Ethics Review Committee

Standard Operating Procedures

for submitting research proposals

Pan American Health Organization
Regional Office of the World Health Organization

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Acknowledgements

We are pleased to present the Pan American Health Organization's Ethics Review Committee's (PAHOERC) Standard Operating Procedures for the submission of research proposals.
These standard operating procedures were approved by the Director, Dr. Mirta Roses-Periago
1 May 2009.

These Standard Operating Procedures were created and reviewed by PAHOERC Members in collaboration with representatives from the offices of Legal Affairs, Procurement, Human Rights, the Bioethics Program, and the Ethics Officer, and The World Health's Organization Ethics Review Committee Secretariat. The discussions were coordinated by the PAHOERC Secretariat, housed within the Research Promotion and Development team (THR/RP). We would like to acknowledge the contributions by PAHOERC Members and Observers, and the PAHOERC Secretariat.

Your comments and feedback are welcome and can be submitted to PAHOERC@PAHO.ORG. Updates and additional information is available at http://www.paho.org/researchportal

Chessa Lutter, President PAHOERC
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Content

Overview of the Ethics Review Committee

I

The purpose of these Standard Operating Procedures (SOPs) is to delineate the structure and process followed by the Ethics Review Committee of the Pan American Health Organization (PAHOERC) for review of proposals, including the requirements for research proposals submitted for ethical review.

A. Purpose of PAHOERC

PAHOERC was reinstated in June 2006 by PAHO's Director to assess the ethical implications of research projects involving human subjects. These include:

1. Ensuring that any research in humans in which PAHO is involved meets ethical standards;

2. Ensuring that research is appropriate for addressing open research question(s) and delivers outcomes likely to contribute to health and equity;

3. Coordinating educational and capacity-building activities in areas relevant to research and research ethics;

4. Establishing, organizing and maintaining the institutional memory, indexing and filing on decisions, activities and documents, and maintaining information resources relevant to PAHOERC.

The role of PAHOERC is to ensure that research in humans in which PAHO is involved:

1. Meets ethical standards and is in accordance with three basic ethical principles: respect for persons, beneficence and justice;

2. Has sound methodological standards, adheres to reliable and transparent processes, and provides an added value to participants, researchers, and the community;

3. Is registered in PAHO's Research Registry.

B. Fundamental Ethical Principles

PAHOERC follows the guidelines set by The World Medical Association Declaration of Helsinki and The Council for International Organizations of Medical Sciences (CIOMS), international/regional human rights treaties and standards, and other norms and guidelines for research in human subjects, abiding with ethical principles for medical research involving human subjects, including research on identifiable human material and data.

What is Subject to Review

II

A. Scope of Review

All research that uses human subjects, tissues/specimens from humans, data/records from human subjects, or surveys of human subjects funded or technically supported by PAHO requires review and approval from PAHOERC. Research involving humans includes, but is not limited to:

1. Studies of a physiological, biochemical, pathological or social process.

2. Response to a specific intervention including diagnostic, preventive or therapeutic measures; or studies designed to determine the consequences for individuals and communities of implementing preventive or therapeutic measures.

3. Studies concerning human health-related behavior in a variety of circumstances and environments.

A research proposal is not subject to review by PAHOERC when:

1. It does not involve human subjects.

2. The data (including health-care records and specimens) being studied already exists and is either publicly available or recorded by the investigator in such a manner that the identity of individuals cannot be established.

3. Public officials are interviewed in their official capacity on issues that are in the public domain.

4. Proposals in which the intervention is limited to public health surveillance or monitoring of public health programs carried out pursuant to statutory or regulatory authority.

B. Who is Responsible for Submitting Research proposals to PAHOERC?

In order to ensure that appropriate ethical review has occurred for all research involving human subjects funded or otherwise technically supported by PAHO, the Responsible PAHO Staff Member, working in close consultation with the Principal Investigator, shall submit the research proposal to the PAHOERC Secretariat through PAHO's Research Registry (see section III).

C. Requirements for Proposals

1. The research conforms to the fundamental ethical principles described under section I.

2. The research has been approved by all appropriate ethical review committees at the institutional and/or national level in the setting where the research will be undertaken.

3. The Principal Investigator and the institution under whose auspices the research will be conducted have committed to safeguard the rights and welfare of the research team in accordance with PAHO's ethical standards for research outlined in these SOPs. They are also committed to adhere to any other requirements/conditions made by PAHOERC in granting approval. The Principal Investigator will inform PAHOERC, the Responsible PAHO Staff Member, and any other Ethics Review Committee (ERC) or Institutional Review Board (IRB) involved in the study, of any relevant changes in the research proposal or its implementation, prior to that change being implemented.

Submission Process

III

A. Responsible PAHO Staff Member

All proposals must be submitted by a PAHO staff member, who is either the Principal Investigator or working in close consultation with the Principal Investigator. The Responsible PAHO Staff Member has the responsibility to ensure that the required documentation for each proposal is complete, and will become the contact person for PAHOERC regarding the proposal.

B. Submitting a Research Proposal

All research proposals must be sent electronically by the Responsible PAHO Staff Member using PAHO's Research Registry http://mc.manuscriptcentral.com/paho; other communications should be addressed to PAHOERC@paho.org. Research proposals can only be submitted through a PAHO staff member. The Responsible PAHO Staff Member will ensure that for each research proposal, all required documentation is complete.

