The Ethics Review Committee (WPRO-ERC)

Standard Operating Procedures

World Health Organization
Western Pacific Region

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We are pleased to present Standard Operating Procedures for the Ethics Review Committee of Western Pacific Regional office of WHO (WPRO-ERC). These standard operating procedures were approved by the Regional Director, Dr. Shin Young-soo on November 1 2009.

These Standard Operating Procedures were created and reviewed by WPRO-ERC Members. The World Health's Organization Ethics Review Committee Secretariat. The discussions were coordinated by the WPRO-ERC Secretariat, housed within the Information, Evidence and Research (IER) technical unit in the Division of Health Sector Development. We would like to acknowledge the contributions by WHO-ERC, WPRO-ERC Members and Observers, and the WPRO-ERC Secretariat. Your comments and feedback are welcome and can be submitted to WPRO-ERC@wpro.who.int. Updates and additional information is available at http://www.wpro.who.int/researchportal

Dr. John Ehrenberg, Chair, WPRO-ERC
Dr. Susan Mercado, Vice-Chair, WPRO-ERC
Dr. Manju Rani, Secretary WPRO-ERC

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I

Overview of the Ethics Review Committee

These standard operating Procedures (hereinafter "SOP") delineate the structure, functions and process (including the review criteria) to be followed by the Ethics Review Committee of the WHO regional office for Western Pacific Region (hereinafter "the Committee" or "WPRO-ERC") for ethical review of research proposals submitted to it. The SOP will override any other administrative rules or procedures specified elsewhere before October 2010. The relevant section in WPRO handbook dealing with this issue has been revised accordingly.

A. The Purpose of WPRO-ERC

The key functions of WPRO-ERC will include:

1. Ensuring that any research involving human participants in which WPRO/WHO is involved either as funder, manager, technical assistance partner or collaborator meets ethical standards in accordance with three basic ethical principles: respect for persons, beneficence, and justice;

2. Ensuring that the proposed research design is scientifically sound and appropriate for addressing research questions and will not unnecessarily expose research participants to risk;

B. Fundamental Ethical Standards

WPRO-ERC follows the guidelines set by World Medical Association in Declaration of Helsinki and by The Council for International Organization of Medical Sciences (CIOMS). It will also be guided by other international/regional human rights treaties and standards as relevant, abiding with the ethical principles for research involving human subjects, including research on identifiable human material and data.

WPRO-ERC Structure

II

A. Members

The Committee shall consist of at least 15 members excluding the Senior Technical Officer (Health Research Policy), who serves as an ex-officio member and Secretary to WPRO-ERC. The Regional Director will appoint two of those members to serve as Chair and Vice-chair of WPRO-ERC.

1. The Committee shall have an appropriate gender balance, and at least two members (a single member may have multiple expertises) must have the following expertise or background in each of the following areas:

   a) biostatistics, epidemiology and research methodologies

   b) social or behavioural research

   c) health systems, preferably also with health economics background

   d) communicable diseases

   e) non-communicable diseases

   f) human rights, gender and/or law

2. At least one of the appointed members will be from a non-health background.

3. Members who are WPRO staff shall serve in an individual capacity and not as official representatives of any unit or programme of the organization. They may not be able to delegate their responsibilities as member of WPRO-ERC to any other technical staff in their unit/program.

4. There shall be at least one member in the Committee not employed by WPRO. These members shall be known as "non-affiliated members". These members will also serve in an individual capacity and not as official representative of their organization.

5. Neither affiliated nor non-affiliated members will receive any remuneration or compensation for specifically serving on the committee or attending its meetings.

B. Appointment of Members

Members shall be appointed by the Regional Director for a two-year term, renewable once for a maximum of two consecutive terms.

1. Members shall be appointed based on but not limited to:
    a) Their willingness to commit the time required for their duties on WPRO-ERC;
    b) Their expert knowledge in medicine, science, or another field, as appropriate; and
    c) Their willingness to acquire knowledge of research ethics through appropriate training and education within two months of beginning service on the Committee.
2. Notwithstanding their term of appointment, the service of WPRO staff on the Committee shall in any event end when their employment terminates. For WPRO 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 break they shall not perform functions for the Committee.
3. Members unable to fulfill their responsibilities may submit a letter of resignation to the Regional Director (copying the Secretariat) for the consideration of Regional Director.
4. Each member shall attend at least 50% of the meetings.
5. To ensure the independence of the Committee and the ability of its members to exercise their judgment concerning matters coming before the Committee, they may only be removed from the Committee by the Regional Director in the event of:
    a) Failure to attend three consecutive meetings for which they had previously committed, without informing the Secretariat in advance prior to the meetings;
    b) Failure to attend at least 40% of the WPRO-ERC meetings in any given year;
    c) Failure to perform the functions expected of Committee members, including serving as primary reviewer of assigned research proposals; or
    d) Flagrant departure from WPRO-ERC SOPs.

