THE NATIONAL ASSEMBLY
OF THE REPUBLIC OF COSTA RICA
DECREES:

# BIOMEDICAL RESEARCH REGULATORY LAW

## CHAPTER I

## GENERAL PROVISIONS

### ARTICLE 1.- Scope of the law

The object of this law is to regulate biomedical research involving human subjects in health, in the public and private sectors.

### ARTICLE 2.- Definitions

For purposes of this law, the following definitions apply:

**Autonomy:** the ability of individuals to make decisions without influence from other people or external pressures.

**Adverse event or reaction that would be attributable to experimentation**: an unfavorable occurrence that:

a) results in death,
b) is life-threatening,
c) the participant requires hospitalization or an extension of the existing hospitalization,
d) it causes inability or persistent or significant disability, or produces a congenital anomaly or birth defect.

**Multicenter:** clinical study conducted in accordance with a unique protocol in more than one place and, therefore, carried out by more than one investigator.

**Stages of vaccine development:**

**Phase I:** Refers to the first introduction of a vaccine trial in a human population to initially determine its safety and biological effects, including its immunogenicity. This phase may include studies of dose and route of administration.

**Phase II:** Refers to the initial trials to determine the effectiveness of the vaccine in a limited number of volunteers; this phase focuses on immunogenicity.

**Phase III:** Its aim is to evaluate the safety and effectiveness in disease prevention more comprehensively, involving a larger number of volunteers in a generally adequately controlled multicenter study.

**Phases of drug development:**

**Phase I**: Is the introduction of a drug in humans for the first time. Involves the participation of healthy volunteers to assess at which levels of drug use toxicity is observed. It continues with the dose-response studies in patients to determine the safety of the drug and, in some cases, initial evidence of their effectiveness.

These studies aim to establish a preliminary evaluation of the safety and pharmacokinetic profile and, where possible, a pharmacodynamic profile. Unless duly justified exceptions, they are carried out in small groups of healthy volunteers. Bioequivalence studies also belong to this phase, as these are also conducted in healthy volunteers.

**Phase II:** Consists of controlled clinical trials designed to demonstrate effectiveness and relative safety. Usually performed on a limited number of closely monitored patients.

**Phase III:** Performed after establishing a reasonable likelihood of the drug's effectiveness and aims to obtain additional information on its effectiveness for specific indications and a more precise definition of the adverse effects associated to the drug. This phase includes controlled and non-controlled studies.

**Phase IV:** Trials are conducted after the national drug registration agency has approved a drug for distribution or marketing. These trials may include research aimed at exploring a specific pharmacological effect, establishing the frequency of adverse events or determining the effects of the long-term administration of a drug.

**Intervention:** All actions of any order related to research involving human subjects, which may affect all or in part, individually or collectively, in one way or another, the dignity and identity, the integrity and welfare of people or any of their human rights and fundamental freedoms. This research differs from observational studies in which there is no intervention.

**Biomedical research:** A type of activity designed to develop or contribute to generalizable knowledge on health in human beings. It may be observational, epidemiological, or non-interventional or experimental, clinical or interventional. For the purposes of this law, any reference to biomedical research will be understood as research on humans in health.

**Observational, epidemiological or interventional biomedical research:** Research in which no diagnostic or therapeutic procedures are performed with experimental purposes, nor are the participating individuals submitted to conditions controlled by the investigator. For the purposes of this law, any reference to observational research is understood as observational, non-interventional epidemiological or biomedical research involving human subjects in health.

**Experimental, clinical or biomedical or interventional research:** any scientific research in the area of health in which a preventive, diagnostic or therapeutic intervention is applied to human subjects, in order to discover or verify the clinical, pharmacological or pharmacodynamic effects of an investigational product, a medical device or a medical or surgical procedure; or thaat attemps to identify any adverse reactions to a product, device or experimental procedure; or study the absorption, distribution, distribution, metabolism and excretion of an investigational product, in order to assess its safety and efficacy or evaluate the outcome of an untested psychological intervention. For the purposes of this law, any reference to clinical research will be understood as experimental, clinical or interventional biomedical research in human beings in health.

**Investigator:** A person exercising a profession recognized in the country of Costa Rica, accredited by the CONIS (National Board of Health Research) for biomedical research, given his/her scientific training. The investigator is responsible for conducting the investigation. If a team is conducting the study at a site, the investigator responsible for the team will be called the principal investigator.

**Contract management organization**: An individual or organization that enters into a private contract with the sponsor, the contract research organization (CRO) and/or investigator, to perform one or more of the tasks and functions of the investigator in the execution of the study . It must be accredited by the CONIS.

**Contract research organization:** person or organization that enters into a private contract with the sponsor to perform one or more of the sponsor's tasks and functions related to the study. It must be accredited by the CONIS.

**Participant:** An individual who participates in a biomedical research project, either as a direct recipient of an intervention, as a control, or as an element of the observation. The individual can be a healthy person who voluntarily participates in the investigation, or a person with a condition unrelated to the research process who voluntarily participates, or a person, usually a patient whose condition is relevant to the use of the product studied or to answer the questions that are being investigated.

**Sponsor:** An individual, company, public or private entity or organization, that is national or foreign, that takes responsibility for the initiation, management, funding and publication of the results of an investigation and that also assumes coverage of costs and severance.

**Placebo:** Substance lacking therapeutic action by itself.

**Impartial witness:** A person that is independent of the biomedical research who cannot be influenced by people involved in the biomedical research (i.e., the sponsor, the contract management organization, the contract research organization, the investigator or the officers, employees or representatives of both), or a family member of the participant, who is present in the process of signing the informed consent.

**Protocol:** A document that describes the hypothesis, objective or objectives, design, methodology, statistical considerations and organization of a study. It also provides the background, rationale and justification of the study.

**ARTICLE 3.- Protection of human subjects**

The lives, health, interest, welfare and dignity of participants involved in a health investigation that involves human beings will prevail over the interests of science, or economic or commercial interests.

All health research involving human subjects must respond to a human rights approach.

**ARTICLE 4.- Principles of biomedical research**

All research on health involving human subjects should be governed by the principles of respect for the dignity of persons, beneficence, non-maleficence, autonomy and distributive justice.

Aside from the above, the respective scientific ethics committee must ensure that it meets the requirements of social and scientific value, scientific validity, non-discriminatory and fair selection of participating populations, a favorable risk-benefit ratio, independent assessment, informed consent and respect for participants. The framework of all scientific research should be a human rights approach.

**ARTICLE 5: Gratuity**

Participation in biomedical research must always be voluntary, so participants will not be paid. Only the costs eventually incurred in by a subject for participating in the investigation will be reimbursed.

In the case of bioequivalence studies, in addition to acknowledging expenses, compensation to the participants will be allowed for their voluntary participation. Such remuneration must be approved previously by the IRB ensuring that these payments are proportional to the study design. The scientific ethics committee that evaluates research must establish and implement special protection measures for participants during recruitment and development, in order to protect the principle of autonomy.

**ARTICLE 6. - Obligations**

It is the obligation of the government, in research involving human subjects:

a) To ensure the rights and safety of participants involved in the research activity.

b) To ensure compliance with ethical norms that guide research on human subjects.

c) To establish strict mechanisms for regulation, control and monitoring of biomedical research, that ensure the protection of the people participating, as well as the proper conduction of the research.

d) To fuarantee the right to research in institutions of higher education.

e) To promote scientific and technical research directed to meet the needs and health problems of the Costa Rican population.

f) To promote scientific and technical research in all structures of the National Health System, as well as in institutions of higher education.

g) To promote the training of personnel of the National Health System in the theoretical, practical and ethical-legal principles of research.

h) To promote and encourage the conduction of clinical studies, bioequivalence studies and other studies contemplated under this law, by the national pharmaceutical industry, in coordination with public institutions and when these are aimed to solve the health-related needs and problems of the Costa Rican population.