C. Documentation Required

Each research proposal must include all of the information listed below to be considered for review:

1. Proof of approval by a local Ethics Review Board and/or if necessary, national authorities. The letter should be issued by the country where the research project will be conducted. In cases where there is more than one country involved, a letter from each participating country will be required by PAHOERC.

2. A structured abstract (less than 300 words) providing a succinct summary of the research question, the population and interventions involved, main outcomes, methods, potential risks for subjects, and names of participating institutions and countries. The abstract should briefly mention the potential value of this research for public health.

3. Disclosure by researchers of their funding sources, sponsors, institutional affiliations and other possible sources of conflicts of interest: real, apparent or perceived, or incentives for people participating in the study.

4. A complete research proposal that includes:
   - Brief background and justification
   - Objective/purpose of study and a brief statement as to why the research question(s) is relevant

- Methodology/procedures/analysis plan
- Sampling methodology and sample size calculations
- Limitations/delimitations
- Significance of study with a careful assessment of predictable risks and burdens to the individuals and communities involved in the research in comparison with foreseeable benefits to them and to other individuals or communities affected by the condition under investigation
- Budget and timelines
- References

5. Curriculum vitae (abbreviated, 2 pages) of the Principal Investigator and any co-investigators. The Principal Investigator and co-investigators shall submit a signed Declaration of Interests form (see definitions in glossary about conflicts of interest and members of the research team). The Principal Investigator shall also submit a written declaration disclosing any conflicts of interest affecting the research and/or research team, or about the emergence of material conflicts of interest that may arise during the course of the project. (See section VIII-D about procedures for how PAHOERC will address potential conflicts of interest.)

6. Disclosure of previous reviews by other ethical or scientific boards or committees, and a copy of the conclusions, recommendations and changes that were incorporated.

7. Informed consent documentation (annex 1 provides examples); any forms that will be used in the study; and a description of how the subjects will be protected, including how data safety and monitoring will work and how deaths and unexpected events will be prevented or analyzed and dealt with. The process of informed consent is one of the most important parts of planning a research study. It is important that human subjects exercise their right of free will when deciding to participate. It is equally important that subjects be given the correct information, comprehend what is being said and read to them, and be given the time to make their own decision about participation. The language of the informed consent must be comprehensible to the research subject (or their guardian). In most cases this may include a document written in a language that the subject can understand at a fifth-grade reading level. The following should take place during the consent process:
   - Review of recruitment materials
   - Verbal instructions
   - Written material (when appropriate)
   - Questions/answer sessions
   - Agreement by documented signature when appropriate (most situations)

Subjects must be informed that it is their right to withdraw from a study at any time. The consent form must be communicated in suitable and effective ways to any subjects including those with disabilities. Children and other vulnerable subjects may need information presented as simply and straightforwardly as possible (see section V).

In cases where the potential subject cannot read the consent form, it must be read to the individual and a witness signature is required on the form, indicating that they were present during the reading/interpreting of the consent form and that it was presented in a manner that was comprehendible to the subject. If for any reason the informed consent process is waived (e.g. studies in some vulnerable populations such as those listed under section V-A), a clear justification has to be provided as well as any alternative arrangements.

Once a proposal has been submitted, the PAHOERC Secretariat will inform the Responsible PAHO Staff Member whether the documentation is complete or incomplete. Incomplete submissions will not be reviewed.

Note*: When the study design corresponds to a clinical trial, PAHOERC requires submission of proof of registration in a database that is linked to the Search Portal of the International Clinical Trial Register Platform of the World Health Organization (http://www.who.int/ictrp/), prior to the recruitment of the first research subject. If a trial has already been registered, the relevant identification number should be provided at the time the proposal is submitted.*

Review Process

IV

A. Identification Number

Once the required documentation is verified, a unique identifier (ID) will be assigned to the proposal and a written confirmation will be sent to the Responsible PAHO Staff Member.

B. Screening Committee

The Screening Committee is comprised of at least three PAHOERC Members and at least one representative of the Secretariat. The Screening Committee's role is to determine whether a proposal is exempt from review in order to expedite decisions for those proposals that do not require review. The Screening Committee must reach consensus in determining whether a proposal requires ethical review. If the Screening Committee cannot agree whether a proposal is subject to review, the proposal will be subject to Committee Review.

Proposals that may not necessarily require review include but are not limited to:

1. Proposals registered in PAHO's Research Registry when the study has been reviewed and approved by World Health Organization's Ethics Review Committee (WHOERC). WHOERC approval needs to have been uploaded in PAHO's Research Registry.

2. The observation of public behavior.

Research that requires Committee Review includes but is not limited to:

1. Research involving children or other vulnerable populations.

2. Research that involves quasi-experimental or experimental interventions, drugs or devices.

3. Research that involves invasive procedures.

4. Research that involves deception.

5. Research that involve sensitive questions or information that can result in stigmatization, discrimination, persecution, prosecution or indictment, or unnecessary stressful situations to participants.

A research project may not begin until PAHOERC approves a research proposal or declares that a proposal does not require Full Committee Review.

If the Screening Committee finds that, in accordance with the criteria set forth in the subparagraphs above, a proposal does not require Review by PAHOERC, the proposal shall be classified as "does not require review by PAHOERC." An official letter will be sent to the Responsible PAHO Staff Member by the Secretariat, and an appropriate notation will be documented and reflected in PAHO's Research Registry.

