the amendment to the Regulations of the General Health Law on Research for Health was published in the Official Gazette of the Federation, through which it is established that **the registry of Ethics Committees in Investigation will be carried out before the National Bioethics Commission.**

3. Description of the Research Ethics Committees

The RECs are part of the commitment to institutional transparency assumed by the establishments - where research with human beings is carried out - with the regulatory authorities, the participants in the research and with society as a whole; representing the public guarantee of respect for the dignity, equality and human rights of the participants.

3.1 Definition

The Research Ethics Committees are collegiate, autonomous, institutional, multidisciplinary, plural and consultative bodies, (General Provision of CEI 2012, FOURTH) whose main purpose is to protect the rights, dignity and well-being of the subjects that participate in health research, through the evaluation, ruling and follow-up of the research submitted for its consideration. It should be noted that the name of the Research Ethics Committee by itself alludes to the purpose of its work, *ie* the evaluation of ethical aspects in research. In this sense, the CEI are:

- **Autonomous:** They are independent of all kinds of influences; professional, institutional, political and/or market, among others.

- **Institutional:** They belong to, are integrated into, and operate in an establishment for medical care in the public, social, or private sector of the National Health System (LGS, article 41 Bis) or a health institution (LGS, article 98) or institutions of higher education where research with human beings is carried out. • **Multidisciplinary:** They promote the convergence of knowledge from different disciplines, by involving specialists in areas related to health care and life sciences; including specialists in scientific and methodological aspects, and good clinical practices, at least one member must have knowledge in bioethics and research ethics. • **Plural:** They recognize and promote diversity, generating consensus to reach agreements between diverse positions, through a deliberation process that starts from shared minimums.

- **Advisory:** They serve as advisory bodies for the heads of establishments and institutions for the issuance of reports, opinions or recommendations of a general nature, with respect to the approval of investigations in their units of responsibility.

3.2 Objectives

In accordance with the FIFTH General Provision for CEI 2012, the objectives of the committee are:

- Contribute to safeguarding the dignity, rights, safety and well-being of all current or potential research participants.
- Act in the interest of the participants and the communities involved in the research, taking into consideration the national and international regulations on ethics in research.
- Ensure that the benefits and burdens[5] of research are distributed among all groups and classes in society, taking into account age, gender, economic status, culture, and ethnic considerations.

3.3 Functions

In accordance with the SIXTH General Provision of CEI 2012, the functions of the committee are:

- Review, evaluate and rule on research protocols involving human beings. us.
- Formulate and follow up on the ethical recommendations that correspond to the research protocols.
- Develop guidelines and institutional ethical guidelines for health research, in accordance with current regulatory provisions.
- Advise researchers for optimal ethical implementation of their protocols.
- Submit within the first thirty calendar days of the year, an annual activity report to the owner or director of the establishment, as well as to the National Bioethics Commission.
- Participate, with other Research Ethics Committees, in the joint evaluation of research protocols when warranted. • Assist in the application of the Law, the Regulations and other applicable provisions in matters of health research.

3.3.1 Resolution function

The RECs in the performance of their functions must respect and comply with the ethical and legal principles set forth in the current applicable provisions, subject to supervision by the competent authorities.

[5] The equitable distribution of benefits and burdens in the selection of individuals refers to the fact that potential individuals to participate in research should be selected for scientific reasons and not because they are easy to recruit due to their difficult social or economic situation or the ease with which they can be recruited. handled, for further reference see CIOMS Guideline 3.

The resolution function includes the following activities:

- Evaluate and issue a written opinion on the research protocols with human beings that the principal investigator submits for your consideration, in accordance with the applicable national regulations and, where appropriate, formulate recommendations with an emphasis on the protection of groups in conditions of vulnerability. (Lisker 2013).
- Evaluate and rule on research protocols, in a transparent, independent, competent, timely, quality, free of undue, institutional, professional and commercial influence, as well as promote their scientific integrity and quality.
- Assess the ethical, methodological and regulatory aspects in the area of their competence, to ensure that the research proposal responds to the interests and needs of citizens.
- Evaluate the risks and benefits of the proposed research, among other aspects, to guarantee the welfare and rights of the research subjects.
- Evaluate and dictate the informed consent form in accordance with the applicable regulations.
- Evaluate and rule on the modifications, amendments or any other document related to the previously approved research protocol, when appropriate.
- Participate in the Internal Transplant Committee, where appropriate, in accordance with article 32, section VI of the Regulations of the General Health Law on Transplants.
- Establish collaboration mechanisms with other RECs, ICs and CBs for the joint evaluation of research protocols when warranted.
- Guide researchers in emergency situations or unforeseen eventualities.

3.3.2 Control and monitoring function

Ethical evaluation of human health research goes beyond the initial approval of the REC, continues during its development and extends until the conclusion of the research. It is essential that the CEI know the status of the resolutions it has issued and supervise the development of the investigations it has previously approved. To comply with the foregoing, it is necessary for the REC to inform the researchers who submit their research protocols about the obligation and commitment to notify the REC, in a timely manner, of amendments, modifications, deviations, violations, occurrence of serious adverse events, presentation of partial and final reports, as well as any significant circumstance regarding the safety of the subject under investigation in any

time.

The control and monitoring actions that the CEI must carry out are:

- Know the status of the investigations, that is, if they have been started, concluded, stopped or cancelled. For which the use of a control instrument is required that reflects the status of each of the research protocols received by the CEI (list of protocols) and the opinion issued by the CEI.
- Evaluate and, where appropriate, approve the modifications or amendments to the documents that it has previously approved.
- Know, analyze and make decisions regarding the occurrence of Serious Adverse Events (SAE) in the investigations that they previously approved, both presented in the international sphere and those that occur in the establishments for which the investigation was approved (local). In some cases, the occurrence of these implies requesting amendments to the protocol and informed consent (Research Regulations, section IX of article 21).
- In the case of SAEs occurring in Mexico, know and follow the actions or measures taken by the principal investigator until the subject is free from all risk. Include-

Doing the corresponding report to the establishment, the health authorities or the sponsor in accordance with the applicable provisions.

- Carry out supervision visits to the establishments for which it approves research, to ensure that the informed consent processes are carried out properly and, in general, that the development of the research adheres to good clinical practices.

- Know, analyze and make decisions regarding deviations or violations of protocol.
- Request the competent authorities of the establishment and COFEPRIS (Federal Commission for the Protection against Sanitary Risks) the suspension or review of an investigation when the integrity of the subjects is threatened, if there is a risk of serious injury or in the presence of any event that is an impediment from the ethical or technical point of view to continue with the investigation.
- Prepare and provide reports of its activity to the appropriate instances, in accordance with the applicable provisions.

3.3.3 Educational function

It is the responsibility of the CEI to carry out continuous training and dissemination actions in the area of ethics in research, bioethics and good clinical practices, aimed at: the members of the committee, the staff and researchers of the establishment where it is installed, the potential subjects in the investigation and external researchers requesting evaluation by the CEI.

In this sense, the educational function includes the following activities:

- Contribute to establishing an institutional program of continuing education in research, research ethics, bioethics and good clinical practices for members of the CEI and staff of the establishment.
- Prepare and disseminate educational material in the establishment on the functions, scope and procedures of the CEI.
- Organize and/or manage training or dissemination events for members and internal or external users of the CEI (researchers).
- Contribute to the dissemination and application of applicable regulations on research.

- If applicable, prepare guidelines and institutional ethical guidelines on health research for the establishment where the CEI is installed.

In the case of training actions for the members of the CEI, these must be carried out at least once a year, from the issuance of the corresponding record and preferably by entities external to the institution where it is installed.

3.4 Obligations

The obligations of the Research Ethics Committees are:

- Protect the participants in the research and evaluate, if necessary, the suspension of an investigation or that the participants give their consent again with the new information available (Research Regulations, article 64, sections I and III).

- Receive and evaluate requests from the treating physician, regarding the use **of emergency treatment in conditions that threaten the life of a person,** when it is considered necessary to use an investigational drug or a known drug using different indications, doses and routes of administration. those established (Research Regulations, article 71).

The REC will be informed in advance of the use of the investigational medication, if the investigator anticipates the need for its use in emergency situations. Subsequently, if the use of the drug, indication, dose or new routes of administration arise as unforeseen needs, the CEI will issue an opinion in favor or against approving the planned use or the repetition of the unforeseen use of the drug (Regulation of Investigation, article 71, Section I).

4. Considerations for the operation of the Ethics Committees in Research

4.1 Conflict of interest management

The committee must avoid conflicts of interest in the evaluation of the protocols (General Provision of CEI 2012, TENTH). The General Provisions for the Integration and Functioning of the CEI 2012 define a **conflict of interest** as the situation originated when a person is influenced in his judgment by an intention or purpose other than the one he is obliged to pursue in accordance with the responsibility that he has. performs, whether this conflict is real (proven), apparent (supposed) or potential (eventual or possible risk in the future).

For the purposes of this Guide, it is important to make explicit that in research with human beings the **primary interest** (end to be pursued) includes the promotion and protection of the well-being of the subjects and the integrity of the research. In the operation of the RECs registered with the National Bioethics Commission, they must state under oath that any economic interest will not influence the evaluation of the REC. For further reference, **Annex 1** presents an example of a format for the declaration of conflicts of interest.

The RECs will establish guidelines, mechanisms or guidelines in writing for the management of conflicts of interest and will prevent these circumstances from negatively affecting the protection of the participants and the scientific integrity of the research. The following are some relevant considerations and criteria for managing conflicts of interest:

- Establish the necessary measures to ensure that the members of the committee maintain the protection of the rights of research subjects as their primary interest in an investigation. • Make transparent and document possible conflicts of interest of the researchers, members of the CEI, owners or legal representatives of the establishments or institutions where the CEI has been integrated, or any other actor involved[6].

- Refrain from participating in the analysis and evaluation of investigations in which any member potentially presents a conflict of interest, and record it in the corresponding minutes.

- Recognize and document the actors who have financial, professional, academic interest, concessions or privileges to third parties or of another nature in the research process.
- Develop informative material on conflicts of interest for the members of the CEI and staff of the establishment or institution. • Establish internal operating procedures specifying that REC members will not enter into communication with research sponsors and Contract Research Organizations (CROs). All contact with the sponsor CRO or its representatives will be made through the principal investigator, who

[6] Any actor involved also includes the owners, investors and staff of the establishment or institution.

will directly request any additional information required by the REC (Shuchman 2007).

- Being a member of a CEI will be incompatible with any kind of interest derived from the manufacture and sale of medicines or any other health input that could be involved in the research.

4.2 Resources and financing

"The operating expenses of the CEI must be financed by the establishment or institution, without this meaning a conflict of interest in the functions of the committee" (General Provision of CEI 2012, ELEVENTH); that is, they must come from the budget of the establishments or institutions where the CEIs operate and were registered.

The establishment or institution may receive support from external sources for evaluating protocols. Said support must not be granted directly to any of the members of the CEI, so that the contributions do not lead to conflicts of interest for the performance of the functions of the CEI. Support for the CEI must not be used for purposes other than its operation and must be managed with complete transparency. Likewise, the evaluations of the committee should not mean financial gains for it.