**ARTICLE 7.- Research in public health**

Observational research in public health requires the approval by the Scientific Ethics Committee, hereinafter CEC, except in the case of investigations pertaining to the institutional work per se of the Ministry of Health or of the Costa Rican Social Security Administration, and refers to research associated to:

a) Prevention and control of endemic and epidemic diseases that require the collection of data relevant to health decisions, such as outbreaks or epidemics.

b) Public health surveillance, which incorporates data collection in cards or electronic files that must be submitted to the Ministry of Health to be defined, based on the epidemiological analysis, prevention and control.

c) Evaluation of social programs or evaluation of the results and impact of public health interventions.

d) Intensive pharmacovigilance of medicines and vaccines, so actions pertaining safety, warnings or marketing of thereof can be undertaken.

Investigations pertaining to institutional work per se are those required of the institution in order to carry out the tasks that were assigned to it and that fall within their operating plan, or in the case of emergencies.

Institutions that conduct this type of research should provide a report of the final results of the study to the CONIS.

**ARTICLE 8.- Jurisdiction of the Ministry of Health**

The Ministry of Health, in order to fulfill the scope of this law, will define the public policies for the development of biomedical research.

## CHAPTER II

## INFORMED CONSENT

**ARTICLE 9.- Informed Consent**

The participation of an individual in a research regulated by this law requires the express, specific, written, signed or fingerprinted consent by him/herself or by his/her legal representative, in all the pages of the consent.

Informed consent is the process by which a person voluntarily confirms their willingness to participate in biomedical research.

The purpose of the informed consent is to protect participants, which is why it cannot become a mechanism to legally protect the investigator, the sponsor, the contract management organization and contract research organization.

**ARTICLE 10: Minimum content of the informed consent document**

The information in the informed consent document must be truthful, clear, accurate and written in a way that can be understood by the participants and that is not misleading or coercive. It must contain at least:

a) A statement that the study involves research.

b) The identity of the professional responsible for the investigation and his/her collaborators.

c) An explanation of the objective and purpose of the investigation.

d) The source of funding of the research project.

e) The approximate number and characteristics of the people who will participate.

f) The expected duration of the subject's participation.

g) The procedures to be followed.

h) If blood samples and other biological material are to be obtained, there must be consent and the right to withdraw by the participant on the transfer of biological samples of human material, the testing these will undergo, where they will be analyzed and if their results will be delivered or not. If they are intended to be stored, an indication of where, for how long and for what purposes must be specified.

i) A description of the risks or discomforts that may occur with the investigation.

j) Measures to respond to eventual discomforts or adverse events that may appear.

k) Measures to ensure adequate compensation if the participant suffers any damage as a result of the investigation.

l) Description of the expected benefits for the participant or for others.

m) Manifestation of the strict confidentiality of the information and the measures taken to secure it.

n) Information about the people who have access to the records to verify procedures and data pertaining to the investigation.

ñ) Measures to access information relevant to the participant, arising from the investigation or the overall results thereof.

o) Measures to maintain the confidentiality of research results, and the information of the participants at the time of publication of the results.

p) Indicate any potential future use of of the results of the research.

q) Indicate that, in publications of research results, the person's information will remain confidential.

r) A statement that participation is voluntary and that the person may withdraw from the research at any time without losing the benefits to which the person is otherwise entitled, or be sanctioned in any way for his/her retirement.

s) Clarification of whether or not some financial compensation for food or transportation will be provided.

t) A list of the people who may be contacted if questions about the study and their rights arise. The list must contain at least the phone number or numbers, email address, address of the office and any other appropriate information to locate them.

u) The name, signature, date, time and place where the participant is summoned to hand him/her the copy of the document and the place of signature, as well as the identification number (cedula) of the participant or of his/her legal representative, of the person who explains the informed consent and of the impartial witness who signs the consent, as well as the date of signature.

v) Others as determined by the regulations of this law and those required as per the opinion of the respective scientific ethics committees.

**ARTICLE 11.- Additional content of the informed consent in clinical research**

In clinical research, aside from what was indicated in the previous article, the informed consent must contain:

a) The treatment to be used in the research, the form and probability of assignment to each treatment.

b) The known side effects, risks and discomforts of investigational drugs or equipment.

c) The available alternative, preventive, diagnostic and therapeutic procedures.

d) Precautions men and women of reproductive age and follow-up to given to the woman and the product in case of pregnancy during participation in the investigation.

e) Treatment will continue until the end of the study.

f) Matters related to the insurance policy.

g) Anything else determined by the regulations of this law.

**ARTICLE 12. Approval of the informed consent**

The informed consent and any modifications thereto should be approved, numbered and stamped on all its pages by the Scientific Ethics Committee prior to submission to prospective participants.

In cases of observational investigations, the Scientific Ethics Committee, after a thorough analysis of the content and scope of the research, may waive the signature of informed consent when it considers that this does not affect the rights the people participating.

**ARTICLE 13.- Quality of the information**

Prior to starting any activity associated to the investigation, and before proceeding to sign the informed consent, the participant must be informed in his/her own tongue, in an appropriate and understandable language, of the nature of the investigation, the procedures, the risks and benefits, other therapeutic or diagnostic options, the confidentiality of the information collected and about

*his/her* rights, so that he/she can understand and make the decision of whether or not to participate, freely, voluntarily and knowingly, without coercion, duress, menace, fraud, deceit, manipulation, or any other type of pressure.

The information in the informed consent must be truthful, clear, accurate and in writing, so that it is not misleading, deceptive or coercive, and so that it can be understood by the participants. To this effect, it must be ensured that the procedure for signing the informed consent has the appropriate time and conditions for people to correctly understand the information.

**ARTICLE 14. Informed consent information**

The use of information and data pertaining to the health of people is prohibited purposes not contemplated or permitted in the informed consent or by law.

The person in charge of the research or clinical trials and those responsible for it may only use this information and data relating to the health of the participants in accordance with the purposes expressly provided or as permitted in the informed consent or by law.

**ARTICLE 15. Modification of the conditions**

Any change in the risk-benefit ratio or in the conditions that arise during the investigation shall be reported to the participant, so that he/she, by providing a new consent or an addendum to the main consent, can ratify his/her stay in study or trial, or decide to withdraw from it.

**ARTICLE 16. - Informed consent for people with disabilities**

When a biomedical investigation involves people with disabilities, the information required to provide the informed consent must be provided in conditions and in formats that are accessible and appropriate to their needs.

**ARTICLE 17.- Consent of minors**

When in biomedical research involving minors, the informed consent must be signed by a legal representative or by whoever has his/her legal representation.

In the case of minors over twelve years of age, his/her informed consent must also be obtained; for this, they will be informed about the scope of the investigation with a language that is understandable for them.

If the minor refuses to give his/her consent, his/her judgment prevails over that of his/her legal representative, provided his/her life or health do not depend on their participation in the investigation, in accordance with the provisions of Law No. 7739, Code of Childhood and Adolescence, of January 6, 1998.

All aspects related to the informed consent in minors must be assessed with the participation of the Scientific Ethical Committee, in order for the Committee to be a guarantor of this consent.

The informed consent must be approved, numbered and stamped on all pages by the CEC prior to submission to prospective participants.

**ARTICLE 18.- Consent of legally incapacitated persons**

For biomedical research involving persons declared incapable by a court process, the informed consent must be signed by the legal representative.

## CHAPTER III

## BIOLOGICAL SAMPLES OF HUMAN MATERIAL

**ARTICLE 19.- Use and transfer of biological samples**

The use of biological samples obtained with purposes not contemplated or approved in the informed consent, the law and other applicable laws is prohibited.

Biological samples may only be transferred abroad if justified in accordance with the scientific objectives and the technical criteria of the investigation, or because of the technological constraints of the country. In the case of multicenter studies, where optimal option would be to standardize the methodology and reports of laboratory tests, in accordance with the scientific objectives, the transfer of the samples to a laboratory abroad is permitted.

In order for biological samples to leave the country, prior to exportation, this information must have been provided in the informed consent and the participant must have consented, except for cases in which epidemiological situations endanger public health.

**ARTICLE 20.- Right to withdraw because of the use of biological samples of human material**

The participant in a biomedical investigation has the right to withdraw his/her consent regarding the possible transfer, storage, handling and use of his/her biological samples of human material.

