AAHRPP®

Association for the Accreditation of
Human Research Protection Programs, Inc.®

Addendum: Brazil Law
Governing Research Involving Human Participants

General Comment

Standards and Elements listed below address areas where policies and procedures must address specific requirements in Resolution CNS 466/2012 on guidelines and rules for research involving human participants; Standard Guidelines and Regulatory Research Involving Human Beings; Resolution 251/97 on complementary rules for research with new pharmaceutical products, medicines, vaccines and diagnostic tests, and Resolution 304/2000 on complementary rules for research involving indigenous people.

Domain I: Organization

Standard I-1: The Organization has a systematic and comprehensive Human Research Protection Program with appropriate leadership.

Element I.1.A. The Organization has and follows written policies and procedures for determining when activities are overseen by the Human Research Protection Program.	Research is defined as a formal and systematic process that aims at production, advancement of knowledge or reaching of answers to problems by employing the scientific method. Human research is defined as research that, individually or collectively, involves human beings as participants in its entirety or parts, and engages the participant, directly or indirectly, including the management of their data, information or biological materials. The definition of research must include environmental, nutritional, educational, sociological, economic, physical, psychical, pharmaceutical, clinical and surgical investigations.
Standard I-3: The Organization's transnational research activities are consistent with the ethical principles set forth in its Human Research Protection Program and meet equivalent levels of participant protection as research conducted in the Organization's principal location while complying with local laws and taking into account cultural context	Sponsored studies abroad must also meet the needs of transfer of knowledge and technology for the Brazilian team, where applicable, and, in the case of the development of new drugs, if proven their safety and efficacy, its registration is mandatory in Brazil.

Standard I-5: The Organization measures and improves, when necessary, compliance with organizational policies and procedures and applicable laws, regulations, codes, and guidance. The Organization also measures and improves, when necessary, the quality, effectiveness, and efficiency of the Human Research Protection Program.

Element I.5.D. The Organization has and follows written policies and procedures for addressing allegations and findings of non-compliance with Human Research Protection Program requirements. The Organization works with the Institutional Review Board or Ethics Committee, when appropriate, to ensure that participants are protected when non-compliance occurs. Such policies and procedures include reporting these actions, when appropriate.	Researchers may not analyze data when the protocol is not followed. Approved research may not be discontinued by the leading researcher without justification previously accepted by the CEP.

Standard I-7: The Organization has and follows written policies and procedures to ensure that the use of any investigational or unlicensed test article complies with all applicable legal and regulatory requirements.

Element I.7.A. When research involves investigational or unlicensed test articles, the Organization confirms that the test articles have appropriate regulatory approval or meet exemptions for such approval.	When research is regulated by the Brazilian National Health Vigilance Agency (ANVISA) the following approvals are required: • Permission to conduct the clinical trial must be obtained from the ANVISA in order to conduct the study. • CEP and CONEP approval must be obtained and communicated to the ANSIA in order to conduct the study.
Element I.7.C. The Organization has and follows written policies and procedures for compliance with legal and regulatory requirements governing emergency use of an investigational or unlicensed test article.	In situations to 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 CONETP and ANVISA.

Domain II: Institutional Review Board or Ethics Committee

Standard II-1: The structure and composition of the IRB or EC are appropriate to the amount and nature of the research reviewed and in accordance with requirements of applicable laws, regulations, codes, and guidance.