The participation of the members of the CEI will be honorary. Neither the CEI as a whole, nor any of its members, shall receive any direct or indirect remuneration from the establishment, the CRO sponsor or its representatives, or from any other organization.

It is recommended that the owners of the establishment consider the participation of the members in the committee for purposes of assessing merit; Likewise, support is provided in the following aspects:

- Provide time for their participation in the CEI sessions.
- Manage academic or work recognition for their performance in the CEI.
- Support the training of members inside and outside the institution or establishment.
- Allocate a physical space for the CEI headquarters, both for meetings and for the reception of documents and file protection. • Assign administrative support personnel for the CEI's activity, since it is required to re-document each and every one of the activities carried out by the CEI.

4.3 Privacy and confidentiality of information

The RECs will maintain the confidentiality of the reports they receive from researchers, mainly if the research is related to the development of inputs, technology and other application processes susceptible to patents or commercial development (Research Regulations, article 112). They will protect the privacy of the research subject, identifying him only when the results require it and he authorizes it (Research Regulations, article 16).

Some considerations and criteria for handling privacy and confidentiality of information by the committee are listed below:

- Maintain confidentiality and protection in the handling of information to which each and every one of the members of the CEI has access.
- Establish mechanisms by the REC for the management of confidentiality that include a confidentiality clause in relation to requests for evaluation of protocols, information from the researcher and the research subjects, as well as the meetings in which they deliberate on the research protocols (General Provision of CEI

2016, NINTH). For further reference, **Annex 2** presents an example of an information confidentiality format that the CEI may implement.

- Maintain confidentiality regarding the reports they receive, as well as the information to which the committee has access during the follow-up carried out on the execution of the investigation.

4.4 Scientific integrity

All research involving human beings must observe other ethical aspects, typical of research, such as scientific integrity, confidentiality in the handling of information and the social value of research; Furthermore, it is important to remember that education together with the generation of trust are pillars of scientific research (Litewka 2016, 182).

The function of the REC is not limited to the approval of the research protocol, it must continue during and after the research and promote scientific integrity. The foregoing contemplates the review of the sources and references, the collection and precise registration of the research data, the reliable correlation of the sources with respect to the data, as well as the publication of the results (Koepsell & Ruiz de Chávez 2015). .

Fraud, falsification of results, plagiarism, misrepresentation or other misconduct related to scientific practice or data management must be reported by the REC to the competent authorities upon identification. In order to guarantee the safety of the subjects participating in the research and its scientific integrity, the CEI may request documentation or additional information.

4.5 Transparency and accountability

The CEI is responsible for providing the information it has available regarding the activities it carries out and the resources allocated for its operation, in order to favor accountability and evaluate its operation before the competent authorities, and in your case, for verification visits, supervision, auditing and monitoring.

The committee will implement and have what is necessary to make its management transparent in accordance with the internal rules of the institution or establishment in which it was integrated and functions, as well as the applicable provisions regarding access and transparency of information.

Before the CEI begins its functions, the establishment or institution must provide the following resources:

- Specific facilities with controlled access that allow the performance of its functions under conditions that guarantee the confidentiality of the matters dealt with and documents evaluated.
- You must have an appropriate physical space to carry out physical face-to-face sessions, as well as the necessary supplies for them.
- It must have an appropriate physical space for handling and filing the documents evaluated.
- Computer equipment with sufficient capacity to manage and safeguard the information received, evaluated and generated by the CEI.
- A specific annual economic budget, approved and provided by the institution or establishment, destined for the training activities and continuous training of the members.

4.6 Independence of its operation

The committee must ensure an autonomous, impartial, competent operation free of negative influences, particularly in decision-making regarding the evaluation of the research proposal; will deliberate in a transparent manner and must demonstrate its independence with respect to

of the researchers, sponsors, CRO, as well as of the institution or establishment to which it belongs. The mechanisms to ensure this independence must be established in the internal operating procedures of the REC.

Therefore, the members have the responsibility to report anything that could affect their objectivity or independence in the performance of their duties. In this sense, the CEI may not include members who are related to each other (by affinity or consanguinity), directors, shareholders or equivalent of the establishment. The management personnel of establishments with registered RECs must refrain from participating in the RECs of other establishments, or else declare the potential conflict of interest before the National Bioethics Commission, during the REC registration process, to assess the feasibility of their participation.

5. Members and installation of the Research Ethics Committee

In accordance with articles 41 Bis and 98 of the General Health Law, and article 99 of its Regulations on Health Research, medical care establishments and all health institutions where health research is carried out with human beings, according to their degree of complexity and level of resolution, **will integrate a CEI, under the responsibility of the respective directors or owners** and in accordance with the applicable provisions.

When within the institution or establishment it is not possible to gather the right people to integrate the CEI, the respective director or head may request the support and advice of the committees registered, before the National Bioethics Commission, at the immediately superior level of their own institution or outside it, provided that the requirements established in the applicable provisions are met. In the event that this has not yet been created, they must go to the Commission for the assignment of a committee (Research Regulations, article 107 and General Provision of CEI 2012, THIRTEENTH).

5.1 Integration

It corresponds to the National Bioethics Commission to establish the criteria for the integration and operation of the CEI, therefore, in accordance with the national legislation in force at the publication of this Guide, the integration of the CEI will be subject to the following:

- The committee will have a president, who should not belong to the governing body of the establishment, and at least four members (General Provision of CEI 2016, SEVENTH). • One of the four members will be designated with the position of secretary member.
- In addition to the 4 members, include at least one person, unrelated to professional training in research or medical care, who acts as a representative of the affected nucleus or representative of users of health services, who will watch over the stakeholders. cattle of the research subjects. It is not necessary for them to have a professional license, people with basic education or technical training can be included.
- Seek gender balance among the members of the CEI.
- Be multidisciplinary and be made up of medical personnel from different specialties, including members of the professions of psychology, nursing, social work, sociology, anthropology, philosophy, law (LGS, article 41 Bis), pharmacology, chemistry, hospital pharmacy and other professionals. of health who have a professional license and accredit training and experience in bioethics, research ethics, good clinical practices and that related to the field of research that they evaluate.
- The chairman of the committee may at any time, by consensus of the members of the latter, submit to the consideration of the director or head of the institution or establishment the expansion of the committee's integration (General Provision of CEI 2012, SEVENTH).

5.1.1 Requirements of the members

- The members of the CEI may or may not be assigned to the health unit or establishment (LGS, article 41 Bis). However, it is required that at least the president and the secretary member be assigned to the establishment or institution due to the functions and responsibilities they assume.

- The members must have academic preparation and experience regarding the ethical, methodological and normative aspects involved in the type of research they evaluate.

- The CEI may invite and consult internal or external specialists7, whose intervention will be considered necessary for decision-making regarding the investigation (General Provision of CEI 2016, SEVENTH).
- The participation of all the members of the committee will be honorary (General Provision of CEI 2016, SEVENTH).
- The REC that evaluates research protocols involving groups in conditions of vulnerability or specific populations must have members who are experts in the field or request the advice of internal or external specialists regarding applicable clinical, ethical and psychosocial issues.

- The president of the CEI may not chair the Research Committee8 or the Biosafety Committee9. It is recommended that no member of the CEI participate in more than one CEI, where appropriate, they must have the express acceptance of the director or head of the institution or establishment in addition to the president of the respective CEI, of the participation of the members in more of a committee and that such participation does not undermine the quality of its reviews, nor does it imply a conflict of interest or compromise the confidentiality of the information to which it may have access in each establishment.
- All members must comply with 80% attendance (physical) to the total sessions carried out by the CEI during the school year. In case of non-compliance, the member must be discharged. • No member should belong to the governing body of the institution or establishment. Nor be part of the governing body of establishments that already have a registered CEI.

5.1.2 Changes in the composition of the Research Ethics Committee

The CEI must establish in its rules of operation the procedure by which the members will be elected and provide a policy for the renewal of appointments, to complete the procedure of resignation, dismissal, rotation and staggered substitution. Once the registration is obtained by the National Bioethics Commission, any change to the registration conditions must be approved by this Commission, and you will have to present your request for modification to the previously issued **registration conditions .** For further reference, see section 11.2 of this Guide.

5.1.3 Training and experience of the members

In order to fulfill the objectives, functions and obligations, the members of the committee must have the experience and knowledge in the field of the investigations that they carry out.

[7] Internal or external specialists: Experts who are not members of the CEI, may have an employment relationship with the establishment. to or institution where the CEI is installed (internal) or be totally independent from it (external).

[8] **Research Committee:** Collegiate, autonomous, institutional, interdisciplinary, plural and consultative body, responsible for evaluating and ruling on research projects or protocols with human beings, evaluating the technical quality and scientific merit, verifying that it is carried out in accordance with the principles research scientists.

[9] **Biosafety Committee:** Collegiate, autonomous, institutional, interdisciplinary, plural and consultative body, responsible for determining, within the institution or establishment, the use of ionizing radiation, genetic engineering techniques or infectious and contagious risks, based on the provisions applicable legal requirements and the objective of the investigation to be conducted.

luan. It is up to the members, according to their areas of training and experience, to issue the applicable contributions regarding the ethical, regulatory and methodological aspects of the protocols submitted for their consideration.

In selecting committee members, the following should be considered:
- Have education, training and experience in bioethics or ethics in research and good clinical practices.[10]
- Acquire the commitment to continuously train in the knowledge of bioethics, research ethics and topics related to the type of research they review.
- Be respectful, tolerant, open to dialogue, flexible, prudent, honest and conciliatory.
- Have no conflicts of interest with the functions entrusted within the CEI or, where applicable, declare conflicts of interest.

Permanent training is a requirement for committee members and must include topics related to bioethics, research ethics, Good Clinical Practices, national and international regulatory aspects, as well as knowledge and application of national regulations and this Guide.

5.1.4 Internal or external experts

The CEI may invite and consult internal or external specialists[11], whose intervention is considered necessary for decision-making regarding any of the research projects that are submitted for evaluation by the CEI (General Provision of CEI 2016, SEVENTH). The experience and trajectory of these specialists can support the review of applicable legal, clinical, ethical, methodological and psychosocial issues.

People who are invited to collaborate with the CEI as specialists in some subject, also called "external consultants", are NOT considered members of the CEI, so they do not assume any position in it nor will they be considered for the purposes of the procedure, modification or renewal. of the CEI registry; however, they must sign a confidentiality clause and a declaration of no conflict of interest.

The collaboration of the guests as specialists will be honorary (General Provision of CEI 2016, SEVENTH) and they may participate personally in the sessions or send their technical comments regarding specific aspects of the research projects. In any case, they will have a voice but no vote, so they cannot participate in the deliberations and decisions of the members of the CEI.

5.2 Appointment of members

The mechanism for appointing the members of the CEI must be transparent and free from influences that could compromise their independence with respect to the evaluations in which they participate.

