# PAN AMERICAN HEALTH ORGANIZATION ETHICS REVIEW COMMITTEE

## Standard Operating Procedures

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Pan American Health Organization
World Health Organization
REGIONAL OFFICE FOR THE Americas

PAHO

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## I. Overview of the ethics review committee

The purpose of these Standard Operating Procedures (SOPs) is to outline the institutional function, structure, scope of review, review process, and membership criteria of the Pan American Health Organization Ethics Review Committee (PAHOERC) pursuant to PAHO/WHO E-Manual Policy XV.3.1 WHO Research Ethics Review Committee.

### A. Purpose of PAHOERC

PAHOERC was established by PAHO's Director (hereafter Director) to ensure that research conducted with the Organization's involvement meets international ethical standards. PAHOERC is thus tasked with:

- Conducting ethics review of all research with human participants that is financially or technically supported by PAHO
- Coordinating educational and capacity-building activities in areas relevant to research ethics.
- Facilitating and promoting the incorporation of ethical standards in research.
- Establishing, organizing, and maintaining institutional memory relevant to all research with human participants conducted with PAHO's financial or technical involvement and to the operations of PAHOERC.

The PAHOERC Secretariat (hereafter Secretariat) is housed in PAHO's Regional Program on Bioethics. PAHOERC is an independent entity that reports to the Director.

### B. Ethical standards

The *World Medical Association (WMA) Declaration of Helsinki* and the *International Ethical Guidelines for Health-related Research Involving Humans* of the Council for International Organizations of Medical Sciences (CIOMS) stipulate that all research with human participants must be reviewed and approved by an independent committee prior to its initiation. They also provide the ethical guidance for the review of research protocols. PAHOERC conducts an independent and thorough ethical analysis and deliberation of each research protocol that it determines requires PAHOERC review, based on the guidance set in the Declaration of Helsinki and the CIOMS Guidelines (see Appendix II: References). Ethics review must always be conducted before the initiation of any research with human participants. Ethics review and

approval cannot be conducted or provided retroactively. Approved research should further be monitored throughout the conduct of the studies, as stipulated by these international standards.

Research conducted with PAHO's involvement must adhere to WHO's Code of Conduct for responsible Research. Failure to obtain appropriate ethics approval and to adhere to the research integrity rules and principles stipulated by the Code will be handled as indicated in WHO's Policy on Misconduct in Research.

In accordance with PAHO/WHO E-Manual Policy 8.2.04, Publications policy, PAHO will not publish the results of research with human participants that was conducted without prior PAHOERC approval.

## II. What is subject to PAHOERC review?

All research with human participants conducted with PAHO's financial or technical involvement must undergo PAHOERC review and receive written approval before its initiation (PAHO/WHO E-Manual Policy XV.3.1 WHO Research Ethics Review Committee). This includes research proposals related to health emergencies declared by PAHO/WHO. Financial involvement includes both monetary and in-kind donations that make it possible to conduct research. Technical involvement can include, but is not limited to, intellectual contributions to the research project, even if PAHO personnel is not listed as investigators. Alternatively, research with human participants that is conducted with financial or technical involvement from PAHO may also proceed if it obtains approval from the World Health Organization Ethics Review Committee (WHO-ERC).

A proposal must meet the following two conditions to be considered "research with human participants:"

- *Research*: any social science, biomedical, behavioral, or epidemiological activity that entails systematic collection or analysis of data with the intent to develop or contribute to generalizable knowledge.
- *Human participants*: human beings (i) who become individually identifiable through investigator's collection, preparation, or use of biological material or medical or other records, or (ii) who are exposed to manipulation, intervention, observation, or other interaction with investigators either directly or through alteration of their environment.

Determinations about whether or not a proposal constitutes research with human participants shall be made by PAHOERC following the procedures stipulated in these SOPs. Investigators, project managers and their supervisors, and any personnel enabling the PAHO's financial or technical involvement are not in a position to determine whether their own proposal should be exempt from PAHOERC review at any stage of a protocol's development; they are in a conflict of interest.

Proposals detailing activities that do not aim to produce generalizable knowledge or do not involve human participants in the ways described above do not fit the definition of research with human participants and will be considered exempt from PAHOERC review (see section IV.D Exemptions from PAHOERC review). Exempt does not signify an endorsement of the research; rather, that the proposal falls outside PAHOERC's purview and will not be reviewed.

Proposals may include components that consist of research with human participants that reside within larger projects; such components must undergo ethics review.