If the Screening Committee finds that, in accordance with the criteria set forth in the subparagraphs above, the study does requires review, external peer review will be obtained by the Secretariat before a proposal is sent for Full Committee Review.

For clinical trials, registration (as described in the note in section III-C) must be completed before recruiting the first subject.

C. Full Committee Review

1. PAHOERC Meetings

The Secretariat organizes meetings at regular intervals, usually monthly. An annual schedule will be disseminated in advance by the President.

2. Criteria Used for Review by Committee

The following are criteria used in the review by the Committee:

a. The research is relevant and the study design is adequate to address the question(s) posed. The sampling frame is adequate to make inferences relevant to target populations and the sample size gives adequate statistical power.
b. Fairness of subject selection.
c. Beneficence: risks to subjects are minimized and a sound research design is implemented without exposing participants to avoidable risks; the benefit-risk balance seems reasonable and safeguards are included to protect human rights, fundamental freedoms and welfare of participants, with particular care being paid to vulnerable subjects.
d. Voluntariness: recruitment practices do not involve coercion.
e. Confidentiality: provisions are made to protect the privacy of subjects and the confidentiality of data.
f. Informed consent process and forms are presented in a comprehensible and suitable manner for the population where the research is being conducted. Informed consent sought and documented prospectively for each subject or legally authorized representative.
g. Data monitoring procedures are in place to provide for the reasonable safety of all involved in the research, including the subjects.

3. Decisions of Committee Review

The review of a research proposal will result in one of the following actions:

a) Approved: the research proposal is approved as submitted. This does not preclude PAHOERC from sending comments for the consideration of the research team, or requesting proof of trial registration when appropriate.
b) Conditionally Approved: the research proposal has not yet been approved; it requires the completion of one or more requirements before approval can be granted. When the requirements are met, a letter of approval will be issued. The Committee will determine who will issue the approval (i.e. Secretariat, Screening Committee, Committee).
c) Not approved: the research proposal is not approved. It may reflect that the research proposal is rejected outright, or that further information, clarification or revision is required.
d) Does not require review by PAHOERC.

Once a decision is made, a letter is issued to the Responsible PAHO Staff Member informing them of the outcome of the Committee Review. Each communication includes:

a) PAHOERC's research proposal ID and date the proposal was received
b) Name of Responsible PAHO Staff Member
c) Names of investigators
d) Title of proposal
e) Date(s) of review and decision, and name of review body (i.e. Screening Committee, Committee)
f) The decision
g) Comments, questions, or suggestions (if applicable)

If the research proposal was either Conditionally Approved or Not Approved, the Principal Investigator needs to address the comments in the PAHOERC letter before resubmitting the research proposal. For clinical trials, proof of trial registration is required (see Note under section III-C).

Research proposals that were Conditionally Approved may be sent for Committee Review upon resubmission or may be sent to the Screening Committee or the Secretariat for approval.

Research Proposals that were Not Approved must be sent for Committee Review upon resubmission.

Any proposed changes or amendments to the research proposal or informed consent process and/or forms must be approved by PAHOERC's Secretariat prior to initiation.

Special Considerations for Vulnerable Populations V

A. Definition of Vulnerable Populations

Vulnerable populations are defined as:

1. Children, including newborns and minors (those under the age of 18 years) (see section V-B);

2. Fertilized ova, pregnant women and viable fetuses (see section V-C);

3. People whose judgment or capacity to make free-willed, informed decisions is limited or compromised. Cognitively impaired persons with conditions that affect their decision-making abilities;

4. Subjects with limited civil freedom, such as wards of state, residents or clients of institutions for the mentally ill, populations under judiciary care, and persons in long-term care facilities, among others;

5. Subjects recruited from emergency medical facilities, intensive care units, older persons in long-term care facilities, life threatening situations or the like;

6. Subjects whose economic conditions predispose them to certain incentives (see section V-D).

7. Populations subject to stigma and discrimination.

B. Studies Involving Children

In accordance with the United Nations Convention on the Rights of the Child, special considerations must be made when performing research on children (those under the age of 18 years). These include the use of additional forms and signatures; informing minors about the risks associated with pregnancy testing; and the inclusion of children in research projects to broaden the scope of knowledge of the effect of treatments on the future growth and development of children (http://www2.ohchr.org/english/law/crc.htm).

C. Studies Involving Women

In a manner consistent with the United Nations Convention on the Elimination of all forms of Discrimination against Women, pregnant and lactating women are classified as a vulnerable population because their condition leads to risk for both the mother and the fetus or breastfeeding offspring. Protections for these populations may include the use of witnesses during the consenting process, requiring consultants or patient

advocates to monitor the consent process, and limiting the scope of research activities. In addition, principal investigators must give scientific justification for the exclusion of potentially pregnant, pregnant and lactating women.

D. Vulnerability Because of Economic Status or Other Factors

Subjects should not be coerced into participating in a research study because of inappropriate inducements. PAHOERC reviews consent process and forms to ensure that any inducements offered are appropriate. Additional considerations may be necessary.

Research Proposal Variations

VI

A. Multi-Center Studies

A research proposal that involves human subjects and that is to be carried out at more than one center requires PAHOERC review. However, the multi-centre nature of such proposals could result in different scenarios for the review process.

