RESOLUTION **Nº** 466, OF DECEMBER 12, 2012.

The Plenary of the National Health Council in its 240th Ordinary Meeting, held on December 11 and 12, 2012, in the exercise of its regulatory powers and attributions conferred by Law **No.** 8,080, of September 19, 1990, and by Law **No.** 8,142, of December 28, 1990, and

Considering respect for human dignity and the special protection due to participants in scientific research involving human beings;

Considering the development and ethical engagement, which is inherent to scientific and technological development;

Considering the progress of science and technology, which has revealed another perception of life and ways of life, with repercussions not only on the conception and prolongation of human life, but also on habits, culture and human behavior in the real and virtual environments available, which change and innovate at an accelerated and continuous pace;

Considering the progress of science and technology, which must imply current and potential benefits for human beings, for the community in which they are inserted and for society, nationally and universally, enabling the promotion of well-being and quality of life and promoting the defense and preservation of the environment, for present and future generations;

Considering the ethical issues raised by progress and advancement of science and technology, rooted in all areas of human knowledge;

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

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

Considering recent international documents, reflecting the great scientific and technological discoveries of the 20th and 21st centuries, especially the Declaration of Helsinki, adopted in 1964 and its versions of 1975, 1983, 1989, 1996 and 2000; the International Covenant on Economic, Social and Cultural Rights, of 1966; the International Covenant on Civil and Political Rights, 1966; the Universal Declaration on the Human Genome and Human Rights, 1997; the International Declaration on Human Genetic Data, 2003; and the Universal Declaration on Bioethics and Human Rights, 2004;

Considering the Federal Constitution of the Federative Republic of Brazil, whose objectives and foundations of sovereignty, citizenship, human dignity, social values of work and free enterprise and political pluralism and the objectives of building a free, fair and supportive society, of guaranteeing national development, of eradicating poverty and marginalization and reducing social and regional inequalities and of promoting the good of all, without any type of prejudice or discrimination, are in line with international documents on ethics, human rights and development;

Considering the related and pertinent Brazilian legislation; and

Considering the provisions of Resolution **No.** 196/96, of the National Health Council, of the Ministry of Health, which imposes periodic reviews to it, according to needs in the technical-scientific and ethical areas.

R E S O L V E:

Approve the following guidelines and regulatory standards for research involving human beings:

I – PRELIMINARY PROVISIONS

This Resolution incorporates, from the perspective of the individual and collectives, bioethical references, such as autonomy, non-maleficence, beneficence, justice and equity, among others.

others, and aims to ensure the rights and duties that concern research participants, the scientific community and the State.

Research projects involving human beings must comply with this Resolution.

II - TERMS AND DEFINITIONS

This Resolution adopts the following definitions:

II.1 - research findings - facts or information found by the researcher during the research and which are considered relevant to the participants or participating communities;

II.2 - free and informed consent - consent of the research participant, child, adolescent or legally incapable, free from vices (simulation, fraud or error), dependence, subordination or intimidation. Such participants must be informed about the nature of the research, its objectives, methods, expected benefits, potential risks and the discomfort it may cause them, to the extent of their understanding and respected in their singularities;

II.3 - assistance to the research participant:

II.3.1 - immediate assistance – is emergency assistance and without any cost to the research participant, in situations in which he/she needs it; and

II.3.2 - comprehensive assistance – is that provided to address complications and damages arising, directly or indirectly, from the research;

II.4 - benefits of research - direct or indirect, immediate or subsequent benefit obtained by the participant and/or their community as a result of their participation in the research;

II.5 - free and informed consent - consent of the research participant and/or his/her legal representative, free from defects (simulation, fraud or error), dependence, subordination or intimidation, after full and detailed clarification about the nature of the research, its objectives, methods, expected benefits, potential risks and the inconvenience that it may cause;

II.6 - damage associated with or resulting from the research - immediate or subsequent harm, direct or indirect, to the individual or to the community, resulting from the research;

II.7 - compensation - material coverage for repair of damage caused by the research to the research participant;