Element II.1.A. The IRB or EC membership permits appropriate representation at the meeting for the types of research under review, and this is reflected on the IRB or EC roster. The IRB or EC has one or more unaffiliated members; one or more members who represent the general perspective of participants; one or more members who do not have scientific expertise; one or more members who have scientific or scholarly expertise; and, when the IRB or EC regularly reviews research that involves vulnerable participants, one or more members who are knowledgeable about or experienced in working with such participants.	Each ethics committee (CEP) must comply with requirements in Resolution CNS 466/2012 and Resolution 304/2000 to have at least seven members with appropriate gender representation: • Professionals from the health sciences. ○ A licensed physician, if research involving an ANVISA-regulated or FDA-regulated article is involved. • Legal scholars, theologians, sociologists, philosophers, or bioethicists. • At least one member of society, representing the users of the institution. • At least one member who represents the perspective of research participants, such as a former or current research participants or a research participant advocate. • At least one member who is independent of the research organization. • A licensed physician, if research involving an ANVISA-regulated or FDA-regulated article is involved. • No more than half its members may come from a single professional category. • At least half of its members must have experience in research. (An individual may fulfill more than one role) When vulnerable groups or communities are to be enrolled in research, a representative of such prospective research participant population must be must participate in the CEP. When research involves Indigenous populations, a consultant thoroughly familiar with the customs and traditions of the community must participate in the CEP.
Element II.1.C. The Organization has and follows written policies and procedures to separate competing business interests from ethics review functions.	Members of CEP must not be paid for the performance of their task, however, they can receive reimbursement for the expenses incurred for transportation, lodging and meals, being indispensable that they are dispensed in their work schedules in CEP from other obligations in the institutions and/or organizations to which they serve, given the character

	of public relevance of this function.
Standard II-2: The Research Review Unit systematically evaluated each research protocol or plan to ensure the protection of participants.	
Element II.2.C: The IRB or EC has and follows written policies and procedures for conducting meetings by the convened IRB or EC.	A quorum must be present for research to be approved. • A quorum consists of the majority of ethics committee members present, but not fewer than five members. • The following members must be present to conduct business: o At least one professional from the health sciences. ▪ A licensed physician, if research involves an investigational article regulated by ANVISA or the FDA. o At least one non-scientist. o At least one individual who is not affiliated with the research institution. o When vulnerable groups or communities are to be enrolled in research, a representative of such prospective research participants must be must participate in the CEP. o When research involves Indigenous populations, a consultant thoroughly familiar with the customs and traditions of the community must participate in the CEP. (Note that a single member may represent more than one category.)
Element II.2.D. The IRB or EC has and follows written policies and procedures to conduct reviews by the convened IRB or EC. **Element II.2.D.1. – Initial review** **Element II.2.D.2. – Continuing review** **Element II.2.D.3. – Review of proposed modifications to previously approved research**	Policies and procedures have the ethics committee (CEP) use the following criteria for approval for all reviews of research, including initial review, continuing review, and review of a modification to previously approved research (when the modification affects a criterion for approval): • Research is conducted in accordance with the scientific principles that justify it and the concrete possibility of answering uncertainties. • Human research is based on prior laboratory experiments with animals or on other scientific facts. • Human research is carried out only when the knowledge to be obtained cannot be otherwise acquired. • When evaluating risks and benefits, both actual and potential, both individual and collective, that the CEP always favors the probability of foreseen benefits, rather than predictable risks, and ensures that benefits are maximized and distress and risks are minimized. • The research follows appropriate methodology. If a random distribution of the research participants 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 participants. • The use of use of placebos, is fully justified, as applicable, in terms of non-maleficence and of methodological requirement. • Participants or their legal guardians provide voluntary and informed consent. • Necessary human and material resources exist to ensure the well-being of the research participants, and the qualifications of the researcher are harmonized with the proposed research project.

