

## RESOLUTION N° 196/96 ON RESEARCH INVOLVING HUMAN SUBJECTS

The National Health Council Plenary Assembly, in fulfillment of its mandate, in its fiftieth ninth Ordinary Meeting realized in October 9th and 10th 1996, as set forth in Law n° 8.080 of 19 September 1990 and in Law n° 8.142 of 28 December 1990, resolves:

To approve the following guidelines and regulating norms for research involving human subjects.

### I PREAMBLE

This Resolution is based on the main international documents that gave rise to declarations and guidelines on research involving human subjects: the Nuremberg Code (1947); Declaration of Human Rights (1948); Declaration of Helsinki (1964, and its later versions dated 1975, 1983 and 1989); International Agreement on Civil and Political Rights (UN, 1966, approved by the Brazilian National Congress in 1992); Proposed International Guidelines for Biomedical Research Involving Human subjects (Council for International Organizations of Medical Science/World Health Organization 1982 and 1993); and International Guidelines for Ethical Review of Epidemiological Studies (CIOMS, 1991). It also meets the provisions of the Constitution of the Federative Republic of Brazil of 1988 and related Brazilian legislation: Consumer Rights Code; Civil Code and Penal Codes; Statute of Children and Adolescents; Basic Health Law N° 8.080 of 19 September 1990 (establishing the terms for health care and the organization and operation of corresponding services); Law N° 8.142 of 28 December 1990 (community participation in the management of the Unified Health System); Decree N° 99.438 of 7 August 1990 (organization and competence of the National Health Council); Decree N° 98.830 of 15 January 1990 (collection of scientific material and data by foreigners in Brazil); Law N° 8.489 of 18 November 1992 and Decree N° 879 of 22 July 1993 (removal of tissues, organs and other parts of the human body for humanitarian and scientific purposes); Law N° 8.501 of 30 November 1992 (utilization of cadavers); Law N° 8.974 of 5 January 1995 (use of genetic engineering techniques and release of genetically modified organisms into the environment); Law N° 9.279 of 14 May 1996 (regulates the rights and duties pertaining to industrial property); and pertinent statutes.

This Resolution includes, from the point of view of the individual and communities, the four basic principles of bioethics: autonomy, non-maleficence, beneficence, and justice, among others, and aims at ensuring the rights and duties of the scientific community, the research subjects and the State.

The contextual nature of these consideration requires that periodical reviews of this Resolution be made, according to the needs of the technical-scientific and ethics areas.

It is further emphasized that each thematic area and each modality of research must both respect the principles set forth in this text and meet all specific regulations and sectorial requirements.

### II TERMS AND DEFINITIONS

Within the scope of this Resolution, the following terms are thus defined:

- II.1 **Research** - class of activities designed to develop or contribute to generalizable knowledge. Generalizable knowledge consists of theories, relationships or principles, or the accumulation of information on which they are based, that can be corroborated by accepted scientific methods of observation and inference.
- II.2 **Research involving human subjects** - research that individually or collectively, directly

or indirectly, involves a human subject, totally or partially, including the management of information and materials.

- II.3 **Research Protocol** - document describing the fundamental aspects of the investigation, information about the research subjects, and the qualification of the researchers and all responsible parties.
- II.4 **Main researcher** - person responsible for the coordination and execution of the research and for the integrity and well-being of the research subjects.
- II.5 **Research institution** - private or public, legally constituted and authorized organization in which scientific investigations are carried out.
- II.6 **Promoter** - individual or institution responsible for promoting the research.
- II.7 **Sponsor** - individual or corporation that provides financial support to the research.
- II.8 **Research risk** - possibility of injury to the physical, psychic, moral, intellectual, social, cultural, or spiritual dimensions of the human subject, during any phase of an investigation, or resulting therefrom.
- II.9 **Injury associated to or resulting from research** - immediate or delayed injury to an individual or community, with proven, direct or indirect, causal relationship resulting from the scientific study.
- II.10 **Research subject** - a participant researched individually or collectively, on a voluntary basis, without any form of remuneration.
- II.11 **Freely given and informed consent** - agreement of the research subject and/or his/her legal guardian, without flaws (simulation, fraud, or error), dependency, subordination, or intimidation, after a complete and detailed explanation about the nature of the research, its objectives, methods, foreseen benefits, potential risks, and discomfort that such research may cause, set forth in a term of consent, authorizing the subject's voluntary participation in the research.
- II.12 **Indemnity** - financial compensation provided as a reparation of immediate or delayed injury caused by research to a human subject of such research.
- II.13 **Reimbursement** - coverage of expenditures incurred by the research subject, only as a result of his/her participation in the research.
- II.14 **Committees on Ethics in Research (CER)** - interdisciplinary and independent collegiate bodies, with *munus publico*, of consultative, deliberative or educational nature, created to defend the interests of the research subjects, in their integrity and dignity, and to contribute to the development of research within ethical standards.
- II.15 **Vulnerability** - pertaining to the state of individuals or groups that, for any reason or motive, have their capacity for self-determination reduced, particularly as refers to freely giving their informed consent.
- II.16 **Disability** - pertaining to possible research subjects whose civil capacity to give his/her freely given and informed consent is impaired, and must be assisted or represented in accordance with the Brazilian legislation in effect.