## III. Submission Process

### A. Responsible PAHO personnel duties

To ensure that all research with human participants funded or technically supported by PAHO has received the appropriate ethics review, the responsible PAHO personnel directly or indirectly in contact with the Principal Investigator (PI), serving as PI, or working in the technical area related to the research proposal shall serve as the point of contact for PAHOERC's review process of that protocol. If the responsible PAHO personnel is not PAHO staff, they will need to obtain approval from their first-level supervisor before serving as the point of contact for the research project and include the first-level supervisor's name in their submission to PAHOERC. Responsible PAHO personnel duties are:

1. Ensuring that all PIs, whether internal or external researchers, are aware of the PAHOERC review requirement and do not initiate their research before obtaining a PAHOERC approval.
2. Ensuring a timely electronic submission of the research proposal to PAHOERC through ProEthos.

3. Coordinating with the PI and the research team as appropriate, ensuring that requests from the Secretariat are addressed throughout the PAHOERC review process and throughout the duration of the project in a thorough and timely manner.
4. Ensuring that the research is conducted in accordance with relevant national regulations and research integrity standards established by WHO's Code of Conduct for responsible Research.
5. Transferring the current duties of the responsible PAHO personnel to the appropriate PAHO personnel in the event that he/she departs PAHO or is reassigned to different activities.

**B. Principal Investigators' duties:**

1. Commit to maintaining transparent communications with the Secretariat through ProEthos or through the PAHOERC email address: pahoerc@paho.org, and copying the Responsible PAHO personnel on all communications.
2. Submit the proposal, revisions, progress reports, reports of adverse events, amendments, and any other information through ProEthos.
3. Respond to the Secretariat's requests within the established deadlines and in accordance with the SOPs.
4. Carry out studies in accordance with international ethical standards and national regulations.
5. Carry out studies in accordance with the approved protocol, except when immediate action is necessary to prevent harm to participants.
6. Comply with the monitoring plan established by PAHOERC.
7. Register clinical trials in a registry that feeds WHO's International Clinical Trials Registry Platform (ICTRP) before enrolling participants.
8. Continuously inform participants, using friendly language, about the progress of the study including emerging scientific evidence and study results.
9. Submit final reports of studies to PAHOERC.
10. Other duties necessary for the ethical conduct of the research.

## C. Electronic submissions to PAHOERC

PAHOERC only accepts research proposals submitted electronically, through ProEthos. The responsible PAHO personnel is responsible for the online submission of their proposal to PAHOERC. Responsible PAHO personnel and PIs must be attentive to the communication process with the Secretariat to ensure that PAHOERC's requests are efficiently addressed. Submissions are considered ready for full PAHOERC review if they include the following elements:

1. **Research protocol.** A complete research protocol should include:
    - Abstract (less than 300 words).
    - Brief background and justification for the study, including the up-to-date, previously published evidence, if available.
    - Study objective(s) and brief statements as to how the research question(s) are relevant for the context.
    - Methodology, including sampling methodology and relevant calculations, inclusion and exclusion criteria, participant selection process, variables, and data analysis plan that supports the objective(s) and research question(s).
    - Limitations and delimitations of the study.
    - Assessment of predictable risks and burdens to individuals and communities involved in the research, and a description of how they will be minimized and addressed.
    - Instrument(s). Questionnaires, scripts for focus groups, ratings scales, diagrams, and tools to collect information that will be used with humans. Information about the prior validation of the instruments should be included, if available.
    - Plans for community engagement
    - Samples or data sharing plans, if any.
    - A plan for the publication and dissemination of the research results, indicating the process by which they will be communicated to the public and health authorities, if appropriate.
    - A plan for making available any intervention that has been found effective, if appropriate.

- References.
- Decisions of other research ethics committees or scientific committees that have reviewed the proposal. Approvals must be in the form of an official letter, issued by a REC based in the country where the study will take place. In cases where the study will take place in more than one country, local ethics approval from each participating country is required and the protocol must be adapted to adhere to the regulations of each country. The review process can start upon submission of complete proposal documentation along with local ethics approval from any one of the countries in which the study will take place. Any previous reviews by other ethics or scientific boards or committees that approved or rejected the proposal or that required it to be modified must be included in the protocol. For studies conducted entirely online, such as those consisting primarily of emailed surveys sent out to multiple countries, a single approval, obtained in the country from which the study is being led, may be sufficient.
- Informed consent documentation (in the language of the potential participants). If research involves minors of an age at which that is appropriate to provide consent, a document for the assent process and a parental permission form must be included. If an oral consent process is planned, a script should be provided. If a waiver of informed consent is requested, a clear justification must be provided.
- Conflict of interest declaration statement. This statement must disclose all funding sources, sponsors, institutional affiliations, and any other sources of potential conflict of interest.
- A budget and timeline.
- Names, institutional affiliation, responsibilities and CVs (2 pages max.) for the PI and co-investigators. CVs should identify experience relevant to their role in the study and research ethics training.
- For clinical trials, documentation also includes proof of clinical trial registration in a registry that is part of the WHO International Clinical Trial Registry Platform (ICTRP: http://www.who.int/ictrp/en/). To meet this requirement, the identification number of the trial must be provided and included in the informed consent forms. Investigators should include their intent to register their studies as part of the study procedure

detailed in the research protocol and to publicly disclose their results (http://www.who.int/ictrp/results/reporting/en/).