	• The research plan includes procedures that will ensure confidentiality and privacy, protection of the image and non-stigmatization of the research participants, 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. • Preliminary research is developed and conducted, preferably, in fully capable individuals. Vulnerable individuals or groups should not be research participants 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. • When research involves communities, investigators must respect the cultural, social, moral, religious, and ethical values, as well as the mores and habits, when research involves communities. • Whenever possible, to guarantee that 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. • 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. • Results of the research are communicated 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 participants and guaranteeing that they will not be stigmatized or their self-esteem diminished. • Research participants are ensured the benefits resulting from the research project, in terms of social return, access to procedures, products or research agents. • Research participants are ensured of receiving required follow-up, treatment, or orientation, in screening surveys; to demonstrate that benefits prevail over risks and burdens. • At the end of the study all participants are ensured of receiving free and indefinite access to the best proven prophylactic, diagnostic and therapeutic methods that have been shown effective, provided by the sponsor: ○ Access is also guaranteed in the interval between the end of individual participation and the end of the study, where, in this case, this guarantee may be given through an extension study, according to an adequately justified analysis of the participant's physician. • The absence of conflicts of interest between the researcher and the research participants or sponsor of the research project is guaranteed. • Evidence is submitted, in case of research conducted abroad or with

	external cooperation, of commitments and advantages to the research participants 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 CEP an authorization issued in the country of origin. The CEP 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 is able to independently develop similar projects. • Biological material and data obtained in the research is used only for the purposes set forth in the research project protocol. • Consideration of additional risks and benefits when research is carried out in women in the reproductive age or pregnant women, as well as possible interference with the fertility, pregnancy, embryo or fetus, labor, puerperium, nursing and the newborn. • Whether research in pregnant women must be preceded by research in non-pregnant women, except when the basic objective of such research is pregnancy. • Multi-center studies facilitate the participation of the researchers who will conduct the research in the overall design of the research project • Research is discontinued only after the CEP that initially approved it has analyzed the reasons for interrupting it. • Provisions to ensure the freely given and informed consent of target individualsor his or her legal guardian and the protection of vulnerable groups and the legally disabled. • When research involves children and adolescents, individuals who are mentally ill or disturbed, and persons with substantially impaired or diminished autonomy, the choice of said research participants must be clearly justified and specified in the research protocol, which must be approved by the CEP and meet all the requirements of freely given and informed consent, through the legal guardian of the prospective research participant, without detriment to the right of information of the individual, within the limits of his/her capacity of understanding. • Voluntary 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 centers, shelters, homes, religious or other institutions, ensuring them complete freedom to participate, or not, in the research, without any retaliation. • In the event it is impossible to record the freely given and informed consent of the research participant, such fact must be duly documented, with an explanation of the causes and the technical opinion of the CEP. • 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.

	The review of CEP will culminate in the placement one of the following categories: • Approved. • pending: when CEP considers necessary the correction of the protocol presented, and requests specific revision, modification or relevant information that should be answered in the time stipulated in the operating standard. • not approved. CEP may, if it considers it appropriate and convenient in the course of the ethical review, request information, documents and other items required in the perfect clarification of issues, where the the procedure is suspended until the receipt of the requested information; Of the decisions that have not been approved, there may be an appeal to CEP within 30 days, whenever some new fact appears to substantiate the need for a re-examination; CEP should determine the archiving of research protocol where the lead researcher does not meet, in a timely fashion, the requests that have been made. The also the protocol may also be considered removed when requested by the leading researcher. The CEP must submit quarterly reports to the National Commission on Research Ethics (CONEP), 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.
Element II.2.F. The IRB or EC has and follows written policies and procedures for addressing unanticipated problems involving risks to participants or others, and for reporting these actions, when appropriate.	The CEP is responsible for: • Monitoring the development of projects through monthly reports from researchers and other monitoring strategies, according to the risk inherent in the research. • Receiving reports of abuse or adverse facts which might alter the normal course of the study, decide on the continuance, modification or suspension of research, and, if necessary, request the adequacy of the statement of consent. • Requesting the establishment of determining the direction of the organization or public agency responsible in the case of knowledge or allegations of irregularities in research involving human participants, and having proof, or if appropriate, reporting it to CONEP and, where applicable, to other agencies.
Standard II-3: The IRB or EC approves each research protocol or plan according to criteria based on applicable laws, regulations, codes, and guidance.	
Element II.3.A. The IRB or EC has and follows written policies and procedures for identifying and analyzing risks and identifying measures to minimize such risks. The analysis of risk includes a determination that the risks to participants are reasonable in relation to the potential benefits to participants and to society	In evaluating the risks and potential benefits of research, the ethics committee (CEP) must guarantee, whenever possible, that 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.
Element II.3.F. The IRB or EC has and follows written policies and	Free and informed consent is defined as consent given by the research