### III ETHICAL ASPECTS OF RESEARCH INVOLVING HUMAN SUBJECTS.

Research involving human subjects must meet the fundamental scientific and ethical requirements.

#### III.1 Ethics in research signifies:

- a) freely given and informed consent of target-individuals and the protection of vulnerable groups and the legally disabled (**autonomy**). To that end, research involving human subjects must always preserve their dignity, respect their autonomy and defend them in their vulnerability;
- b) weighing risks and benefits, both actual and potential, individual and collective (**beneficence**), making a commitment to maximize benefits and minimize distress and risks;
- c) ensuring that predictable injury will be prevented (**non-maleficence**);
- d) social relevance of the research, with significant advantages to the research subjects and minimization of the burden to vulnerable individuals, which guarantees equal consideration of all interests involved and preserves the socio-humanitarian purpose of research (**justice and equality**).

III.2 Any procedure which involves human subjects and has not been fully accepted in the scientific literature, regardless of its nature, will be considered research and, therefore, must comply with the guidelines set forth in this Resolution. The above mentioned procedures include, *inter alia*, those of instrumental, environmental, nutritional, educational, sociological, economic, physical, psychical or biological nature, whether pharmaceutical, clinical or surgical, regardless of their purpose being prevention, diagnosis, or therapy.

III.3 Research involving human subjects, regardless of the field of knowledge, must comply with the following requirements:

- a) to be in accordance with the scientific principles that justify it and the concrete possibility of answering uncertainties;
- b) to be based on prior laboratory experiments with animals or on other scientific facts;
- c) to be carried out only when the knowledge to be obtained cannot be otherwise acquired;
- d) to always favour the probability of foreseen benefits, rather than predictable risks;
- e) to follow appropriate methodology. If a random distribution of the research subjects into experimental and control groups is necessary, it is essential that it not be possible, *a priori*, to establish the advantages of a given procedure over the other, through a review of literature, observation, or other methods not involving human subjects;
- f) to fully justify, as applicable, the use of placebos, in terms of non-maleficence and of methodological requirement;
- g) to have the freely given and informed consent of the research subject and/or his/her legal guardian;
- h) to have the necessary human and material resources to ensure the well-being of the

research subjects and to harmonize the qualifications of the researcher and the proposed research project;