**ARTICLE 21. Transfer agreements**

In order to transfer any biological sample outside the country, there must an agreement of transfer agreement biological material, signed by the legal authorities of the institutions involved, the investigator and the sending institution, and by the investigator and the receiving institution.

**ARTICLE 22.- Retention and destruction of biological samples of human material**

The biological samples of human material will be kept only as long as necessary for the purposes that justified their collection, unless the participant has given his/her explicit consent for further use. This consent may be revoked by the participant completely or for certain purposes at any time. When the revocation refers to any use of the sample, the immediate destruction of said sample will follow and the laboratory will issue a written certificate of destruction of the sample, except for samples that have been anonymized.

In the case of biological samples of human material that are to be preserved, the participant will be informed of the location and of the storage conditions, objectives, future uses, transfer to third parties and conditions to apply for their destruction, in accordance with the rules that apply to the destruction of biological samples, except for samples that have been anonymized.

**ARTICLE 23.- Donation or transfer of biological samples of human material**

In order to donate or lease to another party a biological sample of human material, a specific informed consent for any these purposes must be obtained. It should make clear the location and storage conditions, the objectives of this conservation, the future uses of the samples and the possibility of transferring the samples to third parties.

The donation and use of human biological samples in an investigation may not be provided reimbursed, nor any other type of compensation provided to the participant; moreover, the sale of biological samples have been obtained for a biomedical research is prohibited.

## CHAPTER IV

## RIGHTS AND OBLIGATIONS OF PARTICIPANTS

**ARTICLE 24.- Right to recant**

The research participants will have the right to, without any explanation, renounce their participation at any time. In those cases where the abrupt withdrawal implies a risk to the health of the participant, the mechanisms that minimize risk shall be established.

Such renouncement will not cause any harm or inconvenience to the participants, for their right to health or in the exercise of any other of their rights.

**ARTICLE 25.- Right to confidentiality**

Using data on the health of persons for purposes other than those for which consent was given is prohibited.

People participating in an investigation shall be entitled to confidentiality about their identity, personal information and their health, as well as about the treatments or the results of the analyses or procedures to which they were subjected and other personal information, except where the law requires otherwise.

Individuals or entities who have access to confidential information of the participants shall take all necessary measures to ensure that the privacy, confidentiality, integrity and dignity of the participants will not be affected. To this end, any person who, in the exercise of his/her functions, in an investigation involving human subjects, has access to personal or confidential documents related to the investigation, shall be subject to the duty of confidentiality.

The obligation of confidentiality does not apply if any of the following conditions exist, which must be recorded and be agreed to by the participant in the informed consent:

a) When required by the scientific ethics committee that approved the research.

b) When required by the National Council on Health Research, in order to meet the inspection and surveillance requirements of a research.

c) When the monitor or auditor need to verify the data contained in the clinical records of research participants for purposes of an audit or monitoring by the sponsor or competent regulatory authority.

d) When requested by a competent judicial authority.

e) When a medical emergency occurs to the participant.

f) When the physician responsible for the clinical care needs to know said information for the purposes of treating his/her patient.

**ARTICLE 26.- Transfer of data**

The transfer of personal data to third parties outside the research involving human subjects shall require the participant's express written consent.

If the data obtained from the participant data were to reveal personal information pertaining to his/her family members, the transfer to third parties will require the express written consent of all concerned.

**ARTICLE 27.- Right to information**

The research participants are entitled:

a) To access, personally or through his/her legal representative, the results of their analyses, when these have not been subjected to processes of dissociation or anonymization, if the study design allows it.

b) To be informed about the progress , about the unexpected adverse events that occur and about the overall results of the investigation.

c) To be respected in terms of the ethnic, cultural and social characteristics of the community or population group to which they belong.

d) For all the verbal and written information to be provided in an understandable language and in the participants' own tongue.

e) To be informed of the discovered diseases that are not part of the research process.

f) To access and obtain a copy of his/her personal file, which shall contain all the information pertaining to the investigation or clinical trial.

**ARTICLE 28.- Right to benefits resulting from the research**

Participants in clinical research will be entitled to enjoy the preventive, therapeutic and diagnostic treatments generated by the study for free, as long as they require them, if it has been demonstrated that these are beneficial to health, provided the prescription of these methods or treatments is endorsed by the professionals in charge of treating and monitoring the patient, and in accordance with what is stated in this law.

**ARTICLE 29.- Right to health care**

No participants in biomedical research will lose their right to health care that would be entitled to receive before, during or after their participation in an investigation.

**ARTICLE 30.- Right to damage awards**

People who have suffered damage to their health as a result of their participation in an investigation will receive the appropriate compensation in accordance with this law and its regulations.

**ARTICLE 31.- Protection policy to participants**

The clinical research must be covered by a liability insurance policy to protect participants from any damages arising from the research, throughout its duration, from the start of the research and for two years at least after the participant's participation in the research has ended. The policies shall be issued in accordance with the principle of proportionality and dignity of human life, and shall be enforceable in the country. The scientific ethics committees must assess the policy submitted and define the period of validity, taking into account the minimum basis set forth in this law.

The Ministry of Health will regulate the process to ensure the participants have access to the benefits of health research insurance.

**ARTICLE 32.- Information for people involved in biomedical research**

In the informed consent that is provided the potential participant, proof or copy of the policy must be provided, indicating the number, the entity that issues it, the term of protection, the conditions the policy will have and procedure for accessing it by the participants.

**ARTICLE 33.- Obligations of participants in a biomedical research**

The obligations of the participants in research involving human subjects involve the following:

a) To comply with the indications and instructions given.

b) To inform the investigator about adverse events they experience in a timely manner.

c) To inform the treating physician about their participation in a clinical research.

d) Other aspects determined by the regulations of this law.

## CHAPTER V

## NATIONAL HEALTH RESEARCH COUNCIL

**ARTICLE 34.- National Health Research Council**

The National Health Research Council, hereinafter CONIS, was created as a multidisciplinary, independent body of an ethical, technical and scientific nature, under the Ministry of Health, with a high degree of maximum decentralization and instrumental legal personality.

The CONIS will have an administrative structure as defined via regulation, and will have its own internal audit, in accordance with Law No. 8292, the General Internal Control Law of July 31, 2002, and Law No. 7428, the Organic Law of the General Treasury Inspector's Office the Republic, on September 7, 1994.

**ARTICLE 35.- Purposes of the CONIS**

The purposes of the CONIS will be to ensure the quality of the investigation and their strict adherence to human rights. Its members shall exercise an independent judgment, decisions avoiding the influence of political and commercial interests in their decisions.

**ARTICLE 36.- Composition of the National Health Research Council**

The CONIS shall consist of seven regular members, each with a deputy, who shall attend meetings in the absence of the regular member.

The CONIS shall consist of:

a) Health Minister or his/her deputy officer and his/her alternate, who shall preside.

b) The Minister of Science and Technology or the official to whom he delegates and his/her alternate. If the minister delegates his/her representation, both the proprietor and the alternate shall be specialists in research. Otherwise, at least the alternate shall be a specialist in this field.

c) A human rights lawyer and his/her deputy, appointed by the Bar Association of Costa Rica.

d) A representative of the Costa Rican Social Security Administration (CCSS), preferably of the Center for Strategic Development and Information in Health and Social Security (CENDEISSS) of the Social Security Adminsitration and his/her deputy. The Steering Board may not designate any of the people who, at that time, are part of its members.

e) A representative of the National Council of Rectors (CONARE) and an alternate, who miust be a specialist in bioethics.

f) A property representative and an alternate, member of of Professional Associations of Physicians and Surgeons; Pharmacists; Surgical Dentists and Microbiologists, appointed by the boards of the respective professional bodies. The regulations of this law shall establish the procedure for appointment and the way they will alternate each year, the proprietary positions and the deputizing between four the professional associations, so that the positions are rotated.

g) A regular member and one deputy representing the community, which for this purpose shall be appointed by the Office of the Ombudsman. The procedure for the election of the person representing the community will be determined by the Office of the Ombudsman.

