Série Cadernos Técnicos

Versão Preliminar

NORMAS PARA PESQUISA ENVOLVENDO SERES HUMANOS

(Res. CNS 196/96 e outras)

Conselho Nacional de Saúde
Comissão Nacional de Ética em Pesquisa - CONEP
Brasil

Série Cadernos Técnicos

Preliminary Version

RULES ON RESEARCH INVOLVING HUMAN SUBJECTS

(Res. CNS 196/96 and others)

National Health Council
National Commission for Research Ethics - CONEP
Brazil

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Rules on research involving human subjects
(Res. CNS 196/96 and others)

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INTODUCTION

The permanent improvement of the standards for research involving human beings has been a noteworthy characteristic of the scientific community in Brazil. In addition to intense efforts to maintain nationally and internationally recognized institutions, our science and technology area has shown great sensitivity and social commitment, with special emphasis on the relentless defense of the citizenship rights of human beings who are subjects of research.

These rights are specifically set forth in the main resolutions and norms of the National Health Council (CNS) on Research Involving Human Beings, placing Brazil among the most advanced countries in this noble field of activities.

At present there are 255 Research Ethics Committees (CEP) already approved and operating in the country, and another 40 have been submitted for approval. A large number of research projects have received the go-ahead of the CEPs from the ethics standpoint, of which 1,040 belong to the eight special thematic areas and were evaluated by the National Commission on Research Ethics (CONEP) during its first three years of existence. The improvement of the quality of the CEPs has led to an intensification of the decentralization process, in which CONEP carefully monitors the gradual transfer of its competencies to the CEPs, including responsibilities over research on special thematic areas.

It must be emphasized that the impressive progress of the National Health Council in this area in the last eleven years not only included the fulfillment of its legal obligations to exert Social Control, but also helped eliminate important gaps in the field of Management of Science, Technology and Ethics of Health Research Ethics. These gaps were definitely eliminated from the structure of the Ministry of Health by the creation of the Department of Science and Technology of the Secretariat of Health Policies in 1999. This agency has shown great skill and

commitment in our development of health science and technology and in managing the monitoring of the ethics component of research involving human beings.

Much progress has been made in the development of the interfaces of the competencies of the National Health Council and its National Commission on Research Ethics, which work in the field of Social Control, on the one hand, and the Department of Health Science and Technology of the SPS/MS, which works in the field of Management, on the other. This is a very promissory event because it shall facilitate, for the first time, the coexistence of these two bodies and their synergetic action.

Lastly, another important piece of information is the revitalization of the Inter-sectorial Commission on Science and Technology of the National Health Council, whose joint action with CONEP/CNS and DECIT/SPS/MS shall certainly enable our country to overcome other challenges in the fields of Technology Evaluation and Ethics in the Allocation of Health Resources, among others.

NELSON RODRIGUES DOS SANTOS
General Coordinator of the
NATIONAL HEALTH COUNCIL

RESOLUTION N° 196/96 ON RESEARCH INVOLVING HUMAN SUBJECTS

The National Health Council, in fulfillment of its mandate, as set forth in Decree N° 93933 of 14 January 1987, 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 for Research Ethics (CEP) - 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 procedures 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 RESEARCH ETHICS (CEP)

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

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

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

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

VII.4 - Membership - The CEP 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 CEP may vary, depending on the specificities of the institution and the lines of research to be analyzed.

VII.5 - The membership of CEP 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 CEP may also have *ad hoc* consultants internal or external to the institution, whose function is to provide the CEP 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 CEP 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 CEP.

VII.8 - CEP 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 CEP - The membership of every CEP 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 CEP, during the first work meeting. The members of the CEP will be elected to a three-year renewable mandate.

VII.10 - Remuneration - The members of the CEP 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 CEP may also be reimbursed for expenditures incurred with food, lodging and transportation.

VII.11 - Archives - The CEP 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 CEP 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 Research Ethics (CEP):

a) to review all protocols of research involving human subjects, including multicentre research; the CEP 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 Commission for Research Ethics (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 CEP 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 Commission for Research Ethics (CONEP/MS) and, if necessary, to other agencies; and

h) to keep regular and permanent communication with CONEP/MS.