- For research proposals related to PAHO/WHO-declared emergencies, it may be also required to provide a plan for minimizing risks, as appropriate.

A unique identifier will be assigned to every proposal upon submission, and written confirmation will be sent to the responsible PAHO personnel and the PI. PAHOERC's Secretariat reviews all submissions and informs the responsible PAHO personnel and PIs if the electronic protocol is deficient or if any section is incomplete and provides a deadline by which to provide the missing information or documents. PAHOERC can initiate the screening of protocols in development provided that enough information to conduct such a screening is included (see IV.A) is included. The Secretariat maintains a regular dialogue with responsible PAHO personnel and PIs from the date of submission to the time a decision is issued to ensure that the protocol is complete and adequate for ethics review, and to facilitate the review process.

## IV. Review process

### A. Screening

Screening is the first stage of PAHOERC review. Screening is the process by which PAHOERC members determine whether a proposal constitutes research with human participants and thus requires full ethics review by PAHOERC (see section II. What is subject to PAHOERC review?). The process is initiated by the Secretariat and conducted electronically after confirming that the submission meets the requirements set out in section III.B. Electronic submissions to PAHOERC or the minimum information necessary for a consultation. Consultations must include at least:

- Abstract.
- Objectives.
- A brief description of activities to be carried out that involve persons, their data or samples.
- Names and institutional affiliations of the team that is responsible for the proposal.

- PAHOERC may request additional documentation (e.g. draft questionnaires) if needed to fully understand the proposal.

The concurrence of at least three members is necessary to determine whether or not the proposal constitutes research with human participants.

If members are not able to reach a determination based on the information submitted, the Secretariat will request additional information. If it is determined that the proposal constitutes research with human participants and thus needs full PAHOERC review, the Secretariat will inform the responsible PAHO personnel and the PI about the decision, assess if the submission includes all the elements listed above, and request any missing elements be forwarded and/or incomplete elements be completed.

### B. Exemptions from full PAHOERC review

If during the screening process at least three members decide that a protocol does not meet the definition of research with human participants, an exemption from PAHOERC review will be issued. Such a decision does not exempt investigators from complying with any local or national-level laws or regulations, including submitting their protocol to a research ethics committee in the country where the study takes place. An exemption from PAHOERC review does not imply that the proposal has been deemed ethically acceptable; rather, it indicates that PAHOERC has established that it does not need to conduct a full review of the proposal.

PAHOERC encourages all investigators, PAHO staff and their counterparts to conduct all activities that do not constitute research with human participants ethically. For example, if an activity is granted an exemption from PAHOERC review because it is considered "public health surveillance," investigators are encouraged to consult *WHO guidelines on ethical issues in public health surveillance* for additional ethics guidance.

### C. Full committee review

Proposals must include all of the elements identified above in section III.B Electronic submissions to PAHOERC for a full review of the committee to proceed. Only proposals that are considered complete within two weeks of a PAHOERC meeting will be included in the agenda.

The Secretariat will seek an external review of the proposal by an expert in the topic of the study before the proposal undergoes full committee review. PAHOERC may decide to proceed

without such external review in cases in which the committee considers that the expertise of its members suffices for a thorough scientific assessment of the proposal.

The Secretariat organizes meetings at regular intervals, usually monthly. An annual schedule is disseminated to PAHOERC members and observers in advance. PIs and responsible PAHO personnel may be asked in advance to be available during the meeting that their proposal will undergo review to answer questions that may arise during the committee's deliberations.

An ethics analysis in accordance with the international ethical guidance listed above will be conducted of each proposal at the meetings. The following considerations will be used by PAHOERC to guide its deliberations as necessary: (1) social value, (2) scientific validity, (3) fair participant selection, (4) favorable risk-benefit ratio, (5) informed consent process, and (6) respect for participants (see Appendix II: Guiding questions for ethics review).

A quorum of five members is required to issue a decision on a proposal (see VII. E Attendance). PAHOERC will make decisions by consensus or through a simple majority vote.