CONIS members shall hold office for a period of five years and may be reappointed. The community representative shall be appointed for a maximum period of three years and may not be reappointed. CONIS members may be dismissed from their positions for the reasons stated in the regulations of this law.

CONIS members may not be appointed simultaneously in CONIS or any other scientific ethics committee (CEC).

**ARTICLE 37.- Allowances**

CONIS members will be remunerated by fees per meeting, the amount of which equals to eighty percent (80%) of the allowances paid to members of the Board of the Costa Rican Social Security Adminsitration per session. The number of paid monthly sessions may not exceed ten sessions per month, between ordinary and extraordinary sessions.

The CONIS will have ordinary sessions once a week and, extraordinarily, whenever necessary, by means of a summon made by the president or by not less than two of its members.

No member of the CONIS may receive directly or indirectly any remuneration or material recognition by sponsors, investigators, contract management organizations or contract research organizations. CONIS members who incur in this fault will be dismissed from their positions.

**ARTICLE 38 - Academic and professional requirements for being part of the CONIS**

CONIS members, both proprietary and deputies, shall be professionals in the fields of human rights, bioethics, clinical research, epidemiology, public health or health services.

To hold a position in the CONIS requires at least:

a) Hold a university degree with at least a bachelor's degree and be registered at the corresponding association.

b) Have an acknowledged and proven repute.

These requirements do not apply to subsection g) and in the case of the person holding the position of minister, referred to in Article 36 of this law.

**ARTICLE 39.- Revocation of appointment**

The national health research council, by simple agreement, may request the body or the corresponding institution that the appointment of any member be revoked for unexcused absences, failure to perform his/her functions within the CONIS or due to a conflict of interest.

**ARTICLE 40.- Ad hoc members and special committees**

The CONIS may incorporate, transiently and to the extent deemed necessary, consultants or experts who are not entitled to vote. It can also form subcommittees or working groups for the technical analysis of specific projects or topics. The people who make up the National Health Research Council cannot be a part, simultaneously, of any other scientific ethics committee of the country. The CONIS is authorized to cancel under the institutional budget for consultants or hire experts required to meet the objectives of this Law.

**ARTICLE 41.- Confidentiality agreement and declaration of conflict of interest**

CONIS members and all staff must sign, before starting work, a confidentiality agreement, a declaration of activities and conflict of interest, and refrain from taking part in the deliberations and votes that have a direct, indirect or familiar interest in the matter under consideration; to do so, they must disclose any conflicts of interest that may affect their objectivity.

**ARTICLE 42.- Quorum**

The quorum will be integrated with the presence of a majority of the members. The agreements will be made with the concurrent vote of a majority of those present. When a tie occurs, the president will solve it with his/her casting vote. The resignation or termination of a member shall not entail the disintegration of the body, provided that the required quorum for meetings is maintained.

**ARTICLE 43.- Functions of the CONIS**

The following will be functions of the CONIS:

a) To regulate, supervise and monitor biomedical investigations and to ensure the life, health, interest, welfare and dignity of the people.

b) To accredit, register and monitor the operation of the CECs, both public and private, to the contract management organizations (CMO) and contract research organizations (CRO).

c) To accredit the investigators conducting biomedical research.

d) To resolve, in a period not exceeding three months, conflicts between the investigators and the CEC.

e) To be aware of and promptly resolve complaints or claims against investigators, CROs, CMOs, the CEC or the entities these depend on.

f) To supervise and inspect any CMO, CRO, CEC, investigator or research project to verify compliance with established norms.

g) To suspend, for reasons of proven emergency or cancel at any time, the approval of a research project, if it is determined that it is in danger freedom, dignity, privacy, health or welfare of the participants.

h) Suspend, temporarily or permanently, the accreditation of a CEC or investigator, if it is determined that is not meeting the provisions of this Law.

i) To promote and encourage training in bioethics research, at a national level in general, and in particular to the CEC, sponsors and investigators.

j) To report in writing to the health authorities of the health regions of the Ministry of Health, on approved investigations that are to be developed in its jurisdiction.

k) To manage the budget in this law. l) To submit an annual report of functions to the institutions represented in the CONIS.

m) To verify that the CEC have adequate and sufficient financial resources to operate. The CONIS may require entities that constitute the CEC to provide them with adequate and sufficient human and material resources for their proper functioning.

n) To maintain a national registry of all biomedical research being conducted in private and public sites in the country, verifying that the CEC must send the information when approving an investigation and before this. Said registry will be publicly available.

ñ) To keep a record of national or local health entities that perform biomedical research.

o) To establish a national registry of investigators.

p) To maintain a national registry of contract research organizations and contract management organizations.

q) Keep an updated record of the CEC and investigators, sponsors, and CMO and CRO that have been penalized for violation of this law.

r) Keep a record of publications and presentations at scientific activities of the results of the biomedical investigations approved in the country.

s) Define, on a yearly basis, work plans and budgets required to perform their duties.

t) To ensure compliance with ethical standards that guide biomedical research. To implement an information system for biomedical research, accessible at all times, with updated databases on approved and rejected investigations, investigators, CEC, CROs and CMOs registered, information and guidance for potential research participants.

u) To maintain a national registry of investigations that have been rejected and the reasons behind that decision.

y) To keep a duly legalized minute book that contains all of its meetings and agreements with the CONIS.

**w)** To keep track of sanctioned investigators and the reasons that motivated the sanction.

**x)** Any other duties established by the regulations of this law.

**ARTICLE 44.- Inspection**

The CONIS have powers of inspection for the CEC, CMO, CRO, investigators and biomedical research, as it deems necessary. To this effect, the CONIS will have the following functions:

a) To conduct inspections at any level, in order to verify that the requirements established by this law are met.

b) To advise ex officio or upon request the CEC, CMO, CRO and investigators on matters within its competence.

c) To solve queries for the CEC, CMO, CRO and investigators on matters within its competence, .

d) To notify the parties involved of the findings in the inspections that have been carried out.

e) To start the administrative and judicial procedures that apply if it is determined there has been a violation of this law, within the time limits established in regulations.

f) The rest of the functions that are attributed to it in regulations.

The subjects referred to in this article shall provide the information required by the CONIS, within the period that it determines, under penalty of incurring in the sanctions established in this law.

The CONIS must hire and train the necessary staff to perform the functions conferred to it by this article.

**ARTICLE 45.- Budget**

The budget of the CONIS shall comprise the following resources:

a) The amount of revenue from registration and inscription of investigations.

b) Bequests, grants and donations from institutions or public organizations and state contributions.

c) Whatever its financial resources generate.

d) The income earned by way of accreditation, certifications, registrations for educational activities and, in general, by the provision of the services provided.

e) The amount of fines generated by the application of this law.

The CONIS will be subject to compliance with the principles and Liability Regime established in the X and XI items of Law No. 8131, Financial Management of the Republic and Public Budgets, dated September 18, 2001. In all other respects, the CONIS is exempt of the scope and application of this law. In the audit, the CONIS will be subject only to the provisions of the Comptroller General of the Republic.

## CHAPTER VI

## SCIENTIFIC ETHICS COMMITTEES

**ARTICLE 46.- Scientific Ethics Committees**

Any public or private, within the facilities of which biomedical research is conducted may establish a scientific ethics committee, hereinafter CEC, of independent judgment, trained in research bioethics and duly accredited by the CONIS.

The Ministry of Health will appoint a CEC that will be responsible for the approval of Phase I clinical trials, as well as theapproval of research investigators and/or independent, public or private entities that do not have a CEC.

Independent investigators and/or public or private entities that do not have a CEC may also submit the research project to any CEC that has been duly accredited by the CONIS.

Public or private entities that create a CEC are required to ensure it has sufficient independence of judgment and performance, as well as all the resources to fulfill their obligations.

**ARTICLE 47.- Integration**

The CEC should be multidisciplinary in its composition and its members should be of recognized integrity, at least one scientific expert with experience in research and one person representing the interests of the community, appointed by mechanisms that seek the widest consultation and participation possible, in accordance with the respective regulations. They must have a minimum of five members and shall be governed by the rules laid down in this law and its internal regulations.