procedures to evaluate the consent process and to require that the Researcher appropriately document the consent process.	participant, child, subo or legally incompetent, free of bias (simulation, fraud or error), dependence, subordination, or intimidation. Such participants should be informed about the nature of the research, its aims, methods, anticipated benefits, potential risks, and any discomfort that may arise, to the extent of their understanding and respecting their singularities. Consent documents must include the disclosure that research participants 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. Consent documents must include a statement clarifying, where appropriate, the possibility of inclusion of participants in the control group or placebo group, explaining clearly the meaning of this possibility. Consent documents must contain the declaration of the researcher responsible that expresses compliance with the requirements contained in Resolution CNS 466/2012. Consent documents must be developed in two copies, initialed on every page and signed, at the end, by the invited research participant, or his legal representative, as well as the investigator, or the person(s) by that delegate(s) it, and the portions containing the signatures must be on the same sheet. Both copies must include the address and telephone or other contact of those responsible for research and the local CEP and of CONEP, when relevant. In research that depends on restriction of information to participants, this fact should be fully explained and justified by the investigator responsible for the CEP/CONEP System. The data obtained from the research participants may not be used for purposes other than those set out in the protocol or free and informed consent. When conducting research 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.
Element II.3.G. The IRB or EC has and follows written policies and procedures for approving waivers or alterations of the consent process and waivers of consent documentation.	Where it is not feasible to obtain the statement of consent or the obtaining consent signifies substantial risks to privacy and confidentiality of the participant or the bonds of trust between researcher and research participant, the waiver of the free and informed consent should be reasonably requested by the responsible researcher from the CEP/CONEP system for consideration, participant to a posterior clarification process.
Standard II-4: The IRB or EC provides additional protections for individuals who are vulnerable to coercion or undue influence and participate in research.	
Element II.4.A. The IRB or EC has and follows written policies and procedures for determining the risks to prospective participants who are vulnerable to coercion or undue influence and ensuring that additional protections are provided as required by applicable	Vulnerability is defined as state of persons or groups who, for whatever reason or reasons, have their capacity for self-determination reduced or prevented, or otherwise are unable to resist, especially with regard to free and informed consent. When pregnant women are to be enrolled in research in pregnant women must be preceded by research in non-pregnant women, except when the

laws, regulations, codes, and guidance.	basic objective of such research is pregnancy. Policies and procedures should describe criteria used by the ethics committee (CEP) when reviewing research involving Indigenous populations. Examples include the following criteria: • When evaluating the benefits and advantages resulting from the development of research, the ethics committee should consider the needs of targeted individuals and groups of the study, or similar societies and/or national societies, taking into account the promotion and maintenance of welfare, preservation and protection of biological and cultural diversity, collective and individual health and the contribution to the development of knowledge and own technology. • Respect for the participants' view of the world, the costumes, aesthetic attitudes, religious beliefs, social organization, philosophies, linguistics differences and political structure. • Not allow physical, mental, psychological or intellectual and social exploration of the indigenous. • Not allow situations that can put at risk the integrity and the physical, mental and social welfare of the indigenous. • Have the agreement of the targeted community which can be obtained through the respective indigenous organizations or local councils, respecting the individual consent, which in common agreement with the referred communities will designate the mediator to the contact between the researcher and the community. • Guarantee equality of consideration of the involved interests, taking into account the vulnerability of the group in question. • That research is not conducted in isolated indigenous communities, exempt in special cases, and only with detailed justification. • Researchers may not patent chemical products and biological material of any kind, obtained from research involving indigenous peoples. • The formation of DNA banks, of cell lineage or any other biological material related to indigenous peoples, is not permitted without the explicit agreement of the involved community, without the presentation of detailed proposal in the research protocol to be submitted to the CEP and CONEP and the formal approval of these Committees. • The non-observance of any of those items above should be communicated to the institutional CEP and to the CONEP of the National Health Council, to take appropriate steps. Research on individuals with the diagnosis of brain death must meet the following requirements: • Document proving brain death. • Explicit consent, with advance directive in the person's will, or consent of family members and/or legal representative. • Respect for human dignity. • Absence of additional financial-economic burden to the family. • No negative consequence for other patients awaiting admission or treatment. • Possibility of obtaining relevant or new scientific knowledge, that