For the composition of the committee, it will be necessary for the director or head of the institution or establishment to issue a certificate of appointment (General Provision of CEI 2012, NINTH) to each of the members. The certificate must contain at least the following requirements:

[10] With the exception of the representative of health service users

[11] Internal or external specialists: Expert staff outside the members of the CEI may or may not be attached to the establishment. to the institution.

- Full name of the designated person, consistent with the document proving their profession, the latter with the exception of the representative of the affected nucleus or users of health services.

- Position of the member, which will correspond only to president, secretary member, member or representative of the affected nucleus or users of health services.
- Duration of the position (the members will last three years in their position).
- Confidentiality clause signed by each member in relation to the research projects received by the CEI, with information provided by the researcher and the research subjects, which will be submitted to the consideration of the committee, as well as the meetings in which that deliberates on the protocols.

- The express indication that the incorporation to the committee will be honorary.

The period of management of the CEI will be three years, at its end, the members of the CEI will propose a list of three to the director or owner of the establishment, in order to designate the new president, as well as the renewal of the rest of the members. In the process, it will be ensured that the positions of president and secretary member repeat functions only once and that the committee is replaced in a staggered manner.

Whatever the period of appointment of members (first time, renewal, substitution, etc.), it should be considered that:

- The director or head of the institution or establishment must designate the president, who will have the power to propose the head of the institution to the rest of the members.
- The president will designate the four minimum required members. • The secretary member will be appointed by the president, from among the four minimum members required. • The members of the committee will select the representative of the affected nucleus or of users of health services, subject to the provisions of the applicable regulations (General Provision of CEI 2016, SEVENTH).

For further reference, see **Annex 3** corresponding to an example of a *member designation* letter .

5.2.1 Functions of the members

All members of the committee will have voice and vote of equal value, internal or external specialists will have voice but no vote.

president

- Coordinate the activities of the CEI, as well as convene, organize and preside over physical face-to-face sessions in accordance with the CEI's internal operating procedure.
- Implement mechanisms for the prevention and detection of conflicts of interest within the CEI.
- Carry out the process of appointment and renewal of the members in accordance with the internal operating procedures of the CEI.
- Sign the opinions or resolutions issued by the CEI. • Promote continuous internal and external training activities of the CEI, including the population of the establishment.

- Issue the information and reports of the CEI and provide them to the corresponding instances.
- Ensure compliance with the submission of the CEI's annual activity report to the competent authorities in a timely manner.
- Attend at least 80% of the sessions, physically in person. • Carry out all those functions related to those indicated.

vocal secretary

- Coordinate the preparation of documents and operating procedures for the integration and development of the functions of the CEI.
- Propose to the members, the annual program of activities that includes the development of the three functions of the CEI, requesting their contributions.
- Propose to the members the annual program of ordinary sessions, which must be approved and published in the first month of the year. • Prepare and provide the work agendas that will be addressed in the session and send the CEI members the necessary documentation prior to each session, in accordance with its internal operating procedures.

- Receive the issues that are proposed to be discussed in the CEI sessions, check that the information is adequate and sufficient to include it in the work agendas.
- Establish information and communication mechanisms with all members.
- Act as an interlocutor in the absence of the president and on behalf of the REC in relation to communication with researchers, the establishment or institution and the regulatory agencies or corresponding instances, in accordance with their internal operating procedures.

- Summon all members, at the express request of the president, to CEI meetings well in advance, in accordance with its internal operating procedures.
- Prepare the minutes of each session, with the characteristics indicated in section 6.2.3 of this Guide.
- Ensure that the documentation of the decisions made during the sessions is available for review, if applicable. • Collaborate in training, updating and dissemination activities among the staff of the institution or establishment.

- Prepare partial or annual reports on the activities of the CEI and submit them for the consideration of the members of the CEI, in order to issue them in a timely manner to whomever is appropriate.
- Keep the file of the CEI up to date, by registering activities and documentary evidence.

- Attend at least 80% of the sessions, physically in person.
- Carry out the functions of the president in the event of vacancy, absence or illness12.
- Perform any other function assigned by the president in relation to the operation of the CEI.

Vowels

- Systematically evaluate the research protocols and any other information or document submitted for consideration by the secretary member to comply with the functions, objectives and obligations of the CEI.
- Participate physically in the meetings for the analysis, evaluation and opinion of the research protocols submitted for your consideration.
- Follow up on the agreements reached and identify issues that could be the subject of deliberation by the CEI.
- Collaborate in the selection and renewal of committee members, by reviewing compliance with the requirements for their designation, experience and training.
- Collaborate in training activities, updating bioethics and other CEI actions with staff and the population of the establishment's area of influx.
- They must attend at least 80% of the sessions, physically in person. • Perform any other function assigned by the president in relation to the operation of the CEI.

[12] The absence of the president or secretary member must be documented and justified.

Representatives of the affected nucleus or users of health services

- Check that the research protocol, the informed consent form and any other information addressed to the research subjects are explicit enough to be understood by potential research participants.
- Ensure that research in subordinate groups13 adheres to ethical principles and the characteristics described in article 58 of the Research Regulations.
- Attend at least 80% of the sessions, physically in person.

5.3 Installation

The CEI must be installed under the responsibility of the director or head of the institution or establishment, by means of an installation certificate, which will state its integration, its address and the other requirements indicated in the applicable provisions (Provision General of CEI 2016, SEVENTH). For further reference, **Annex 4** presents an example of a record CEI installation.

The installation certificate must contain at least the following information:

- Name or business name of the institution or establishment.
- Address of the institution or establishment to which the CEI belongs.
- Name, profession and position held by each of the members of the CEI.
- Legal basis containing the powers of the director or head of the institution or establishment to install the CEI.
- Statement from the director or head of the institution or establishment stating that the CEI is established under his or her responsibility.
- Autograph signature of the director or head of the institution or establishment.
- Place, date and time of installation of the Committee.

6. Procedures for the operation of the Research Ethics Committee

6.1 Operating rules

The committee will formulate its rules of operation, which must have the approval of the director or head of the institution or establishment, specifying the functions of its members, the activities and functions of the committee, as well as the internal mechanisms of operation in the sessions, in accordance with the criteria established in this Guide (General Provision of CEI 2012, TENTH).

The operating rules of the CEI may include, but are not limited to, regulations, guidelines, operation manuals and internal operating procedure manuals, which must be available for review at the request of the interested parties and particularly of the competent authorities.

6.1.1 Essential internal operating procedures

The National Bioethics Commission promotes with this Guide the development of standardized internal operating procedures, under which it will carry out the fulfillment of its objectives, functions and obligations; in such a way that they promote the consistent application of ethical principles, as well as ensure and demonstrate quality in the review and monitoring of research.

[13] In accordance with article 57 of the Investigation Regulations, subordinate groups are understood to be the following: students, laboratory and hospital workers, employees, members of the armed forces, inmates in prisons or social rehabilitation centers and other groups. of the population, in which informed consent may be influenced by some authority.

RECs must establish their internal operating procedures in writing, considering at least the following:

- Determination of its composition, including the position and qualifications of each member, as well as the functions they assume.
- Determination of the obligations of the establishment under which the committee is installed, as well as those of the owner or director.
- Annual calendar of sessions.
- Session conduction scheme, frequency and type according to their classification; for further reference, see section 6.2 of this Guide. • Scheme of notifications, communication and summons to the members.
- Commitment of minimum attendance of 80% to the sessions physically in person, as well as determination of the quorum to hold the meeting in accordance with section 6.1 of this Guide.
- Conducting the review of the protocol and related documentation, as well as the reviews subsequent ones.
- Review elements of the research proposal and its documents.
- Characteristics and content of the minutes or records of the session.
- Specifications of the reports that the investigator must provide to the REC, for example: deviations from the protocol, modifications that increase the risk to the subjects or significantly affect the conduct of the study, serious adverse events or new information that may negatively influence safety. of the subjects or the conduct of the study.
- Notification of the REC's decision, in a timely manner and in writing, regarding the decision on the investigation, the reasons for the determination, and the procedure for appealing the decision or resolution.
- Scheme for issuing the opinion and maximum time for issuing it, in accordance with section 6.1 of this Guide.
- Follow-up scheme, type, frequency and elements to be supervised by the CEI for previously approved research.
- Records and archive of the documentation received and evaluated by the CEI.
- Determination of the procedure before total or partial resignation of the members.
- Determination of the procedure of the changes of members.

6.2 Internal operating mechanisms in sessions

The committee will formulate its rules of operation, which must include the internal mechanisms of operation in the sessions, in accordance with the criteria established in the *Agreement* and this Guide (General Provision of CEI 2012, TENTH).

6.2.1 Classification of sessions

- **Ordinary sessions:** they are established through the annual work program, with specific dates and times. The CEI must include in its annual program at least six ordinary sessions. The possibility of holding sessions more frequently should be considered in those institutions or establishments where there is great activity in health research.
- **Extraordinary sessions:** they are held at the express request and based on situations related to the work of the CEI, the researchers, the participants or the institution.
  They are carried out at the call of the president, justified by the high volume of health research or by justified priorities in the establishment or institution.
- **Expedited reviews:** they are carried out for evaluations of administrative amendments, inclusions or addition of center without change in documents previously evaluated by the CEI in ordinary session, typographical corrections, change of investigator,

etc. This type of review may not be used to evaluate initial protocols or substantive amendments.

6.2.2 Requirements for sessions and reviews14

The sessions and reviews of the CEI must meet the following conditions:

- The annual calendar of sessions should be made known to those interested in January.
- The agenda and the documents corresponding to each session will be delivered at least seven working days before the meeting. In the case of extraordinary sessions, these will be delivered three days in advance.
- All the members of the CEI must be summoned to each session and a quorum will be considered to exist if the chairman of the committee is present and half plus one of its members is present. In the absence of the president and the secretary member physically in person, the quorum will not be recognized15.
- At the request of the CEI, the principal investigator may be invited to present the research proposal, to delve into specific issues or to clarify doubts. This practice is desirable to shorten review times and optimize communication between the CEI and the investigator.
- Internal or external specialists may be invited to the sessions or to submit written comments, and they must abide by the confidentiality criteria applicable to the rest of the members of the CEI. For further reference, see section 5.2.1 of this Guide.
- The CEI may meet jointly with the Research Committee and, where appropriate, with the Biosafety Committee of the same establishment or institution16. • In cases that by their nature are required, such as in the evaluation of multi-center studies, the REC may meet jointly with the REC of other establishments, for the assessment and opinion of these protocols, respecting the internal regulations of each participating institution.
- In the event of a conflict of interest in any of the members of the CEI, they must be declared disqualified for that particular deliberation and cannot be counted towards completing the quorum. This condition must be documented in the corresponding minute or minutes, in accordance with section 4.1 of this Guide.
- Expedited reviews do not require the necessary quorum for ordinary and extraordinary sessions. The matters of these reviews can be executed by the president and/or secretary member, as well as by the members that are determined for said activity.
  The observations made in these reviews must be reported at the next meeting of the CEI, for its information.