II.8 - institution proposing research - organization, public or private, legitimately constituted and qualified, to which the responsible researcher is linked;

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

II.10 - research participant - an individual who, in an informed and voluntary manner, or with the clarification and authorization of his/her legal guardian(s), accepts to be researched. Participation must be free of charge, except in Phase I or bioequivalence clinical trials;

II.11 - sponsor - natural or legal person, public or private, that supports the research, through financing, infrastructure, human resources or institutional support actions;

II.12 - research - formal and systematic process that aims to produce, advance knowledge and/or obtain answers to problems through the use of the scientific method;

II.13 - research into human reproduction - research that deals with the functioning of the reproductive system, procreation and factors that affect the reproductive health of humans, and in these studies all those affected by the procedures will be considered “research participants”;

II.14 - research involving human beings - research that, individually or collectively, has as a participant the human being, in its entirety or parts thereof, and involves it directly or indirectly, including the management of its data, information or biological materials;

II.15 - researcher - member of the research team, jointly responsible for the integrity and well-being of research participants;

II.16 - responsible researcher - person responsible for coordinating the research and co-responsible for the integrity and well-being of research participants;

II.17 - research protocol - set of documents containing the description of the research in its fundamental aspects and information relating to the research participant, the qualifications of the researchers and all responsible bodies;

II.18 - prior material provision - material compensation, exclusively for transportation and food expenses of the participant and their companions, when necessary, prior to their participation in the research;

II.19 - final report - is the one presented after the end of the research, totaling your results;

II.20 - partial report - is one presented during the research demonstrating relevant facts and partial results of its development;

II.21 - reimbursement - material compensation, exclusively for expenses of the participant and their companions, when necessary, such as transportation and food;

II.22 - research risk - possibility of damage to the physical, psychological, moral, intellectual, social, cultural or spiritual dimension of the human being, in any research and resulting from it;

II.23 - Free and Informed Consent Form - TCLE - document in which the free and informed consent of the participant and/or their legal guardian is expressed, in writing, and must contain all necessary information, in clear and objective language, easy to understand, for the most complete clarification about the research in which they intend to participate;

II.24 - Consent Form - document prepared in language accessible to minors or those legally incapacitated, through which, after the research participants have been duly informed, they will explicitly agree to participate in the research, without prejudice to the consent of their legal guardians; and

II.25 - vulnerability - state of people or groups who, for whatever reasons or motives, have their capacity for self-determination reduced or impeded, or are in any way prevented from offering resistance, especially with regard to free and informed consent.

III - ETHICAL ASPECTS OF RESEARCH INVOLVING HUMAN BEINGS

Research involving human beings must comply with the relevant ethical and scientific foundations.

III.1 - Research ethics implies:

a) respect for the research participant in their dignity and autonomy, recognizing their vulnerability, ensuring their willingness to contribute and remain, or not, in the research, through an express, free and informed statement;

b) weighing up risks and benefits, both known and potential, individual or collectives, committing to maximum benefits and minimum damage and risks;

c) assurance that foreseeable damage will be avoided; and

d) social relevance of the research, which guarantees equal consideration of the interests involved, without losing the sense of its socio-humanitarian purpose.

III.2 - Research, in any area of knowledge involving human beings, must observe the following requirements:

a) be appropriate to the scientific principles that justify it and have concrete possibilities of responding to uncertainties;

b) be based on scientific facts, previous experimentation and/or assumptions appropriate to the specific area of research;

c) be carried out only when the knowledge sought to be obtained cannot be obtained by other means;

d) always seek to ensure that the expected benefits prevail over the foreseeable risks and/or discomforts;

e) use appropriate methods to answer the questions studied, specifying them whether the research is qualitative, quantitative or quali-quantitative;

f) if there is a need for random distribution of research participants into experimental and control groups, ensure that, *a priori,* it is not possible to establish the

advantages of one procedure over another, through literature review, observational methods or methods that do not involve human beings;

g) obtain free and informed consent from the research participant and/or their legal representative, including in cases of research that, by their nature, justifiably implies *a posteriori consent;*