VII.14 - Role of the CEP:

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 CEP 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 Commission for Research Ethics (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 CEPs 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 CEP 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 Commission for Research Ethics (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 Research Ethics (CEP);

b) to register institutional and other CEPs;

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 CEP 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-oficio* 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 CEP;

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 Commission for Research Ethics 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 Comittees for Research Ethics 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 CEP 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 CEP, 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 CEP;

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 CEP the interruption of the project or the non-publication of its results.

IX.3 - Each institutional Committee for Research Ethics must register at the National Commission for Research Ethics (CONEP/MS).

IX.4 - After a research project has been approved, the CEP will be co-responsible for the ethical aspects of the research.

IX.5 - The projects approved by the CEP 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 CEP.

IX.6 - Research on new medical drugs, vaccines, diagnostic tests, and health equipment and devices must be forwarded to CONEP/MS by the CEP 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 CEP and/or CONEP, as applicable.

IX.8 - The institutional CEPs 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 Commission for Research Ethics (CONEP/MS); and

b) setting up norms for the registration of institutional CEPs.

X.2 - The Executive Workgroup must fulfill its mandate in 180 days.

X.3 - The CEP 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.

NATIONAL HEALTH COUNCIL
RESOLUTION Nº 240, DATED 5 JUNE 1997

The Plenary of the National Health Council in its 66th Regular Meeting, held on 4 and 5 June 1997, in the exercise of its competencies, as set forth in its by-laws, and the attributions in Law 8.080 and Law 8.142, respectively dated 19 September 1990 and 28 December 1990, and considering the need to define the term "users" for the purpose of participation in the Committee for Research Ethics of institutions, as established in National Health Council Resolution CNS 196/96, item VII.4, Resolves that:

a) the term "users" shall have a broad interpretation contemplating multiple collectivities that benefit from the work executed by the Institution;

b) representatives of users are people who are able to express the points of view and interests of individuals and/or groups who are subjects of research in a given institution and representative of collective interests and divers groups;

c) in the case of reference institutions that focus on specific publics or pathologies, the representatives of the "users" must necessarily belong to the target population of said units or to an organized group that defends their interests;

d) in places where there are forums or councils representing the users and/or patients of specific pathologies and handicaps, said organizations are empowered to indicate the representatives in the Ethics Committees; and

e) the respective Municipal Health Council shall be informed of the names of the representatives of users indicated to Committee for Research Ethics.

CARLOS CÉSAR S. DE ALBUQUERQUE
President of the National Health Council

I hereby ratify CNS Resolution nº 240, dated 5 June 1997, in the terms of the Decree on the Delegation of Competency dated 12 November 1991.

CARLOS CÉSAR S. DE ALBUQUERQUE
Minister of State for Health

NATIONAL HEALTH COUNCIL
RESOLUTION Nº 251, DATED 7 AUGUST 1997

Plenary of the National Health Council in its 15th Special Meeting, held on 5 August 1997, in the exercise of its competencies, as set forth in its by-laws, and the attributions in Law nº 8.080 and Law nº 8.142, respectively dated 19 September 1990 and 28 December 1990, Resolves:

To approve the following norms of research involving human beings in the thematic area of research with new pharmaceutical products, medicines, vaccines, and diagnostic tests:

I - PREAMBLE

I.1 - This Resolution incorporates all provisions contained in Resolution 196/96 of the National Health Council on Guidelines and Norms Regulating Research Involving Human Beings, which this Resolution complements in the specific thematic area of research with new pharmaceutical products, medicines, vaccines, and diagnostic tests.

I.2 - It also refers to the Resolution on the Common Market Group (GMC) Nº 129/96, signed by Brazil, which establishes the technical regulations for ascertaining [the implementation of] good practices in clinical research.

I.3 - The norms, resolutions and regulations issued by the Health Surveillance Secretariat of the Ministry of Health (SVS/MS) should be fully complied with, and SVS/MS authorization is required to execute and subsequently follow up and control the technical development of research projects in [the area of] Clinical Pharmacology (Phases I, II, III, and IV of products not yet registered in the country) and Bioavailability and Bioequivalence. Research projects in this area should comply with the provisions of Law nº 6.360 (23 September 1976), regulated by Decree Nº 79.094 (5 January 1977).

I.4 - In any clinical essay and particularly when there are conflicts of interests associated with new products, the dignity and well-being of the research subject must prevail over any other interests, whether economic, scientific, or of the community.

I.5 - It is essential that all research in this thematic area be founded on recognized scientific norms and on knowledge based on in vitro laboratory experiments and pertinent literature.