6.2.3 Records of sessions and reviews

For the legal and administrative purposes of each session or review, the corresponding minutes or minutes must be drawn up no more than 10 business days after the session; It will have the autograph signature only of those attending the physical face-to-face session, as well as establishing, in the internal operating procedures of the CEI, the procedure for approving these, their content, their protection and filing.

It is the function of the secretary member, in accordance with section 5.2.1 of this Guide, to prepare the minutes, which must include the following information:

[14] The CEI may define in its internal operating procedures the mechanisms for evaluating investigations without considered risk. Ranking the classification of article 17 of the Regulation on research for health.

[15] Except for unencumbered revisions

[16] The opinion issued may correspond to a single opinion or the opinion of each committee in accordance with its internal operating procedures.

- Place and date of the session.
- Type of session according to the classification cited in section 6.2.1 of this Guide.

- Indicate if the session was recorded.
- Consecutive numbering of the minutes or minutes per year.
- Name, position and signature of those attending the face-to-face physical session.
- Agenda, or if applicable as an annex.
- Issues dealt with.
- Include the comments, suggestions or contributions issued by the attendees in the face-to-face physical session.
- Agreements generated in the session.
- Topics or pending issues.
- Opinion issued by the Committee.
- Indicate the name and position of the members who declared potential conflicts of interest and the actions carried out in this regard.
- If applicable, indicate the participation of internal or external specialists and the mechanisms to send their technical comments regarding the research proposal, including their comments issued.

7. Criteria for evaluating research

7.1. General considerations in the evaluation

Bioethics does not recommend a specific set of rules or policies, but rather provides a structure or guidance for evaluating problems and determining appropriate courses of action:

- The research protocols submitted for evaluation by the CEI must comply with the criteria and provisions applicable in the country. Provide sufficient and timely information to the REC to evaluate the research proposal as a whole.
- The RECs must be familiar with the different methodologies and make the applicable ethical considerations for each type of proposed research.17
- The ethical analysis of research should reflect the provisions of national legislation, as well as international recommendations, cultural values and human rights instruments.

- The REC must base its evaluation on a coherent and consistent methodology, documented in accordance with its internal operating procedures. It will have to indicate the grounds on which its resolution is based, with concrete evidence of the comments issued and the decisions adopted, for which the use of an evaluation instrument of minimum ethical aspects is recommended.

7.2 Ethical aspects for the evaluation of protocols

As part of the systematic evaluation that the committee must carry out with respect to the research proposal submitted for its consideration, the REC must assess at least the following
(Emanuel, Wendler & Grady 2000):

- **Scientific value:** To be ethical, research with human beings must have scientific and social value and, consequently, help improve the health or well-being of the population, test a hypothesis that can generate important information about the

[17] Human **health research** may include but is not limited to: A) Phase I to IV clinical trials with drugs, vaccines, or medical devices; B) Bioequivalence and biocomparability studies; C) Research with organs, tissues and cells; D) Epidemiological investigations; E) Research in social sciences; F) Behavioral studies; G) Post marketing studies; H) Observational studies applying surveys or review of files, among others.

structure or function of human biological systems, even when such information does not have immediate practical applications. Some examples of health research with no scientific or social value include research that partially or fully duplicates proven results, is not generalizable, a banal hypothesis, or one in which the intervention cannot be carried out in a practical way even if it is effective. Social value is an ethical requirement that ensures responsible use of limited resources and avoids exploitation.

- **Scientific relevance in the design and conduct of the study:** Ethical considerations are an integral part of the research throughout it, from the formulation of the research question to the publication of results. Although the fundamental responsibility of the RECs is to review the ethical aspects of research involving human beings, they must assess whether the research lacks relevance and scientific rigor that could cause harm or greater risks to the participants and therefore therefore not ethical. Scientific relevance is a non-negotiable requirement.

- **Participant selection criteria:** The identification and selection of potential research subjects must be equitable, regardless of age, gender, socioeconomic group, or culture. It is required that it be science and not vulnerability, social stigma, powerlessness or factors unrelated to the purpose of the research, that determine potential participants. Equitable selection requires that all groups be offered the opportunity to participate in research unless there are good scientific or risk reasons that restrict their eligibility.

- **Proportionality in risks and benefits:** Risk is defined as the combination of the probability that an event with negative consequences will occur. In research, the degree of risk and benefit is uncertain and in the case of research with human beings it can only be justified when: 1. Potential risks are minimized; two. The possible benefits for the participants individually or for society are maximized; and 3. The possible benefits are proportional to or exceed the anticipated risks (Research Regulations, article 15).

- **Independent evaluation:** Potential conflicts of interest for the approval of a research protocol are minimized when the evaluation is independent and the research with human subjects is reviewed by experts who are not involved in the study and who have the authority to approve, condition or, in extreme cases, reject or cancel the investigation.

- **Respect for participants:** It is important to protect the privacy of research participants, offer them the opportunity to withdraw from the study, and ensure that they are being continuously evaluated during the study.

- **Informed Consent: Informed** consent is a process by which an individual, after receiving the necessary information, makes a voluntary decision to participate, or not, in a research study. Informed consent is recorded by means of a document, signed and dated. It consists of two parts, the first in which information about the proposed research is provided and the second which is the formal act in which the research subject agrees with his signature to participate in the research. For further reference, see **Annex** 5.

8. Decision making

Committee decisions regarding research should be based on a process of inclusive discussion and deliberation. The president of the CEI is responsible for ensuring that all members participate in said process, ensuring that sufficient time is available and that the meeting is held in an atmosphere of respect that allows the expression of different points of view.

During the meetings, a discussion will begin on the documentation submitted for consideration by the CEI and the corresponding opinion will be issued. In this regard, it should be considered that:

- The decisions of the CEI will be made by consensus, which implies that none of the members should consider the decision as unacceptable. Decisions will never be made by vote.
- Only the members of the CEI physically present at the session may issue opinions for decision-making on the investigations. • Investigators, sponsors and other people directly involved in the study should not be present during the deliberation.

The resolutions issued by the CEI must be based on solid and substantiated arguments. In the case of research projects that are ruled as "pending approval", the CEI must provide clear suggestions to the researcher for the new version and revision of the protocol; when the opinion is "not approved", it must be based on clear and specific arguments, stating the procedure to submit the request for review again, if it were the case.
case.

8.1 Resolution of the protocol evaluation

The CEI must establish in its rules of operation the resolution mechanism, the time it comprises and the type of resolution. For the purposes of this Guide, resolutions are classified as opinions:

- **Approved:** Meets all established requirements. In the case of an approving resolution, it must include its validity, which may correspond to up to one year.

- **Pending approval: a.** It requires major modifications and must be evaluated by the CEI, in plenary session, when said modifications are made. **b.** It requires minor modifications and may be evaluated expeditiously, in accordance with what is established in the corresponding section. **c.** Conditioned or in the process of valuation. More information is required or doubts arose during the protocol review process.

  In the case of an opinion pending approval, the time to resolve the observations by the principal investigator must be included, which does not exceed 30 calendar days from the date of receipt of the observations.

- **Not approved:** Research proposal rejected for ethical, methodological or regulatory reasons that warrant a major restructuring.

8.2 Communication of the evaluation result

The opinion18 must be notified in writing to the requesting principal investigator within the period indicated in the applicable provisions or, where appropriate, in the operating procedures.

[18] The opinion corresponding to the first evaluation of the CEI, in the event that modifications are required by the CEI to the protocol or its documentation, is the responsibility of the principal investigator to deliver it in a timely manner, the time will not be counted until the investigator attends to the observations required by the CIS.

internal tives of the CEI; It is suggested that it be sent within a period not exceeding five business days after the session has been held, or if applicable, not exceeding 30 calendar days from the date of request for review. For further reference in **Annex 6**
An example of an opinion on the evaluation of research is presented, particularly in the case of clinical trials that must be authorized by COFEPRIS (LGS, article 102).

The decisions made by the Committee will only be valid when there is an established *quorum* , in accordance with section 6.2.2 of this Guide.

9. Documentation and archive of the Research Ethics Committee

The documentation and archive of the CEI must be physically safeguarded19 in the facilities of the establishment to which the registration of the Committee was issued by the National Bioethics Commission.20

9.1 File characteristics

A person responsible for the CEI file must be appointed and have facilities for exclusive use and restricted access. The documentation should preferably be filed grouped by study and in such a way as to guarantee its confidentiality.

9.2 Duration of the safeguard

The CEI will keep all the essential documents reviewed and related to each evaluated investigation, for up to 5 years after its completion or during the period established in the applicable provisions. The CEI must define the manner of destruction or disposal at the end of the safeguard period.

9.3 Essential file information

The CEI must keep a copy of the complete file submitted to the National Bioethics Commission to obtain the CEI's registration and, where appropriate, requests for modification and renewal.

Information of the members of the CEI

- Updated curriculum vitae of each member of the CEI.
- Original letter of declaration of no conflict of interest, with the frequency of signature that the CEI determines in its internal operating procedures.21
- Certificates of training of each member of the CEI.

CEI operation

- Annual calendar of CEI sessions.
- Correspondence received, documentation sent by the researchers, as well as the communication exchanged with them and other actors.
- Records of expenses or use of the resources received, in accordance with the principles expressed in this guide and with the procedures of the committee.

[19] Unless applicable legal provision that establishes another condition or mechanism.

[20] For further reference, it must correspond to the address of the establishment established in the CEI registration certificate.

[21] The CEI will determine the periodicity of the signature of the letter of declaration of No Conflict of Interest of each member of the CEI that must correspond to at least one letter signed for the period of appointment in the position of three years, in its case determine if the signature is implemented for each research proposal evaluated or on an annual basis.

Evidence of evaluations

- File of each research proposal evaluated, including at least: research protocol and its amendments, informed consent form, researcher's manual or product monograph or equivalent22, written material delivered to the research subject, and other applicable documentation.
- Physical or electronic list per year, of each and every one of the research protocols evaluated and in follow-up. • Original of each act or minute of session carried out by the CEI.23
- Original of each resolution issued and its respective supporting documentation.

Follow-up evidence

- Periodic reports on the approved investigation and the final report.
- Follow-up report delivered by the principal investigator to the CEI regarding the status of each investigation, with the periodicity determined by the CEI24, considering at least one annual report.
- Report of each serious adverse event report received by the REC regarding each investigation it has approved.

The committee must keep the documentation related to its integration, operation and registration for up to three years after the conclusion of its activities and the procedure for transferring the file and its person in charge at the establishment where the CEI registration was granted must be defined.

10. Role of the researcher with respect to the Research Ethics Committee

In accordance with the Mexican legal framework, health research must be carried out by health experts and professionals (Research Regulation, Article 114) with knowledge and experience to care for the integrity of the human being, under the responsibility of a health care institution. to health, that acts under the supervision of the competent health authorities and that has the necessary human and material resources, which guarantee the well-being of the research subject (Research Regulations, article 14 section VI).

