

RESOLUTION No. 466, OF 12 DECEMBER 2012

During session of the National Council of Health at its 240th General Meeting held on December 11 and 12, 2012, in the discharge of its official authorities and duties, conferred upon it by Law 8080 of September 19, 1990, and Law 8142 of December 28, 1990, and

Considering the respect for human dignity and the special protection to the members of the scientific researches involving human beings;

Considering the development and ethical commitment, inherent to the techno-scientific development;

Considering the evolution of science and technology which unveiled another perception of life and its ways of living, with impacts not only in conception and in lengthening of the human life span, as in costumes, culture, human behavior upon real and virtual means available changing and innovating at a continuous and fast pace;

Considering the progress of science and technology, which may imply in current and potential benefits to the human being, the community in which he/she is inserted and the national and universal society, making it possible to promote well-being and quality of life, and promoting the protection and preservation of the environment for the current and future generations;

Considering the ethical grounds subjects raised by the progress and growth of science and technology, rooted in all areas of human knowledge;

Considering that all growth and progress must always respect the dignity, freedom and autonomy of the human being;

Considering the documents that form the pillars of recognition and affirming dignity, freedom and autonomy of the human being, such as Nuremberg Code, from 1947, and the Universal Declaration of Human Rights, from 1948;

Considering recent international documents, a reflection from the great scientific and technological discoveries from the XX and XXI centuries, particularly the Helsinque Declaration, adopted in 1964 and its versions from 1975, 1983, 1989, 1996 and 2000; the International Pact regarding Economical, Social and Cultural Rights, from 1966; the International Pact regarding Civil and Political Laws, from 1966; the Universal Declaration regarding Human Genoma and Human Rights, from 1997; the International Declaration regarding Human Genes Data, from 2003; and the Universal Declaration regarding Bioethics and Human Rights, from 2004;

Considering the Federal Constitution of the Federal Republic of Brazil, which objectives and foundations of sovereignty, citizenship, human dignity, labor and free enterprise social values and political pluralism and the objectives of building a free, fair and caring society, to ensure national development, to end poverty and marginalization and to reduce social and regional inequalities and to promote the well being of all, without any type of prejudice or discrimination, are consistent with the international documents of ethics, human rights and development;

Considering the related and relevant Brazilian Legislation; and

Considering the Resolution no. 196/96, of the National Council of Health, from the Ministry of Health, that states periodic reviews to it according to the needs on techno-scientific and ethical areas.

DECIDES:

To approve the following guidelines and standards regulating researches involving human beings:

I – PRELIMINARY PROVISIONS

This Resolution consolidates bioethical benchmarks from the view point of the individual and the communities, such as autonomy, non maleficence, beneficence, justice and equity, among others, and it seeks to

ensure the rights and duties that refer to the participants of the research, to the scientific community and the State.

Projects of research involving human beings must attend to this Resolution.

II – TERMS AND DEFINITIONS

This Resolution adopts the following definitions:

II.1 – research findings – facts or information met by the investigator along the study and considered as relevant to the participants or communities involved;

II.2 – informed consent agreement – an agreement of the research participant, child, teenager or legally unable, free of vice (simulation, fraud or error), dependence, subordination or intimidation. Such research participants must be clarified about the nature of research, its objectives, methods, expected benefits, potential risks and the discomfort that it might occur by reason of said investigation, according to their comprehension and respecting their singularities;

II.3 – assistance to the research participant:

II.3.1 – immediate assistance – considered as an emergency and with no cost of any kind to the research participant, in situations that he/she may need it; and

II.3.2 – full assistance – that provided to attend complications and damages caused directly or indirectly by the research;

II.4 – research benefits – immediate or posterior, direct or indirect profit, attained by the participant and/or his/her community caused by his/her participation in the research;

II.5 – informed consent form – an agreement from the research participant and/or from his/her legal representative, free of vice (simulation, fraud or error), dependence, subordination or intimidation following a complete and detailed explanation of the nature of the research, its objectives, methods, expected benefits, potential risks and discomfort that might occur by reason of said investigation;