I.6 - It is necessary that the investigation of new products be justified and that such products actually result in significant progress when compared with existing products.

II - TERMS AND DEFINITIONS

II.1 - Research of new pharmaceutical products, medicines, vaccines or diagnostic tests. It refers to Phase I, II or III research with these types of products or with products not yet registered in the country, even in Phase IV, when the research focuses on their use with modalities, indications, dosages, or paths of administration different from those established at the time registration was authorized, including their use in combinations, as well as bioavailability and bioequivalence studies.

II.2 - The terms listed below, which are part of the Common Market Group Resolution (GMC Nº 129/96), are hereby incorporated into this Resolution.

a) **Phase I**
It is the first study with human beings, in small groups of usually healthy volunteers, of a new active principle or a new formulation, usually investigated using human volunteers. The purpose of such research is to establish a preliminary notion of the safety and pharmacokinetic profile, and, if possible, the phamacodynamics profile [of the product].

b) **Phase II** (Pilot-Scale Therapeutic Study)
The objectives of the Pilot-Scale Therapeutic Study are to demonstrate the activity [of the product] and to ascertain the short-term safety of the active principle in patients affected by a given disease or pathological condition. The research is carried out on a limited (small) number of individuals and is frequently followed by an administration study. It should also be possible to establish the dose/response ratio for the purpose of

obtaining sound background for the description of the extended therapeutic studies (Phase III).

c) Phase III (Extended Therapeutic Study)

These studies are performed on a large and varied number of patients, for the purpose of determining:

- the result of short-term and long-term risks/ benefits of the active principle formulations; and
- in a global (general) manner, the relative therapeutic value.

In this phase, the type and profile of the most frequent adverse reactions are studied, as well as the especial characteristics of the medication and/or therapeutic specialty, for example, clinically relevant interactions, main factors that modify the effect, such as age, etc.

d) Phase IV

This is research performed when the product and/or therapeutic specialty is commercially available.

This research is based on the characteristics under which the medicine and/or therapeutic specialty was authorized. These are usually post-commercialization surveillance studies that aim at establishing the therapeutic value, [verifying] the emergence of new adverse reactions and/or confirming the frequency of known adverse reactions, as well as the treatment strategies.

The same ethical and scientific norms applied in the research in the previous phases should be used in Phase IV research.

Once a medicine and/or therapeutic specialty is already commercially available, the clinical research performed to explore new indications, new methods of administration, or new combinations (associations), etc. shall be considered research of a new medicine and/or therapeutic specialty.

e) Pharmacokinetics

As a rule, it is all the modifications a biological system causes on an active principle.

In operational terms, it is the study of kinetics (quantitative relation between the independent variable 'time' and the dependent variable 'concentration') of the absorption, distribution, biotransformation, and excretion of medicines (active principle and/or its metabolites).

f) Pharmacodynamics
It is all the modifications an active principle causes in a biological system. From a practical standpoint, it is the study of the biochemical and physiological effects of medicines and their action mechanisms.

g) Margin of Safety
It is the pharmacodynamics indicator that expresses the difference between the toxic dose (for example, the DL 50) and the effective dose (for example, the DE 50).

h) Therapeutic Margin
It is the ratio of the maximum tolerated dose, also toxic dose, to the therapeutic dose (toxic dose/ therapeutic dose). In clinical pharmacology, the therapeutic margin is used as equivalent of the Therapeutic Indicator.

III - RESPONSABILITY OF THE RESEARCHER

III.1 - The unremittable and untrasferable responsability of the researcher to [comply with] the terms of Resolution 196/96 is hereby reaffirmed. All obligations provided for in said Resolution are equally reaffirmed, particularly the guarantee of conditions [required] to care for research subjects.

III.2 - The researcher shall be responsible for:

a) submitting a complete research project to the Committee for Research Ethics (CEP), in the terms of Resolution 196/96 and this Resolution;

b) maintaining a file for each research subject, for a period of five years, after the end of the research,

due compliance being given to the confidentiality and secrecy of the records;

c) submitting a detailed report as requested or established by the CEP, the National Commission for Research Ethics (CONEP), or the Health Surveillance Secretariat (SVS/MS);.

d) informing the CEP of any occurrence of collateral effects and/or unexpected adverse reactions;

e) communicating also any proposed changes in the project and/or justification of interruptions, keeping in abeyance until the matter is appreciated by the CEP, except in urgent cases to safeguard the safety of research subjects; in the latter case, the CEP should be notified immediately afterwards;

f) making available to CEP, CONEP and the SVS/MS all duly required information;

g) continuously analyzing the findings, throughout the research, for the purpose of detecting, as soon as possible, the advantages of one treatment over another or preventing adverse effects on research subjects;

h) submitting regular reports within the time periods established by the CEP, with at least one report every six months and one final report;

i) providing the patient's physician and the patient him/herself access to the results of tests and treatment whenever requested and/or indicated; and

j) recommending that no individual be selected as research subject before a year has passed from his/her participation in another research, unless that individual were to directly benefit from it.