Both the members and support staff of the CEC must sign a confidentiality agreement and a declaration of conflict of interest.

**ARTICLE 48.- Functions and responsibilities of the scientific ethics committee (CEC)**

The functions and duties of the CEC are:

**a)** To ensure that in biomedical investigations life, health, interest, welfare and human dignity are held under strict respect and that the requirements and criteria for scientific rigor and ethical rules governing the matter are met, including the process of informed consent, the expertise and experience of the investigators, and the requirements established in this law.

b) To protect the rights, safety, freedom, dignity and welfare of human subjects participating in biomedical research.

c) To take into account the principle of justice, so that the benefits and drawbacks of the research are equitably distributed among all social groups and classes.

d) To dictate its internal rules of operation, which must be approved by the CONIS as a requirement for accreditation.

e) To consider, approve or reject research projects involving human subjects within the timeframes established in its internal regulations.

f) To provide information to update the National Register of Biomedical Investigations when approving an investigation and before it starts.

g) To consider, approve or reject applications for the renewal of biomedical research projects, within the timeframes established in the regulations of this law.

h) To consider, approve or reject the amendments to the original protocol, informed consent and informed assent.

i) To suspend or cancel, at any time, the execution of a research project, if it is determined it could endanger the health or welfare of the participants.

j) To keep a duly legalized minute book that contains all of its meetings and a file for each of the projects submitted to it for review.

k) To monitor the implementation of projects through the reports submitted periodically by the principal investigator and carry out, at least once a year, an audit of each institution and research site. It must also review the end of study report.

l) To review, record and report to all the CONIS the serious or unexpected adverse events and the relevant situations that occur during the development of the research that are reported to the CEC.

m) To preserve and guard the project files submitted to it, as well as any documentation that supports its actions for a period of fifteen years after the completion of each investigation.

n) To submit quarterly and annual reports to the management CONIS, including investigations that have been approved, rejected, suspended, canceled, and completed, amendments to ongoing investigations, the inspections carried out and the list of ongoing investigations.

ñ) To provide training to its members, so that they receive regular training and continuing education related to bioethics and biomedical research.

o) To guarantee investigators the opportunity to present the objections they deem necessary regarding the resolutions of the CEC.

p) To inform the CONIS and competent institutional authorities about irregularities or breaches to this law.

q) To immediately evacuate the queries of research participants when they request information concerning their rights and to process, as soon as possible, the complaints these may have regarding the investigation or the actions of an investigator or of his human team.

r) To comply with the provisions of the Ministry of Health and the CONIS in terms of their competence.

s) The payments to be made to the CEC for the review process of research projects submitted for their review, possible approval and for the monitoring, renewal and inspection of approved projects will be determined by the CEC after analysis of relevant costs and in accordance with the regulations of this law.

t) To keep a record of publications or presentations that are made of the results of the investigations approved by the committee.

u) To notify the National Children's Trust when investigation on minors have been approved, for whatever proceeds.

v) The others established by the regulations of this law.

**ARTICLE 49.- Incompatibilities**

The following may not be part of the CEC:

a) Members of the boards of directors of public institutions or private companies promoting biomedical research, when participating directly or by proxy stake in private companies of a nature or their spouse, partner or companion or some of their relatives by consanguinity or affinity, including up the third degree.

b) Officers of the public or private entity in which the committee is established, in which they or their spouse or partner, or any relative by consanguinity or affinity , including up to the third degree, hold positions of leadership or direction that involve the power to decide on the authorization of biomedical research projects.

When one member of a CEC has ties involving a risk of conflict of interest, in accordance with Article 38 of Law No. 8422, the Law against Corruption and Illicit Enrichment in Public Service, of October 6, 2004, as amended, and other rules of law, he/she shall not participate in the administrative process, approval, control and monitoring of that specific investigation.

**ARTICLE 50.- Budget and resources**

The entities that constitute a CEC should provide them with the necessary human and material resources to fulfill their duties and obligations.

## CHAPTER VII

## OBLIGATIONS OF THE INVESTIGATOR, SPONSORS, CONTRACT MANAGEMENT ORGANIZATIONS AND CONTRACT RESEARCH ORGANIZATIONS

**ARTICLE 51.- Obligations of the investigator**

The obligations of the investigator in charge of conducting the biomedical investigation are:

a) To strictly respect life, health and human dignity and fulfill the requirements and criteria of scientific rigor and ethical rules governing the matter and the requirements established by this law.

b) To stay up-to-date on bioethical issues and good clinical practice.

c) To guarantee that the conduction of biomedical research involves, in all cases, that the routine care, procedures and treatments required by participants take precedence over the development of the investigation.

d) To having the academic background, training and experience necessary to assume the responsibility for the proper conduct of the biomedical investigation.

e) To have a sufficient number of qualified staff and adequate facilities available to conduct biomedical research.

f) To ensure that the members who are part of the research team have the adequate qualifications and experience for the investigation proposed in the exercise of his/her profession, in accordance with the provisions of Law No. 5395, General Health Law of October 30, 1973. For students undertaking undergraduate, graduate and postgraduate studies, the respective CEC may exempt them from this requirement to the extent to which this does not involve a risk to the participants.

g) To submit the duly accredited research protocol to the CEC and, before starting any activity related to the research, have the respective approval.

h) To be fully familiarized with the research protocol and informed consent and, in the case of clinical trials, the investigator's brochure and the drug, equipment or material under investigation.

i) To comply with the provisions of the research protocol approved by the CEC.

j) To ensure the correct and timely attainment of the informed consent by the participants or their legal representative, when the corresponding CEC has not exempted him/her from this requirement.

k) To keep a control of the drugs, equipment or materials in clinical trials.

l) To ensure that the data reported in the biomedical investigation is accurate, legible, complete and in submitted within the required time.

m) To ensure that persons for whom the planned investigation represents a special risk are excluded from it.

n) To submit for review to the respective CEC all amendments to the protocol that occur before changes can be implemented, provided this does not involve a risk to the participants.

**ñ)** To submit international safety reports to the respective CEC, in case of investigations or multicenter studies.

o) To report to the CEC, within a maximum timeframe of twenty-four hours, all serious adverse events or unexpected problems occurred in biomedical research under his/her charge.

p) To submit reports to the CEC about the progress of the investigations by means of quarterly and annual reports.

q) To provide counsel to research participants about their rights throughout the development of the investigation.

r) To ensure, by appropriate control, that the potential health benefits of participating outweigh the risks.

s) To immediately report the participants and the CEC, in case of early termination of the investigation, a detailed explanation of this suspension. In case of clinical trials, to ensure a treatment and monitoring program for each of the participants.

t) To custody all the documentation of each investigation in a file for a period of fifteen years after the investigation has been completed.

u) To submit a copy of the final report and final results of the investigation, as required by the CEC that approved it.

v) To make available to participants the information deemed relevant to their health.

w) To meet the ethical, scientific and administrative obligations that may be imposed by the sponsor of the research, the CEC, the CONIS or any regulatory body, with interest in verifying the protection of the rights of research participants, in accordance with current legislation.

x) To declare any potential conflict of interest prior to, and during, the conduction of the investigation.

y) When an organization is designated to conduct an investigation (contract management organization), it must sign a contract in which the obligations and responsibilities assumed by said organization are established.

z) To comply with the provisions of the Ministry of Health, the CONIS and the CEC in terms of its competence.

**aa)** To submit to the CEC that approved the investigation and to the CONIS a copy of the publications and/or certification of participation in scientific activities of the results of the investigation.

**ARTICLE 52.- Publication of results of biomedical research**

It is the obligation of the investigator to publish or present, in a conference or scientific activity, the results of the biomedical investigations he/she carries out. By publishing the results of biomedical research, the investigators must respect the accuracy of the data and results obtained, and to present both positive and negative results, include the full amount of financing sources of information and research funding bodies, and indicate the institution or health institutions where the research took place. Similarly, in publications, respect of the right to confidentiality of participants will be upheld.