h) have the necessary human and material resources to guarantee the well-being of the research participant, and the researcher(s) must have adequate professional capacity to carry out their role in the proposed project;

i) provide for procedures that ensure confidentiality and privacy, image protection and non-stigmatization of research participants, guaranteeing that information is not used to the detriment of individuals and/or communities, including in terms of self-esteem, prestige and/or economic-financial aspects;

j) be developed preferably in individuals with full autonomy. Vulnerable individuals or groups should not be research participants when the desired information can be obtained through participants with full autonomy, unless the research can bring benefits to vulnerable individuals or groups;

k) always respect cultural, social, moral, religious and ethical values, such as also habits and customs, when research involves communities;

(l) ensure that community-based research, whenever possible, will result in benefits that continue to be felt after its completion. Where there is a real benefit in the interest of the community in encouraging or stimulating changes in customs or behavior, the research protocol should, whenever possible, include provisions for communicating such benefit to individuals and/or communities;

m) communicate to the competent authorities, as well as to the bodies authorized by Social Control, the results and/or findings of the research, whenever these can contribute to improving the living conditions of the community, while preserving the image and ensuring that the research participants are not stigmatized;

n) ensure that research participants benefit from the project, whether in terms of social return, access to research procedures, products or agents;

o) ensure that research participants have the conditions for monitoring, treatment, comprehensive assistance and guidance, as appropriate, as long as necessary, including in screening research;

p) to demonstrate, in research conducted abroad or with foreign cooperation, the commitments and advantages for the research participants and for Brazil resulting from their implementation. In these cases, the researcher and the national institution responsible for the research in Brazil must be identified. Studies sponsored abroad must also meet the needs of knowledge and technology transfer to the Brazilian team, when applicable. Furthermore, in the case of the development of new drugs, if their safety and efficacy are proven, their registration in Brazil is mandatory;

q) use the material and data obtained in the research exclusively for the purpose provided for in its protocol, or in accordance with the participant's consent; r) take into account, in research carried out on women of childbearing age or pregnant women, the assessment of risks and benefits and possible interference with fertility, pregnancy, the embryo or fetus, labor, the puerperium, lactation and the newborn;

s) consider that research on pregnant women must be preceded by research on women outside the gestational period, except when pregnancy is the fundamental object of the research;

t) guarantee, for women who expressly declare themselves to be free from the risk of pregnancy, either because they do not engage in sexual practices or because they engage in them in a non-reproductive manner, the right to participate in research without the mandatory use of contraceptives; and

u) be discontinued only after analysis and manifestation, by the CEP/CONEP/CNS/MS System that approved it, of the reasons for such discontinuation, except in cases of justified urgency for the benefit of its participants.

III.3 - Research that uses experimental methodologies in the biomedical field, involving human beings, in addition to what is recommended in item III.2, they must also:

a) be based on prior experimentation, carried out in laboratories, using whether animals or other experimental models and scientific evidence, when relevant;

b) have fully justified, when applicable, the use of placebo, in terms of non-maleficence and methodological necessity, and the benefits, risks, difficulties and effectiveness of a new therapeutic method must be tested, comparing it with the best current prophylactic, diagnostic and therapeutic methods. This does not exclude the use of placebo or any treatment in studies in which there are no proven methods of prophylaxis, diagnosis or treatment; c) use the biological material and data obtained in the research exclusively for the

purpose provided for in its protocol, or in accordance with the consent given by the research participant; and

d) ensure that all participants at the end of the study, on behalf of the sponsor, have free and indefinite access to the best prophylactic, diagnostic and therapeutic methods that have proven effective:

d.1) access will also be guaranteed in the interval between the end of individual participation and the end of the study, in which case this guarantee may be given through an extension study, in accordance with a duly justified analysis by the participant's attending physician.

IV – FREE AND INFORMED CONSENT PROCESS

Due respect for human dignity requires that all research be carried out with the free and informed consent of participants, individuals or groups who, by themselves and/or their legal representatives, express their agreement to participate in the research.