- i) to plan procedures that will ensure confidentiality and privacy, protection of the image and non-stigmatization of the research subjects, guaranteeing that the information obtained will not be used to the detriment of individuals and/or communities, including injury to their self-esteem, prestige and/or economic or financial status;
- j) to be developed, preferably, in fully capable individuals. Vulnerable individuals or groups should not be research subjects when the desired information can be obtained from fully capable individuals, unless the research is to directly benefit the vulnerable individuals or groups. In such cases, the rights of individuals or groups that wish to participate in the research must be guaranteed, and their vulnerability and legal incapacitation assuredly protected;
- l) to respect the cultural, social, moral, religious, and ethical values, as well as the mores and habits, when research involves communities;
- m) to guarantee that, whenever possible, research in communities is translated into benefits whose effects continue to be felt after the research is concluded. The project must analyze the needs of each of the members of the community and existing differences among them, and make clear how such differences will be respected;
- n) to guarantee the individuals and communities where the research was undertaken a return on the benefits obtained in the research. When it is really beneficial to foster or encourage changes in practices or behaviors in the interest of a community, the research protocol must include, whenever possible, provisions to communicate such benefits to the individuals and/or communities;
- o) to communicate the results of the research to the health authorities, whenever such results can contribute to the improvement in the health of society at large, preserving, however, the image of the research subjects and guaranteeing that they will not be stigmatized or their self-esteem diminished;
- p) to ensure the research subjects the benefits resulting from the research project, in terms of social return, access to procedures, products or research agents;
- q) to ensure the research subjects the required follow-up, treatment, or orientation, in screening surveys; to demonstrate that benefits prevail over risks and burdens;
- r) to guarantee the absence of conflicts of interest between the researcher and the research subjects or sponsor of the research project;
- s) to submit evidence, in case of research conducted abroad or with external cooperation, of commitments and advantages to the research subjects and to Brazil, which will result from the implementation of the research. In such cases, the researcher and national institution co-responsible for the research must be identified. The protocol must comply with the requirements of the Declaration of Helsinki and include, among the documents submitted to the evaluation of the Committee for Ethics in Research of the Brazilian institution, an authorization issued in the country of origin. The Committee for Ethics in Research will require compliance with its own ethical parameters. Studies sponsored by external organizations must also respond to training needs in Brazil, so that the country be able to independently develop similar projects.

- t) to use the biological material and data obtained in the research only for the purposes set forth in the research project protocol;
- u) to take into account, in research carried out in women in the reproductive age or pregnant women, the evaluation of risks and benefits, as well as possible interference with the fertility, pregnancy, embryo or fetus, labor, puerperium, nursing and the new born;
- v) to consider that research in pregnant women must be preceded by research in non-pregnant women, except when the basic objective of such research is pregnancy;
- x) to foster, in multi-centre studies, the participation of the researchers who will conduct the research in the overall design of the research project; and
- z) to discontinue the research project only after the Committee for Ethics in Research that initially approved it has analyzed the reasons for interrupting it.

#### **IV FREELY GIVEN AND INFORMED CONSENT**

In order to respect human dignity, research must only be carried out after informed consent has been freely given by the prospective research subjects, whether individuals or groups, who have expressed their agreement to participate in the research, on their own behalf and/or through their legal guardians.

**IV.1** Accessible language must be used in providing the prospective subjects information about the research, always including the following points:

- a) rationale, aims and methods to be used in the research;
- b) any foreseeable risks or discomfort to the subject, as well as benefits that might reasonably be expected, associated with participation in the research;
- c) existing alternative methods;
- d) medical follow up and care to be provided to the subjects of research, as well as the identity of those responsible for such actions;
- e) assurance of information about the methodology, before and during the research, including the possibility of inclusion in a control or placebo group;
- f) freedom of the individual to refuse participation or withdraw his/her consent, at any time during the research, without any penalty or loss of benefits to which he/she would otherwise be entitled;
- g) extend to which confidentiality of records will be maintained, so as to safeguard the privacy of the research subjects;
- h) forms of reimbursement of current expenditures resulting from participation in the research; and
- i) types of indemnity to cover possible injury resulting from the research.

**IV.2** The terms of freely given and informed consent must meet the following requirements:

- a) they must be drawn up by the main researcher and express compliance with each of the

above mentioned requirements;

- b)** they must be approved by the Committee for Ethics in Research that evaluates the research;
- c)** they must be signed by or identified with the fingerprint of each and every research subject or their legal guardians; and
- d)** an original and a copy must be signed by the research subject, the latter to be kept by the research subject or his/her legal guardian and the former to be filed.

**IV.3** In the event there is any hindrance to the freedom of or access to the information required by the research subject for giving adequate consent, the following requirements must be fulfilled:

- a)** in research involving children and adolescents, individuals who are mentally ill or disturbed, and persons with substantially impaired or diminished autonomy, the choice of said research subjects must be clearly justified and specified in the research protocol, which must be approved by the Committee for Ethics in Research and meet all the requirements of freely given and informed consent, through the legal guardian of the prospective research subject, without detriment to the right of information of the individual, within the limits of his/her capacity of understanding;
- b)** freedom of consent must be particularly guaranteed to those individuals who, although adults and capable, are exposed to specific conditioning or to the influence of authority, specially students, military personnel, employees, prison inmates, inmates of rehabilitation centres, shelters, homes, religious or other institutions, ensuring them complete freedom to participate, or not, in the research, without any retaliation;
- c)** in the event it is impossible to record the freely given and informed consent of the research subject, such fact must be duly documented, with an explanation of the causes and the technical opinion of the Committee for Ethics in Research;
- d)** research on individuals diagnosed as brain dead can only be carried out after meeting the following conditions:
  - document proving brain death (death certificate);
  - explicit consent of the relatives and/or legal guardian, or prior statement by the individual;
  - total respect for the dignity of the human subject, and not mutilation or violation of the body;
  - no additional financial burden for the family;
  - no deleterious effect to other patients awaiting admission or treatment;
  - possibility of obtaining scientific knowledge which is relevant, new, or unobtainable through other means;
- e)** in communities with a different culture, including Indigenous communities, prior consent must be obtained from the community, through its leaders, without foregoing, however, efforts to obtain individual consent;
- f)** when the merit of the research depends on some restriction of information to the subjects, such fact must be duly stated and justified by the researchers, and submitted to the Committee for Ethics in Research. The data obtained from such research subjects cannot be used for purposes other than those contemplated in the protocol and/or terms of consent.

## **V RISKS AND BENEFITS**

Any research involving human subjects involves risks. Possible injury may be immediate or delayed and may involve an individual or a community.

**V.1** Despite potential risks, research involving human subjects will be admissible provided that:

- a)** it is highly probable that it will generate knowledge that will permit understanding, preventing, or attenuating a problem that affects the well-being of the research subjects and other individuals;
- b)** the risk is justified by the importance of the expected benefit; and
- c)** the benefit is greater than or equal to other, already established, prevention, diagnosis or treatment alternatives.

**V.2** Research without direct benefit to individuals must include conditions easily tolerated by the research subjects, considering their physical, psychological, social, and educational status.

**V.3** If the main researcher perceives any risk or injury to the health of the research subjects, resulting therefrom and unforeseen in the terms of consent, he/she must interrupt the research immediately. Likewise, as soon as the advantage of a method under study has been demonstrated, the project must be interrupted and all research subjects must be offered the benefits of the best regime.

**V.4** The Committee for Ethics in Research of the institution must be informed of any adverse effects or relevant facts that alter the normal course of the study.

**V.5** The researcher, the sponsor and the institution must assume full responsibility for providing comprehensive care to the research subjects, as regards complications and injury resulting from foreseen risks.

**V.6** Research subjects that suffer any type of injury resulting from their participation in the research, regardless of such injury having been foreseen in the terms of consent, or not, have the right to receive comprehensive medical care, as well as an indemnity.

**V.7** Under not circumstance will the research subject be required to waive his/her right to indemnity for injury resulting from the research. The form used in obtaining the freely given and informed consent of the research subjects must not contain any clause exempting the researcher from responsibility or depriving any individual of his/her legal rights, including the right to seek an indemnity for injury resulting from the research.

## **VI RESEARCH PROTOCOL**

Any research protocol submitted to ethical review will only be considered if the following documents, in the Portuguese language, have been attached:

**VI.1** title page: name of the project; name, identity card number, tax-payer number, mailing address, and telephone number of the main researcher and the sponsor of the research;

and the name and signatures of the main officers of the institution and/or organization;

**VI.2** a description of the research, including the following items:

- a) description of the purposes and hypothesis to be tested;
- b) scientific background and data justifying the research. If the purpose is to test a new health product or device, whether external or domestic, the status of registration at the regulatory agencies in the country of origin must also be indicated;
- c) detailed and comprehensive description of the research project (material and methods, number and characteristics of patients, expected results, and bibliography);
- d) critical analysis of the risks and benefits;
- e) total duration of the research, after approval has been obtained;
- f) terms of responsibility of the researcher, institution, promoter, and sponsor of the research;
- g) statement about the criteria to be used to interrupt or close the research;
- h) location of the research: detailed description of the health services, centres, communities, and institutions in which the various stages of the research will take place;
- i) demonstration of the existence of the infrastructure required to execute the research and deal with possible problems resulting therefrom, with the documented agreement of the institution;
- j) detailed financial budget: funds, sources and destination, as well as the form or value of remuneration of the researcher;
- l) statement about the preexisting agreement on the property of the information generated in the research, demonstrating the absence of any restrictive clause referring to the public dissemination of the results, except when a patent is sought; in the latter case, the results must be published as soon as the patent process has been concluded;
- m) declaration about the results of research being made public, whether favourable or not; and
- n) declaration about the use and destination of the material and/or data collected in the research.