II.6 – damage related to or caused by the research – immediate or posterior, direct or indirect offense, to the individual or community, caused by the research;

II.7 – compensation – material coverage for compensating damages caused by the research to its participants;

II.8 – research applicant institution – public or private organization, legitimated and qualified, to which the leading researcher is linked to;

II.9 – research co-participating institution – public or private organization, legitimated and qualified, in which some of the stages or steps of the research are developed;

II.10 – research participant – the individual who accepts to be studied on a voluntary and informed basis or under the clarification and authorization of his/her legal representatives. The participation must be free of charge, except Phase I or Bioequivalence clinical researches;

II.11 – sponsor – public or private individual or legal entity that supports the research, throughout financial shares, infrastructure, human resources or institutional support;

II.12 – research – a formal and systematic process which aims at the production, at the advancement of knowledge and/or at obtaining answers to problems by using a scientific methodology;

II.13 – research in human reproduction – researches engaged with the functions of the reproductive system, procreation and factors that affect the reproductive health of humans, considering as “research participants” all those who were affected by its procedures;

II.14 – research involving human beings – researches involving, individually or collectively and directly or indirectly, human beings as a whole or part thereof, including handling of his/her data, information or biological materials;

II.15 – investigator – a member of the research team, co-responsible for the integrity and welfare of all participants of the research;

II.16 – leading researcher – a person in charge of the coordination of the research and co-responsible for the integrity and welfare of all participants of the research;

II.17 – research protocol – a set of documents describing the research regarding its fundamental aspects and the information related to the research participants, the researcher's qualification and all responsible bodies;

II.18 – previous material compensation – material compensation dedicated exclusively for expenses related to transportation and meal for the research participant and his/her companion(s), and if necessary, prior to his/her participation in the research;

II.19 – final report – the one presented after the closure of the research, totaling its results;

II.20 – partial report – the one presented during the research showing relevant facts and partial results of its development;

II.21 – indemnification – material compensation dedicated exclusively for expenses related to transportation and meal for the research participant and his/her companion(s), whenever necessary;

II.22 – research risks – possible damage to the human being physical, psychic, moral, intellectual, social, cultural or spiritual dimension, caused by and from any research;

II.23 – Informed Consent Form (ICF) – a document specifying the research participant and/or his/her legal representative's consent statement, in the form of a written consent, and it must contain all necessary information, in a clear and objective language, so the participant and/or his legal representative clearly understand about the research to which he/she is willing to participate;

II.24 – Consent Term – a document prepared for minors or legally incapable for their easy understanding allowing them, after being clearly informed about the research, to state their will to participate in the research without prejudice to the consent of their legal representatives; and

II.25 – vulnerability – the condition of individuals or groups that, for any reason whatsoever, have their self-judgment capability reduced or disabled, or by any means they are prevented to resist to the opposition, especially when it comes to the informed consent form.

III – ETHICAL ASPECTS OF RESEARCHES INVOLVING HUMAN BEINGS

The researches involving human beings must attend to the relevant ethical and scientific grounds.

III.1 – Ethics of research involve:

- a) respect the research participant's dignity and autonomy, recognizing his/her vulnerability, ensuring his/her will to contribute and remain, or not, in the research, by means of express, free and informed statement;
- b) balance known and potential, individual or collective, risks and benefits committing to the maximum of benefits and to the minimum of risks and damages;
- c) ensure that known damages will be avoided; and
- d) social relevance of investigation, ensuring the equated weighting of interests involved with no loss to the sense of its social-humanitarian purpose.