6. Except in the case of removal for cause, members shall serve until their successors are named.

C. Chair and Vice-Chair

1. Appointment

   a) The Regional Director shall appoint a Chair and a Vice Chair of the Committee from among its members on the recommendation of the Director, Division of Health Sector Development.

   b) Appointment as Chair and Vice-Chair shall be for a maximum two renewable terms of two years each, or for the duration of the membership, whichever is shorter.

2. Responsibilities

   The Chair or, when the Chair is absent or unable to carry out the responsibilities of the office, the Vice-Chair, shall, in addition to such other functions provided for in these Rules:

   a) Preside at meetings of the WPRO-ERC.

   b) Sign, on behalf of the Committee, the review outcomes and recommendations on the proposals reviewed by the Committee;

   c) Name the members of any subcommittees or ad hoc committees;

   d) Convey to the Regional Director the Committee's advice on matters related to the ethics of research involving human participants or to the activities and responsibilities of the Committee;

   e) Work with and provide general direction to the Secretary regarding the operation of the Committee and the Secretariat; and

   f) Recommend to the Regional Director possible new members, endeavoring to ensure appropriate balance of expertise, gender, geography, and cross-division involvement.

3. The Chair will hand over the responsibility of the office to the Vice Chair whenever proposals from the Chair's immediate area of work are being reviewed or discussed.

Similarly, the Vice-Chair shall not act as the Chair if proposals from their immediate area of work are being reviewed or discussed. (See section VI for more details regarding conflict of interest). In the event that neither the Chair nor the Vice-Chair is available, the Chair will designate in writing, the WPRO-ERC member who will be authorized to act on behalf of the Chair.

References hereinafter to the Chair in these Rules shall refer to whichever officer is fulfilling the role of Chair.

D. Secretary

1. The Secretary of the Committee shall be the Senior Technical Officer (Health Research Policy) in the technical unit of Health Information, Evidence and Research (IER) in the Division of Health Sector Development in WPRO. The Secretary shall be assisted by an administrative staff as required to fulfil the function of the Secretariat of the Committee. When necessary, the Secretary can delegate representation for meetings and administrative issues to another member of the IER. However, neither the Secretary nor the delegated persons will count towards quorum.

2. Responsibilities

   In addition to such other functions as are provided in these Rules, the Secretary shall:

   a) Serve as a member of WPRO-ERC (ex-officio position).

   b) Certify, on behalf of organization, which research proposals have been duly approved by WPRO-ERC in accordance with these procedures.

   c) Make available to WHO staff and new members of WPRO-ERC information and educational materials and training on ethical issues relating to research with human participants.

   d) Take appropriate steps to make the standards employed by the WPRO-ERC in reviewing research known and accessible to WPRO staff and to investigators who carry out research involving human participants funded or otherwise supported by WPRO.

   e) Ensure that the secretariat operates in an efficient, accountable and transparent manner, specifically by

i) Liaising with the Chair and the Committee members on policy issues relating to the WPRO-ERC;

ii) Ensuring any administrative assistance that may be needed by the Chair and members in carrying out the Committee's functions;

iii) Maintaining a Registry of research proposals involving human participants submitted for Committee review ("WPRO Research Registry);

iv) Undertaking a preliminary review of all submitted proposals to assess whether the proposal is complete, and if not, to liaise with the WPRO technical officer in order to bring it up to the required standards;

v) Scheduling, coordinating and organizing WPRO-ERC meetings at such intervals and in such a manner as specified in these Rules or as otherwise directed by the Committee to ensure prompt reviews of new and pending research proposals;

vi) Informing the responsible WPRO staff member in a timely manner of the Committee's decision for each research proposal reviewed;

vii) Timely drafting of meeting minutes, the annual Report, and other such reports as may be required, regarding the work of the Secretariat and of the Committee;

viii) Work with the Chair and other officials to obtain for WPRO-ERC such approvals, evaluations, or accreditation of its research ethics review processes as are necessary and appropriate;

f) Maintaining and archiving the following documentation:

i) A copy of these Standard Operating Procedures and any amendments;

ii) An up-to-date list of all WPRO-ERC members, with their terms of service, titles, and curriculum vitae or other biographical information sufficient to describe their qualifications (e.g., educational background, current employer, and relevant area(s) of expertise);

iii) A full set of minutes of WPRO-ERC meetings and decisions, and such additional detailed records as the Committee may require;

iv) WPRO's Research Registry data documenting the status of all research proposals submitted to the Committee (e.g., whether exempt from review, approved, awaiting changes before action, or not approved);

v) Copies of all research proposals submitted to WPRO-ERC, including comments from any scientific or technical bodies and any other Research Ethics Committees that reviewed any such proposal;