Ethics review of a proposal will result in one of the following decisions:

1. *Approval*. Unless otherwise noted, approval is granted to a proposal for two years from the date of the approval. Extensions of approval may be requested if needed; these must be submitted through ProEthos and will be reviewed in an expedited manner by the Secretariat on behalf of the committee. Any proposed changes to the approved research proposal must be approved by the Secretariat prior to implementation of such changes. This includes proposals to conduct an approved study in a new site or country. The approval of a proposal does not prevent PAHOERC from sending comments for the consideration of the research team, or from requesting proof of clinical trial registration when appropriate. PAHOERC may withdraw approval for the study as explained in sections VI.A Continuing oversight of approved protocols and IX. Non-compliance.
2. *Revision*. In response to PAHOERC observations required for approval: investigators are required to respond to each observation provided by PAHOERC, making any necessary corrections to the protocol, instruments, or consent documents. When reviewing the proposal, the committee may determine that the Secretariat can assess: (a.) whether the observations are adequately addressed, (b.) if such assessment must be done in consultation with the members who participated in the original meeting, or (c.) if the revised proposal must be reviewed again at a PAHOERC meeting, (d.) a deadline by

which investigators must respond to the observations. PAHOERC's observations will be organized according to the six research ethics considerations listed above.

3. *Non*-approval. Proposals will receive a non-approval if the committee determines that a research proposal is unethical, if the responses to PAHOERC's observations are deemed unsatisfactory, or if no response to PAHOERC's observations is submitted within 30 days of the issue date, unless there is a prior request from the investigators to extend that time. Proposals that receive a non-approval must be substantively revised and resubmitted as new proposals through ProEthos to be reconsidered by PAHOERC. Resubmissions must include confirmation that the updated version of the study has been reviewed or amended by an ERC in the country where the study will take place.

4. Exempt from review. PAHOERC may determine that a proposal does not constitute research with human participants and therefore issue an exemption.

**D. Appeals process**

Responsible PAHO personnel and PIs may submit an appeal to PAHOERC if they do not agree with PAHOERC's decision. Appeals must be submitted to the Secretariat in writing, listing the specific reasons for the appeal and providing the references that support their arguments. Appeals must be sent to pahoerc@paho.org within 30 days of receipt of PAHOERC's decision. In the interest of maintaining impartiality, PAHOERC will endeavor to invite an external reviewer to assess the protocol and the decision in question. PAHOERC reserves the right to review the appeal during a full PAHOERC meeting.

**E. Expedited review**

An expedited review is conducted by the Secretariat without convening the committee. Expedited reviews can only be conducted for studies that use the same protocol as another study that has received a prior approval from PAHOERC or WHO-ERC and are being submitted for implementation in a different location. Studies that depart from the previously approved protocol will not be eligible for expedited review by the Secretariat. PAHOERC will be informed at the monthly meeting about proposals that have undergone expedited review and have been approved by the Secretariat.

### F. Ethics review during PAHO/WHO-declared emergencies

Requests for review of research proposals related to health emergencies are prioritized. PAHOERC will endeavor to schedule virtual meetings to review an emergency-related research proposal within two business days of receiving the proposal through ProEthos

A quorum of five members is necessary for decision-making. Quorum should include members with experience and knowledge relevant to the review of research. If appropriate, *ad hoc* members with expertise in the topic of the proposal will be involved in the review and granted full decision-making capacity.

If members are unable to participate in the meeting, they will be considered for quorum if they submit their reviews electronically to the Secretariat in advance of the meeting or shortly thereafter (e.g. through ProEthos, email, or Microsoft Teams). In these cases, PAHOERC will conduct a staggered review and the Secretariat will send summaries of the deliberations to all members through email or ProEthos at the relevant stages of the process.

PAHOERC will endeavor to send additional requests for information, observations, or a decision as soon as possible after finalizing the review of an emergency-related proposal and no later than 24 hours after the review process is completed (see Catalyzing Ethical Research in Emergencies. Ethics Guidance, Lessons Learned from the COVID-19 Pandemic, and Pending Agenda).

## V. Research Proposal Variations

### A. Multi-country studies

Research with human participants that will use the same research protocol in several different countries requires that ethics approval be obtained for each country. Approval from PAHOERC (or, alternatively, from WHO-ERC) must be obtained for each country in which the study will be conducted. If PAHOERC or WHO-ERC has already approved the study for one country, an expedited review will be conducted for any additional country in which the study will be carried out. For each additional country where the study will take place, a cover letter should be included that details any differences from the previously approved protocol.

### B. Nested studies

Any study that is part of another, i.e. "nested" within another study, shall be reviewed in the same way as any other research proposal. The protocol for the main study should be submitted along with the proposal for the nested study. While the protocol for the main study may not be formally reviewed by PAHOERC, the committee must be satisfied with its ethical aspects and possess documentation of its ethics approval before initiating review of the nested study.

### C. Clinical trials

PAHOERC considers a “clinical trial” to be any research that adheres to WHO’s definition: “any research study that prospectively assigns human participants or groups of humans to one or more health-related interventions to evaluate the effects on health outcomes” (http://www.who.int/ictrp/en/). Interventions are not required to be pharmacologic. Clinical trials are reviewed in the same way as other research protocols, with the additional requirement that they must be registered in a registry that is part of ICTRP before enrolling research participants.