	cannot be otherwise obtained. • That there is an official communication channel with the government, to easily clarify doubts for all those involved in research projects, equally for patients diagnosed with brain death. • In communities whose culture recognizes the authority of the group leader or the collective over the individual, obtaining of permission that research complies with such particularity, participant to individual consent, where possible and desirable. When the Brazilian legislation has governmental powers, such as the National Indian Foundation - FUNAI, in the case of indigenous communities, for protection of these communities, such instances must authorize research in advance.
Standard II-5: The IRB or EC provides additional protections for individuals who are vulnerable to coercion or undue influence and participate in research.	
Element II.5.A. The IRB or EC maintains a complete set of materials relevant to the review of the research protocol or plan for a period of time sufficient to comply with legal and regulatory requirements, Sponsor requirements, and organizational policies and procedures.	The CEP must keep the research project, its protocol and respective reports on file for five years after the conclusion of the research. The CEP is responsible for safeguarding the confidentiality of all information obtained in carrying out its duties and the filing of the complete protocol. The CEP must forward, after reasoned analysis, CONEP's competencies protocols, observing carefully all the documentation that must accompany this referral, according to the current operating standard, including detailed proof of costs as well as funding sources needed for research. The CEP must maintain regular and ongoing communication with CONEP, through its Executive Secretariat.
Domain III: Researcher and Research Staff	
Standard III-1: In addition to following applicable laws and regulations, Researchers and Research Staff adhere to ethical principles and standards appropriate for their discipline. In designing and conducting research studies, Researchers and Staff have the protection of the rights and welfare of research participants as a primary concern.	
Element III.1.C. Researchers employ sound study design in accordance with the standards of their discipline. Researchers design studies in a manner that minimizes risks to participants.	In research in the area of health, as soon as a significant advantage of an intervention is established over another, the investigator should assess the need to adjust or suspend the ongoing study aiming to provide everyone the benefits of the best regime.
Element III.2.C. Researchers and Research Staff follow the requirements of the research protocol or plan and adhere to the policies and procedures of the Organization and to the requirements or determinations of the IRB or EC.	The main researchers must submit to the CEP an affidavit that they will comply with Resolution CNS 466/2012. It is up to the researcher to: • submit the properly instructed protocol to CEP or CONEP, awaiting the decision of the ethical approval before starting the research. • prepare the statement of consent. • develop the project. • prepare and submit partial and final reports. • provide information requested by the CEP or CONEP. • keep the research data on file, physical or digital, under their custody and responsibility for a period of five years after the completion of the research. • submit the results of the research for publication, with due credit to

	associate researchers and technical staff member of the project. • provide a reasoned justification to CEP or CONEP of any interruption of the project or the non-publication of the results.
Element III.2.D. Researchers and Research Staff follow reporting requirements in accordance with applicable laws, regulations, codes, and guidance; the Organization's policies and procedures; and the IRB's or EC's requirements.	The leadresearcher, when realizing any significant risk or harm to the research participant, provided, or not, in the statement of consent, must report it immediately to the CEP/CONEP System, and evaluate, as an emergency, the need to adjust or suspend the study.