**VI.3** information about the research subject:

- a) a description of the characteristics of the population to be studied: size, age bracket, sex, colour (Brazilian Geographical and Historical Institute - IBGE classification), general health status, social classes and groups, etc; explanation of the reasons for using vulnerable groups;
- b) a description of any methods that directly affect the research subjects;
- c) a clear statement about the sources of research material, such as specimens, records and data to be obtained from human subjects. It is necessary to indicate if the material

will be obtained specifically for the purpose of the research, or used for other purposes;

- d) description of the plans for recruiting the individuals and the procedures to be used, as well as the admission and withdrawal criteria;
- e) submit the specific form or terms of consent to be used in the research to the approval of the Committee for Ethics in Research, including information about the circumstances in which the informed consent will be obtained, who will obtain it and the nature of the information to be supplied to the research subjects;
- f) description of any anticipated risks and evaluation of their probability and severity;
- g) description of the measures to be used to protect against or minimize any possible risks. When appropriate, description of the measures to be used to ensure the necessary health care, in the case of injury to the individuals. Description of the procedures to be used to monitor data collection and to ensure the safety of the individuals, including safeguarding confidentiality; and
- h) estimates of any reimbursements to be made to the research subjects, which cannot be so large as to interfere in the autonomy of the individual, or of his/her legal guardian, to decide whether to participate in the research.

**VI.4** qualification of researchers: *Curriculum vitae* of the main researcher and other participants.

**VI.5** affidavit from the main researchers and the institution that the terms of this Resolution will fully enforced.

## **VII COMMITTEE FOR ETHICS IN RESEARCH (CER)**

Any research involving human subjects must be submitted to the appreciation of a Committee for Ethics in Research (CER).

**VII.1** The institutions in which research involving human subjects are carried out must set up a Committee for Ethics in Research (CER), as needed.

**VII.2** In the event a CER cannot be set up, the institution or the main researcher must submit the research project to the appreciation of the Committee for Ethics in Research (CER) of another institution, preferably to those indicated by the National Committee for Ethics in Research (CONEP/MS).

**VII.3** **Organization** - The institution will be responsible for the organization and creation of the CER, in accordance with the regulatory guidelines and norms set forth in this Resolution, as well as for providing the CER the necessary conditions for its operation.

**VII.4** **Membership** - The CER will be constituted by a group of no less than seven (7) members. Its membership must include professionals from the health, exact, social, and human sciences, including, for example, legal scholars, theologians, sociologists, philosophers, bioethicists, and at least one member of society, representing the users of the institution. The membership of the CER may vary, depending on the specificities of the institution and the lines of research to be analyzed.

**VII.5** The membership of CERs must always be multi- and transdisciplinary in nature; not more

than half its members may come from a single professional category; and both sexes must be represented. The CER may also have *ad hoc* consultants internal or external to the institution, whose function is to provide the CER technical input.

- VII.6** In the case of research in vulnerable groups, communities and the society at large, a representative of such prospective research subjects must be invited to be an *ad hoc* member of the CER and participate in the analysis of the specific project.
- VII.7** In the case of research in Indigenous populations, a consultant thoroughly familiar with the customs and traditions of the community must participate in the CER.
- VII.8** CER members must exempt themselves from decision making whenever directly involved in the research being analyzed.
- VII.9** **Selection and mandate of the Members of the CER** - The membership of every CER must be defined by the institution, and at least half of its members must have experience in research and be elected by their peers. The chairman will be selected by and among the members of the CER, during the first work meeting. The members of the CER will be elected to a three-year renewable mandate.
- VII.10 Remuneration** - The members of the CER cannot be remunerated for participating in the committee. It is recommended, however, that they be exempted from other duties, by the institutions that employ them, during the time devoted to work in the committee. The members of the CER may also be reimbursed for expenditures incurred with food, lodging and transportation.
- VII.11 Archives** - The CER must keep the research project, its protocol and respective reports on file for five (5) years after the conclusion of the research.
- VII.12 Autonomy of work** - In the fulfillment of their function, the members of the CER must have complete decision-making autonomy and must maintain any information received confidential. Thus, they cannot be subjected to any type of pressure from their supervisors, or from other interested parties in a given research; must guard against financial involvement; and must not be submitted to conflicts of interest.
- VII.13 Duties of the Committee for Ethics in Research (CER):**
- a) to review all protocols of research involving human subjects, including multicentre research; the CER will be responsible for all decisions pertaining the ethics of the research to be developed by the institution, so as ensure the integrity and rights of volunteers participating in said research;