### D. Standardized protocols

PAHOERC and WHO-ERC may review and approve standardized protocols with the aim of catalyzing ethical research on a particular topic or in health emergencies. Standardized protocols are also called master protocols. Approved standardized protocols must be adjusted later to consider the specific context where the study will be conducted. These “site-specific protocols” must obtain ethics approval in the country where the study will be conducted, as well as approval from PAHOERC or WHO-ERC. PAHOERC will review these protocols in an expedited manner unless they depart substantively from the previously approved standardized protocols, or if the relevant evidence base has undergone significant changes since the time the standardized protocol was written.

## VI. Continuing monitoring of approved studies

### A. Continuing monitoring

PAHOERC shall ensure continuing monitoring of approved research proposals with human participants. The Secretariat will monitor approved proposals every year.

Responsible PAHO personnel or the PI shall report any substantial amendments in an approved research proposal to PAHOERC. Amendments must be submitted through ProEthos and include their description and justification, the final version of the amended document(s), and the version with track changes. Examples of substantial amendments include:

1. Changes in sample size, sampling procedures or settings; change in the PI and/or key member(s) of the research team; changes in funding sources or conflicts of interest.
2. Changes in the recommendations by other research ethics committees; new knowledge that alters the balance of benefits and risks.
3. Early termination of a study and the reasons behind the decision (e.g. a request by a local safety and data monitoring committee; the risks outweigh the benefits to the study participants; the research questions have been decisively answered; natural disasters or other external factors).

Changes may be implemented only after obtaining PAHOERC approval with the exception of modifications urgently needed to protect the wellbeing or important interests of participants already enrolled in the study.

The Secretariat will determine whether the proposed changes are subject to full committee review.

PAHOERC may withdraw its approval of a proposal. Examples of circumstances that would require withdrawal of approval are:

- Local ethics approval is withdrawn.
- Presentation of fraudulent documentation.
- Failure to report substantial changes or departure from the protocol.

In those cases, PAHOERC will communicate the decision to other research ethics committees that approved the proposal.

Once a research proposal has been completed or discontinued, the responsible PAHO Personnel for the study shall notify PAHOERC and submit a brief final technical report on the study within 60 days of completion or discontinuation of the research. The PI is encouraged to inform the responsible PAHO personnel of references and links to relevant publications issued subsequent to the study, link them in trial registries when appropriate, and keep the registries up-to-date.

### B. 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. These incidents or serious problems may involve the conduct of the study or the participation in the study (e.g. problems with recruitment or consent process). Such events do not have to be physical in nature; an event could involve psychological harm or threats to privacy or participant's safety.

Adverse or unexpected events must be reported immediately to the local research ethics committees that approved the study. The responsible PAHO personnel or PI for the study must notify PAHOERC in writing about adverse or unexpected events within five working days of the PI's discovery of the occurrence. Additionally, the responsible PAHO personnel for the study must immediately notify PAHOERC in writing about any decisions made by the PI and/or review, safety or monitoring committees in response to adverse or unexpected events. Examples include:

- Injuries or complaints associated with the study procedures and/or problems involving the conduct of the study.
- Any possible breach of human subject protections and confidentiality (e.g., 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 PI to determine whether there is a change in the benefits and risks to participants that requires modifications to the proposal.

### C. Ethics monitoring of emergency-related research

Amendments, reports, and other communications regarding an emergency-related protocol must be submitted through ProEthos. Amendments requesting substantial revisions may be subject to review during an additional PAHOERC virtual meeting; in such cases, PAHOERC will endeavor to hold a meeting within 48 hours of the receipt of the additional documentation.

PAHOERC will closely monitor approved research related to the emergency. The Secretariat may designate an ERC member or group to be in charge of monitoring a particular research protocol.

If new evidence emerges, researchers must evaluate it expeditiously to identify whether it affects the research they are conducting. They must promptly send PAHOERC a report that includes the following:

- a summary of the most important points from their review of new evidence,
- references consulted, and
- justification for the way in which the research will proceed (whether the study will be continued, modified, suspended, or terminated).

PAHOERC will review the protocol on the basis of the new evidence and approve, as appropriate, the measures proposed by the researchers. PAHOERC may request additional measures as needed, including temporarily suspending it, or withdrawing its approval. PAHOERC will communicate its decision immediately to the local ERCs and the relevant health authorities. Any change to the protocol should be promptly recorded in the respective research registries.

## VII. Protocols for the emergency use of unproven interventions outside of research

### A. MEURI Overview

Protocols for the use of unproven interventions outside of a research protocol in emergency situations, i.e., under the Monitored emergency use of unregistered and experimental interventions (MEURI) framework, will be reviewed in the same timeframe as research protocols and in accordance with the relevant ethical criteria (see *Chapter 5 of Catalyzing Ethical Research in Emergencies. Ethics Guidance, Lessons Learned from the COVID-19 Pandemic, and Pending Agenda)*.