The CONIS may dispense with the publication of the results of biomedical investigations, in the case of results with little input.

**Article 53.- Obligations of the sponsor**

The following are obligations of the sponsor:

a) To ensure and document that the electronic data systems meet the requirements of completeness, accuracy, reliability and consistency in the implementation proposed and that they maintain a security system that prevents unauthorized data access.

b) To properly select the investigator, his/her team and the institution where the research will be conducted.

c) To supervise the conduction of investigations and implement a system of quality standard.

d) To ensure that the investigator and the entity carrying out the investigation have adequate funding, adequate material resources, by signing contracts containing such conditions.

e) To define and obtain an agreement with the investigator to conduct the investigation in accordance with good clinical practice, the national regulatory requirements and the protocol approved by the CEC.

f) To verify that research it sponsors has been approved by the respective CEC accredited in the country.

g) To provide adequate and ongoing training on scientific and ethical research methodologies to the investigator and his human team.

h) To verify that the investigator reports to CEC cases in which he/she found deviations from the approved protocol.

i) To cover the costs of treating those participants who suffered an injury as a result of the investigation.

j) To compensate participants who suffer injuries, or heirs in case of death as a direct result of the clinical research and relevant to the procedures in this, as long as these are not inherent risks of drugs and/or standard procedures; for this, he/she must have an insurance policy in force covering from the beginning of the investigation and up to a minimum of two years after completion of the participant's participation in the investigation. To ensure legal coverage and liability policy for the investigator and his/her team, in order to cope with possible claims for injury attributable to the clinical investigation, provided that it is not due to negligence, incompetence or violations to the protocol, in which case the responsibility falls on the investigator.

k) To provide participants, free of charge and after the conclusion of a clinical investigation, with the drug, device or procedure that has been investigated, unless:

i. The drug, device or procedure ceases to be effective for the participant or he/she does not require it, which shall be established by the treating physician by a duly justified resolution, which will become part of the record and will be reported to the CEC within three business days after it has been issued.

ii. The development of said drug, device or procedure is suspended.

iii. The investigator certifies that it is not essential for preserving the participant's health and there are therapeutic alternatives.

iv. The patient did not grant the informed consent required for continued treatment.

l) To notify the investigator, the CEC and the CONIS about the reasons for the suspension of a biomedical investigation.

m) To ensure the investigator, the CEC and the participants that the suspension of a biomedical investigation will not affect the participants.

n) To certify that, in biomedical investigations, the investigational products (including the active comparator and placebo if applicable), are manufactured according to good manufacturing practices, that storage conditions be indicated, that the packages prevent contamination or deterioration during transport and storage, that coding and labeling be in Spanish and that the requirements established via regulation are met.

ñ) To ensure the timely delivery of investigational products, to keep records of shipment, receipt, disposition, return and destruction of these products.

o) To document the financial aspects of research in an agreement between the sponsor and the investigator.

p) The sponsor may transfer any or all of its duties and functions related to the investigation to a contract research organization (CRO), but will retain the ultimate responsibility for the quality and integrity of research data.

q) Any task and function related to the investigation, which is transferred and assumed by a CRO, should be specified in writing. All obligations hereunder, which are made to sponsor in this law, also apply to the CRO as far as it has assumed the duties and functions of the sponsor.

r) To comply with the provisions of the Ministry of Health, the CONIS and the CEC in terms of its competence.

s) To guard in a file all the documentation of each investigation, for a period of fifteen years after the investigation has concluded.

t) To send a copy of the final report and the final results of the investigation to the CEC and CONIS, which shall publish in the digital record it will create for that purpose.

u) To make available to participants the information deemed relevant to their health.

v) To meet the ethical, scientific and administrative obligations imposed by the CEC, the CONIS or any regulatory body, with interest in verifying the protection of the dignity and rights of research participants, in accordance with the laws and international ethical guidelines for experimental clinical research.

w) To declare any potential conflict of interest prior to and during the conduction of the investigation.

x) When designating organization to conduct a research (contract management organization, CMO), it must sign a contract in which the obligations and responsibilities assumed by the organization are established.

y) Forward, to the CEC that approved the investigation and CONIS, copies of publications and/or certification of participation in scientific activities of the results of the investigation.

**ARTICLE 54.- Obligations of the contract management organization and the contract research organization**

The obligations of the contract management organization (hereinafter CMO) and the contract research organization (hereinafter CRO) are the following:

a) To issue the CEC quarterly and annual management reports.

b) To submit to the CEC, for registration, the document of the agreement subscribed with the sponsor of the investigation or with the investigator, in order to know the tasks and functions that have been transferred to it. Moreover, it must also transfer the CEC any modification to this agreement within a period of eight working days.

c) All the ones the sponsor or investigator has transferred to it through a contract or contractual documents held between them.

d) To respond, in solidarity with the sponsor or investigator, to any eventual damages or losses caused by the tasks or functions that have been transferred to it.

## CHAPTER VIII
## RESEARCH INVOLVING HUMAN SUBJECTS

**ARTICLE 55 -. Approvals and authorizations**

All investigations, prior to beginning, must have the written approval of a duly accredited CEC and, if it is to be carried out in a public or private health center, must also have the consent of the corresponding authority or authorities. No authority, public or private, may authorize an investigation without the approval of the respective CEC.

For research requiring the import of drugs, equipment, devices and supplies related to approved research, approvals and authorizations set forth in the preceding paragraph will be essential prerequisites for import to the investigator.

**ARTICLE 56.- Monitoring and follow-up of the investigations**

In all cases, the conduction of the investigation must must comply with the content of the project to which the authorization was granted.

Health authorities shall have, at all times, inspecting powers on the investigation and may have access to the individual medical records of research participants, for which they must keep, at all times, their confidential nature.

Health authorities, the CONIS or the CEC may provisionally suspend the investigation authorized in the cases in which the requirements established by this law have not been observed or whenever there are indications that the health, integrity and safety of the participants is in danger, having to protect their rights at all times. Said measures shall be applied in the opening act of the administrative process and must be dictated as a preliminary act, in order to ensure the rights and safety of the participants, as well as the due process. Moreover, all interested parties shall be notified, including the authorities of the health center where the research was being conducted.

**ARTICLE 57.- Inapplicability of positive silence**

The figure of positive silence, governed by Article 330 of Law No. 6227, General Law of Public Administration of May 2, 1978, shall not apply to the processes of approval, inspection, control and monitoring of biomedical research projects, in any of its forms.

**ARTICLE 58.- Contract**

All biomedical investigations that have sponsorship outside of the public or private entity where said activities are carried out, must have a contract in which the rights and obligations of both the sponsor and the investigator who conduct the investigation are regulated. This contract must indicate the payment agreed to for conducting the investigation and must include a clause whereby the sponsor is responsible for the short-term and long-term adverse events that arise as a result thereof. The absence of such a clause does not relieve the sponsor of its responsibility. The contract must be signed by the representative of the sponsor, the principal investigator and a representative of the public or private entity, and must be signed prior to the initiation of the investigation.

**ARTICLE 59.- Prohibition to the heads of public and private institutions**

The leaders and officials of public and private institutions are forbidden from authorizing the development of biomedical research or, for the same purpose, assigning resources to any entities under their charge, if said investigations do not have the prior approval of a CEC. The respective authorities of the hospitals of the Costa Rican Social Security Administration, where an experimental clinical investigation is intended to be carried out, may refuse the provision of the resources referred to in this article if they deem that yielding some kind of resource could affect patient care and the health care service said institution is in charge of.

**ARTICLE 60.- Fee**

For the purposes of registering a biomedical research project, the principal investigator shall pay the CONIS a sum equal to three percent (3%) of the total budget of the investigation. For these purposes, the investigator, the sponsor, the CMO or CRO shall submit to the CEC copy of the signed contract with it, and it shall be the duty of the CEC to send a copy of this document to the CONIS, in accordance with the instructions in this law. This amount must be paid to CONIS when requesting registration of the project approved.