IV - RESEARCH PROTOCOL

IV.1 - The protocol must include all items stipulated in Chapter VI of Resolution 196/96, in addition to the basic pharmacological information appropriate to the phase of the research project, in compliance with Res. GMC 129/96 - Mercosul – including the following:

a) specifications and rationale of the clinical research phase in which the study is to be carried out, demonstrating that prior phases have been concluded;

b) description of the pharmacological substance or product being investigated, including its chemical formula and/or structure, in addition to a brief summary of relevant physical, chemical and pharmaceutical properties. Any structural similarity to other known chemical compounds should also be mentioned;

c) detailed preclinical information is required to justify the phase of the project, including a report on the experimental studies (materials and methods, animals used, laboratory tests, pharmacodynamics data, margin of safety, therapeutic margin, pharmaco-kinetics, and toxicology, in the case of drugs, medicines, or vaccines). The preclinical results must be accompanied by a discussion of the relevance of the findings in connection with the expected therapeutic effects and possible undesirable effects in human beings;

d) the preclinical toxicology data should include the study of acute toxicology, subacute toxicology with repeated doses and chronic toxicity (repeated doses);

e) the toxicology studies should be performed in at least three animal species, one of which must be a non-rodent mammal; both sexes must be included in the studies;

f) in studying acute toxicity, two paths of administration must be used, one of which must be related to that recommended for the therapeutic use being proposed and the other must be a path that will ensure the absorption of the pharmaceutical product;

g) in subacute toxicity, repeated dose and chronic toxicity studies the path of administration should be related to the proposed therapeutic use and the experiment should last at least 24 weeks;

h) in the preclinical phase, the toxicity studies should also include an analysis of the effects on fertility, embryo-toxicity, mutagenicity, oncogenic (carcinogenic) potential, and other studies, according to the nature of the pharmaceutical product and the therapeutic proposal;

i) depending on the importance of the project, in view of the lack of time and in the absence of other therapeutic methods, the CEP may approve projects that have not fulfilled all clinical pharmacology phases; in this case, approval must also be obtained from CONEP and the SVS/MS;

j) information about the status of the research and product registration in the country of origin;

k) the detailed clinical information obtained during the prior phases, as regards safety, pharmaco-dynamics, effectiveness, and dose-response observed in studies using human beings, whether healthy volunteers or patients. If possible, there should be a separate summary of each essay, with a description of the objectives, design, method, results (safety and effectiveness), and conclusions. In the case of a large number of studies, the summary must encompass groups by phase, in order to facilitate a discussion of the results and their implications;

l) justification for the use of a placebo and possible suspension of treatment (washout);

m) access to the medicine being tested must be assured by the sponsor or by the institution, researcher, or promoter, if there is no sponsor, in the event its superiority to the conventional treatment is proven;

n) in multiple center studies the researcher must, to the extent possible, participate in the design of the project. If this is not possible, the researcher must formally state that he/she agrees with the existing design and that he/she will follow it;

o) the sponsor must provide the researcher all data about the pharmaceutical product;

p) funding must not be tied to the per capita payment of the subjects effectively recruited;

q) the protocol must be accompanied by the terms of consent. In the case of subjects not fully capable of self-determination, in addition to the consent from the individual legally responsible for the proposed research subject, it is necessary to take into account the expressed wishes of the proposed research subject, even when not fully capable (for example, the elderly) or not fully developed (for example, children); and

r) in the case of research on psychiatric patients, whenever possible consent should be obtained from the patient him/herself. It is mandatory that the level of capability to express free and informed consent of each psychiatric patient be established by a psychiatrist other than the researcher involved in the project.

In the case of drugs with psychopharmacological action, a critical analysis must be made of the possible risks of causing dependency.