### B. Submission of MEURI protocols

The use of the intervention must be proposed as part of a protocol submitted through ProEthos. The protocol should include at least the following elements:

- background;
- scientific justification, based on the recommendations of a scientific committee or recommendations issued by PAHO/WHO;

- objectives;
- population to be offered the intervention;
- risks and potential benefits;
- measures to minimize risks;
- scientific data to be collected that may provide information on the intervention's safety and efficacy;
- plan to offer the intervention;
- informed consent documents and details about the process;
- measures to protect confidentiality;
- data sharing plan; and
- proposal for the transition to research.

PAHOERC will require the differentiated registration of MEURI protocols in registries that feed WHO's ICTRP.

### C. Monitoring of MEURI protocols

PAHOERC will monitor the emergency use of the unproven intervention to ensure that it remains justified in light of newly available evidence. PAHOERC may require modifications to the intervention or the way it is offered, or else its suspension or termination. For monitoring purposes, PAHOERC will promote rapid and efficient mechanisms for communication and coordination with health authorities and health care professionals responsible for the intervention offered under the MEURI framework.

## VIII. PAHOERC membership

### A. Membership overview

PAHOERC operates independently and reports directly to the PAHO Director. The Organization must ensure that PAHOERC has a diverse, gender-balanced, and multidisciplinary membership. Members serve in an individual capacity and do not participate as official representatives of any entity.

PAHOERC consists of a minimum of 11 and a maximum of 15 internal members, inclusive of the secretary, and at least one member external to PAHO. Members are appointed by the PAHO Director based on their willingness to commit the time required to fulfill their duties on PAHOERC and/or their knowledge and experience in research or research ethics. Upon

appointment, members shall submit to the Secretariat a declaration to abide by these Standard Operating Procedures.

Decisions on initiation or termination of membership shall be guided by the objective of achieving a balanced staggering of membership turnover and ensuring diversity of expertise while maintaining a balance for gender. New membership on any given year should not consist of more than 30% of PAHOERC members. PAHOERC must include as a member at least one person whose background is not in research.

Members who find that they are unable to fulfill their duties may resign by notifying the Secretariat. Notwithstanding their term of appointment, the service of PAHO staff on PAHOERC shall end upon termination of their employment, although former staff may later be reappointed to serve as a PAHOERC external member. 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.

Members may only be removed from PAHOERC by the PAHO Director. Circumstances under which the PAHO Director may remove a member include failure to perform the functions expected of members and 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. Duties**

Members are responsible for attending and participating in committee meetings. Members are expected to be fully prepared for the reviews they undertake. Members should undergo training on research ethics within six months of beginning service on PAHOERC unless they have obtained prior research ethics training and commit to participating in ongoing trainings on topics relevant to the work of the committee. They should strive to remain impartial and objective and keep demands for information and other material to a realistic level. They should use their expertise to make balanced judgments based on the evidence presented and must declare any conflicts of interest to the president or the secretariat before initiation of a review process. Member responsibilities shall be reflected in the staff members' work objectives.

All PAHOERC members and the Secretariat are expected to contemplate the operations of PAHOERC to identify problems and to offer suggestions as well as contribute to the implementation of solutions that will improve the quality and efficiency of PAHOERC's work.

During emergencies, PAHOERC members should respond promptly to requests from the Secretariat and adhere to the timelines for ethics review and monitoring described in these SOPs.

### C. Confidentiality

The deliberations of PAHOERC are confidential and all involved in the review process, including external reviewers, are bound to respect such confidentiality. The president will 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 can 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. If a third party is invited to contribute background information or clarifications, they may not be present during PAHOERC's 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 PI, 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 conflict of interest, as well as the appearance of such conflicts, is important to ensure both the quality and credibility of the process of ethics review of proposals for research with human participants. PAHO therefore takes seriously the need for investigators, responsible PAHO Personnel, members, observers and the Secretariat to avoid both conflicts of interest and the appearance of such conflicts. As participants in an expert technical group, members are required to complete a conflict-of-interest form (Chapter VI Procurement Sub-Chapter VI.1 General Procurement Requirements)(WHO/PAHO III.1.2 Declaration of Interests). Members must also complete the annual Declaration of Interests form issued by the PAHO Ethics Office.

It is important that all reviewers of research proposals avoid, when possible, and disclose, as appropriate, circumstances that may affect their ability to provide objective judgment and assessment of proposals and must recuse themselves from any related deliberations. The president and secretary must ensure appropriate action is taken to minimize bias and address conflicts of interest and will excuse members when conflicts arise. Members should advise the Secretariat of any research that they are involved in from the point of its submittal to PAHOERC and through the electronic screening process, so that they may be excluded from the related review process. During monthly meetings, members may not be present for discussions or deliberations of any protocols for which they will serve as a co-investigator or on which they have provided advice.