The Free and Informed Consent Process is understood to be all the steps that must necessarily be observed so that the person invited to participate in a research study can express themselves, in an autonomous, conscious, free and informed manner.

IV.1 - The initial stage of the Free and Informed Consent Process is to provide information to the person invited to participate in the research, at which time the researcher, or a person delegated by him/her and under his/her responsibility, must:

a) seek the most appropriate time, condition and place for the clarification to be carried out, considering, for this purpose, the peculiarities of the person invited to participate in the research and their privacy;

b) provide information in clear and accessible language, using the most appropriate strategies for the culture, age group, socioeconomic status and autonomy of those invited to participate in the research; and

c) allow adequate time for the person invited to participate in the research to reflect, consulting, if necessary, their family members or other people who can help them make a free and informed decision.

IV.2 - Once the initial clarification stage has been completed, the researcher in charge, or a person delegated by him/her, must present the Informed Consent Form to the person invited to participate in the research, or to his/her legal representative, so that he/she can read and understand it, before granting his/her free and informed consent.

IV.3 - The Free and Informed Consent Form must contain, without exception:

a) justification, objectives and procedures that will be used in the research, with details of the methods to be used, informing the possibility of inclusion in a control or experimental group, when applicable;

b) explanation of possible discomforts and risks arising from participation in the research, in addition to the expected benefits of such participation and presentation of the measures and precautions to be taken to avoid and/or reduce adverse effects and conditions that may cause harm, considering the characteristics and context of the research participant;

c) clarification on the form of monitoring and assistance to which research participants will be entitled, including considering benefits and monitoring after the end and/or interruption of the research;

d) guarantee of full freedom to the research participant, to refuse to participate or withdraw your consent, at any stage of the research, without any penalty;

e) guarantee of maintaining the confidentiality and privacy of research participants during all phases of the research; f) guarantee
that the research participant will receive a copy of the Term of
Free and Informed Consent;
g) explanation of the reimbursement guarantee and how the expenses incurred by the research participants and resulting from it will be covered; and
h) explanation of the guarantee of compensation for any damages arising from the research.

IV.4 - The Free and Informed Consent Form in research using experimental methodologies in the biomedical field, involving human beings, in addition to that provided for in item IV.3 above, must mandatorily observe the following: a) explain, when relevant,
existing alternative therapeutic methods; b) clarify, when relevant, the possibility of
including the participant in
control group or placebo, clearly explaining the meaning of this possibility; and
c) not require the research participant, under any argument, to waive the right to compensation for damages. The Informed Consent Form must not contain any reservation that removes this responsibility or that implies that the research participant waives his/her rights, including the right to seek compensation for any damages.
IV.5 - The Free and Informed Consent Form must also:
a) contain a statement from the responsible researcher expressing compliance with the requirements contained in items IV.3 and IV.4, the latter if applicable;
b) be adapted, by the responsible researcher, in research with foreign cooperation conceived at an international level, to ethical standards and local culture, always using clear language that is accessible to everyone and, in particular, to research participants, taking special care to ensure that it is easy to read and understand;
c) be approved by the CEP to which the project was presented and by CONEP, when applicable; and
d) be prepared in two copies, initialed on all pages and signed, at the end, by the person invited to participate in the research, or by his/her legal representative, as well as by the researcher in charge, or by the person(s) delegated by him/her, with the signature pages being on the same page. Both copies must include the address and telephone number or other contact details of those responsible for the research and the local postal code and CONEP, when applicable.