III.2 – In any area of knowledge involving human beings, the researches shall comply with the following demands:

- a) shall be appropriate to the scientific values that justifies it and with concrete possibilities of responding to uncertainties;
- b) shall be founded in scientific grounds, previous testing and/or appropriate assumptions to the specific area of investigation;
- c) shall be performed only when the expected knowledge cannot be obtained through other means;
- d) always seek for the expected benefits to prevail regarding risks and/or foreseeable discomforts;
- e) use the appropriate methodology to answer the studied subjects specifying if a qualitative, quantitative or quali-quantitative investigation;

- f) if there is a need to allocate the research participants randomly into experimental and control groups, ensure beforehand that it is not possible to establish the advantages of a procedure over another, by reviewing literature, observation methods or methods that do not involve human beings;
- g) obtain a deliberate consent statement from the research participant and/or his/her legal representative, including on cases where, due to their nature, the researches imply in *posteriori* consent;
- h) count on human resources and materials necessary to ensure the research participant's wellbeing, and the investigator(s) must have appropriate professional capability to develop his/her function in the proposed project;
- i) provide procedures ensuring confidentiality and privacy, image protection and avoiding stigmatization of the research participants, and to guarantee the non-use of information to the detriment of people and/or communities, including in terms of self-esteem, prestige and/or economic and financial aspects;
- j) to be preferably developed on individuals with full autonomy. Individuals or vulnerable groups shall not participate in the research when the expected information may be obtained with participants fully capable, unless the research may bring benefits to the individuals or vulnerable groups.
- k) always respect cultural, social, moral, religious and ethical values, as well as habits and practices, when involving communities in researches;
- l) ensure, wherever possible, that researches within communities become beneficial to their effects and continue after their conclusion. When there is a real benefit to motivate or stimulate changes of habits or behaviors for the sake of the community, the research protocol shall include, wherever possible, willingness to communicate such advantage to the people and/or community;
- m) communicate the competent authorities, as well as to the bodies legitimized by the Social Control, the results and/or findings of the research, every time they can contribute to improving living conditions of the community, preserving, however, the image and ensuring that the research participants will not be stigmatized;
- n) ensure the benefits resulting from the project to the research participants, whether in terms of social return, access to procedures, products or research agents;
- o) ensure the monitoring conditions, treatment, full assistance and guidance to the research participants, according to the case, while needed, including those in tracking researches;
- p) present evidence of commitments and advantages to the research participants and Brazil resulting from the performance thereof for researches carried out abroad or with foreign cooperation. In these cases, the investigator and national institution responsible for the research in Brazil must be identified. The studies sponsored abroad must also respond, when applicable, to the needs of transferring knowledge and technology to the Brazilian team and, in case of developing new drugs, their registration in Brazil are mandatory, if safety and effectiveness are proven;
- q) use the material and data obtained from the research solely for the purposes identified in its protocol or according to the participant's consent statement;
- r) consider evaluating risks and benefits and eventual interferences regarding fertility, pregnancy, embryo or fetus, childbirth, puerperium, lactation and newborn in researches carried out in pregnant women or those in the childbearing age;
- s) consider that the researches carried out in pregnant women must be performed before those carried out in women after their gestational period, except for researches to which pregnancy is the main purpose;
- t) women who declare themselves with no risk of pregnancy, whether by sexual relation or by no means of reproduction, guarantee the right to participate on es without the compulsory use of contraceptives; and

- u) discontinue research only after analysis of reasons for such discontinuation by the CEP/CONEP/CNS/MS System approving such study, unless in cases of justified urgency to the benefit of their participants.

III.3 – The researches using experimental methodologies in the biomedical area, involving human beings, besides that recommended in item III.2, shall:

- a) be founded on previous experimentation carried out in labs using animals or other experimental models and scientific evidence, when appropriate;
- b) when using placebo, such use shall be fully justified as to its non maleficence and methodology requirements, where the benefits, risks, difficulties and effectiveness of a new therapeutic method shall be tested, comparing it to the best current prophylactic, diagnostic and therapeutic methods. It is not included the use of placebo or any other treatment to studies where there are no proven methods of prophylaxis, diagnosis or treatment;
- c) use the biological material and data obtained from the study solely to that intended purpose in the protocol, or according to the consent granted by the research participant; and
- d) guarantee to all participants, at the end of the study and for unlimited time, free access to the best prophylactic, diagnostic and therapeutic methods that have proven their efficiency;
- d.1) the access will also be guaranteed in the interval between the end of the individual's participation and the end of the study, in which case this guarantee could be granted by means of an extension study, according to a duly justified analysis from the doctor assisting the research participant.