1. When PAHO is the lead agency funding or organizing the research, an expedited review process by the PAHOERC Screening Committee may be utilized to add new centers to an approved research proposal. (See section IV-B for description of Screening Committee.)
   a. Once PAHOERC has approved a research proposal for the first center as a "master protocol," the review and approval of additional research sites for the same project may be undertaken on an expedited basis. Each new potential site will be given a new ID in the Research Registry, with a notation that it is derived from a particular master protocol.
   b. In such a situation, expedited review may be limited to determining whether the research proposal remains unchanged from the master protocol; whether any variations in the local circumstances (in terms of the characteristics of the population, the local manifestation or nature of the disease, etc.) could adversely affect the benefit-risk ratio, the minimization of risk, or the validity of informed consent; and whether translations of information and documentation have been prepared in an adequate and culturally appropriate fashion.
   c. If, in light of their determinations on these factors, PAHOERC agrees that an additional research site may be added, the extension of the project to that site will be recorded in PAHO's Research Registry as "Approved" and will be reported to the Responsible PAHO Staff Member. If deemed “Not Approved”, the Responsible PAHO Staff Member will be informed.
   d. For clinical trials, the Responsible PAHO Staff Member will ensure that research registries remain valid and accurate, updating them accordingly.

2. When PAHO staff are involved in only one or a few sites of a multi-center study being led by scientists unaffiliated with the Organization and when another Institutional Review Board (IRB) or Ethics Review Committee has been designated as the "lead ethical review committee" for the study with the aim of promoting consistent and uniform conditions for the research at all sites, PAHOERC may choose to postpone review of the research proposal until such Committee has completed its review.

a. The Responsible PAHO Staff Member for the research proposal shall submit the results of the review by the lead Ethics Review Committee (including any explanations, requirements, or other comments) to the Secretariat. When this documentation is received, the PAHOERC will commence its review of the proposal.
b. The decision to postpone a review should be made in a manner that will not unduly delay the decision on PAHO's involvement in the study.

B. Nested Studies

Any study that is part of another, i.e., "nested" within another study, will be subject to the procedures and criteria for review as set forth in these procedures. Nevertheless, the Responsible PAHO Staff Member shall also submit the proposal for the main study. While the main proposal does not need to not be formally reviewed by PAHOERC, it should be satisfied with the ethical aspects of the main study before approving the nested study.

Continuing Oversight and Monitoring

VII

The Organization's obligation to ensure continuing oversight of approved research proposals with human subjects, which it funds or otherwise supports, creates responsibilities beyond the obligation to perform continuing reviews.

1. The Principal Investigator will inform the Responsible PAHO Staff Member of any material changes in an approved research proposal prior to or during implementation; these shall be immediately reported to PAHOERC. Examples of material changes include but are not limited to:
   a. Substantial changes in sample size, sampling procedures or settings; change in the Principal Investigator and/or key member(s) of the research team; changes in funding sources or conflicts of interest.
   b. Substantial changes to the duration of the study; recommendations by other ethical review committees; new knowledge that alters the balance of benefits and risks.
   c. Early termination of a study and the reasons behind the decision (e.g. a request by a local safety and data monitoring committee; the balance between benefits and risks has been established; the research questions have been decisively answered; natural disasters or other external factors).

2. When a report of proposed changes in the proposal or informed consent process and/or forms of a research proposal that PAHOERC has previously approved is received, the Screening Committee will determine whether the proposed changes should be subject to Committee Review.

3. Pending PAHOERC's decision, which it will endeavor to produce within a reasonable time, the changes proposed for the research proposal should not be instituted, with the exception of any modifications urgently needed to protect the well-being or important interests of subjects already enrolled in the study.

4. PAHOERC may withdraw its approval of a proposal. Examples include but are not limited to:
   a. Local ethical approval is withdrawn.
   b. Presentation of fraudulent documentation.
   c. Failure to report critical changes, departure from the protocol and safety procedures.
   d. Conflict with international/regional human rights law(s) and or national policy.

Once a research proposal has been completed or discontinued, the Responsible PAHO Staff Member shall report this and submit a final report on the study.

The Principal Investigator is encouraged to inform the Responsible PAHO Staff Member of references and links to relevant publications subsequent to the study, link them in trial registries when appropriate, and keep the registries up-to-date.

PAHOERC Membership

VIII

A. Appointment

PAHOERC membership is by appointment of the PAHO Director (hereafter "Director"), for two-year terms with the option of a one-year extension. The Committee consists of up to 13 members including the head of the Research Promotion and Development Team (RP), who serves as an ex-officio permanent member and Secretary to PAHOERC. The Director will appoint two of those members to serve as President and Vice-President of PAHOERC.

After three continuous years of membership, a recess of at least one year is required. Members shall serve in an individual capacity and not as official representatives of any entity. Members (including the President and Vice-President) shall not receive compensation specifically for serving on PAHOERC.

1. Members shall be appointed based on but not limited to:
   a. Their willingness to commit the time required for their duties on PAHOERC;
   b. Their knowledge and experience in research;
   c. Their knowledge of research ethics, which they possess at the time of appointment or acquire through appropriate training and education within six months of beginning service on PAHOERC.

2. When necessary, membership terms may be set for periods of less than a full term in order to achieve a balanced staggering of membership turnover.