2. All project related documentation shall be retained for a period of three years after the closure of the project, and all secretariat related documentation (meeting agenda, minutes of meetings, annual reports, reports etc.) shall be retained for a period of five years, unless otherwise advised by the Records and Archive department of WHO;

E. Ad hoc Committee Members

The Secretariat of WPRO-ERC shall maintain a roster of ad hoc members with expertise on specific health issues; and their expertise shall be called upon by the Committee depending on the need and the topic of the research proposal in review. When called upon by the WPRO-ERC, ad hoc members 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.

WPRO-ERC Meetings

III

A. Frequency

1. Meetings of the Committee shall be convened and organized by the Secretariat ad hoc, depending upon the number and timing of research proposals received by the Secretariat for review.

2. The secretariat will ensure a meeting of WPRO-ERC within three weeks of receiving the proposal by the Secretariat.

3. The Secretariat shall provide the Committee members with at least one week's notice of all meetings, together with a copy of the proposed agenda and required meeting materials.

B. Attendance

1. Meetings of the Committee may only be attended by members, the Secretary and the Secretariat staff and such additional persons as are permitted under these Rules to be present for a particular meeting or a portion thereof.

2. Committee members are responsible for attending the meetings they agree in advance to attend or, if they are unable to do so, for notifying the Secretariat as far in advance as possible to enable the Secretariat to arrange for alternate dates of the meeting if the required quorum is not attained.

3. The responsibility of attending and participating in Committee meetings shall be borne equitably by all members, and the Secretariat shall keep records of the service of each member and distribute assignments accordingly.

4. At the invitation of the Chair, the WPRO staff member responsible for a submitted proposal (or in his/her absence such other person(s) designated by the responsible staff member) may attend meetings at which the proposal

will be reviewed, for the purposes of offering additional information and clarifications requested by the Committee.

5. The Chair may invite additional staff of WHO, other UN agencies or experts to provide advice on special issues, when the Chair considers that their expertise is needed for the review of a research proposal or for other matters before the Committee. When consulted on a research proposal, such experts may attend those portions of the meeting at which the proposal is being reviewed and participate in the discussion thereof.

6. In the interest of transparency and improving the wider understanding of the work of the WPRO-ERC, the Chair may also, at his/her discretion; invite a limited number of individuals as observers to the WPRO-ERC meetings. Observers may attend the entire meeting to which they have been invited, but may not take part in discussions, unless explicitly invited by the Chair to do so. The Chair at his/her discretion, may decide to request the invited observers to depart from the meeting room during specific portions of the discussions.

C. Confidentiality

1. The project documentation and the deliberations of the Committee are confidential and all WPRO-ERC members are bound to respect such confidentiality.

2. All experts and all observers invited to any WPRO-ERC meeting must commit to maintain confidentiality regarding the Committee's work for each meeting that they are invited to attend.

3. In order to ensure that the Committee is able to engage in candid evaluation of research proposals, the minutes of its meetings and all other WPRO-ERC records shall be kept in such a manner that the points discussed are recorded without ascribing the views or conclusions to particular members of the Committee. [Annex 5 for template for recording minutes]

4. In all communications from the Committee and Secretariat, reasonable steps will be taken not to reveal confidential or proprietary information concerning any research proposal or investigator. Such measures, however, shall not interfere

with the ability of the Committee to fully perform its function.

D. Quorum

At least seven members, including the Chair, must be present to constitute a quorum. A meeting can only commence once a quorum is obtained. If at any time during the meeting the quorum is lost, the meeting must be concluded. Members of the Secretariat and other experts or observers do not count towards the quorum.

E. Meeting records

Minutes shall be recorded by the Secretariat following the template provided at Annex 5 for all meetings and shall be submitted to the Chair, and subsequently to the Committee for approval.