IV – PROCESS OF INFORMED CONSENT FORM

Due respect to human dignity requires that every research be carried out after subjects, individuals or groups, or their legal representatives have given the respective informed consent form expressing their agreement to participate in the research.

The Process of the Informed Consent Form refers to all steps the guests need to observe to participate in a research and to be able to manifest themselves as autonomous, conscientious, free and informed.

IV.1 – The first step of the Process of the Informed Consent Form refers to clarify the guests about their participation in the research, where the investigator or person delegated by him/her or under his/her responsibility should:

- a) look for the right moment, condition or place to carry out the clarification taking into account the guests' peculiarities and privacy to participate in the research;
- b) provide clear and accessible information using the most appropriate strategies referred to the culture, age, socio-economic conditions and autonomy of the subjects participating in the research; and
- c) grant the appropriate time so that the subjects participating in the research could think and consult, if necessary, their family or other people to help them take an informed consent decision.

IV.2 – Once the first step of clarification is completed, the investigator or person delegated by him/her shall submit the Informed Consent Form to the guest participating in the research, or to his/her legal representative, to be read and understood before the concession of the consent statement.

IV.3 – The Informed Consent must contain:

- a) justification, objectives and procedures that will be used in the research detailing the methods applied, notifying the possibility of their inclusion into control or experimental group, when applicable;
- b) explanation of potential discomforts and risks resulting from participating in the research, besides the benefits expected from such participation and presenting measures and cautions to avoid and/or lower effects and adverse conditions that may cause damage, taking into account characteristics and context of the research participant;
- c) clarification regarding monitoring and assistance that the research participants are entitled to, including the benefits and monitoring following the closure and/or interruption of the research;

- d) granting of total freedom to the research participant to refuse to participate or to remove his/her consent at any stage of the research, with no penalty;
- e) granting of maintaining confidentiality and privacy of all research participants during all stages of research;
- f) granting the research participant a copy of the Informed Consent Form;
- g) explanation of the reimbursement guarantee and how will the expenses of the research participants be covered and thereof;
- h) explanation of the indemnification guarantee in the case of eventual damages caused by the research.

IV.4 – The Informed Consent Form used in researches adopting experimental methodologies in the biomedical area, involving human beings, besides that expected on item IV.3 above, must contain, necessarily, the following:

- a) explanation, where appropriate, of the existing alternative treatment methods;
- b) clarification , where appropriate, regarding the possibility of including the participant into a control group or placebo, clearly explaining the significance of that possibility; and
- c) do not demand from the research participant, under any justification, a waiver of indemnification for damages. The Informed Consent Form shall not include any liability disclaimer nor imply waiver by the research participant of his/her legal rights, including the right to procure indemnification for potential damages.

IV.5 – The Informed Consent Form should also:

- a) contain a statement of the leading researcher expressing the compliance with the requirements specified on items IV.3 and, where applicable, IV.4;
- b) be adapted to the ethical rules and to the local culture, by the leading researcher, on researches with foreign cooperation elaborated abroad, with clear and accessible language to all and particularly to the participants of the research, taking special care for easy reading and understanding;
- c) be approved by CEP to which the project was presented and by CONEP, when applicable; and
- d) be elaborated in 2 copies and with all pages initialed and signed at the end by the guest invited to participate in the research, or by his/her legal representative, as well as by the leading researcher or those delegated by him/her, and with all signed pages on the same sheet. Both copies shall state the address and contact number or other of those responsible for the research, of the local CEP and CONEP, when applicable.