For the purposes of this Guide, the health professional, that is, the principal investigator, will be in charge of the technical direction of the investigation (Research Regulations, article 116), which includes at least the following activities:

- Conduct the investigation in accordance with the provisions of the protocol approved by the CEI.
- Submit to the CEI the evaluation of any amendment to the previously approved protocol or its documents, if applicable, the exceptions to the evaluation of amendments by the CEI. It should be noted that the security amendments must follow the applicable provisions. 25
- Prepare and present the partial and final reports of the investigation.

Conducting the investigation involves the following responsibilities:

- You must know the relevant aspects of ethics in research, particularly in cases involving populations in a situation of vulnerability, in accordance with TITLE TWO of the Regulations of the General Law of Health in the Matter of Research for Health.
- Will be directly responsible for the scientific and ethical aspects of the proposed research

[22] When it comes to clinical trials, this is intervention research.

[23] The acts or minutes must be numbered by year and consecutive number.

[24] The periodicity must correspond to that established in the respective internal operating procedure.

[25] See the considerations or exceptions for the implementation of security amendments in the applicable provisions.

and to submit the evaluation request to the CEI. In such a way that the committee can carry it out completely. It should be remembered that the protocol must contain the information referred to in the applicable provisions.

- Communicate to the CEI regarding the premature termination or suspension of the investigation, the reasons and the results obtained up to that moment. • Submit to the CEI the final report that includes the results of the investigation and report on its publication, contemplating adverse or negative results as a result of the investigation. • Inform the CEI of any serious adverse event, with the periodicity established in the approved protocol and in the CEI procedures manual, both in accordance with the provisions applicable in Mexico. In case of reporting a serious adverse event, the committee will review it and take the corresponding actions to minimize the potential risk to the subjects.

- Obtain the informed consent of potential research subjects before starting the research, unless you have received explicit written approval from an REC of the exception26 to informed consent for justifiable reasons.

11. Procedures associated with the registration of Research Ethics Committees

The owners of health establishments and institutions will register the Research Ethics Committee, Research Committee and Biosafety Committee27 with the Secretariat, which will determine the characteristics and frequency of the reports to be provided. In the case of Research Ethics Committees, registration will be made before the National Bioethics Commission (Research Regulations, article 101).

The medical care establishments of the National Health System or the health institutions where health research is carried out with human beings must apply to the National Bioethics Commission, through the general director, owner or legal representative,28 in accordance with the legal nature of the requesting establishment, the CEI registration of its establishment.

The establishments that may have the CEI registration will be those that meet the requirements set forth in the General Health Law, in its Regulations on Health Research and other applicable provisions, whose infrastructure must guarantee the technical, material, human and financial, as well as the facilities, equipment and technology to carry out the tests, studies, trials, and other activities necessary to carry out research with human beings, respecting the human rights and dignity of the subjects participating in the research. .

Classification of requests

For purposes of submitting applications to the National Bioethics Commission, they will be classified as:

- Application for initial or new registration.
- Request for modification of the registration conditions. • Application for registration renewal.

[26] The informed consent letter will be obtained from the research subject, if applicable, from their legal representative or the closest relative, except when the condition of the subject incapacitates or prevents granting it, the legal representative or the relative is not available and ceasing to use the research medication represents an almost absolute risk of death (Research Regulations, article 71, section II).

[27] The Research and Biosafety Committee is registered with COFEPRIS.

[28] It is the person who, by virtue of a legal act, acts on behalf of the principal (company or establishment) to carry out certain actions.

Characteristics of the requests

They must comply with the following:29

- Appear by the interested party, in physical format, before the National Bioethics Commission located at Calzada Arenal number 134, Colonia El Arenal Tepepan, Tlalpan Delegation, CP 14610, Mexico, Mexico City:
  - In person, by appointment.
  - Sending documents by certified mail or certified parcel, with acknowledgment of receipt and prepaid guide.
- Contact the National Bioethics Commissioner at the Directorate of Bioethics Committees.
- Appear in the strict order established in this Guide.
- Be presented in printed form with a legible folio on each page with text on the upper right side, all simple copies must be legible and complete.

Classification of the documentation presented

The applicant must classify the documentation submitted to the National Bioethics Commission as public information or confidential information. In case of being reserved, you must indicate in brackets the data that is confidential. The documents must contain the legends: *public information or confidential information,* justifying, in the case of the latter, the reason why it is assigned the character of confidential or reserved information.30

Elements of the registration certificate31

The record of registration, in addition to the requirements of any administrative act provided for in the Law Code of Administrative Procedure and the Federal Code of Civil Procedures of supplementary application, contains the following elements:

- Details of the establishment:
  - Name of the owner or business name of the establishment to which the CEI belongs.
  - Name of the establishment.
- Address of the establishment where the CEI is located.
- Single registration alphanumeric key.
- Issue date. • Validity.
- Signature of the head of the National Bioethics Commission.

Reception of the resolution

Only the health officer, legal representative and/or authorized persons may collect the respective resolution at the facilities of the National Bioethics Commission, in accordance with the application form submitted to the Commission. If you have received a resolution, and detected any erroneous information in the letter issued, you must submit the request for internal correction within a period not exceeding 10 calendar days from the receipt of your letter.

11.1 Application for initial or new registration

The registration application must be submitted to the National Bioethics Commission, on working days and hours, in the format32 and with the requirements detailed in the AGREEMENT that amends and adds the diverse one by which the General Provisions are issued. for Integra The application presentation characteristics

[29] apply for initial or new registration, modifications and renewal of the CEI registration.

[30] The information classification of the applications to be submitted applies to initial or new registration, modifications and renewal of the CEI registration.

[31] The elements of the CEI registration certificate apply for initial or new registration, modifications and renewal of the CEI registration.

[32] The formats referred to in this Guide will be available for filling out or downloading on the Commission's Internet Portal National Bioethics https://www.gob.mx/salud/conbioetica

tion and Operation of the Research Ethics Committees and the hospital units that must have them are established, in accordance with the criteria established by the National Bioethics Commission, published on October 31, 2012, published in the DOF on October 11, 2012. January 2016 (General Provision of CEI 2016, TWELFTH).

requirements

1. Original **application for registration of the Research Ethics Committee** (the format is available in the General Provisions 2016 as well as on the Internet portal of the National Commission) duly completed and with the autograph signature of the director, owner or legal representative of the establishment. • Statement under protest to tell the truth, that the data provided is correct and in which he undertakes to provide, at the request of the National Bioethics Commission, the information, data or documents that are required.

2. Original **self-assessment format** duly completed and with autograph signature of the director, owner or legal representative of the establishment.
3. Original **CEI installation certificate** according to section 5.3 of this Guide.
4. Original of the **certificates of appointment** of each of the members of the committee, according to section 5.2 of this Guide.
5. Simple copy of the **professional license** of each one of the members of the committee, except in the case of the representative of the affected nucleus or of the users of the health services.

6. Original of the **curriculum vitae** of each one of the members of the committee. • Present in the format of a curricular capsule of no more than 10 pages.
   - Include the autograph signature of the respective member on the last sheet and signature on each previous sheet.
   - Include the position, position and current affiliation.
   - Include your academic background.
   - Include representative scientific production related to their functions in the committee. tea, no more than 10 posts.
   - Include your experience in clinical practice, research areas or related to duties on the committee.
7. Simple copy **of training certificates** in bioethics and/or Research Ethics of the members of the committee, except for the representative of the affected nucleus or of the users of the health services. Issued in the last 5 years before the filing of the registration application.

8. Simple copy of the **document with which the legal representation of the establishment,** and original or certified copy for comparison.
9. Simple copy of the **health license** of the establishment and original or certified copy for comparison.
   - For health care establishments, submit a simple copy of the health license.
   - For higher education institutions, submit a simple copy of the agreement with the health care establishment for medical emergency care, if applicable.
   - For clinical units, authorized third parties to carry out interchangeability and biocomparability tests, submit a simple copy of the current authorization issued by COFE PRIS. In this case, the CEI registration will be valid as long as the authorization issued by COFEPRIS remains in force.

   - For other types of establishments not contemplated above, it will be reviewed on a case-by-case basis, and the corresponding information must be submitted to prove its research activities with human beings, if applicable, with the respective authorization from the competent authority.

10. Simple copy of the **notice of appointment of the health manager** of the establishment and original or certified copy for comparison.
    - The notice is submitted to COFEPRIS or the federal entities within the scope of its competition.
11. Simple copy of its **operating rules**
    - The rules of operation must include at least what is indicated in the section 6.1 of this Guide.
12. Simple copy of its **policies, guidelines or guides in adherence to good practices** facility **clinics .**
    - They must include at least what is indicated in section 6.1 of this Guide.
13. **Internal operating procedure to follow up** on the approved protocols.
    - They must include at least what is indicated in section 6.1 of this Guide.
14. **Manifestation under protest to tell the truth** that the establishment is in the **cases provided for in articles 41 bis and 98 of the general health law**

    and has the infrastructure that guarantees the technical, material, human and financial capacity, as well as the facilities, equipment and technology to carry out the tests, studies, trials, verifications and other activities necessary to carry out research activities with human beings, in accordance with the criteria established in current regulations.

    - Submit in free written format, on letterhead, dated, addressed to the National Bioethics Commissioner and with the autograph signature of the director, owner or legal representative of the establishment.
15. **Demonstration under protest to tell the truth** that the requesting establishment **has the necessary facilities** to protect the participants in research, the personnel and equipment necessary for the attention of any medical emergency, the procedures for the hospitalization of patients in case of be necessary and with more guidelines established in the Good Research Practices and current regulations.

    - Submit in free written format, on letterhead, dated, addressed to the National Bioethics Commissioner and with the autograph signature of the director, owner or legal representative of the establishment.

In order to guarantee the safety of the subjects participating in the research and the scientific integrity of the research, the Commission reserves the right to request additional documentation or information (General Provisions of the CEI 2016) or, through supervision visits, evaluate the information presented in the application and verify compliance with the provisions that support the CEI registration. This visit scheme will be subject to the characteristics (except the administrative process item) and minimum aspects to be evaluated referred to in section 12.2.2 Supervision visits of this Guide, but unlike these, the persons authorized to receive notifications in the CEI registration request will be informed in advance about the date and time they will occur.

Resolution of the application

Terms and deadlines: The Commission, within a period of ten business days, counted from the business day following the presentation of the application, will admit it for processing or, where appropriate, will prevent the applicant so that rectify the omissions of your request within the term of fifteen business days, counted from the business day following the date on which said prevention was notified, aware that in case of not doing so, the request will be considered as not submitted.

Once the application has been admitted for processing, the Commission will have a period of thirty business days to notify the applicant of its origin or to issue the corresponding registration certificate (General Provision of CEI 2016, TWELFTH).

Validity of the registration certificate: It will be three years. The registration certificate must be displayed in a visible place in the establishment and, if applicable, on its website. The registration number must appear in all official communications issued by the committee33.
Likewise, the purpose and functions of the committee must be posted in the establishment in a visible place for the general public (General Provision of CEI 2016, TWELFTH BIS).