The funds corresponding to the fees mentioned in this article funds will be used to finance the following activities:

a) The proper functioning of the CONIS.

b) Training CONIS members and staff on issues pertaining to investigation, regulation and related topics.

c) Promoting interest in biomedical research, either directly or collaborating with projects or programs organized by health authorities and the scientific community integrated by the public sector.

d) Collaborating and encouraging improvement activities of the research process and dissemination of bioethics, and the rights of users of health services and of participants in research projects.

e) Funding of projects of interest in public health, as defined by the Ministry of Health.

**ARTICLE 61.- Exemption**

The following investigations are exempt from paying the fee stipulated in the previous article:

a) Those classified as public interest by the Executive Branch of the government.

b) Those considered a health priority by the Ministry of Health.

c) Any research conducted by students in higher education in order to obtain an undergraduate, graduate, postgraduate or similar degree.

d) Independent investigators without sponsorship, provided that their development and results are without commercial purposes.

e) The investigations carried out by programs and research projects by state universities.

The above does not apply, under any circumstances, to investigations sponsored by pharmaceutical corporations or organizations for profit.

**ARTICLE 62.- Protection of records**

All information concerning the investigation conducted on human subjects must be recorded in the patient's file and protected for a period of thirty years in the health institution or clinic where it was carried out.

**ARTICLE 63.- Use of placebo**

The benefits, risks, burdens and effectiveness of all biomedical research must be tested against the best current proven intervention, except in the following circumstances:

a) The use of a placebo is acceptable in studies where there is no existing treatment or intervention being tested.

b) When due to methodological, scientific and compelling reasons, the use of placebo is necessary to determine the efficacy and safety of an intervention that does not involve a risk of serious or irreversible damage for the patients receiving placebo.

## CHAPTER IX

## INVESTIGATIONS ON VULNERABLE GROUPS

**ARTICLE 64.- Minors and people without volitional and cognitive abilities**

Clinical research in which that a person with legal inability, whether it be a minor or a person judicially declared as having no volitional and cognitive ability, may only be carried out when it is anticipated that the results can produce real and direct benefits to their health, or when no comparable results can be obtained in subjects that are older or capable of giving their consent.

When it is foreseeable that clinical research is not going to produce results in direct benefit to the health of these participants, the research may be authorized in exceptional circumstances, given the following conditions:

a) That the investigation has the purpose of contributing to the understanding of the disease or leads to a result that is beneficial to others of the same age with the same disease or condition.

b) That the investigations entails a risk and burden that are minimal to the participant.

**ARTICLE 65.- Persons highly dependent healthcare**

Clinical investigations should be evaluated with particular care when performed on particularly vulnerable human beings, at the discretion of the CEC, because of their high dependence on healthcare and/or their limited ability to understand the information provided and to freely express their willingness to participate, or both circumstances. Biomedical investigations will require additional conditions and procedures for protection when performed on:

a) People with disability who are highly dependent on care and attention.

b) People with moderate to severe cognitive impairment.

c) Serious psychiatric patients, whether or not they are hospitalized.

d) People in health emergencies.

e) Critically ill patients in intensive care.

f) Terminally ill patients.

These investigations shall meet at least the following conditions:

1) They may not be contrary to the patient's best interest.

2) They will seek therapeutic benefit with a reasonable chance of superiority over standard treatment.

3) They may not have a higher risk than the very conditions of the patient and alternative methods of treatment.

4) The informed consent process will be implemented in the most reasonable way possible to meet their demands, including the involvement of families and the authorized representative.

5) In cases where the patient is not the person giving the consent, he/she will be informed as soon as possible and may withdraw from the research without consequence for due care and attention.

6) Any other conditions defined by the regulations of this law.

**ARTICLE 66.- Emigrant indigenous communities and particularly vulnerable groups**

Clinical research in vulnerable groups may be carried out only to the extent that the following circumstances are accredited:

a) That research is done in order to try and benefit the community in an ailment that is its own and characteristic of this disease or another of high prevalence.

b) The investigator and the sponsor commit to reliably respect the value system, worldview and culture of the community that will participate in the study, and adapt the design and study procedures to the customs of each original community.

c) That the consent of each participant belonging to an indigenous community is preceded by information provided in the native language of their culture, if he/she does not understand Spanish and, in either case, that the investigator ensure the understanding of the information and the freedom of the decision taken by the participant.

d) That research has the approval of a CEC which was held with the presence of a representative of the community, elected by the community itself, and with the authorization of the CONIS.

**ARTICLE 67.- Subordinate Groups**

Research involving human subjects, carried out on individuals or groups who are under authority of a the investigators or that of a third, or in certain situations of dependency that could harm or affect their autonomy and that do not pose a direct benefit for research participants, require special attention for the implementation of this law. Subordinate groups in terms authority should be considered, including students, residents and/or concurrent in medicine or other health sciences, people deprived of liberty and officials of the police and security. These investigations may only be conducted if the following conditions are met:

a) The research is done in order to achieve a benefit for the subordinate group under study.

b) The investigation cannot be conducted in unsubordinated population groups.

c) The investigation involves minimal risk or burden to the people included in the study.

**ARTICLE 68.- Clinical research with women or breastfeeding women**

Pregnant or breastfeeding women should not participate in a clinical investigation unless the following conditions are met simultaneously:

a) Comparable results cannot be obtained in women who are not pregnant or breastfeeding.

b) The investigation involves a minimal risk to their health, the health of the product of conception in any of the stages of pregnancy or breastfeeding, or the benefit outweighs the risk.

c) The objective of the research is to obtain new knowledge for the benefit of other women or of the product of conception at any stage of pregnancy or breastfeeding.

**ARTICLE 69.- Clinical investigations with people deprived of liberty**

People who are deprived of liberty must not be unreasonably denied the opportunity to participate in clinical research or to have access to medicines, vaccines and other research elements that may represent a therapeutic or preventive benefit for them.

Special attention must be paid to ensure the voluntariness of consent in this population, applying an adequately proven scientific methodology that reasonably ensures that the consent of those deprived of liberty is unquestionably voluntary.

## CHAPTER X

## SANCTIONS

**ARTICLE 70.- Sanitary and administrative measures**

The Ministry of Health, the CONIS or the CEC, as appropriate, shall know of and issue the relevant health and administrative measures to prevent or amend those actions contrary to this law incurred by investigators, sponsors and any other party that is involved in a research project; all this without prejudice to the civil, criminal or disciplinary liability that may correspond to the offender.

**ARTICLE 71.- Precautionary Measures**

During the pendency of administrative proceedings or investigations in court questioning the legality of the activity of the investigator, the sponsor or the CEC, CRO or CMO and for purposes of protecting the health and safety of research participants , the competent authority may impose the necessary precautionary measures.

The investigations, the investigator or the approval of research projects may suspended temporarily or permanently, partially or completely, in case the administrative authority or the judiciary court deem it necessary.

The competent body, in a reasoned decision and after hearing the parties concerned, must resolve whether to confirm, modify or revoke the adopted measure. To do this, it must apply the procedure laid down in the Code of Administrative Litigation.

**ARTICLE 72.- Violations by the investigator, the sponsor, the CRO or the CMO**

The CONIS, after due process, may impose a fine of up to thirty percent (30%) of the total value of the investigation if the investigator, the sponsor, the CRO or the CMO commits any of the following offenses:

a) To have provided false information or to have omitted relevant information during the approval process or the execution of a research project.

b) To begin a research project without the proper approval by the CEC.

c) To fail or unreasonably delay compliance with the obligations under this Law.

d) Any other breach of the obligations imposed on them by law.

To determine the applicable penalty, the seriousness of the offense by the investigator, the sponsor, the CRO or CMO or employees, agents or officers of the company shall be taken into account, as well as the repeated offenses against this law. The CONIS will publish the list of sanctioned investigators, sponsors, CROs or CMOs, on the website of the Ministry of Health.