IV.6 – In the event where there is any restriction to freedom or explanation required to the appropriate consent, the following shall be complied with as well:

- a) researches involving children and adolescents, individuals mentally disturbed or ill and those who have their capacity to consent substantially reduced, shall include in the protocol unquestionable justification for the choice of such individuals approved by CEP, and by CONEP, and comply with all requirements of informed consent statement by means of their legal representatives and the research participant, to the fullest extent of his/her capacity, is guaranteed the right to information;
- b) freedom to consent shall be specifically guaranteed to those individuals that, although fully capable, are exposed to specific conditioning or authority influence, featuring situations restricting their autonomy, specially students, members of the armed forces, employees, prisoners rehabilitation, shelters, nursing homes or religious associations interns and alike, in addition to be free to decide whether or not to participate in the research, with no retaliation of any kind;
- c) researches with individuals diagnosed with encephalic death may comply with the following requirements:
 - c.1) documentary evidence of encephalic death;

- c.2) a written consent from family members and/or legal representative or documentary evidence of individual's will to participate in researches;
 - c.3) respect to human dignity;
 - c.4) no additional economic-financial burden to the family;
 - c.5) no prejudice to other patients awaiting hospitalization or treatment; and
 - c.6) likely to acquire new, relevant scientific knowledge which cannot be so acquired any other way;
- d) the existence of an official government communication channel to clarify doubts to all those involved in the research projects, as well as for those cases of encephalic death diagnosis; and
- e) in group culture communities recognizing the leader's authority or the collectiveness upon the individual, the authorization for the research should respect such feature, without the prejudice of individual consent, when possible and desirable. The authorization for the research should be granted in advance by government bodies when the Brazilian Legislation rules upon their competence, like it is the case of the National Indian Foundation (FUNAI), where indigenous communities are under their own responsibility.

IV.7 – The research depending on restriction to information to the research participants, such restriction shall be fully explained and justified by the leading researcher and submitted to the CEP/CONEP. Data collected from the research participants may not be used for any other purposes other than those specified in the protocol and/or informed consent statement.

IV.8 – In cases where unfeasible to obtain the Informed Consent Form or that its obtaining may imply to substantial risks to the privacy and confidentiality of the research participant's data or to the bonds of trust between investigator and investigated, the dismissal of such Statement Form must be rightly requested by the investigator to the CEP/CONEP System, for evaluation, without prejudice to the subsequent clarification process.

V - RISKS AND BENEFITS

Every research with human beings is considered to involve risks of different types. The bigger and more evident the risks, the bigger should be the care offered by CEP/CONEP to minimize them and protect the research participants. Possibilities for immediate or further damages must be analyzed at an individual and collective level. The analysis of risks is an indispensable part to the ethical analysis which generates the monitoring plan that shall be offered by the CEP/CONEP System in each specific case.

V.1 – Researches involving human beings will be admissible when:

- a) the risk is justified by the expected benefit; and
- b) in case of experimental researches referred to health, the benefit is bigger, or, at least, equal to the already established options for prevention, diagnosis and treatment.

V.2 – Researches with solely indirect benefits to their participants are admissible as long as their physical, psychological, moral, intellectual, social, cultural and spiritual dimensions are considered.

V.3 – The leading researcher must immediately communicate to the CEP/CONEP System any significant risk or damage the research participant may suffer, stated or not in the Informed Consent Form and evaluate as an emergency the need to adjust or suspend the study.

V.4 – In the health area researches, the researcher shall evaluate the need to adjust or suspend the ongoing study as soon as the significant superiority of an intervention over other comparative(s) are recognized, aiming at offering all subjects the benefits of the best regimen.

V.5 – The CEP/CONEP System shall be informed of any relevant fact that may change the regular course of the studies approved by it and, specifically, in those researches related to health, to be informed of the adverse effects and the significant superiority of a research upon other or other comparatives.

V.6 – The investigator, the sponsor and the institutions and/or organizations involved in different stages of the researches shall provide immediate assistance, in terms of item II.3, as well as to be responsible for the complete assistance to all subjects when referred to complications and damages caused by such research.

V.7 – Every research subject who come to suffer any damages whatsoever in the future, whether or not indicated in the consent statement and resulting from his/her participation shall be entitled to indemnification on the part of the investigator, sponsor and institutions involved in the different stages of the research.

VI – RESEARCH PROTOCOL

The protocol to be submitted to ethical review will only be subject to examination if accompanied with all documentation required by the CEP/CONEP System, considering the nature and specificities of each research. *Plataforma BRASIL* is the official system for launching researches for the CEP/CONEP System analysis and monitoring.