IV.6 - In cases of restriction of freedom or clarification necessary for adequate consent, the following must also be observed: a) in research whose
guests are children, adolescents, people with mental disorders or illnesses or in a situation of substantially reduced decision-making capacity, there must be a clear justification for their choice, specified in the protocol and approved by the CEP and by CONEP, when applicable. In these cases, the stages of clarification and free and informed consent must be followed, through the legal representatives of those invited to participate in the research, preserving their right to information, to the limit of their capacity;

b) freedom of consent should be particularly guaranteed for those research participants who, although fully capable, are exposed to specific conditions or to the influence of authority, characterizing situations that may limit autonomy, such as students, military personnel, employees, prisoners and inmates in rehabilitation centers, shelters, asylums, religious associations and similar, ensuring them complete freedom to participate or not in the research, without any reprisals;

c) research on people diagnosed with brain death must meet the following requirements:

c.1) document proving brain death; c.2) explicit
consent, advance directive of the person, or consent
family members and/or legal representative;
c.3) respect for human dignity;
c.4) absence of additional economic-financial burden on the family;

c.5) no harm to other patients awaiting hospitalization or treatment;

and

c.6) possibility of obtaining relevant or new scientific knowledge that cannot be obtained in any other way;

d) that there be an official government communication channel that clarifies doubts in an accessible way for those involved in research projects, also for cases of diagnosis with brain death; and

e) in communities whose group culture recognizes the authority of the leader or collective over the individual, obtaining authorization for research must respect this particularity, without prejudice to individual consent, when possible and desirable. When Brazilian legislation provides for the competence of government agencies, such as the National Indian Foundation – FUNAI, in the case of indigenous communities, under the guardianship of such communities, such agencies must authorize the research in advance.

IV.7 - In research that depends on restricting information to its participants, this fact must be duly explained and justified by the researcher responsible to the CEP/CONEP System. Data obtained from research participants may not be used for purposes other than those provided for in the protocol and/or in the free and informed consent.

IV.8 - In cases where it is not feasible to obtain the Free and Informed Consent Form or where obtaining it means substantial risks to the privacy and confidentiality of the participant's data or to the bonds of trust between the researcher and the researched, the exemption from the TCLE must be justifiably requested by the responsible researcher to the CEP/CONEP System, for assessment, without prejudice to the subsequent clarification process.

V – RISKS AND BENEFITS

All research involving human beings involves risks of varying types and degrees. The greater and more evident the risks, the greater the care required to minimize them and the protection offered by the CEP/CONEP System to participants. The possibilities of immediate or subsequent harm, on an individual or collective level, must be analyzed. Risk analysis is an essential component of ethical analysis, resulting in the monitoring plan that must be offered by the CEP/CONEP System in each specific case.

V.1 - Research involving human beings will be admissible when: a) the risk is justified by the expected benefit; and

b) in the case of experimental research in the health area, the benefit is greater, or, in the minimum, equal to the alternatives already established for prevention, diagnosis and treatment.

V.2 - Research whose benefits to its participants are exclusively indirect is admissible, provided that the physical, psychological, moral, intellectual, social, cultural or spiritual dimensions of these are considered.

V.3 - The responsible researcher, upon noticing any significant risk or harm to the research participant, whether or not foreseen in the Free and Informed Consent Form, must immediately communicate the fact to the CEP/CONEP System and assess, on an emergency basis, the need to adapt or suspend the study.

V.4 - In health research, as soon as the significant superiority of one intervention over another comparative intervention(s) is confirmed, the researcher must assess the need to adapt or suspend the ongoing study, aiming to offer everyone the benefits of the best regime.

V.5 - The CEP/CONEP System must be informed of all relevant facts that alter the normal course of the studies approved by it and, specifically, in research in the health area, of adverse effects and the significant superiority of one intervention over another or other comparatives.

V.6 - The researcher, the sponsor and the institutions and/or organizations involved in the different phases of the research must provide immediate assistance, in accordance with item II.3, as well as be responsible for providing full assistance to research participants with regard to complications and damages arising from the research.

V.7 - Research participants who suffer any type of harm resulting from their participation in the research, whether or not provided for in the Free and Informed Consent Form

That being said, they are entitled to compensation from the researcher, the sponsor and the institutions involved in the different phases of the research.

VI – RESEARCH PROTOCOL

The protocol to be submitted for ethical review will only be assessed if all documentation requested by the CEP/CONEP System is presented, considering the nature and specificities of each research. The BRASIL Platform is the official system for launching research for analysis and monitoring by the CEP/CONEP System.