- b)** to issue written technical opinions, within thirty (30) days, clearly identifying the assay, documents studied and date of review. The review of each protocol will lead to its being classified in one of the following categories:
- approved;
  - pending action: when the committee considers that the protocol is acceptable, but identifies certain problems in the protocol, the consent form, or both, and recommends changes or requests relevant information within sixty (60) days;
  - withdrawn: when said deadline is not met, and the protocols are still pending;
  - not approved; and
  - approved and submitted, together with the respective technical opinion, to the appreciation of the National Committee for Ethics in Research (CONEP/MS), as stipulated in chapter VIII, item 4.c.
- c)** to safeguard the confidentiality of all data obtained during their work and to file the complete protocol, which will remain available to the health authorities;
- d)** to monitor the development of the research projects, by means of annual reports from the researchers;
- e)** to act as consultant and educational source, fostering reflection about ethics in science;
- f)** to receive from the research subjects, or any other interested party, reports of abuses or adverse facts which may alter the normal course of the study, and decide on the continuance, modification, or suspension of the research, and, if necessary, adapt the terms of consent. Any research interrupted without a justification accepted by the CER that approved its implementation will be considered unethical;
- g)** to require that the institution investigate reports of irregularities of an ethical nature and if such reports are found to be true, communicate the fact to the National Committee for Ethics in Research (CONEP/MS) and, if necessary, to other agencies; and
- h)** to keep regular and permanent communication with CONEP/MS.

#### **VII.14 Role of the CER:**

- a)** The ethical review of each and every proposal of research involving human subjects cannot be dissociated from the scientific analysis of said proposal. Any research unaccompanied by the respective protocol will not be analyzed by the committee.
- b)** Each CER must establish its own bylaws, including the working methodology, such as minutes taking, annual plan of activities, frequency of meetings, minimum number of members necessary to begin a meeting, deadlines for issuing technical opinions, criteria for requesting technical input from experts, decision-making model, etc.

### **VIII NATIONAL COMMITTEE FOR ETHICS IN RESEARCH (CONEP/MS)**

The National Committee for Ethics in Research (CONEP/MS) is an independent collegiate body, accountable to the National Health Council and with powers to provide consultancy and to deliberate, regulate, and inform.

The Ministry of Health will adopt the necessary measures for the full operation of the National Committee for Ethics in Research and its Executive Secretariat.

**VIII.1 Membership:** The CONEP will be constituted of thirteen (13) regular members, and respective alternate members. It must have multi- and transdisciplinary representation and include both male and female members. Five of the members must be well-known individuals in the field of ethics in research and health and eight, personalities having made noteworthy contributions to theology, law and other fields of knowledge, one of whom must always come from the health management area. The members must be selected from indicative lists drawn up by institutions whose CERs are registered at CONEP. Seven (7) members will be selected by the National Health Council and six (6), by drawing lots. The CONEP may also have consultants and *ad hoc* members, and representation of the users.

**VIII.2** Each CER may indicate two names.

**VIII.3** The members of CONEP are elected to a four-year mandate; seven or six of the members will be renewed, alternatively, every two years.

**VIII.4 Duties of the National Committee for Ethics in Research (CONEP/MS)** - The CONEP is responsible for reviewing all ethical aspects of research involving human subjects, as well as adapting and updating pertinent guidelines and norms. The CONEP will consult society whenever necessary. Its duties include, *inter alia*:

- a) to foster the creation of institutional and other Committees for Ethics in Research (CER);
- b) to register institutional and other CERs;
- c) to approve, within sixty (60) days, and monitor the protocols of research in special areas, such as:
  - 1 - human genetics;
  - 2 - human reproduction;
  - 3 - pharmaceutical products, medical drugs, vaccines, and diagnostic tests, either new (phases I, II and III) or without registration in the country (even in phase IV), or when the research is related to the use of products that have modes, indications, doses, or ways of administration different from those previously established, including their combined use;
  - 4 - health equipment, inputs and devices, either new or without registration in the country;
  - 5 - new procedures not yet established in the literature;
  - 6 - Indigenous populations;
  - 7 - projects involving biosafety;
  - 8 - research coordinated from abroad or with the participation of foreigners, and research involving the sending of biological material to foreign countries; and
  - 9 - research projects which a CER considers worthy of analysis by CONEP;
- d) to promote specific ethical standards for research, including research in special areas, as well as recommendations for the application of said standards;

- e) to act as final appellate body, *ex-officio* or on the basis of regularly supplied information, claims, or requests made by interested parties, and to decide the matter at issue within than sixty (60) days;
- f) to review responsibilities, forbid or interrupt research, on a temporary or permanent basis, and to request protocols of research for ethical review, including protocols already approved by a CER;
- g) to set up an information system to monitor the ethical aspects of research involving human subjects in the country, and to keep the databases updated;
- h) to provide input and advice to the Ministry of Health, the National Health Council and other agencies of the Unified Health System, as well as to the government and society at large, on ethical issues pertaining to research on human subjects;
- i) to disseminate information about this and other norms related to ethics in research involving human subjects;
- j) the CONEP, together with other sectors of the Ministry of Health, will establish norms and criteria for the accreditation of Research Centres. Said accreditation must be proposed by the sectors of the Ministry of Health, according to their needs, and approved by the National Health Council; and
- l) to establish its own bylaws.

**VIII.5** The National Committee for Ethics in Research will submit to the consideration of the National Health Council:

- a) proposals of general ethical standards to be applied to research involving human subjects, including changes to this norm;
- b) annual work plans; and
- c) annual reports of its activities, including a summary of all Committees for Ethics in Research established and research projects analyzed.

## **IX OPERATIONALIZATION**

- IX.1** Each and every research project involving human subjects must comply with the recommendations set forth in this Resolution and the documents endorsed in its preamble. The responsibility of the researcher cannot be transferred or refused, and includes all ethical and legal aspects.
- IX.2** The researcher must:
- a)** submit a duly documented protocol of research to the CER and await the decision of said body before beginning the research;
  - b)** conduct the research project as set forth in the protocol;
  - c)** draw up and submit partial and final reports;
  - d)** submit any data requested by the CER, at any time;
  - e)** keep in a file, under his/her guard, for five years, all research data, including individual records and all other documents recommended by the CER;
  - f)** submit the results for publication, with due credit given to the associate researchers and technical personnel participating in the project; and
  - g)** justify to the CER the interruption of the project or the non-publication of its results.
- IX.3** Each institutional Committee for Ethics in Research must register at the National Committee for Ethics in Research (CONEP/MS).
- IX.4** After a research project has been approved, the CER will be co-responsible for the ethical aspects of the research.
- IX.5** The projects approved by the CER can be considered approved, with the exception of those in special areas, which must be submitted to the consideration of CONEP/MS, after being approved by the institutional CER.
- IX.6** Research on new medical drugs, vaccines, diagnostic tests, and health equipment and devices must be forwarded to CONEP/MS by the CER and, after issuing a technical opinion, by CONEP/MS to the Secretary of Health Surveillance.
- IX.7** The research financing agencies and publishing body of scientific journals must demand documented evidence of the research having been approved by the CER and/or CONEP, as applicable.
- IX.8** The institutional CERs must submit quarterly reports to CONEP/MS, together with a list of the research projects analyzed, approved and concluded, as well as on-going research projects; they must immediately report any research project interrupted.

## **X TRANSITORY PROVISIONS**

- x.1** The Executive Workgroup (EWG) established by Resolution CNS 170/95 will assume the duties of CONEP until the CONEP is established and will be responsible for:

- a)** taking all measures required to establish the National Committee for Ethics in Research (CONEP/MS); and
- b)** setting up norms for the registration of institutional CERs.
- X.2** The Executive Workgroup must fulfill its mandate in 180 days.
- X.3** The CER of each institutions must survey and analyze, within ninety (90) days, all on-going research projects involving human subjects and sent CONEP a list of said projects.
- X.4** Resolution 01/88 is hereby revoked.