VII – CEP/CONEP SYSTEM

It is integrated by the National Commission of Ethics in Research – CONEP/CNS/MS of the National Council of Health and by the Committees of Ethic in Research – CEP – composing a system using mechanisms, tools and proper instruments of inter-relationship, cooperatively, aiming especially the protection of Brazil's research participants, in a coordinated and decentralized manner by means of an accreditation process.

VII.1 – Researches involving human beings shall be submitted to the CEP/CONEP System evaluation, which by analyzing and deciding, it becomes the co-responsible for guaranteeing protection to all research participants.

VII.2 – The CEP are interdisciplinary and independent groups of a public function and advisory, deliberate, and educational nature, established to protect the interests of all research participants in their integrity and dignity and to contribute to the research development according to ethical standards:

VII.2.1 – institutions and/or organizations performing researches involving human beings shall establish one or more Committees of Ethic in Researches – CEP, according to their own needs, and meeting the normative criteria; and

VII.2.2 – in case of a non existing CEP in the applicant institution or in case of an investigator with no institutional affiliation, it shall be CONEP's responsibility to indicate a CEP to perform the analysis of the research among those presenting the best conditions for monitoring such research.

VII.3 – CONEP is a collegiate body that is advisory, deliberative, legislative, educational and independent in nature and is linked to the National Council of Health/MS.

VII.4 – The ethical review of projects involving human beings shall be associated to its scientific analysis.

VII.5 – Members of CEP/CONEP System shall be fully independent to make any decision they deem appropriate in the discharge of their duties, safeguarding the confidentiality of the information received. Hence, they shall not be subject to any pressure whatsoever on the part of higher-ranked personnel or third parties interested in a certain research. They should avoid taking decisions when involved in the research under analysis.

VII.6 – Members of CEP and CONEP may not receive any compensation for the discharge of their duties, and may only receive reimbursement of expenses related to transportation, lodging and meal. It is recommended, however, that during the regular working hours at CEP, or at CONEP, they are dismissed from their other obligations in the institutions and/or organizations to which they render services given the public relevance of the function.

VIII – COMMITTEES OF ETHIC IN RESEARCH (CEP)

DUTIES:

VIII.1 – evaluate protocols of research involving human beings, with priority given to subjects related to public relevance and strategic interests for the Unified Health System (SUS) priorities' agenda, based on the epidemiological indicators providing a duly justified opinion, always guided, among others, by the impersonality,

transparency, reasonability, proportionality and efficiency principles within deadlines laid down by operational standards, avoiding redundancies that may result in slowing down the analysis;

VIII.2 – perform an advisory and educational role in matters related to ethics; and

VIII.3 – elaborate its Bylaws.

IX – NATIONAL COMMISSION OF ETHICS IN RESEARCHES (CONEP)

DUTIES:

IX.1 – examine all ethical aspects of researches involving human beings, as well as to adapt and update all applicable rules, for which purpose they may refer to the society whenever they judge necessary;

IX.2 – promote popular participation in initiatives of Social Control in Researches with Human Beings, besides establishing institutional CEP and other bodies, whenever such creation may imply in the strengthening of protecting the research participants in Brazil;

IX.3 – register and supervise the operation and cancel the registry of any other CEP that may form the CEP/CONEP System;

IX.4 - evaluate protocols of research involving human beings, providing a duly justified opinion, always guided, among others, by the impersonality, transparency, reasonability, proportionality and efficiency principles within deadlines laid down by operational standards, avoiding redundancies that may result in slowing down the analysis;

1. human genetics, when the project may involve:

1.1 shipments of human genetics overseas or any other human biological material for obtaining genetic material, except in those cases where there is cooperation with the Brazilian Government;

1.2 storage of biological material or human genetic data abroad and within the country, when part of an agreement with foreign institutions or with commercial institutions;

1.3 changes in the genetic structure of human cells for *in vivo* use;

1.4 researches in genetics of human reproduction (reprogenetics);

1.5 researches of genetics in behavior; and

1.6 researches in which irreversible dissociation of research participant's data is expected;