### E. Attendance

Virtual or in-person committee meetings may only be attended by members, appointed observers, the secretary and the Secretariat staff, and invited third parties. Members are responsible for notifying the Secretariat of their availability for meetings 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.

To constitute a quorum, five PAHOERC members must be present in a meeting. Members are equally responsible for attending meetings and ensuring that quorum is met. If a quorum is not met, no decisions may be issued. However, preliminary reviews of protocols can be conducted, and the members may address other matters relevant to PAHOERC. Observers and support staff do not count towards quorum.

Minutes that record attendance, issues discussed, and decisions made on proposals will be produced by the Secretariat and shared with members for their approval.

## VIII. Special roles

### 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 position, the vice president) shall, amongst other functions described in these SOPs:

1. Preside at meetings of PAHOERC.
2. Convey PAHOERC's advice to the PAHO Director on matters related to the ethics of research involving human participants and the activities and responsibilities of PAHOERC.
3. Approve the annual report on the work of PAHOERC.
4. Provide general direction to the secretary regarding the operations of PAHOERC and the Secretariat.
5. Recommend potential new members to the PAHO Director, endeavoring to ensure appropriate balance of expertise and gender.
6. In consultation with the secretary, establish an annual meeting schedule.
7. In consultation with the secretary, call for auxiliary meetings to review research during PAHO-declared emergencies and make the relevant decisions regarding quorum for those meetings.
8. In consultation with the secretary, prepare and present to the PAHO Director a budget for the bi-annual operation of PAHOERC.

In the event that the vice president is unable to carry out these responsibilities, then the president shall name a delegate among PAHOERC members.

**B. Secretary**

The secretary of PAHOERC is appointed by and reports to the PAHO 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. The secretary shall, amongst other functions described in these SOPs:

1. Serve as a member of PAHOERC.

2. Ensure that the Secretariat operates in an efficient, accountable, and transparent manner specifically by:

    a. Liaising with the president, vice president, and other members or observers, on policy issues relating to PAHOERC and the protection of human participants in research funded or supported by PAHO.

    b. Managing the digital registry of projects and coordinating its management with the President.

    c. Facilitating the timely progress of research protocol reviews through close communication with members and researchers.

    d. Maintaining a record of the following documentation:

        - All relevant proposal documentation, including amendments, comments from any scientific or technical bodies and any other research ethics committees that review any such research proposal, final research reports, as well as any other information generated during review and oversight processes.
        - A copy of these SOPs and any amendments.
        - 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 after separating from PAHOERC.
        - A full set of minutes of PAHOERC meetings and decisions, and such additional detailed records as PAHOERC may require. These documents shall be stored within ProEthos as part of PAHO's institutional memory.
        - Information regarding the status of all research proposals submitted to PAHOERC.

- Documents relevant to active and finished research proposals shall be kept for at least 7 years after a decision on the proposal has been made and, if approved, for at least 10 years after the date of completion or discontinuation of the project.
- The annual schedule of PAHOERC meetings.
- Any other materials required for the efficient functioning of PAHOERC.

3. Undertaking a preliminary review of all research proposals' documentation submitted to determine whether the documentation is complete, and if not, liaising with the responsible PAHO personnel and PI to complete the submission and ensure that the proposal is ready for committee review.

4. Providing assistance to PAHO staff, PIs and other relevant stakeholders in matters pertaining to ethics review (requirements for submitting applications, internal processes, timelines, and other aspects).

5. 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.

6. Requesting external reviews of research proposals, ensuring conflicts of interest are declared and managed before documentation is sent.

7. Organizing the PAHOERC meetings. This includes:

    - Distributing relevant documentation to members, including ad-hoc reviews
    - Scheduling meetings
    - Ensuring quorum
    - Preparing the minutes, decisions, the annual report and other Documentation regarding the work of the Secretariat and PAHOERC, as may be required, in coordination with the President.
    - Requesting the registration of clinical trials in a registry that feeds ICTRP.

- Promptly informing the relevant responsible PAHO personnel and PIs of PAHOERC's decisions on each research proposal.
- Providing the necessary administrative support for the PAHOERC-related activities of the committee.
- Liaising with WHO-ERC
- Report, as appropriate, on research proposals that have been approved by PAHOERC
- Make appropriate information readily available to PAHO staff about PAHOERC and international ethical guidelines; use and update appropriate communication technologies to share information about PAHOERC and research ethics to relevant constituencies.
- Other duties necessary for the proper functioning of PAHOERC.

### C. Observers

The PAHO Director can appoint observers representing a PAHO entity or program (for example Ethics, Legal, Procurement, and External Relations). 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 quorum.

## IX. Non-compliance

Research with human participants that involves PAHO and is conducted or initiated without prior PAHOERC approval is considered "non-compliant." Protocol violations, namely situations in which research has been conducted in a manner that differs from the protocol that has been approved by PAHOERC, are also considered "non-compliant." PAHOERC may withdraw its approval in cases of non-compliant research.