3. Decisions about reappointments should be guided by the objective of not having more than 40% of PAHOERC consist of new members in any year.

4. Members unable to fulfill their responsibilities may submit a letter of resignation to the Director (copying the Secretariat) for the Director's consideration.

5. Notwithstanding their term of appointment, the service of PAHO staff on PAHOERC shall in any event end when their employment terminates, although former staff may later be reappointed to PAHOERC. In the case of PAHO staff members on short-term contracts, breaks between contracts of up to one month shall not be considered termination of appointment for the purposes of this rule, although during such breaks they shall not perform functions for PAHOERC.

6. Members may only be removed from PAHOERC by the Director. Examples of circumstances under which the Director will remove a member include but are not limited to:

a. Failure to attend at least 60% of PAHOERC's meetings in any given year.
b. Failure to perform the functions expected of members.
c. Flagrant departure from PAHOERC's SOPs.

Except in the case of removal for cause, members shall serve until their successors are named; special consideration will be given when a member is transferred to a new duty station.

B. Responsibilities

Members' responsibilities should be reflected in the staff members' work objectives. It is expected that members will be fully prepared for the reviews they undertake. They should strive to remain impartial and objective and keep demands for information and other material to a realistic minimum. They should use their expertise to make balanced judgments based on the evidence presented and must declare their conflicts of interest.

All Committee Members and the Secretariat are held accountable for scrutinizing the operations of PAHOERC in order to identify problems and to offer suggestions and contribute to the implementation of solutions that will improve the quality and efficiency of PAHOERC's work.

Such suggestions should typically be presented to the President, who will review the suggestion and consult with the Secretary. If they conclude that the suggestion would improve the functioning of PAHOERC, the Secretary shall either place the suggestion on the agenda for discussion at the next meeting or, if it merely amounts to an administrative adjustment, institute same and provide to all affected parties notification of the change.

C. Confidentiality

The deliberations of PAHOERC are confidential and all involved in the review process are bound to respect such confidentiality. The President shall provide a reminder of the requirement for confidentiality at the beginning of each meeting; otherwise, members may only discuss the information with other PAHO staff on a "need to know" basis.

To ensure that PAHOERC is able to engage in candid evaluation of research proposals, the minutes of its meetings and all other PAHOERC records shall be kept in such a manner that the points discussed are fully described without ascribing the views or conclusions to specific members. In the event that a third party is invited to contribute background information or clarifications, such person must not be present during PAHOERC deliberations.

In all communications from PAHOERC and the Secretariat, reasonable steps will be taken not to reveal confidential or proprietary information concerning any research proposal or Principal Investigator, and members involved in reviews are required to safely dispose of documents that are no longer necessary.

Information related to PAHOERC's final decisions is not confidential and may be disclosed.

D. Conflicts of Interest

Avoiding conflicts of interest as well as the appearance of such conflicts is important to ensure both the quality and credibility of research with human subjects. PAHO therefore takes seriously the need for investigators, Responsible PAHO Staff Members, PAHOERC Members and the Secretariat to avoid both conflicts of interest and the appearance of such conflicts. Any member with a conflict of interest shall recuse themselves from the relevant deliberations. The President, Vice-President or Secretary may also excuse members when conflicts arise.

PAHOERC shall ensure that the resolution to any situation involving a potential conflict of interest avoids not only the occurrence of unacceptable conflicts but also the appearance of such conflicts.

It is important that all reviewers of research proposals avoid, when possible, and disclose as appropriate, situations that affect their ability to provide objective judgment and assessment of proposals. The President and Secretary must ensure appropriate action is taken to minimize bias and address conflicts of interest.

E. Attendance

Meetings may only be attended by members, appointed observers, the Secretary and the Secretariat staff, or invited third parties. Members are responsible for notifying the Secretariat of their attendance as far in advance as possible.

Invited third parties may attend the meetings to provide additional information but must depart prior to the commencement of the deliberations.

F. Quorum

Five PAHOERC Members including the President (or Vice-President) and Secretary (or their delegate), must be present to constitute a quorum. If the quorum is not met, the meeting shall not review proposals, but can address other matters relevant to PAHOERC. Observers and support staff do not count towards the quorum.

Special Memberships

IX

A. President and Vice-President

The Director shall appoint a President and a Vice-President of PAHOERC from among its members. The President or, when the President is absent or unable to carry out the responsibilities of the office, the Vice-President, shall, in addition to such other functions provided for in these SOPs:

- Preside at meetings of PAHOERC;
- Name the members of any subcommittees or ad-hoc committees within PAHOERC (the President can delegate this responsibility to the Secretary);
- Convey to the Director PAHOERC's advice on matters related to the ethics of research involving human subjects and the activities and responsibilities of PAHOERC;
- Approve the Annual Report on the work of PAHOERC and the Secretariat;
- Provide general direction to the Secretary regarding the operations of PAHOERC and the Secretariat;
- Recommend potential new members to the Director, endeavoring to ensure appropriate balance of expertise, gender, geography, and cross-entity involvement;
- In consultation with the Secretary, establish an annual meeting schedule.

References hereinafter to the President in these SOPs shall refer to whichever officer is fulfilling the role of President.