2. human reproduction: researches interested in the functioning of the reproductive system, procreation and factors affecting the human reproductive health, shall consider as "research participant's" all those who are affected by the procedures thereof. It will be up to CONEP to analyze the project when it involves:

2.1 – assisted reproduction;

2.2 – gametes, pre-embryos, embryos and fetus manipulation; and

2.3 – fetal medicine, when involving invasive procedures;

3. therapy equipments and devices, new or not registered in the country;

4. new invasive therapy procedures;

5. studies with indigenous populations;

6. research projects involving genetically modified organisms (GMOs), embryonic stem cells and organisms representing high collective risk, including organisms related to them, in areas of: experimentation, construction, growing, manipulation, transportation, transfer, import, export, storage, release into the environment and disposal;

7. setting up and functioning protocols of biobanks for research purposes;

8. researches with coordination and/or sponsorship originated outside Brazil, except those with the Brazilian Government co-sponsorship; and

9. projects that, at the discretion of CEP and duly justified, were judged as worthy of analysis by CONEP;

IX.5 – strengthen the participation of CEPs through a continuous process of training, qualification and accreditation;

IX.6 – coordinate the CEPs accreditation process, appointing them responsibilities originally from CONEP, according to their skill levels;

IX.7 – analyze and monitor, directly and indirectly, within the standards deadline, the research protocols that may involve needs for a higher protection related to their research participants, specially the risks thereof. Within such scope, it shall always be considered as first priority and, or in association, the national interests in the scientific and technological development, as the basis for determining the relevance and opportunity for performing such researches;

IX.8 – analyze and monitor, directly and indirectly, research protocols with conflict of interests that make the fair local analysis difficult and not viable;

IX.9 – rightly analyze any CEP/CONEP System protocol, whenever appropriate; and

IX.10 – analyze, urgently and with special processing, research protocols with relevant public interest such as those that contribute to the public health, justice and reduction of social inequalities and technological premises, upon request of the Ministry of Health or other organization of Public Administration, or even at the discretion of CONEP/CNS Plenary.

X – ETHICAL ANALYSYS PROCEDURES

X.1 – CEPs ETHICAL ANALYSIS

DUTIES:

1. it is CEP's responsibility to issue, after analysis, a duly reasoned opinion in which the collegiate decision is presented in a clear, objective and detailed manner, respecting the deadline laid down in the operating standard;
2. forward CONEP's duties protocols after an informed analysis, according to the current operating standards taking special care of all documentation that must follow such forwarding, including the detailed proof of expenses and the financing resources necessary for the research;
3. CEP shall also be responsible for:
 - a) keeping the confidential custody of all data obtained while on duty and filing the complete protocol;
 - b) monitoring the project's development through biannual reports from investigators and other monitoring strategies, according to the risk inherent to the research;
 - c) CEP shall keep the project, protocol and corresponding reports filed for a five-year period after the closure of the study, and such filing may be digitally processed.
 - d) receiving complaints of abuse and notifications about adverse facts that might alter the study's regular course, deciding on the continuation, modification or discontinuation of the research, requesting, if applicable, the change of the Statement Consent;
 - e) requiring the opening of a research to the institution's and/or organization's board, or to the public competent bodies, if known any case of complaints of irregularities in the researches involving human beings and, if proved the existence of such complaints, communicate the fact to CONEP and, where applicable, to other authorities; and
 - f) maintain a regular and ongoing communication with CONEP, through its Executive Secretariat.

X.2 – PROCEDURE OF CONEP's ETHICAL ANALYSIS:

1. it is CONEP's responsibility to issue a duly reasoned opinion, respecting the deadline to be laid down in the Operating Standard, with a clear, objective and detailed analysis of all elements and documents of the project;

2. CONEP shall also be responsible for the direct or indirect monitoring of all research protocols within its duties; and
3. the provisions about the Procedures of CEP's Ethical Analysis are applied to CONEP in cases where it operates as CEP.