It is necessary for the CEI of the institution or establishment to have a valid registry so that the opinions of the protocols or their follow-up are valid before the national health authority. If there is no current registration, the REC has the obligation to inform the principal investigator. In the event of ongoing investigations and no REC with current registration, the owner or director of the establishment must ensure that the monitoring of the protocols is carried out by a REC with current registration issued by the National Bioethics Commission.

11.2 Request for modification to the registration conditions

Types of modification

For the purposes of this Guide, modifications to the CEI registration conditions include, but are not limited to:

A. Errata (typographical errors).
B. Change or substitution of members (departures, registrations or new position).
C. Change of address of the establishment.
D. Change in the document that accredits the legal representation of the establishment.
E. Change of legal representative, director or owner of the institution or establishment.
F. Change in operating rules of the CEI or internal operating procedures.
G. Change in operating procedure to follow up on approved protocols.
H.Other

General requirements

1. Free letter describing the reason for the modification, on letterhead, dated, addressed to the National Bioethics Commissioner and with the autograph signature of the director, owner or legal representative of the establishment.
2. CEI registration certificate previously issued, in original with autograph signature.

Requirements by type of modification

A. Errata (typographical errors).
- Comparative table of changes.

B. Change or substitution of members (departures, registrations or new position).
- Original certificate of installation of the CEI with the characteristics indicated in the section 5.3 of this Guide.
- Original of the certificates of appointment of each of the members of the committee, in accordance with the characteristics indicated in section 5.2 of this Guide.
- Simple copy of the professional license of each one of the members of the committee, except in the case of the representative of the affected nucleus or of the users of the health services.

[33] The registration number of the CEI must appear in the opinion issued by the committee.

- Original curriculum vitae of each of the members of the committee.
  - ÿ Submit in a curricular capsule format of no more than 10 pages.
  - ÿ Include the autograph signature of the respective member on the last sheet and signature on each previous sheet.
  - ÿ Include the position, position and current affiliation.
  - ÿ Include your academic background.
  - ÿ Include representative scientific production related to their functions in the committee, no more than 10 publications.
  - ÿ Include your experience in clinical practice, research areas or related to duties on the committee.
- Simple copy of training certificates in bioethics and/or research ethics of the members of the committee, except for the representative of the affected nucleus or of the users of the health services.
- In the event that the modification of the member affects the contact data of the CEI, it is written free of cancellation, registration and/or incorporation of contact data.

C. Change of address of the establishment.

- Document issued by the competent authority that certifies the new domicile corresponding to the name of the establishment to which the CEI registration was previously issued.

D. Change of legal representative or director or owner of the institution or establishment.

- Simple copy of the new document accrediting the legal representation of the establishment or appointment of the new director or owner, and original or certified copy for comparison.

E. Change in operating rules of the CEI or internal operating procedures.

- Simple copy of the new rules of operation, policies, guidelines or guides in adherence to the good clinical practices of the establishment; The rules of operation must include at least what is indicated in section 6.1 of this Guide.

F. Change in operating procedure to follow up on approved protocols.

- New internal operating procedure to monitor the approved protocols, must include at least what is indicated in section 6.1 of this Guide.

G. Other.

- It will be attended according to the characteristics and type of modification.

In order to guarantee the safety of the subjects participating in the research and its scientific integrity, the Commission reserves the right to request additional documentation or information (General Provisions of the CEI 2016).

11.3 Application for renewal of registration

Presentation of the application

For the renewal of the registration certificate, the director, owner or legal representative of the establishment must submit the corresponding request to the Commission, within 45 business days prior to the expiration of its validity, in the format (Form available at General Provisions 2016) and with the requirements detailed below:

requirements

1. Original of the **request to renew the registration of the Research Ethics Committee** duly requested and with the autograph signature of the director, owner or legal representative of the establishment.
2. Previously issued CEI registration certificate, in original with autograph signature.

3. Original of the **certificates of appointment** of each one of the members of the committee, in accordance with the characteristics indicated in section 5.3 of this Guide.
4. Simple copy of the **professional** license of each one of the members of the Committee, except in the case of the representative of the affected nucleus or of the users of the health services.

5. Original of the **curriculum vitae** of each one of the members of the committee. • Submit in curricular capsule format no longer than 10 pages.
   - Include the autograph signature of the respective member on the last sheet and signature on each previous sheet.
   - Include the position, position and current affiliation.
   - Include your academic background.
   - Include representative scientific production related to their duties on the committee, no more than 10 publications.
   - Include your experience in clinical practice, research areas or related to the functions on the committee.

6. Simple copy **of training certificates** in bioethics and/or research ethics of the members of the Committee, except for the representative of the affected nucleus or of the users of the health services. Issued with a date after the issuance of the last certificate of registration of the CEI.

7. Simple copy of the acknowledgment of receipt of the last three **annual reports** filed with the National Bioethics Commission.
8. Simple copy of the **document with which the legal representation of the state is accredited establishment,** and original or certified copy for comparison.
9. Simple copy of the **Sanitary License** of the establishment and original or certified copy for comparison.
   - For health care establishments, submit a simple copy of the health license ria.
   - For higher education institutions, submit a simple copy of the agreement with the medical care establishment for medical emergency care.
   - For clinical units, a third party authorized to carry out interchangeability and biocomparability tests, submit a simple copy of the current authorization issued by COFE PRIS. In this case, the CEI registration will be valid as long as the authorization issued by COFEPRIS remains in force.

   - For other types of establishments not contemplated above, it will be reviewed on a case-by-case basis, and the corresponding information must be submitted to prove its research activities with human beings, where appropriate, with the respective authorization from the competent authority.

Resolution of the request

Terms and deadlines: The Commission, within a period of ten business days, counted from the business day following the presentation of the application, will admit it for processing or, where appropriate, will prevent the applicant so that he corrects the omissions of his application within a term of fifteen business days, counted from the business day following the date on which said prevention has been notified, being warned that in case of not doing so, the application will be considered not submitted (General Provision of CEI 2016, TWELFTH BIS).

Once the application has been admitted for processing, the Commission will have a period of thirty business days to notify the applicant of its origin or to issue the certificate of renewal of the corresponding registration.

Validity of the registration certificate: It will be three years. The new registration certificate issued must be displayed in a visible place in the establishment and, if applicable, on its website. The registration number must appear in all official communications issued by the committee. Likewise, the purpose and functions of the committee must be posted in the establishment in a visible place for the general public (General Provision of CEI 2016, TWELFTH BIS).

In order to guarantee the safety of the subjects participating in the research and its scientific integrity, the Commission reserves the right to request additional documentation or information (General Provisions for CEI 2016).

12. Follow-up of the National Bioethics Commission to the Committees Research Ethics

One of the powers of the National Bioethics Commission is to evaluate and monitor the integration and operation of the Research Ethics Committees, in coordination with the competent authorities. In this regard, this section deals specifically with the CIS monitoring activities carried out by the Commission.

12.1 Follow-up definition

Monitoring of the RECs is a set of permanent activities carried out by the National Bioethics Commission to assess that their integration and operation complies with current applicable provisions and the criteria established by the Commission in this regard, as well as how to ensure that the committees perform with the highest quality standards, respecting the fundamental ethical principles and the applicable regulations in the field of health research.

12.2 Monitoring instruments

They are the formats, documents and actions, which may be applied jointly or separately, designed to evaluate the functioning of the CEI. The main instruments that the National Bioethics Commission may apply are detailed below.

12.2.1 Annual activity report

Definition: It is a mandatory document that must be presented, within the first thirty calendar days of the year, to the National Bioethics Commission and to the owner or director of the establishment, the CEI with registration (General Provision of CEI 2016, SIXTH PROVISION, SECTION V) . In this regard, the National Commission designs and distributes the electronic formats to present the annual activity report, these can be made up of one or more files or formats.

The president of the CEI is responsible for the presentation of the annual activity report34, who will state under oath that the information provided was reviewed and authorized by him. Once the report is received, the National Commission will evaluate and process its content and will issue the corresponding observations or acknowledgment, which is an essential requirement for the application for renewal of the CEI registration.

Items covered in the annual report

As its name indicates, this activity reports information regarding the integration and operation of the CEI during the immediately preceding year, regardless of the month in which

[34] For the annual activity report, the rest of the members can support its preparation, however, the authorization of the information contained therein is the responsibility of the president.

have received your registration. Listed below, by way of example but not limitation, are the aspects included in the annual report:

a) General data of the CEI and the establishment.

b) General information.

- Report of modifications to the registration conditions, for further reference see section 11.2.
- Information on the integration of the CEI (for example, characteristics of the members, professional training, as well as all relevant information).
- Report on the characteristics, frequency and duration of the CEI sessions, as well as the annual calendar.

c) Exercise of the resolution function.

- Report on the investigations received and evaluated by the CEI (quantity, types of submission, characteristics, names of the principal investigators, opinion issued by the CEI, etc.).

d) Exercise of the educational function.

- Preparation and dissemination of guidelines or guidelines on health research among the staff of the establishment.
- Training activities for CEI members.
- Training activities for establishment personnel.

e) Exercise of the control and monitoring function.

- Report on activities of control and monitoring of protocols approved by the CEI.

f) Technical, human and material resources of the CEI.

g) Capacity and scope of the CEI operation.

It is important to point out that the formats provided by the National Bioethics Commission do not request confidential information regarding the research or personal or sensitive data of the research subjects. In this sense, the information related to the investigations adheres to those data considered for the National Registry of Clinical Trials (RNEC) operated by COFEPRIS.

12.2.2 Supervisory visits

Definition: The supervision visit is an administrative act in which authorized personnel of the National Bioethics Commission go to the establishments that have a Research Ethics Committee registration, in order to verify *in situ* that they comply with the legal provisions. applicable, as well as evaluate its integration, operation, performance and adherence to procedures in accordance with the information entered in your application.

In addition to the above, the supervision visits constitute a mechanism to provide feedback on the functioning of the CEI and standardize its operation at the national level, while at the same time allowing the National Commission to have specific information on the work of the CEI to carry out actions and strategies related to the strengthening of health research with human beings and research ethics in our country

Characteristics of the visits: Due to the purpose and nature of the supervision visits to the CEIs, they are carried out in conjunction with COFEPRIS, which, within the scope of its powers, also evaluates that the CEI complies with the legislation. applicable.

The schedule of visits considers a representative sample of registered RECs, so all RECs registered with the National Bioethics Commission are likely to be visited. In this sense, it is important to point out that the visits are carried out:

- ***Without notice.*** For the purpose of evaluating the regular functioning of the committee, the visits are not made known in advance to the committees. Designated personnel notify and initiate the visit the same day they attend the establishment.
- ***Throughout the year and throughout the national territory.*** They are established through the annual visit plan that covers all the states that have CEI registered or in process.
- ***With strict adherence to law.*** The staff of the National Bioethics Commission is trained to maintain transparency during the process and safeguard the rights of the people who attend or participate in the visit.
- ***They involve an administrative procedure.*** The visits initiate a process before the National Bioethics Commission, to which the CEI must provide timely follow-up. Here is a brief outline of what it consists of:

1. The designated personnel carry out the visit and during it a circumstantial record is generated where the information obtained is recorded.
2. Based on the evidence and information collected, an official letter is generated where the findings derived from the visit are notified, as well as the actions, evidence and time to correct them.
3. The CEI sends the documentation and evidence to the National Commission to respond to the office of finds.
4. The National Bioethics Commission evaluates the evidence and issues a resolution in this regard.