VII – CEP/CONEP SYSTEM

It is integrated by the National Research Ethics Commission - CONEP/CNS/MS of the National Health Council and by the Research Ethics Committees - CEP - making up a system that uses its own mechanisms, tools and instruments for interrelation, in a cooperative work that aims, especially, to protect research participants in Brazil, in a coordinated and decentralized manner through an accreditation process.

VII.1 - Research involving human beings must be submitted for assessment by the CEP/CONEP System, which, upon analysis and decision, becomes jointly responsible for ensuring the protection of participants.

VII.2 - The CEPs are interdisciplinary and independent collegiate bodies, of public relevance, of a consultative, deliberative and educational nature, created to defend the interests of research participants in their integrity and dignity and to contribute to the development of research within ethical standards:

VII.2.1 - institutions and/or organizations in which research involving human beings is carried out may establish one or more Research Ethics Committees (CEP), according to their needs and meeting the normative criteria; and

VII.2.2 - in the absence of a CEP at the proposing institution or in the case of a researcher without institutional ties, CONEP will be responsible for indicating a CEP to carry out the analysis of the research among those that present the best conditions to monitor it.

VII.3 - CONEP is a collegiate body, of a consultative, deliberative nature, normative, educational and independent, linked to the National Health Council/MS.

VII.4 - The ethical review of research projects involving human beings must be associated with its scientific analysis.

VII.5 - The members of the CEP/CONEP System must have, in the exercise of their their functions, complete independence in decision-making, keeping the information known strictly confidential. In this way, they cannot suffer any type of pressure from hierarchical superiors or from those interested in a given research.
They must exempt themselves from decision-making when involved in the research under analysis.

VII.6 - Members of the CEP and CONEP may not be paid for performing their duties, and may only receive reimbursement for expenses incurred with transportation, accommodation and food. It is essential that they are exempted, during their working hours at the CEP or CONEP, from other obligations in the institutions and/or organizations to which they provide services, given the public relevance of the role.

VIII – RESEARCH ETHICS COMMITTEES (CEP)

RESPONSIBILITIES:

VIII.1 - evaluate research protocols involving human beings, with priority given to topics of public relevance and strategic interest in the SUS priority agenda, based on epidemiological indicators, issuing a duly justified opinion, always guided, among others, by the principles of impartiality, transparency, reasonableness, proportionality and efficiency, within the deadlines established in operational standards, avoiding redundancies that result in slow analysis;

VIII.2 - play an advisory and educational role in matters of ethics; and

VIII.3 - prepare its Internal Regulations.

IX – NATIONAL COMMISSION ON RESEARCH ETHICS (CONEP)

RESPONSIBILITIES:

IX.1 - examine the ethical aspects of research involving human beings, as well as the adequacy and updating of the relevant standards, and may, for this purpose, consult society whenever deemed necessary;

IX.2 - encourage popular participation in initiatives for Social Control of Research with Human Beings, in addition to the creation of institutional CEPs and other bodies, whenever such creation may mean strengthening the protection of research participants in Brazil; IX.3 - register and supervise the operation and cancel the registration of CEPs that make up the CEP/CONEP System;

IX.4 - analyze research protocols involving human beings, issuing a duly justified opinion, always guided, among others, by the principles of impartiality, transparency, reasonableness, proportionality and efficiency, within the deadlines established in operational standards, avoiding redundancies that result in slow analysis;

1. human genetics, when the project involves:

1.1. sending genetic material or any human biological material abroad to obtain genetic material, except in cases where there is cooperation with the Brazilian Government; 1.2. storage of biological material or human genetic data abroad and in the country, when agreed with foreign institutions or in commercial institutions;

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

1.4. research in the area of human reproductive genetics (reprogenetics);

1.5. research in behavioral genetics; and

1.6. research in which the irreversible dissociation of research participants' data is foreseen;