X.3 – COMMON PROVISIONS TO CEP AND CONEP:

1. members of CEP/CONEP shall exempt themselves from the case's analysis and discussion, as well as from decision-making, when involved in the research;
2. CEPs and CONEP may count on *ad hoc* consultants, people belonging to or not, an institution/organization, with the purpose of providing technical support;
3. a research lacking its protocol shall not be analyzed;
4. any approved research that becomes discontinued by the leading researcher, without an acceptable justification satisfactory to the CEP or CONEP, approving such research shall be considered an unethical investigation;
5. CEP's review shall be completed upon its classification under one of the following categories:
 - a) approved;
 - b) outstanding: when CEP considers the correction of the presented protocol as necessary, and requests specific review, change or relevant information, which shall be performed within the deadline laid down in operating standard; and
 - c) not approved;
6. CEP may request, if judged as convenient and appropriate while performing the ethical review, information, documents and others needed for the well understanding of the issues, and discontinue the procedure until confirming the receipt of said elements;
7. should the decision be not approved, it shall be CEP and/or CONEP's responsibility to appeal, within 30 days, whenever a new fact is presented to substantiate the need for a reevaluation;
8. CEPs and CONEP shall determine the research protocol filing in cases where the leading researcher did not meet the requests addressed to him/her within the stated deadline. They shall also consider the withdrawn protocol when requested by the leading researcher;
9. once the project is approved, CEP, or CONEP in situations acting as a CEP or under the operation of its original duties, it becomes the co-responsible for that referred to the research's ethical aspects; and
10. shall be considered as authorized for implementation those projects approved by CEP, or by CONEP when in situations acting originally as a CEP or under the operation of its duties.

XI – LEADING RESEARCHER

XI.1 – The researcher has a non transferable, indeclinable responsibility which includes the following ethical and legal aspects:

XI.2 – The investigator is required to:

- a) submit the duly guided protocol to CEP and CONEP, awaiting for the ethical approval decision before starting the research;
- b) elaborate the Informed Consent Form;
- c) develop project as designed;
- d) prepare and submit interim and final reports;
- e) submit all data requested at any time by CEP or CONEP;
- f) keep under his/her custody and responsibility for 5 years, records of all research data, physical or digital, after the closure of such research;
- g) forward all results for publication, including the respective acknowledgments concerning associate investigators and technical staff participating in the project; and

- h) submit to the relevant CEO or CONEP reasonable, acceptable explanation for discontinuation of a project or non publication of any results.

XII – OTHER PROVISIONS

XII.1 – Every area of research and each research modality, in addition to abide by the provisions contained in this Resolution, shall comply with all branch requirements and specific regulations.

XII.2 – Research promotion agencies and editorial staff of scientific journals shall require documentary evidence of project's approval by the CEP/CONEP System.

XII.3 – By virtue of the contextual nature of all considerations contained herein, this Resolution will be subject to regular reviews to meet the requirements of the technical-scientific and ethical areas.

XIII – RESOLUTIONS AND SPECIFIC RULES

XIII.1 – The assessment procedures of research protocols, as well as the specific aspects of registry, like concession, renewal or cancellation and, also accreditation of Ethical Committees in Research shall be regulated by Resolution from the National Council of Health.

XIII.2 – The accreditation process of Ethical Committees in Research that form the CEP/CONEP System shall be treated by a Resolution from CNS.

XIII.3 – Ethical research specificities in social and human science and others adopting methodologies from those areas shall be addressed in complementary resolution, given their particularities.

XIII.4 – Ethical research specificities with strategic interest for SUS shall be addressed in specific complementary Resolution.

XIII.5 – Procedural and administrative aspects of CEP/CONEP System shall be treated in Operating Standard from CNS.

XIII.6 – Risk typification and gradation in different research methodologies shall be defined by the National Council of Health own rule.

XIV – FINAL PROVISIONS

Resolutions CNS no. 196/96, 303/2000 and 404/2008 are hereby repealed.

This Resolution shall come into force upon publication.

ALEXANDRE ROCHA SANTOS PADILHA
President of the National Council of Health

I approve the Resolution CNS no. 466 of December 12, 2012, pursuant to the terms of the Decree of Delegation of Authority dated November 12, 1991.

ALEXANDRE ROCHA SANTOS PADILHA
Ministry of State for Health