IV Submission of Research Proposals

A. Responsible Person for Submission

All proposals must be submitted by a WPRO staff member, who is associated with the research in any capacity—either as principal investigator, co-investigator, or manager of the research at WPRO level, or providing technical assistance to the principal investigator. The responsible WPRO staff member has the responsibility to ensure that the required documentation, as outlined in subsection B of this section, for each proposal is complete. He/she will also ensure that such research has been authorized by the relevant health authorities in the country where the research will be conducted when so required in the countries concerned. He/She will become the contact person for WPRO-ERC regarding the proposal.

B. Documentation Required at the Time of Submission

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

1. Proof of approval by a local Ethics Review Committee(ERC) or Institutional Review Board (IRB) from the country where the research is proposed to be conducted. The letter should be issued by the ERC or IRB in the country where the research project will be conducted. In cases of involvement of more than one country in the proposed research, a letter from local ERC of each participating country will be required by WPRO-ERC. If the approval has not yet been obtained, a proof of submission of the proposal to the local ERC should be provided. All research proposal will include the name and complete contact details of local ERC in the country that had reviewed or will review the research proposal.

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. The Principal Investigator and co-investigators 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 VI-D about procedures for how WPRO-ERC will address potential conflicts of interest.)

4. A complete research proposal that includes [please see Annex 1 for the recommended format of research proposal and summary sheet:

    - Brief background and justification
    - Objective/purpose of study and a brief statement as to why the research question(s) is relevant
    - Methodology (including sampling methodology and sample size) /procedures/analysis plan
    - Limitations, if any.
    - 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
    - Plans for dissemination of research results to the relevant stakeholders
    - Budget and timelines
    - References

5. Curriculum vitae (abbreviated, 2 pages) of the Principal Investigator and any co-investigators.

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

7. Informed consent documentation (Annex 3 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 participants exercise their right of free will when deciding to participate. It is equally important that participants 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 participant (or their guardian). In most cases this may include a document written in a language that the participant 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)

   Participants 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 participant including those with disabilities. Children and other vulnerable subjects may need information presented as simply and straightforwardly as possible (see section VI).

   In cases where the potential participants 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 comprehensible 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 VI-A), a clear justification has to be provided as well as any alternative arrangements.

8. A certification that all required documentation is attached which may take the form of items checked off on a cover sheet provided by the Committee (Annex 1), and if not, an explanation for any missing documentation and when such documentation will be made available to the Committee.

9. Other documentation as listed in Annex 2 relevant to a research proposal in a specific situations.

C. Submitting a Research Proposal

All research proposals must be submitted electronically by the responsible WPRO staff member using WPRO's Research Registry http://mc.manuscriptcentral.com/wpro ; other communications should be addressed to wproerc@wpro.who.int . Once a proposal has been submitted, the WPROERC secretariat will inform the Responsible WPRO staff member whether the documentation is complete or incomplete within two working days of submission of the proposal. The incomplete submissions will not be reviewed.

Note: *When the study design corresponds to a clinical trial, WPRO-ERC 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 participant. If a trial has already been registered, the relevant identification number should be provided at the time the proposal is submitted.*

V

Review of Research Proposals

A. Identification Number

A unique identifier (ID) will be automatically assigned to the proposal on electronic submission and an automated confirmation for successful submission along with unique ID will be sent to the Responsible WPRO staff member. Once the required documentation is verified by Secretariat, a written confirmation about complete documentation and future course of action including the review date will be sent by the Secretariat to the Responsible WPRO Staff Member.

B. What is Subject to Review: Scope of Review

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

1. Studies of a physiological, biochemical, pathological or social process among human populations.
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.
4. Research involving children or other vulnerable populations
5. Research that involves quasi-experimental or experimental intervention, drugs, devices
6. Research that involves invasive procedures
7. Research that involves deception

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

C. What may not necessarily require review?

Proposal that may not require review by WPRO-ERC include but are not limited to:

1. The research does not involve human participants;
2. The data (including health-care records and specimens) being studied already exist and are either publicly available or are recorded by the investigator in such a manner as to be unidentifiable;
3. Public officials are interviewed in their official capacity on issues that are in the public domain;
4. The intervention is limited to the observation of public behavior; or
5. The intervention is limited to public health surveillance or routine evaluation of health programmes carried out pursuant to statutory or regulatory authority.
6. Proposals registered in WPRO Research Registry when the study has been reviewed and approved by World Health Organizations's Ethics Review Committee (WHOERC). WHOERC approval needs to be uploaded in WPRO's Research registry.