2. Human reproduction: research that deals with the functioning of the reproductive system, procreation and factors that affect the reproductive health of humans, and in these studies, all those affected by the procedures will be considered “research participants”. CONEP will be responsible for analyzing the project when it involves:

2.1. assisted reproduction;

2.2. manipulation of gametes, pre-embryos, embryos and fetus; and

2.3. fetal medicine, when involving invasive procedures;

3. therapeutic equipment and devices, new or not registered in the Country; 4. new invasive therapeutic procedures;

5. studies with indigenous populations; 6. research projects involving genetically modified organisms (GMOs), embryonic stem cells and organisms that represent a high collective risk, including organisms related to them, in the areas of: experimentation, construction, cultivation, handling, transportation, transfer, import, export, storage, release into the environment and disposal; 7. protocols for the establishment and operation of biobanks for research purposes;

8. research with coordination and/or sponsorship originating outside Brazil, except for those with co-sponsorship from the Brazilian Government; and

9. projects that, at the discretion of the CEP and duly justified, are deemed 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 CEP accreditation process, accrediting them according to competence levels that allow them to be delegated responsibilities originating from CONEP;

IX.7 - analyze and monitor, directly or indirectly, within the timeframe stipulated in the regulations, research protocols that involve the need for greater protection in relation to their participants, especially the risks involved. In this scope, the individual and, in an associated manner, national interests in scientific and technological development must always be considered first and foremost, as a basis for determining the relevance and opportunity in carrying out such research;

IX.8 - analyze and monitor, directly or indirectly, research protocols with conflicts of interest that hinder or make a fair local analysis unfeasible;

IX.9 - analyze, with justification, any protocol of the CEP/CONEP System, whenever it considers it pertinent; and IX.10 - analyze,

as a matter of urgency and with special processing, research protocols that are of relevant public interest, such as protocols that contribute to public health, justice and the reduction of social inequalities and technological dependencies, upon request from the Ministry of Health, or another Public Administration body, or at the discretion of the CONEP/CNS Plenary.

X - ETHICAL ANALYSIS PROCEDURE

X.1 - ETHICAL ANALYSIS OF CEP COMPETENCIES:

1. It is the responsibility of the CEP, after analysis, to issue a duly motivated opinion, in which the collegiate body's decision is presented in a clear, objective and detailed manner, within a period stipulated in the operational standard;

2. forward, after a well-founded analysis, the protocols under CONEP's jurisdiction, carefully observing all the documentation that must accompany this forwarding, in accordance with the current operational standard, including detailed proof of costs and sources of financing necessary for the research;

3. The CEPs are also responsible for:

a) maintain confidential custody of all data obtained in the execution of their task and archiving of the complete protocol;

b) monitor the development of projects, through biannual reports from researchers and other monitoring strategies, in accordance with the risk inherent to the research;

c) the CEP must keep the project, protocol and corresponding reports on file for a period of 5 years after the study is completed, and this may be archiving is processed in digital media;

d) receive reports of abuse or notification of adverse events that may alter the normal course of the study, deciding whether to continue, modify or suspend the research, and, if necessary, request the adaptation of the Consent Form;

e) request that the management of the institution and/or organization, or the competent public body, initiate an investigation in the event of knowledge or reports of irregularities in research involving human beings and, if proven, or if relevant, report the fact to CONEP and, where applicable, to other bodies; and

f) maintain regular and permanent communication with CONEP, through its Executive Secretariat.

X.2 - CONEP ETHICAL ANALYSIS PROCEDURE:

1. It is up to CONEP, within the period to be stipulated in the Operational Standard, to issue a duly motivated opinion, with a clear, objective and detailed analysis of all the elements and documents of the project;

2. CONEP is also responsible for monitoring, directly or indirectly, the protocols of research within your competence; and

3. The provisions on the following apply to CONEP, in cases where it operates as a CEP: Ethical Analysis Procedures of CEP.