Non-compliance constitutes research misconduct according to WHO's Code of Conduct for responsible Research, and will be handled as indicated in WHO's Policy on Misconduct in Research.

If PAHOERC is made aware of any instance of non-compliance, the Secretariat will first reach out to the responsible PAHO personnel and PI to gather information about the situation and the status of the research. PAHOERC will report incidents of non-compliance to the responsible PAHO personnel for the study, the relevant unit chiefs and department directors, the PAHO/WHO Representative of the country where the study was conducted, the Legal Office, the

Ethics Office, and the PAHO Director. In cases of protocol violations, PAHOERC will also inform other research ethics committees that approved the study.

## X. Internal monitoring and reporting

At the end of each year of work, the Secretariat shall prepare an Annual report that will be reviewed by PAHOERC members and approved by the president. The annual report shall include:

1. A description of PAHOERC's activities, accomplishments, and any 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.

5. A list detailing PAHOERC's membership.

6. Information on any non-compliance issue that has been brought to PAHOERC's attention.

7. The budgetary status of PAHOERC's work.

8. Any other relevant information.

The secretary shall submit the annual report to the PAHO Director by January 31 of the next year. Once the PAHO Director has approved the annual report, the secretary shall disseminate it to other relevant constituencies.

## Appendix I: International guidance and standards

Council for International Organizations of Medical Sciences (CIOMS). (2016). *International Ethical Guidelines for Health-related Research Involving Humans*. Fourth Edition. Geneva, Switzerland: CIOMS. Retrieved from https://cioms.ch/wp-content/uploads/2017/01/WEB-CIOMS-EthicalGuidelines.pdf

World Health Organization. (2011). *Standards and operational guidance for ethics review of health-related research with human participants*. Geneva, Switzerland: World Health Organization; 2011. Retrieved from http://www.who.int/iris/handle/10665/44783

World Medical Association. (2013). *World Medical Association Declaration of Helsinki ethical principles for medical research involving human subjects*. Retrieved from *https://www.wma.net/policies-post/wma-declaration-of-helsinki-ethical-principles-for-medical-research-involving-human-subjects/*

Pan American Health Organization. (2022). Catalyzing ethical research in emergencies. Ethics guidance, lessons learned from the COVID-19 pandemic, and pending agenda. Washington, D.C. Retrieved from https://iris.paho.org/handle/10665.2/56139

**Appendix II: Guiding questions for ethics review of research with human participants**

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|---|
| *1. Social value*<br>Can this study lead to improvements in health or well-being? Who will benefit from the conduct and results of research? What is the potential value of the research for each of the prospective beneficiaries? |
| *2. Scientific validity*<br>Is the investigation methodologically valid and scientifically (and statistically) sound?<br>Do the scientific and statistical design and methods satisfy generally accepted standards and achieve the objectives of the study? Will the study generate valid and reliable data that can be generalizable?<br>Is the study feasible? Does the study design ensure participants the healthcare interventions they are entitled to? If not, are there methodologically compelling reasons to participate and are participants protected from serious harm? |
| *3. Fair participant selection*<br>What are the criteria to include and exclude participants? Is selection of participants based on scientific criteria? Are research participants selected to minimize risks and maximize potential benefits? If participants are vulnerable, are there adequate safeguards to protect them? Are the risks and potential benefits of the study fairly distributed? |
| *4. Favorable risk-benefit ratio*<br>*What are the physical, psychological, social and economic risks of the study? Can the risks for participants be minimized? Can potential benefits for individuals and society be improved? Do the potential benefits for society and individuals outweigh the risks?* |
| *5. Adequate informed consent*<br>*Is the information provided to potential participants accurate, clear, relevant and complete? Are the recruitment procedures, consent process and incentives appropriate for their culture and context? Is there an appropriate plan for obtaining permission for those who can't consent for themselves? Are the* participants being made aware of their right to refuse to participate and are they actually free to refuse? |

*6. Respect for participants*

*How will the health and well-being of participants be monitored to minimize harms? How will their confidentiality be protected? Can participants withdraw from the study without penalty? What are the plans of care after the study is completed? Will participants be given any new information (including the results of the study)?*

Adapted from: (1) Emanuel E, Wendler D, Grady C. An ethical framework for biomedical research. In: Emanuel E et al. eds. The Oxford textbook of clinical research ethics. New York, NY: Oxford University Press; 2008: 123-135. (2) Emanuel E, Wendler D, Grady C. What makes clinical research ethical? JAMA 2000;283:2701-27711. (3) Emanuel E, Wendler D, Killen J, Grady C. What makes clinical research in developing countries ethical? The benchmarks of ethical research. JID 2004;189:930-937.