**ARTICLE 73.- Violations of the CEC**

The CONIS may impose on employees, agents or officers of a CEC, a fine of up to three hundred times the base salary, according to Law No. 7337, of May 5, 1993, as amended, which is the law creating the concept of base salary for special crimes in the Criminal Code, if any of them commits any of the following offenses:

a) Fails or unreasonably delays the fulfillment of the obligations that the law bestows upon them, as well as any other obligation under this Law, Law No. 5395, the General Health Law of October 30, 1973, in the moral or ethical code of professional associations to which the investigators belong, or the regulations of those bodies of law, or any other applicable statute.

b) Does not resolve or channel, in a timely manner, complaints from people involved in investigations due to damages suffered.

c) Any other breach of the obligations imposed on them by law.

In order to determine the applicable penalty, the seriousness of the offense shall be taken into account, as will the degree of fault or the existence of fraud by employees, agents or officers of CEC, and their regression.

**ARTICLE 74.- Coordination**

The Ministry of Health and the CONIS shall determine the necessary coordination mechanisms for the proper and efficient application of controls, special sanitary measures and the sanctions provided for in this law. The proceeds from fines imposed in this article shall be distributed as follows: fifty percent (50%) to CONIS and fifty percent (50%) to the CEC, if the breach is punishable by a sponsor or a investigator. In the case of imposed fines to the CEC, the product of these will correspond to the CONIS.

**ARTICLE 75.- Challenges**

Appeals at the CONIS may be placed against the resolutions issued by the CEC, in the exercise of its powers. The appeal must be filed within five working days of notification of the corresponding resolution.

The resolution to impose a penalty shall be enforceable against the offender. The CEC or the CONIS, as applicable, will be entitled to collect it.

**ARTICLE 76.- Punitive procedure**

The sanction process will apply the procedure established in Law No. 6227, the General Law of Public Service, of May 2, 1978.

**ARTICLE 77.- Punishable Acts**

If the breach of the obligations under this Law or its regulations were to result in offenses, the Minister of Health, CONIS or CEC, or whoever has knowledge of the offense, as appropriate, shall notify it to the Public Ministry to promote and exercise the relevant criminal proceedings.

**ARTICLE 78.- Undue Experimentation**

Anyone who subjects a person to research for the application of drugs, pharmaceuticals, chemicals, treatments, techniques, devices or procedures without duly informing the experimental status of these and risks they involve, and without the explicit consent written and documented by the victim or his/her legal representative and authorization procedure by a CEC; or whoever has taken advantage of the inability of the victim to issue a consent, coercion, threat, deception, disinformation, manipulation or any other illegal means to obtain such consent, shall be punished with imprisonment of three to eight years.

A person who promotes or performs biomedical scientific research without informed consent validly given by the participants or their legal representative, unless the respective CEC has waived such requirement under this Law, or has been resorted to coercion , threat, deception, disinformation, manipulation, or other unlawful means to obtain such consent, shall be punished by imprisonment of three to eight years.

**ARTICLE 79. Serious undue experimentation**

Imprisonment shall be of five to ten years, when the conduct described in the preceding article are carried out by public officials or investigators who are repeat offenders of the sanctioned behavior, or when these are committed to the detriment of children, women in gestation, elderly people or people unable or who for any reason cannot express their opposition to the practice of the investigation.

**ARTICLE 80. Disqualification**

In addition to the prison term that entails, the judicial authority shall establish the penalty of disqualification for a period of five to ten years for the processes of biomedical research or the exercise of their profession, or both, according to the assessment of the facts, the person who committed the acts described in the preceding articles.

**ARTICLE 81.- Trading in influence with biomedical research**

A prison sentence of one to three years will be imposed to members of scientific ethical committees (CEC) and officials of public and private institutions that permit, facilitate or hire the conduction of biomedical research involving companies or have economic interests in which they, their spouses or partners, or relatives by consanguinity or affinity to the third degree, are part of their boards, participate directly or through another person or entity in its capital stock, or work as investigators.

**ARTICLE 82. Bribes and coercion**

Imprisonment of three to five years shall be imposed to a member of a scientific ethics committee who accepts any gifts from people or companies that carry out biomedical research, without prejudice to other penalties and liabilities as appropriate in accordance with the law .

**ARTICLE 83. Offering of bribes and coercion**

A sentence of three to five years in prison shall be imposed on the the person offering bribes to or exerting coercion on CEC members to obtain favorable results in the authorization or any stage of the investigation, without prejudice to other penalties and responsibilities that come under the legal system.

**ARTICLE 84. Improper use of privileged information**

Whoever, using his/her position in the public service or in the private sector, uses protocols or medical or social records of patients or users to locate, recruit or contact participants for biomedical research that entails economic benefit to him/her, his/her spouse or partner, or his/her relatives by blood or affinity including up to the second degree shall be punished by imprisonment of one to three years, subject to other penalties and liabilities as appropriate in accordance with the law.

## CHAPTER XI

## FINAL PROVISIONS

**ARTICLE 85.- Violation of privacy**

The person who discloses or publishes, in any medium, private information about the participants in a clinical trial without their prior consent shall be punished with a sentence of two to four years of imprisonment.

**ARTICLE 86. Regulations**

The Executive Branch shall implement this Law within six months; however, the lack of regulation does not prevent its implementation.

**ARTICLE 87. Waivers**

Articles 25, 26, 64, 65, 66, 67 and 68 all of the Law No. 5395, Health Law of October 30, 1973 are hereby repealed.

**TRANSIENT I:**

The CEC of public or private entities that are operating under the effective dates of this Law are authorized to continue to do so and start the approval of clinical investigations in strict compliance with the provisions of this law. However, within six months from the date of the constitution and installation of the CONIS, said CEC are required to be accredited by the CONIS, adapting to the requirements of this Law their operation. After this period of six months has expired, the CEC that have not applied for the respective accreditation will automatically lose their license to operate.

**TRANSIENT II:**

The Ministry of Health is authorized to allocate human resources, financial resources and resources of other sorts, as required for the operation of the CONIS, until it does not have the necessary funds to operate and comply fully with the functions which have been assigned to it in this law. Within six months from the effective date of this law, the Ministry of Health will formulate the corresponding budget that contemplates the content for the allocation of spots required for the conformation, strengthening and operation of the powers of the CONIS, and the provision of resources to finance the infrastructure and equipment required for the effective and efficient functioning of said body. The Ministry of Health will send the Ministry of Treasury the corresponding spending plan, in order to include, in the next special budget, a transfer for the CONIS for the total amount resulting from the allocation of those resources.

**TRANSIENT III-**

Within forty-five days of integration and entry of operation of the CONIS, this agency shall submit its first operating budget for approval to the Comptroller General of the Republic. Moreover, in this first budget, the headings that allow to pay retroactive allowances to members of the CONIS for the sessions they had attended and have been held since its installation until the date of approval by the Comptroller General of the Republic of that budget. This authorization also applies to retroactively pay the administrative expenses incurred during the same period.

**TRANSIENT IV. -**

If at the end of sixty working days, as from the publication of this Law or, if applicable, from the date of expiration of the term of appointment to the CONIS of institutions obliged to do so that had not done so, the members who are not appointed will automatically be represented by:

The Minister of Health.

The Minister of Science and Technology.

**a)** The president of the Costa Rican Social Security

**b)** Administration. The president of CONARE.

**c)** The president of the Bar Association of Costa Rica.

**d)** An auditor of any of the professional associations of

**e)** Physicians and Surgeons, Pharmacy, Dental Surgeons or

**f)** Microbiology at the discretion of the Ministry of Health, and a representative of the community appointed by the Minister of Health.

A representative of the public, to be appointed by the Minister of Health.

g)

Members appointed in this way will hold their posts provided the respective owner and his/her deputy have not been appointed in the manner provided in this law or the corresponding regulations. The CONIS members mentioned in the previous paragraph, are required to report and credit to the first session they attend the name of his/her alternate, who shall meet the requirements of this law.

**TRANSIENT V.-**

While the CONIS does not have its own internal audit, it may be audited by the Internal Audit of the Ministry of Health, in accordance with Law No. 8292, the General Internal Control Law of July 31, 2002 and Law No. 7428, the Organic Law of the Comptroller General of the Republic, on September 7, 1994.

In effect from its publication.

**NATIONAL ASSEMBLY:** On the seventh day of April, two thousand and fourteen.