D. Authority to decide on exemption of review

1. The secretariat in consultation with Chair will decide after reviewing the proposal whether the proposal is exempt from review or need to be submitted to full review by WPRO-ERC.
2. If the secretariat and chair decide that, in accordance with the criteria set forth in the section V-C, a proposal does not require review by WPRO-ERC, the proposal shall be classified as 'does not require review by WPRO-ERC'. An official letter will be sent to the Responsible WPRO Staff Member by the Secretariat, and an appropriate notation

will be documented and reflected in WPRO Research Registry. Such notification shall include a brief explanation of the grounds for the exemption and a reminder that the Secretariat must be consulted in the event that material changes are made in the design or execution of the activity in question.

3. If the secretariat and chair cannot agree whether a research proposal qualifies as exempt from review, the proposal will be submitted for review to WPRO-ERC. The Chair may also decide to ask the Responsible WPRO Staff Member to submit research proposals, e.g. multi-regional studies, to the WHO-ERC rather than to WPRO-ERC for ethical review.

4. The secretariat will submit the list of all the proposals that have been reviewed by it in consultation with the Chair and were considered exempt from review to the next meeting of WPRO-ERC. Any member of the Committee may request a re-assessment of the proposals that were deemed to be exempt or eligible for expedited review.

    a) When such a request has been made, the Secretariat shall immediately notify the responsible WPRO staff member not to proceed further with the research project until the Committee has reviewed the matter and he/she has been informed of the outcome.

    b) If the Committee decides to override the determination made by the Chair and the Secretariat, it shall then determine the type of review the proposal shall undergo.

E. WPRO-ERC Review: Basic Procedures

1. All proposals for research involving human participants funded or otherwise supported by WPRO that are not determined to be exempt by Secretariat in consultation with Chair (please see section V-D) will be subject to a review by WPRO-ERC at a convened meeting. Two members of the Committee scheduled to be present at the meeting where a research proposal will be discussed shall be assigned by the Secretariat as "primary reviewers," based on the expertise required to adequately assess the research proposal. Such primary reviewers shall summarize the proposal at the Committee meeting and provide their opinions on its

ethical aspects, including recommendations for action by the Committee. In the event a primary reviewer determines that additional material is needed for review, or that the presence of the Responsible WPRO Staff Member at the WPRO-ERC meeting would be desirable, he/she should promptly notify the Secretariat, who shall then attempt to obtain the needed information.

2. Notwithstanding the informational role of the primary reviewers, all members present at the Committee meeting shall be familiar with each proposal and shall participate in the discussion and in the decision to be taken with respect to each proposal.

3. A Committee decision on research proposals shall be made by consensus. When consensus cannot be reached, the Chairperson can at his/her discretion exercise the following two options:

   a) he/she may ask the Committee to vote. Committee action shall require a two-thirds majority or

   b) he/she may decide that additional information or expert advice is required. If that is the case, consideration on the proposal shall be postponed to the next meeting in order to seek additional information or expert advice. If consensus cannot be reached at the second meeting, then a vote on the Committee decision shall be taken. Committee action shall require a two-thirds majority.

F. WPRO-ERC Review: Criteria for Review

The evaluation of research proposals by WPRO-ERC shall be guided by the Declaration of Helsinki (WMA 2008) [Please see Annex 6], the International Guidelines for Biomedical Research Involving Human Subjects (CIOMS, 2002), and the International Guidelines for Ethical Review of Epidemiological Studies (CIOMS 2008). The Committee may also officially recognize other statements on research ethics or formulate its own standards for particular topics (where such standards do not already exist) in addition to these documents. The committee will use following criteria for review [Annex 4]:

1. The proposed research design is scientifically sound (the hypothesis/objective is clear, and study design is appropriate to prove the hypothesis) and will not unnecessarily expose subjects to risk. In addition, the research

is relevant and will contribute to generalizable knowledge and is worth exposing the research participants to risk/ inconvenience.

2. 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 [see section VI].
3. Fairness of subject selection.
4. Voluntariness: recruitment practices do not involve coercion.
5. Confidentiality: provisions are made to protect the privacy of subjects and the confidentiality of data.
6. 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.
7. Data monitoring procedures are in place to provide for the reasonable safety of all involved in the research, including the subjects.

   Please see Annex 4 for minimum regulatory requirements for WPRO-ERC review, discussion and documentation in the meeting minutes.