B. Secretary

The Secretary of PAHOERC is the head of the Research Promotion and Development Team (RP) and reports to the Director. The Secretary shall be assisted by additional technically qualified and administrative staff designated to fulfill the function of the Secretariat of PAHOERC. When necessary, the Secretary can delegate representation for meetings and administrative issues to another member of the Secretariat. However, delegated persons do not count towards the quorum.

In addition to such other functions as are designated in these procedures, the Secretary shall:

1. Serve as a member of PAHOERC (ex-officio position);

2. Certify, on behalf of the Organization, which research proposals have been duly approved by PAHOERC in accordance with these procedures;

3. Ensure that the Secretariat operates in an efficient, accountable, and transparent manner, specifically by:
   a. Liaising with the President and other members on policy issues relating to PAHOERC and the protection of the rights and interests of human subjects in research funded or supported by PAHO.
   b. Providing any administrative assistance that may be needed by the President and members in carrying out PAHOERC's functions.
   c. Maintaining a Registry of PAHO Research Projects involving human subjects submitted for Committee review (PAHO's Research Registry).
   d. Undertaking a preliminary review of all research proposals submitted to determine whether the proposal is complete, and if not, liaising with the Responsible PAHO Staff Member to bring it up to the required standards.
   e. Ensuring that all necessary reviews of new and pending research proposals are carried out promptly by PAHOERC at such intervals and in such fashion as specified in these SOPs, or as otherwise directed by PAHOERC.
   f. Requesting, when appropriate, the assistance of external reviewers in order to inform the review by PAHOERC members of specific research proposals.
   g. Organizing PAHOERC meetings and promptly informing the relevant Responsible PAHO Staff Member of PAHOERC's decisions on each research proposal.
   h. Providing the necessary administrative support for the PAHOERC-related activities of the President and Vice-President.
   i. Timely drafting of meeting minutes, the Annual Report and other such reports regarding the work of the Secretariat and PAHOERC, as may be required.
   j. Maintaining and archiving the following documentation:
      1. A copy of these SOPs and any amendments.

      2. An up-to-date list of all PAHOERC members. Their terms of service, titles, and curriculum vitae or other biographical information sufficient to describe their qualifications (e.g. educational background and relevant area(s) of expertise) should be stored for at least 5 years.
      3. A full set of minutes of PAHOERC meetings and decisions, and such additional detailed records as PAHOERC may require shall be stored as part of PAHO's institutional memory.

4. PAHO's Research Registry data documenting the status of all research proposals submitted to PAHOERC (e.g., whether exempt from review, approved, awaiting changes before action, or not approved), including for approved research proposals, should be kept for at least 2 years after a project is completed.
5. Copies of all research proposals submitted to PAHOERC, including comments from any scientific or technical bodies and any other Ethics Review Committees that review any such research proposal; documents relevant to active and finished research proposals should be kept for at least 2 years after a decision on the proposal has been made and, if approved, for 2 years after the date of completion or discontinuation of the project.
6. Information related to Ethics Review Committees that have reviewed and research proposals also reviewed by PAHOERC should be kept for at least 2 years after a decision on the proposal has been made and, if approved, for 2 years after the date of completion or discontinuation of the project.
7. An updated list of peer reviewers.
8. The annual schedule of PAHOERC meetings.
9. Any other materials required for the efficient functioning of PAHOERC.

4. Make appropriate information readily available to PAHO staff about PAHOERC, including its SOPs, directives, activities (e.g. meeting times, educational programs, etc.) and decisions on proposals; use and update appropriate communication technologies to share information about PAHOERC and research ethics to relevant constituencies.

C. Observers

The Director can appoint observers representing a PAHO entity or program (for example Bioethics, Ethics, Legal, Procurement, Human Rights, Project Support or Country Support). Observers are expected to participate in the review process and make recommendations but do not vote on research proposals. Their attendance will be recorded but will not contribute towards the quorum of the meeting.

Internal Monitoring of Compliance and Annual Reports

X

At the conclusion of each year of work, the Secretariat shall prepare an Annual Report and submit it for the approval of the President.

The Annual Report shall include:

1. A description of PAHOERC's activities, accomplishments, and any particular challenges or pending issues;

2. A summary of the recommendations and conclusions of any independent evaluation(s) of PAHOERC;

3. Any recommendations for the improvement of PAHOERC, including any that would require a change in PAHOERC's functioning as set forth in these SOPs;

4. Tables summarizing the research proposals reviewed by area and country office and other relevant characteristics that delineate research at PAHO;

5. A listing of the composition of PAHOERC's membership and their attendance;

6. Any other relevant information.

Each year the Secretary shall submit an Annual Report to the Director by January 31. Once the Director has approved the Annual Report, the Secretary shall disseminate it to other relevant constituencies (including WHO counterparts) and post it on the relevant websites.

Glossary

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Adverse events: Creating unfavorable, undesirable or harmful results. They may consist of undesirable and unintended consequences of, or reactions to, procedures experienced by the research participant/subject (see Annex 2 about reporting unexpected events).

Annual report: An annual synoptic document that outlines and analyzes activities, especially summarizing the research proposals reviewed over the past year.

Approved: Formal confirmation that the proposal is satisfactory.

Beneficence: Refers to the ethical obligation to maximize benefits and to minimize harms (CIOMS).

Clinical trial: Any research study that perceptively assigns human participants or groups of humans to one or more health-related interventions to evaluate the effects on health outcomes.