Minimum aspects to be evaluated during a visit: During the visits, adherence to the national legislation that regulates the operation of the RECs is evaluated. Listed below, by way of example but not limitation, are the minimum elements that are subject to review:

a. Information and documentation entered for the CEI registration process.

b. Adherence to operating rules and internal operating procedures evaluates two by the National Bioethics Commission to grant registration.

c. The documentation received by the REC (initial submissions, amendments or modifications, partial or final reports, deviations, reports of serious adverse events, etc.).

d. The documentation generated by the CEI (session minutes, opinions, evaluation instruments, observations and comments, file and communication controls, results of on-site control and follow-up visits, etc.).

and. Evidence of the training of the members of the CEI in matters of ethics in investi tigation, bioethics or good clinical practices.

F. Evidence of the educational work for the staff of the establishment in matters of ethics in research, bioethics or good clinical practices.

g. Files of investigations received and evaluated by the CEI.

h. Archive of the CEI, its characteristics, as well as the control and access mechanisms.

i. Any other relevant information, in accordance with the evaluation instrument that is subject to change and improvement at least once a year.

13. Cancellation of the registration of Research Ethics Committees

Derived from the powers of the National Bioethics Commission with respect to promoting the protection and respect of human rights in the provision of health services and in research; establish and disseminate the criteria and procedures for the integration, operation and registration of Research Ethics Committees, and promote their observance in the National Health System, as well as evaluate and monitor them in coordination with the competent authorities, Scenarios are foreseen in which the CEI could lose the registration previously granted, or the possibility of not obtaining a registration after the application is processed.

In this sense, the cases in which the National Bioethics Commission could cancel the registration of a CEI are described below, by way of example but not limitation:

- Entering false data in the CEI registration application and/or in any of the accompanying documents.
- If the establishment that requested the registration is not in the cases provided for in Articles 41 BIS and 98 of the General Health Law that support its issuance .
- If it is found that the operation and functioning of the CEI is not carried out in accordance with the provisions of national legislation on the matter and the guidelines established by the National Bioethics Commission.
- If there is no evidence that the REC complies with its obligations established in the legislation with respect to evaluating and ruling on research protocols with human beings.
- If the integration, operation or functioning of the CEI puts at risk the protection of the subjects participating in the research.
- If there is evidence of a lack of technical, ethical and legal competence in the evaluation of research protocols.
- If there is evidence of lucrative activities in the operation of the CEI that put at risk the quality of evaluation of the research and therefore the protection of the human beings that participate.
- Do you want to denounce it.

14. Topics of interest

Ethical considerations on biological material in research Human

biological material includes organs, tissues, tissue components, cells, products and corpses of human beings (LGS, article 314, section XVII). Its use and association with personal data is becoming more frequent and important in biomedical research. The collection, storage and use of these materials and the possibility of obtaining biological and genetic information through them represent a challenge from an ethical, legal and social point of view. This is why the population must have confidence that the material will be handled responsibly (CEI Council of Europe Guide).

Research and other activities related to health databases and biobanks must be for the benefit of society, in particular public health objectives (Declaration of Helsinki 2013). From an ethical perspective, it is important to consider the following aspects:

- If the information and biological material are collected for a research project determined and approved by the REC, if applicable, consent must be obtained

specific to the participants. • The
informed consent related to the collection, use, and storage of biological material must make it clear that it will not be used for a purpose other than that originally proposed, and in accordance with the protocol approved by the CEI.
- The collection, use and storage of biological material must guarantee the confidentiality and privacy of the donor. • The commercialization of biological material is prohibited. • It will not exercise undue influence through financial incentives to donors of biological material.

- The collection and transfer of biological material must not, under any circumstances, jeopardize the medical care and safety of the research subject.
- Upon revocation of informed consent, the biological material collected for such purposes must cease to be used, unless they are irreversibly dissociated from the person. Data and biological material that are not irreversibly dissociated should be treated in accordance with the wishes of the owner or donor (International Declaration on Human Genetic Data).

- The REC must require the establishment of time limits for the use of biological material and prohibit the unrestricted use of the material.

Attachments

Annex 1. Example of a declaration format of no conflict of interest

In this form you must indicate if you consider that there is a secondary interest that could unduly influence your responsibility to protect the research subjects.

You are asked to answer questions concerning yourself and your “immediate family members.”35 This form is intended to identify and address existing and potential conflicts of interest. Four questions are included.

1. I have a conflict of interest to report	Otherwise

If you have any conflict, please specify which one:

1. Direct business or economic relationship with the sponsor.	Otherwise
2. Direct professional relationship with the sponsor.	Otherwise
3. Any other thing that could affect their objectivity or independence in the performance of their duties.	Otherwise

If you answered yes to any of the questions above, please provide details:

I declare under oath that the above information is correct.

Date and signature of the member of the Research Ethics Committee

[35] For purposes of this form, “immediate family members” are: (i) your spouse or common-law partner; and (ii) your children.

Annex 2. Example of information confidentiality format

Mexico City to __DD_ of ___MM___YYYY

I declare that according to the appointment and functions that I perform as a **member of the Research Ethics Committee (CEI)** I have no personal, labor, professional, family or business interest that may affect the independent and impartial performance of the position that I perform.

It is hereby stated that I: _____
_____ (FULL NAME), in my capacity as: (POSITION AT THE CEI)
_____ that as a result of the work I perform at _____ and having access
(PROPERTY NAME) to information regarding
(MENTION IN A GENERAL FORM THE INFORMATION CORRESPONDING TO THE FUNCTIONS OF THE CEI) ___

I commit indefinitely to:

1. Maintain the reserve and confidentiality of said information.
2. Do not disclose the content of the information to third parties, individuals or legal entities.
3. Not to use the information directly or indirectly for my own benefit or that of third parties, except to fully fulfill my functions related to the position I perform.
4. Do not fully or partially disclose to any third party the information obtained as a result direct or indirect evidence of the conversations that have taken place.
5. Do not send to third parties, files that contain the information required by the CEI or establishment through email or other means to which you have access, without the respective authorization.
6. In general, keep secrecy and confidentiality of matters that come to my knowledge due to the work I perform and specifically to the information required.

In case of non-compliance with the provisions of this document, I submit to the sanctions contained in (CITE INTERNAL REGULATIONS OF THE ESTABLISHMENT OR APPLICABLE LEGAL PROVISIONS).

_____
Name and signature

Annex 3. Example of letter of appointment of members of the Ethics Committee in research

Logo y nombre de la institución

México, D.F., a _____de _____de ___.

Asunto: Designación del Presidente del Comité de Ética en Investigación del (establecimiento) _____.

C.___ (nombre del director) _____ por medio del presente documento y en función de las atribuciones que me confiere el cargo de la Dirección del establecimiento se nombra al C._____ de profesión _____ como Presidente del Comité Ética en Investigación del (establecimiento).

El cargo tendrá una duración de ___(#)___años y estará sujeto a los procedimientos internos reglamentados por el mismo Comité para efectos de renovación, sustitución y/o renuncia del cargo.

El C._____ se compromete a cumplir con las funciones y obligaciones inherentes al cargo, de manera honorífica, incluyendo la aceptación del acuerdo de confidencialidad. De igual manera, se compromete a no hacer mal uso de la información a la que tenga acceso en apego a la legislación aplicable.

La importante actitud ciudadana de aceptar el cargo de Presidente del Comité Ética en Investigación de nuestro establecimiento honra y demanda, realizar las acciones necesarias, para promover el desarrollo de la cultura bioética, que nuestra sociedad demanda, en la investigación en seres humanos y merece la gratitud sincera en esta encomiable empresa social que el día de hoy Usted inicia.

Atentamente,

C._____

Director de _____

C.c.p

Annex 4. Example of the record of installation of the Research Ethics Committee

In the City of XXX being the XXX hours XXX of the DD/MM/YYYY, XXX meet to formalize the installation of **the Research Ethics Committee (CEI)** of the establishment XXXXX in the consecutive **"CEI".**

The installation of the CEI is carried out under the responsibility of the FULL NAME (director or head of the institution or establishment) based on (REGULATION INTERNAL) ----------

The integration of the CEI is hereby stated in accordance with the following:

ESTABLISHMENT DATA:

- Name or business name of the institution or establishment.
- Address of the institution or establishment to which the CEI belongs.

INTEGRATION:

- Name, profession and position held by each of the members of the CEI.

Name	Cargo	Profession	Business
1……..			
"n"….			

FUNCTIONS OF THE CEI: The powers and obligations of the members of the committee will be those provided in the National Guide for the integration and Operation of Research Ethics Committees, as well as those set forth in the operating rules of the committee issued by this establishment.

FORM OF FINANCING: The operating expenses of the Research Ethics Committee will be covered by the establishment to which this committee belongs.

DECLARATIONS: ---------- ----------

PLACE, DATE AND TIME OF INSTALLATION OF THE COMMITTEE.

AUTOGRAPH SIGNATURE OF THE ATTENDANCE (DIRECTOR OR HEAD AND THE MEMBERS OF THE CEI).

Annex 5. Example of content of the informed consent form

The informed consent form must reflect the information provided to the research subjects, the language used throughout the document must be understood by a student with a primary education level. The form comprises two sections, the first in which the research information is provided, and the second, in which the subject agrees to participate by signing the form together with two witnesses36.

Information

1. It must be stated that the participation of the research subject is voluntary, he may refuse to participate or withdraw from the study at any time, without the need to state the reasons for his decision or without loss of the benefits to which he is entitled.
2. Explain specifically that it is an investigation.
3. Justification and objectives of the investigation.
4. Procedures to be used and their purpose, including identification of experimental procedures

5. Expected inconvenience or risks.
6. The potential benefits that may be obtained, solely in terms of benefits in the state of health or quality of life of the research subject. If there are no direct benefits for the research subject, this aspect must be specified. Under no circumstances may remuneration, free clinical trials or equivalent be referred to as benefits.

7. Existing alternative procedures and treatments that might be advantageous to you. the subject, without the need to participate in the research.
8. The guarantee of receiving answers to any questions and clarification of doubts about the procedures, risks, benefits and other matters related to the research and treatment of the subject.

9. The freedom to withdraw your consent at any time and stop participating in the study, without prejudice to continuing your care and treatment.
10. Assurance that the subject will not be identified and that information related to their privacy will be kept confidential.
11. The commitment to provide updated information obtained during the study even if it could affect the subject's willingness to continue participating.
12. The availability of medical treatment and the compensation to which they would legally be entitled, by the health care institution, in the case of damages that merit it, directly caused by the investigation.