G. Decisions of Committee Review

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

1. Approved: The research proposal is approved as submitted. This does not preclude WPRO-ERC from sending comments for the consideration of the research team, or requesting proof of approval by local ERB or IRB or ERC or proof of clinical trial registration in International Trial registry when appropriate.
2. 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 review the response submitted (i.e. Secretariat, Chair, special reviewers, or Committee) and will be so recorded in the decision and meeting minutes. If the assigned reviewers are not satisfied with the response, the Secretariat will request the Responsible WPRO Staff member to provide further clarifications. Notwithstanding the manner of final review of a proposal that has been conditionally approved, the Secretariat shall confirm a final approval in writing, and have the approval signed off by the Chair of the Committee.

3. Not approved: The research proposal is not approved as submitted either because there is insufficient information to make a decision or the proposal is not ethically sound. However the proposal can be re-submitted for the review by full committee after addressing all those concerns.

4. Does not require review by WPRO-ERC

H. Reporting the Outcome of a Review

The outcome of a review shall be communicated by the Secretariat to the responsible WPRO staff member in writing, together with an explanation of the reasons for the decision. Each communication must include:

a) WPRO-ERC's research proposal ID and date the proposal was received

b) Name of Responsible WPRO Staff Member

c) Names of investigators

d) Title of the Research Proposal

e) Date(s) of review and decision, and name of reviewing body (i.e. Secretariat in consultation with Chair, Full Committee)

f) The decision

g) Comments, questions, or suggestions (if applicable)

I. Continuing Review of Approved Research Proposals

1. When an approved research proposal is planned to extend for more than one year, the research project shall be reviewed by the Committee twelve months after the date of the initial approval, unless the Committee determines that a more frequent review is needed. This review shall occur even if, for administrative or other reasons, work on the project has been delayed, or no participant has been recruited. When the Committee determines that continuing review of an approved project should occur more frequently than once every twelve months or should occur after the accrual of a specified number of participants, the timing of the continuing review shall be set accordingly.

2. Assuming that no substantive changes have been made in the proposal or consent documents, a continuing review may be conducted as an expedited review. Such an expedited review may be carried out by the Secretariat, on behalf of the Committee and will be reported for information to the next Committee meeting.

3. If any substantive changes have been made in the protocol or consent documents, the continuing review shall be conducted as Full Review.

4. Should the process of review lead to a disapproval of the continuation of a previously approved study, this determination shall be immediately communicated to the Responsible WPRO Staff Member, who shall in turn convey it to the Principal Investigator as well as to any other persons, funding agencies or other bodies with whom such reports must be filed pursuant to terms and conditions agreed by WHO. The Responsible WPRO Staff Member shall promptly report back to the WPRO-ERC concerning the date the enrolment of new participants was halted and the manner in which the research project is dealing with the previously enrolled participants.

J. Review of Special Categories of Proposals

1. Multi-Centre Studies: Research projects that are to be conducted at more than one centre require review in the same manner as any other research funded or supported by WPRO that involves human participants, but the multi-centre nature of such projects can lead to two variations in the process of approval.

    a) When WPRO is the lead agency funding or organizing the research, an expedited review by secretariat in consultation with Chair may be utilized to add new centres to an approved research project.

        i) Once the WPRO-ERC has approved a research proposal for the first centre as a "master protocol," the review and approval of additional research centres as sites for the same project can be undertaken on an expedited basis by Secretariat and Chair, but each proposed new site shall be given a new ID in the Registry, with a notation that it is derivative of a particular master protocol. The secretariat, however, will report about all these proposals to Full WPRO-ERC in its next meeting, for the information of all the members.

        ii) In such a situation, expedited review can be limited to determine 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 any translation of information and documentation has been prepared in an adequate and culturally appropriate fashion.

        iii) If the Secretariat and Chair conclude on initial review that the benefit-risk ratio is adversely affected, the proposal will be submitted for full review by the Committee, and the Responsible WPRO Staff Member shall be so informed.

    b) When WHO staff or persons under contract to WPRO/ WHO are involved in only one or a few sites of a

multi-centre study being led by scientists unaffiliated with the Organization and when another Institutional Review Board or Research Ethics Committee has been designated as the "lead ethical review board" for the study with the aim of promoting consistent and uniform conditions for the research at all sites, the Committee may choose to postpone review of the research proposal until such board has completed its review.

i) The decision to postpone review should be made in a manner that will not unduly delay the final decision on WPRO involvement in the study.

ii) A decision to postpone review is dependent upon a determination by the committee that the lead ethics review board for the study is capable of providing review of comparable scope and quality to that which the WPRO-ERC would otherwise provide.

iii) The responsible WPRO staff member for the research proposal shall submit to the Secretariat the results of the review by the lead ethics review board (including any explanations, requirements, or other comments). When this documentation is received, the WPRO-ERC will commence its review of the proposal.