X.3 - COMMON PROVISIONS FOR CEP AND CONEP:

1. CEP/CONEP members must exempt themselves from the analysis and discussion of the case, as well as from decision-making, when involved in the research;

2. CEP and CONEP may count on *ad hoc consultants,* people belonging to, or no, to the institution/organization, for the purpose of providing technical subsidies;

3. research that is not accompanied by the respective protocol should not be analyzed;

4. Approved research that is discontinued by the researcher is considered unethical. responsible, without justification previously accepted by CEP or CONEP;

5. The review of the CEP will result in its classification into one of the following categories:

a) approved;

b) pending: when the CEP considers it necessary to correct the submitted protocol, and requests a specific review, modification or relevant information, which must be met within the period stipulated in the operational standard; and

c) not approved;

6. The CEP may, if it deems it appropriate and convenient, during the course of the ethical review, request information, documents and other information necessary to fully clarify the issues, with the procedure being suspended until the requested elements are received;

7. Decisions not to approve may be appealed to the CEP itself and/or CONEP, within 30 days, whenever any new facts are presented to justify the need for a reanalysis;

8. The CEPs and CONEP must order the archiving of the research protocol in cases where the researcher in charge does not respond, within the specified period, to the requests made to him/her. They may also consider the protocol withdrawn, when requested by the researcher in charge; 9. Once the project has been approved,

the CEP, or CONEP, in cases where it acts as a CEP or in the exercise of its original competence, becomes jointly responsible for the ethical aspects of the research; and

10. Projects approved by the CEP, or by CONEP, in cases where it originally acts as CEP or in the exercise of its powers, are considered authorized for execution.

XI – RESPONSIBLE RESEARCHER

XI.1 - The researcher's responsibility is non-delegable and non-declinable and includes ethical and legal aspects.

XI.2 - It is the researcher's responsibility to:

a) submit the duly instructed protocol to the CEP or CONEP, awaiting the ethical approval decision, before starting the research;

b) prepare the Free and Informed Consent Form;

c) develop the project as outlined;

d) prepare and present partial and final reports;

e) submit data requested by CEP or CONEP at any time;

f) keep the research data in a physical or digital file, under your care and responsibility, for a period of 5 years after the end of the research;

g) forward the research results for publication, with due credit to the associated researchers and technical staff involved in the project; and

h) justify, with reasoned justification, before the CEP or CONEP, the interruption of the project or non-publication of results.

XII - OTHER PROVISIONS

XII.1 - Each thematic area of investigation and each type of research, in addition to respecting the provisions of this Resolution, must comply with sectoral requirements and specific regulations.

XII.2 - Research funding agencies and the editorial board of scientific journals must require documentation proving approval of the project by the CEP/CONEP System.

XII.3 - This Resolution, by its very nature, requires periodic reviews, according to the needs of the ethical, scientific and technological areas.

XIII - RESOLUTIONS AND SPECIFIC RULES

XIII.1 - The procedure for evaluating research protocols, as well as specific aspects of registration, such as granting, renewal or cancellation, and also the accreditation of Research Ethics Committees will be regulated by Resolution of the National Health Council.

XIII.2 - The accreditation process of the Research Ethics Committees that make up the CEP/ CONEP System will be addressed in a CNS Resolution.

XIII.3 - The ethical specificities of research in the social and human sciences and others that use methodologies specific to these areas will be covered in a complementary resolution, given their particularities.

XIII.4 - The ethical specificities of research of strategic interest to the SUS will be covered in a specific complementary Resolution.

XIII.5 - The procedural and administrative aspects of the CEP/CONEP System will be treated in the CNS Operational Standard.

XIII.6 - The typification and gradation of risk in the different research methodologies will be defined in a specific standard by the National Health Council.

XIV – FINAL PROVISIONS

CNS Resolutions Nos. 196/96, 303/2000 and 404/2008 are hereby revoked.

This Resolution shall come into force on the date of its publication.

ALEXANDRE ROCHA SANTOS PADILHA
President of the National Health Council

I hereby approve CNS Resolution **No.** 466 of December 12, 2012, under the terms of the Decree of Delegation of Competence of November 12, 1991.

ALEXANDRE ROCHA SANTOS PADILHA
Minister of State for Health