IV.2 - Including healthy subjects in research.

a) justifying the need to include healthy subject in the research project. Critical analysis of the risks involved.

b) description of how the recruitment will take place; no dependency situation should exist.

c) in the case of drugs with psychopharmacological action, a critical analysis of the risk of causing dependency is necessary.

V - ATTRIBUTIONS OF THE CEP

V.1 - The CEP and the researcher will be jointly responsible for maintaining ethically correct conducts throughout the project and during the implementation of the research. In addition, they should take the following actions.

a) issue a consolidated report explaining the scientific basis of the research project and its relation with the studies in prior phases, including the preclinical phase, with emphasis on safety, toxicity, adverse reactions or effects, effectiveness, and results.

b) approve the justification of the use of a placebo and washout.

c) request partial and final reports from the main researcher establishing the schedule (on a six-monthly basis at least) according to the characteristics of the research. Copies of the reports must be forwarded to the SVS/MS.

d) if announcements in the media are to be used to recruit research subjects, such advertising must be authorized by the CEP. No indication may be given, whether implicitly or explicitly, that the product being investigated is effective and/or safe, or that it is equivalent to or better than other existing products.

e) convene the research subjects for follow up and evaluation.

f) require that the top management of the institution start an inquiry, suspend or interrupt the research and communicate the fact to CONEP and the SVS/MS.

g) any infringement of ethical principles or evidence of fraud of any nature should lead the CEP to request the creation of an Inquiry Committee and to communicate the results [of such inquiry] to CONEP, SVS/MS and other agencies (top management of the Institution, pertinent Regional Councils).

h) communicate the occurrence of serious adverse events to CONEP and the SVS/MS.

i) communicate to the Institution the occurrence or existence of administrative responsibility problems that may interfere with the ethical conduction of the research; report to CONEP and the SVS/MS immediately and, as the case may be, to the Regional Councils.

V.2 - The National Health Council hereby delegates to the CEP authority to approve, from the point of view of ethics, research projects involving new pharmaceutical products, medicines and diagnostic tests, with the provision that the following documents be submitted to CONEP and the SVS/MS:

a) a copy of the consolidated report approving the research project, together with a completed header page;

b) official conclusion on the partial and final reports on the research; and

c) other documents required by CEP, CONEP or the SVS.

V.3 - In research that includes patients submitted to emergency or urgency situations, the CEP must previously approve the conditions or limits for obtaining free and informed consent; in addition, the researcher must inform the research subject, on a timely basis, about his/her participation in the project.

V.4 - Assess whether all adequate measures are being implemented in the case of research with human beings whose capability for self-determination is impaired or limited.

VI - OPERATIONALIZATION

VI.1 - CONEP will exercise its competencies in the terms of Resolution 196/96, with emphasis on the following activities:

a) organizing an information and follow up system (item VIII.9.g of Resolution 196/96) on the basis of the data supplied by the CEPs (consolidated approval report, duly completed header page, partial and final reports, etc.);

b) organizing a system to evaluate and follow up the activities of the CEPs. The system should enable peers, i.e. members of the various CEPs, to exchange information and experience, with reports to CONEP. It should also comply with the specific regulations issued by CONEP;

c) informing the appropriate authorities, particularly the Health Surveillance Secretariat of the Ministry of Health, with a view to appropriate action, proven violations of the ethical standards in the execution of research projects; and

d) supplying the various bodies of the Ministry of Health, particularly the Health Surveillance Secretariat, the information required to fully exercise their respective competencies as regards the research covered in this Resolution.

VI.2 - The Health Surveillance Secretariat/MS shall exercise its attributions in the terms of Resolution 196/96, with especial emphasis on the following activities.

a) reporting, in writing, to CONEP any indication of violation of ethics observed or detected during the execution of the research projects covered in this Resolution;

b) supply, upon request or when pertinent, the information required for the full exercise of the competencies of CONEP;

c) in the case of research involving situations for which there is no recognized treatment ("humanitarian use" or "compassionately"), the release of the product may be authorized as an emergency measure, after CEP approval and ratification by CONEP and the SVS/MS; and

d) standardizing its internal operational procedures with a view to exerting effective health control of the products object of clinical research.

CARLOS CÉSAR S. DE ALBUQUERQUE
Minister of Health of Brazil

I hereby ratify CNS Resolution Nº 251, dated 7 August 1997, in the terms of the Decree on the Delegation of Competency dated 12 November 1991.