2. Nested Studies: Any study which is part of another, i.e., "nested" within another study, shall be subject to the procedures and criteria for review as set forth in these Rules. However, the responsible WPRO staff member shall also submit the protocol for the main study. While the main protocol need not be formally reviewed by the Committee, it should be satisfied with the ethical aspects of the main study before approving the nested study.

K. Continuing Oversight and Monitoring

The Organization's obligation to ensure continuing oversight of approved research projects with human participants, which it funds or otherwise supports, creates responsibilities for the Responsible WPRO Staff Member and for the Committee beyond the obligation to perform continuing reviews.

1. The Responsible WPRO Staff Member for each approved research shall promptly report to WPRO-ERC any developments in the project that might have ethical implications.

2. Principal Investigators shall inform the responsible WPRO staff member of any changes in an approved research proposal or consent documentation proposed to be made prior to implementation, and these shall be immediately reported by the Responsible WPRO Staff Member to the Committee.

    a) When the Secretariat receives a report of changes that are proposed to be made in the protocol or consent documentation of a research project that the Committee has previously approved, a determination shall be made by the Chair and Secretariat in accordance with section V-D whether the proposed changes should be subject to review by the Committee in accordance with these Rules.

    b) Pending the Committee's decision, which it shall endeavor to produce in a timely manner, the changes proposed for the research project shall not be instituted, with the exception of any modifications urgently needed to protect the well-being or important interests of participants already enrolled in the study.

3. Any deaths as well as any serious adverse events or unexpected events that occur to participants during their participation in any approved research project shall be immediately reported by the Principal Investigator to the Responsible WPRO Staff Member as well as to any other persons, ethics review bodies, funding agencies or other bodies with whom such information must be filed pursuant to national regulations and the terms and conditions agreed by WHO. The Responsible WPRO Staff Member must in turn promptly convey such reports to the Secretariat, including the feedback from other review bodies.

    a) The Secretariat shall review all such reports and determine whether the information reported warrants re-review of the research project, with particular attention to the benefit-risk ratio, the adequacy of the steps taken to minimize risk, and the

information provided to prospective participants; such determinations will be reported to the Committee at its next meeting.

b) If the Secretariat determines that such re-review should occur, it shall take place as soon as possible (including through an extraordinary Committee meeting, if necessary under the circumstances).

c) The results of the re-review will be promptly conveyed to the Responsible WPRO Staff Member.

d) It shall remain the obligation of the Responsible WPRO Staff Member, rather than of the Committee, to ensure that adverse event reports, as well as the determinations reached by the Committee in a re-review, are filed with all appropriate persons and agencies, pursuant to terms and conditions agreed by WHO.

4. Procedures on completion of research project:

a) The principal investigator is requested to submit a final report and a financial report (if financially supported by WPRO/WHO) upon completion of the research project, if it had been reviewed by WPRO-ERC earlier, to the Responsible WPRO Staff in relevant technical unit. The final report should also include information on how the results have been used and disseminated to relevant stakeholders.

b) The Responsible WPRO Staff Member shall report the final research project outcome (completion or discontinuation) and submit a final report on the study to the Secretariat. A notation shall be made in the Registry accordingly.

c) The Responsible WPRO Staff Member will also submit a copy of any reports that were published in public domain or any publications in any peer reviewed journals, which will be linked with project ID in the electronic registry.

Special Considerations for Vulnerable Populations

VI

A. Definition of Vulnerable Populations

1. Vulnerable population are those who are relatively (or absolutely) incapable of protecting their own interests, either due to insufficient power, intelligence, education, resources, strength or other needed attributes to protect their own interests (CIOMS, 2002). They may include but not limited to:

    a) Children, including newborns and minors (those under the age of 18 years) (see section VI-C);

    b) Fertilized ova, pregnant women, viable fetuses (see section VI-D)

    c) People whose judgement or capacity to make free-willed, informed decisions is limited or compromised. This includes cognitively impaired persons with conditions that affect their decision-making abilities.

    d) Participants 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.

    e) Participants recruited from emergency medical facilities, intensive care units, older persons in long-term care facilities, life threatening situations or the like;

    f) Participants whose economic conditions predispose them to certain incentives (see section VI-D)

    g) Populations subject to stigma and discrimination.