Conditionally approved: The research proposal has not yet been approved; it requires the completion of one or more requirements before approval can be granted.

Conflict of interest: A conflict between a person's private interests and public obligations.

(The) Council for International Organizations of Medical Sciences (CIOMS): An international, nongovernmental, not-for-profit organization established jointly by WHO and UNESCO in 1949. CIOMS serves the scientific interests of the international biomedical community in general and has been active in promulgating guidelines for the ethical conduct of research, among other activities. CIOMS promulgated guidelines in 1993 entitled *International Ethical Guidelines for Biomedical Research Involving Human Subjects*. These 15 guidelines address issues including informed consent, standards for external review, recruitment of participants, and more. The Guidelines are general instructions and principles of ethical biomedical research. Website: http://www.cioms.ch/

Curriculum vitae: A summary of somebody's educational and work experience.

Data monitoring committee: A board set up by a clinical trial sponsor to evaluate trial progress, safety data, and significant outcomes according to regulatory agencies. This

committee, comprising community representatives and clinical research experts, may also recommend revisions or discontinuation of a clinical trial if the trial objectives remain unmet or safety concerns arise.

Declaration of Helsinki: Guidelines adopted in 1964 by the 18th World Medical Assembly (WMA) (Helsinki, Finland) and revised in 2008 by the 52nd WMA General Assembly, for physicians conducting biomedical research. This declaration outlines clinical trial procedures required to ensure patient safety, consent and ethics committee reviews in human subjects. The Declaration of Helsinki can be found at http://www.wma.net/e/ethicsunit/helsinki.htm (last accessed 4 June 2009).

Declaration of interests: The requirement for members to give notice of their interests in matters related to an item under consideration (see "conflict of interest").

Director: Persons chosen to control and govern the affairs of the Pan American Sanitary Bureau.

Ethics Review Committee (ERC): An independent body constituted of medical, scientific, and nonscientific members, whose responsibility it is to ensure the protection of the rights, safety and well-being of human subjects involved in research by, among other things, reviewing, approving and providing continuing review of trials, of protocols and amendments, and of the methods and materials to be used in obtaining and documenting informed consent from research subjects.

Expedited review process: Review of proposed research by the ERC Secretariat, Screening Committee, or a designated voting member or group of voting members rather than the entire Committee.

Experimental interventions: New or innovative interventions expected to improve a situation (especially medical procedures or applications that are intended to relieve illness or injury) that needs to have its effects assessed to determine if the expected benefits exceed those of other appropriate forms of care.

External peer review: The process of subjecting an author's scholarly work, research, or ideas to the scrutiny of others who are experts in the same field. Peer review requires a community of experts in given (and often narrowly defined) fields, who are qualified and able to perform impartial review. Peer reviewers are subject to declarations of interest (see "conflict of interest").

Federal Wide Assurance (FWA): Institutions conducting clinical studies or research (not otherwise exempt) supported by any agency of the U.S. Department of Health and Human Services (HHS) must have an OHRP-approved assurance of compliance with the HHS regulations (45 CFR 46.103) for the protection of human subjects.

Good clinical practices: A standard for the design, conduct, performance, monitoring, auditing, recording, analyses and reporting of clinical trials that provides assurance that the data and reported results are credible and accurate, and that the rights, integrity and confidentiality of trial participants are protected.

Human subjects: The U.S. Department of Human Services defines human subjects as "a living individual about whom an investigator (whether professional or student) conducting research obtains data through intervention or interaction with the individual or obtains identifiable private information. Regulations governing the use of human subjects in research extend to use of human organs, tissues, and body fluids from identifiable individuals as human subjects and to graphic, written, or recorded information derived from such individuals".

Identifier (ID): A unique number assigned to each proposal received by PAHOERC's Secretariat.

Informed consent documentation: Forms that indicate that a process has been followed for research participants to make the decision to take part in the research of her/his own free will and with an understanding of the potential risks and benefits. If the research involves more than one group of individuals, for example health-care users and health-care providers, a separate informed consent form for each group, tailored specifically for them, must be provided.

Internal monitoring: A plan describing the type of monitoring that will take place while a research proposal is being implemented (e.g. sample of all participants within a site; key data or all data) including the schedule of when these activities are to take place, how they are reported, and a timeframe to resolve any issues found. Internal monitoring seeks to identify unexpected changes in the benefit-risk ratio that warrant modifications to the research protocol and aims to protect research participants.

International Clinical Trial Register Platform: A platform set up by the World Health Organization (meta-register) that collates information from selected registers of research studies that prospectively assign human participants or groups of human participants to one or more health-related interventions to evaluate the effects on health outcomes. Clinical trials may also be referred to as interventional trials. Last accessed on 4 June 2009 at http://www.who.int/ictrp/en/.

Institutional Review Board (IRB): A committee that has been formally designated to approve, monitor and review biomedical and behavioral research involving humans with the aim to protect the rights and welfare of the research subjects.

Lead agency: The agency that has the principal responsibility for carrying out or approving a project.

Multi-center study: Research conducted at multiple sites using a common protocol.

Not approved: The research proposal is not complete for implementation; changes or amendments need to be presented to the Committee for further review.

Observer: Delegated persons or entities appointed by the Director to participate in the review process and make recommendations but who do not vote on research proposals.