CARLOS CÉSAR S. DE ALBUQUERQUE
President of the National Health Council

NATIONAL HEALTH COUNCIL
RESOLUTION Nº 292, DATED 8 JULY 1999

The Plenary of the National Health Council, in its 88th Regular Meeting, held on July 7 and 8, 1999, in the exercise of its competencies, as set forth in its by-laws, and the attributions in Law nº 8.080 and Law nº 8.142, respectively dated 19 September 1990 and 28 December 1990, and CONSIDERING the need for complementary regulation of CNS Resolution Nº 196/96 (Guidelines and Norms Regulating Research Involving Human Beings), a competency of CONEP as stated in item VIII.4.d of that Resolution, as regards the special thematic area "research coordinated abroad or with foreign participation and research that involves sending abroad biological material" (item VIII.4.c.8), RESOLVES to approve the following norm:

I - Definition: Research coordinated abroad or with foreign participation is any research involving the promotion and/or execution of:

a) collaboration with foreign, individuals or companies, whether public or private;

b) sending and/or receiving biological material from a human being;

c) sending and/or receiving data and information collected for inclusion in research findings; and

d) international multiple-center studies.

I.1 - Due compliance being given to the conditions above, the following [research] is not included in this thematic area:

a) research entirely carried out in this country by foreign researchers who belong to the technical staff of a national entity; and
b) research carried out by multinational corporations with headquarters in this country.

II - In all research, it is mandatory:

II.1 - to prove the Brazilian participation and to identify the co-responsible national researchers and institutions; and

II.2 - to set forth the responsibilities, rights and obligations through an agreement of the parts involved [in the research].

III - This Resolution incorporates all provisions contained in Resolution Nº 196/96 of the National Health Council on Guidelines and Norms Regulating Research Involving Human Beings, whose specific thematic area is hereby complemented.

III.1 - CNS Resolutions referring to other thematic areas simultaneously contemplated in the research should complied with.

IV - The burden and benefits arising from the investigation and the research results must be distributed fairly among the parts involved and should be clearly set forth in the protocol.

V - The national researcher and institution should be well aware of the legal norms and regulations on sending material abroad and those that protect industrial property and/or technology transfers (Law Nº 9.279, dated 14 May 1996, which regulates the rights and duties associated with industrial property; Decree Nº 2.553/98, which regulates Law Nº 9.610/98 on copyright), expounding, as the case may be, the agreements established, as well as the legal norms on sending biological material abroad.

VI - During the research, the sponsors and researchers should communicate to the Committees for Research

Ethics (CEP) any relevant information of public interest, in addition to the regular reports required by law.

VII - In preparing the [research] protocol, special attention must be given to the presentation of the following items:

VII.1 - Approval document issued by the Committee for Research Ethics or equivalent institution in the country of origin that will promote or also execute the project.

VII.2 - When the project is not to be developed in the country of origin, a justification should be attached to the protocol, for consideration by the Committee for Research Ethics of the Brazilian institution.

VII.3 - Detailed exposition of the financial resources involved: sources (whether international and foreign and whether there is a national/institutional counterpart); manner and value of the remuneration of the researcher and other human resources; expenditures with infrastructure; and impact on the routine of the health services [rendered by] the institution [where the project will be implemented]. To the extent possible, the financial input should not create situations where health professionals and/or users are discriminated, since these resources could lead to extraordinary benefits for the participants and research subjects.

VII.4 - Statement of the research promoter or sponsor, as the case may be, that the terms of the resolutions on ethics in research involving human beings issued by the National Health Council will be complied with.

VII.5 - Statement on how the biological material and the information and data gathered exclusively for the purpose foreseen in the protocol will be used by all individuals manipulating the material.

VII.6 - Statement of the researcher on the protocol, in the event the researcher was unable to participate in the design of the project.

VIII - According to the attributions set forth in item VIII.4.c.8 of Resolution Nº 196/96, CONEP, after approval by the Committee on Research Ethics of the institution, must appreciate all research included in this thematic area, even when other thematic areas are also included.

VIII.1 - Any case referring to the ethical aspects of research not contemplated in this resolution shall be resolved by the National Commission for Research Ethics.

JOSÉ SERRA
President of the National Health Council

I hereby ratify CNS Resolution Nº 292, dated 8 July 1999, in the terms of the Decree on the Delegation of Competency dated 12 November 1991.

JOSÉ SERRA
Minister of Health of Brazil