13. That if there are additional expenses, these will be absorbed by the research budget tion.
14. The study treatment(s).
15. The form and probability of assignment to each treatment, in the case of studies with several treatment arms.

16. The gratuity of all medicines, products and procedures involved in the investigation. tigation.
17. The circumstances under which the study can be terminated.
18. The duration of the study.
19. The approximate number of research participants
20. There should be the possibility of directly accessing your information records from the research.
21. The researcher's commitments.

[36] Two witnesses: In accordance with the Regulation on Research for Health in Mexico.

22. The commitments assumed by the research subject.
23. Information that the identification data will be kept confidential, ensuring that, if the results of the study are published, the identity of the research subject will be kept confidential and protected.
24. Names and contact details of the principal investigator and the president of the REC, including telephone number available 24 hours in case of emergency.

The informed consent form must be signed by the research subject or his legal representative and two witnesses, a duplicate will be delivered, in accordance with articles 21 and 22 of the Regulations of the General Health Law on Health Research. .

Informed consent in populations in conditions of vulnerability

Vulnerability can be defined as the presence of certain situations in which individuals and/or groups are diminished in their autonomy due to the imposition of social, political and/or economic structures that exclude them from access to mechanisms and instances that are decisive for their quality. of life (Bayón, Mier and Terán 2010). Vulnerability has traditionally been recognized in the condition of being a minor, a woman, a person with a disability, an older adult, suffering from a mental illness, being an immigrant, illiterate, belonging to an ethnic or racial minority, unemployed, homeless, or incarcerated. . However, an individual or group will never be vulnerable per se, so it is preferable to speak of a situation of vulnerability because one of its characteristics is its dynamic and relational condition, it depends on a defined space and time.

According to the Belmont Report, “Respect for persons embodies at least two ethical convictions: the first is that individuals should be treated as autonomous agents, and the second is that people with diminished autonomy have a right to be protected. ”. When reviewing research involving populations in situations of vulnerability, RECs should ensure that additional protection mechanisms are in place to minimize risks specific to each group.

Minors[37]

In addition to the general ethical provisions that must be complied with in all research with human beings, research carried out on minors must ensure that similar studies have previously been carried out on older people and immature animals, except in the case of study conditions that are typical of the neonatal stage or specific conditions of certain ages.

Research classified as risky and likely to directly benefit the minor will be admissible when: A) The risk is justified by the importance of the benefit that the minor will receive, and B) The benefit is equal to or greater than other alternatives already established for diagnosis and treatment.

- When the mental capacity and psychological state of the minor allow it, informed consent must also be obtained, after explaining what is to be done. The Research Ethics Committee may waive compliance with these requirements for justified reasons (Research Regulations, articles 34-39).
- In the text of the informed assent, it must be ensured that the information provided is appropriate for the understanding of minors.

[37] Except in the case of emancipated persons over 16 years of age (Research Regulations, article 34).

- When two people exercise parental authority over a minor, the consent of one of them will only be admissible if the other is irrefutably or manifestly unable to provide it or in the event of imminent risk to the health or life of the minor.

Pregnant women and fetuses

Research on pregnant women and fetuses will only be allowed if it represents an opportunity to understand, prevent or alleviate some serious pathology.

- Pregnant women should not be excluded from research if the risks to the fetus are minimal, the informed consent should mention the possible risk to the fetus.
- For the use of biological material derived from abortions, the informed consent must be independent of that given to perform the abortion and will not include financial compensation.
- To carry out research in pregnant women, during labor, puerperium and lactation, in live or stillbirths, in the use of embryos, deaths or fetuses and for assisted fertilization, it is required to obtain the woman's informed consent letter. and of your spouse or concubine, prior information of the possible risks for the embryo, fetus or newborn in your case.
- The consent of the spouse or common-law partner may only be waived in the event of irrefutable or manifest inability or impossibility to provide it, because the common-law partner is not in charge of the woman, or when there is an imminent risk to the health or life of the woman, embryo, fetus or newborn (Research Regulations, article 43).

Subordinates and students

The following are subordinate groups: students, laboratory and hospital workers, employees, members of the armed forces, inmates in prisons or social rehabilitation centers and other special groups of the population, in which informed consent may be influenced by some authority (Research Regulation, article 58).

- The principal investigator must clearly define the reasons why he plans to recruit the population. subordinate tion.
- It is a requirement for the approval of the protocol, a written statement from the immediate superior or the corresponding authority that there has been no coercion.
- If medical residents or associates are recruited for the research, the program director must provide the REC with a letter of support, this writing must come from a figure with no ties to the study (for example: if the program director conducts research in residents, the letter must come from the Director of the department or the authority in charge of the academic program).
- It is important to consider the confidentiality of the research data for the group of subordinates and students, depending on the nature of the study and the information collected. A breach of confidentiality may affect the person's employment prospects, professional development, study plans, or social relationships within the school or hospital community. The REC will pay particular attention to the principal investigator's plans to safeguard data security.

Annex 6. Example of elements of the opinion of the Research Ethics Committee

The communication of the decision of the CEI regarding the investigation must be issued in a signed letter, dated and include the following information:

1. Identification data of the research proposal reviewed by the CEI.
   a) Number the protocol code
   b) Exact title of the research protocol
2. Identification data of the principal investigator responsible for conducting the investigation and the health facility or institution.
   a) Full name of the principal investigator
   b) Company name and address of the health establishment or institution
3. Detailed description of the documents evaluated and approved, in Spanish or in its case, in another language in accordance with the applicable provisions in force:
   a) Research protocol, version and date of the version
   b) Monograph of the product, investigator's manual or equivalent, version and date of the version, if applicable, depending on the type of research in question.
   c) Informed consent form, version and date of version
   d) Informed assent format, version and date of the version, if any
   e) Announcement (advertisements, propaganda, announcements, among others) through which potential research subjects are invited to participate in the research and all the written material that will be provided to the subjects
4. Precise description of the CEI resolution (approved, conditioned, pending approval or rejected).
5. Validity of the approval of the research issued by the CEI (it is recommended not to exceed one year).
6. In cases where the protocol is not approved (conditional, pending approval or rejected):
   a) Include the reasons why the decision was made
   b) Specify the necessary conditions for its approval, if applicable
   c) Specify the requirements of the CEI and the procedure for a new review
   d) Specify the actions required, in case of a decision pending approval
7. Date and signature of the president of the CEI (consistent with the name indicated in the current registry issued by the National Bioethics Commission).
8. List of the participants in the face-to-face session, if applicable, as an annex to the opinion.
9. The registration number must appear in all official communications issued by the committee (General Provision of CEI 2016, TWELFTH BIS 2).

Glossary

Informed Assent: Acceptance of the minor to be a research subject (Research Regulations, article 37).

Medical care: Set of services that are provided to the user in order to protect, promote and restore their health, as well as provide palliative care to the patient in a terminal situation (Regulations for the Provision of Medical Care Services, article 7).

Well-being: Physical and mental integrity of the subjects participating in a clinical study.

Good Clinical Practice (GCP): Standard for the design, conduct, conduct, monitoring, auditing, registration, analysis and reporting of clinical studies that provides a guarantee that the data and results reported are credible and accurate and that they are protected. the rights, integrity and confidentiality of the study subjects.

Informed Consent: Informed consent is understood as the written agreement, through which the research subject or, where appropriate, their legal representative authorizes their participation in the research, with full knowledge of the nature of the procedures and risks involved. to which it will submit, with the ability to freely choose and without any coercion.

Confidentiality: Do not reveal to others -unless authorized personnel- the information or identity of a subject.

Conflict of interest: Any circumstance or situation in which the professional judgment or integrity of the actions of an individual or the institution with respect to a primary interest is unduly affected by a secondary interest, which may be financial or personal. , such as professional or academic recognition, concessions or privileges to third parties (UN).

Adverse event: Any undesirable medical event that may occur in a research subject during the clinical research stage of a drug or vaccine but that does not necessarily have a causal relationship with it (NOM-220, numeral 4.21).

Amendment: Any change to a document that is part of the research project or protocol, derived from variations in the methodological structure, substitution of the principal investigator or due to the identification of risks in the research subjects. The documents subject to amendment are: project or protocol, informed consent letter, investigator's manual, patient documents, measurement scales and schedule.

Administrative amendment: Any change in a document that is part of the authorization of a research project or protocol for human health issued by the Secretary of Health, derived from modifications to the study documentation that do not affect the design or methodology. of this These amendments may include, but are not limited to: Contact information changes in study documentation; Changes in the signature sheet of the protocol; Format changes and/or typographical corrections; Minor changes in the document, for example standardizing terms, among others.

Substantive amendment: Any change in a document that is part of the authorization of a research project or protocol for human health issued by the Secretary of
Health, derived from variations in the methodological structure, or due to the identification of risks in

the research subjects. These amendments may include, but are not limited to: Changes in the interpretation of scientific documents that affect the validity of the study; Changes in the quality of the product under investigation due to contamination, potency or expiration; Changes in the methodology for conducting the clinical trial; Modification to the sample size; Modification to eligibility criteria; Addition or change of biochemical tests and additional laboratory studies; Addition of treatments; Interim analyses; Changes in the primary evaluation criteria of safety and efficacy, among others.

Annual activity report: It is the document that contains information about the activities developed by the Research Ethics Committee during the fiscal year prior to the year presented. It is delivered both to the director or head of the institution or establishment and to CONBIOÉTICA.

Institution or establishment: Where research for health is carried out, to all those who provide medical care services, belonging to the public, social or private sectors, whatever their denomination, that can carry out preventive, diagnostic, therapeutic and therapeutic activities. of rehabilitation, by itself or subrogated, aimed at maintaining or reintegrating people's health status and carrying out training and development activities for health personnel, as well as research.

Research for health with human beings: In which the human being is the subject of research and which is carried out with the sole purpose of making scientific and technological contributions, to obtain new knowledge in matters of health.

Principal investigator: Health professional, responsible for conducting, coordinating and monitoring the development of said investigation.

Monitoring: Act of monitoring the process of a clinical study and ensuring that it is conducted, recorded and reported in accordance with the protocol, Internal Operating Procedures (IOP), Good Clinical Practice (GCP) and applicable regulatory requirements.

Affected nucleus: Refers to the group of people who suffer from the pathology or with the characteristics indicated in the investigation.

Contract Research Organization (CRO): A commercial, academic, or other person or organization contracted by the sponsor to perform one or more of the sponsor's tasks and functions related to the study.

Sponsor: Natural or legal person who accepts responsibilities to finance an investigation.

Placebo: Inert substance, physically indistinguishable from the study drug.

Research project or protocol for health with human beings: Document that describes the proposal for research for health with human beings, in accordance with the objective and field of application of this standard, composed of at least the chapters on: planning, programming , organization and budgeting structured in a methodological and systematized manner in its different phases of work, which will be carried out under the responsibility, management and supervision of a principal investigator.

Research risk: This is the probability that the research subject suffers some harm as an immediate or late consequence of the study.

Research subject: Individual who gives their informed consent, by themselves or through their legal representative, for certain procedures to be carried out on their person for health research purposes with human beings.

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