Predictable risk: The probability of discomfort or harm to participants in a clinical trial.

President: The highest-ranking member of the Committee as appointed by the Director of the Pan American Sanitary Bureau.

Principal Investigator (PI): The lead scientist for a particular well-defined science (or other academic) project; responsible and accountable for the appropriate conduct of the research.

Public health surveillance: Refers to activities that regulatory and health agencies normally have to carry out to identify variations in health indicators. These involve the monitoring through regular and systematic collection, analysis, and interpretation of health data about conditions of significant impact on public health and their use to drive decisions about health policy and health education.

Quorum: A fixed minimum percentage or number of members of the Committee who must be present before the members can conduct valid business.

Research proposal: A document describing in detail how a research study is to be conducted in practice, including the methodology, a plan for analyzing the results, and a budget. Research proposals describe the processes followed to address questions through the application of scientific method.

Research team: The group of qualified personnel that implements a research proposal; it typically includes a principal investigator, additional investigators, a research coordinator and research assistants.

Responsible PAHO Staff Member: A member of staff responsible for representing PAHO's involvement in the research and liaising with external parties on matters involving a specific research proposal.

Sample size: Typically refers to the number of research subjects that will need to be recruited in a research proposal to address the main research questions with an estimated degree of certainty. Typically denoted n, a positive integer (natural number).

Screening Committee: Formed by at least three PAHOERC members, including one representative from the Secretariat, to screen research proposals or delegate on issues relevant to PAHOERC and to determine whether they need to be presented to the Committee.

Secretariat (PAHOERC Secretariat): A group of staff from the Pan American Sanitary Bureau that provides the administrative and organizational support needed to run the Ethics Review Committee.

Secretary: Head of Secretariat and typically the head of the Research, Promotion and Development Team.

Standard Operating Procedures (SOPs): A document with the rules and procedures relevant to the function of the Ethics Review Committee of the Pan American Health Organization (PAHOERC), including the requirements for research proposals submitted for ethical review.

Unexpected (adverse) events: Any adverse change in health or "side-effect" that occurs in a person who participates in a clinical trial while the patient is receiving the treatment (study medication, application of the study device, etc.) or within a pre-specified period of time after their treatment has been completed. While adverse effects are of particular concern to research subjects, it must be noted that occasionally the term refers to unexpected beneficial effects and that adverse effects can occasionally be anticipated (hence the differentiation between unexpected and adverse effects).

United Nations Convention on the Elimination of all forms of Discrimination against Women: See http://www.un.org/womenwatch/daw/cedaw/.

United Nations Convention on the Rights of the Child: See http://www.unhchr.ch/html/menu3/b/k2crc.htm.

Vice-President: The member of PAHOERC who is designated by the Director to fill in for the President of PAHOERC when the latter is unavailable.

Vulnerable subjects: Group/individual that cannot give informed consent because of limited autonomy, such as children, the mentally ill, prisoners and people who are unconscious or have an impaired judgment (see Section V).

World Health Organization's Ethics Review Committee (WHOERC): A 26-member Committee established and appointed by the Director-General, to ensure the highest ethical standards in research supported by WHO. It is mandated to review all research projects that involve human participants, and are supported, either financially or technically, by WHO. Additional information at http://www.who.int/rpc/research_ethics/erc/en/

Annexes

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1. Examples of guidelines and templates of informed consent forms

- World Health Organization. Informed consent form templates. Accessed on 4 June 2009 at http://www.who.int/rpc/research_ethics/informed_consent/en/

- Federal Wide Assurance (FWA) for the Protection of Human Subjects, Department of Health and Human Services (HHS), Office for Human Research Protections (OHRP), U.S. Government. Last visited on 7 April 2009 at http://www.hhs.gov/ohrp/humansubjects/assurance/filasurt.htm

- Code of Federal Regulations, Title 45, Public Welfare, Department of Health and Human Services (HHS), U.S. Government. Last visited on 7 April 2009 at http://www.hhs.gov/ohrp/humansubjects/guidance/45cfr46.htm

2. Reporting unexpected (adverse) events

Unexpected and adverse events can consist of undesirable or unintended consequences of, or reactions to, procedures experienced by the research participant/subject. These incidents or serious problems may involve (but are not limited to) the conduct of the study, or the subject's participation (i.e. problems with recruitment and/or consent process). Such events do not have to be physical in nature; an event could involve psychological harm and/or threats to privacy or subject safety.

The Responsible PAHO Staff Member must report in writing to PAHOERC any decisions made relating to adverse or unexpected events by the Principal Investigator and/or review, safety or monitoring committees within five working days of being thus informed. Examples include but are not limited to:

1. Injuries or complaints associated with the study procedures and/or problems involving the conduct of the study.

2. Any possible breach of human subject protections and confidentiality (i.e. loss or theft of files, breach of confidentiality, misuse of information, or inappropriate revealing of a subject's identity).

PAHOERC will review the decisions made by the Principal Investigator to determine whether there is an unacceptable change in the benefits and risks to subjects, which may require modifications to the project.

3. Facilitating compliance with government and funding agency requirements.

Considering the need for researchers to have ethics review approvals that are compliant with legislation, rules and/or regulations where research is conducted, sponsored or funded (for example the Federal Wide Assurance of the United States Government), PAHOERC may apply for registration and approval with relevant regulatory agencies.