B. Research Involving Vulnerable Population:

WPRO ERC will be guided by article 17 and articles 26-29 of Helsinki Declaration and Guideline 13 “Research involving

vulnerable persons' (CIOMS, 2002) in reviewing proposal involving vulnerable populations. Article 17 of Helsinki Declaration clearly states that "medical research involving a disadvantaged or vulnerable population or community is only justified if the research is responsive to the health needs and priorities of this population or community and if there is a reasonable likelihood that this population or community stands to benefit from the results of the research".

C. Research 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 age of 18 years). These include the use of additional forms and signatures including adequately informing their parents or other legally authorized representatives or guardians. WPRO-ERC will be guided by Guideline 14 "Research involving Children" of the international Guidelines for Biomedical Research (CIOMS, 2002) in reviewing proposal involving children.

D. Research 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. WPRO-ERC will be guided by Guideline 16 "women as research subjects" and Guideline 17 "pregnant women as research participants" of the international Guidelines for Biomedical Research (CIOMS, 2002) in reviewing proposal involving women.

E. Vulnerability Because of Economic Status or Other Factors

Research participants should not be coerced into participating in a research study because of inappropriate inducements. WPRO-ERC will review consent process and other forms to ensure that inducements offered are appropriate. It will additionally be guided by Guideline 7 "Inducement to Participate" and Guideline 10 of the International Guidelines for Biomedical Research (CIOMS, 2002) and Article 17 of Helsinki Declaration (2008) in reviewing proposals involving research in population and communities with limited resources.

Conflicts of Interest

VII

The avoidance of conflicts of interest or the appearance thereof, is important to ensure both the quality and credibility of research ethics review. WPRO-ERC will therefore take necessary steps to avoid conflicts of interest and the appearance of conflicts of interest for investigators, Responsible WPRO Staff Members, the Committee members and Secretariat.

1. It is important that all persons participating in the submission and review of proposals involving human research avoid situations that could affect their ability to provide objective guidance for, or review of, research proposals regarding particular drugs, devices, vaccines, or other interventions.

2. The Committee shall ensure that its resolution of any situation involving a potential conflict of interest avoids not only the occurrence of unacceptable interests but also the appearance of such conflicts of interest.

3. In all cases in which a conflict of interest is revealed, but it is not so material as to warrant not approving the project, the Committee shall determine the type of description of such interest that needs to be included in the information provided to prospective participants in the research and shall ensure that the consent documentation also includes an appropriate disclosure.

A. Investigators

1. The Principal Investigator who will conduct the research should not have any material conflict of interest or any other interests that may damage the scientific objectivity of the research.

2. All Principal Investigators involved in the proposed research proposal have to clearly mention in the proposal cover page that they do not have any conflict of interest with the proposed research.

3. The Committee shall approve a research proposal only if it concludes that the Principal Investigator does not have

any material conflict of interest or that such interests are not sufficient to damage the scientific objectivity of the research (in light of other means such as the independence of other investigators or the oversight of a monitoring board to counterbalance the interest).

B. WPRO-ERC members: Financial Conflict

1. WPRO staff members on the Committee and Committee Secretariat are bound by Staff Rule 110.7.1 to inform the Regional Director of any interest they, as well as their spouses and dependent children, may have in any entity that has a commercial interest or a common area of activity in the work of WHO. In the case of an interest in an entity having a commercial interest or common area of activity involving a research proposal submitted to the Committee, all such staff members shall inform the Secretariat.

3. Non-affiliated members shall agree to be bound by the same obligation of disclosure to the Secretariat with respect to interests in an entity having a commercial interest or common area of activity involving a project submitted to the Committee.

C. WPRO-ERC members: Role Conflicts

A Committee member who is also a responsible WPRO staff member for a proposal under review or is connected closely to a proposal (such as being on the same team as the responsible officer submitting the proposal or being in a supervisory position with the submitting responsible staff member) would have a conflict of interest if he or she participated in the ethics review of the proposal.

D. Resolution of Conflict

1. When asked to perform an expedited review or to be a primary reviewer, a Committee member a financial or role conflict shall disclose such a conflict and decline to undertake the review.

2. Members of the Committee having reported a financial or role conflict may, unless the Chair determines otherwise, comment on the matter before the Committee but may not

participate in the Committee's decision on the matter, and the Chair (subject to being overruled by the Committee) may impose additional restrictions (such as requesting the member to leave the meeting while the matter is discussed) as he/she believes are warranted under the circumstances. The conflict of interest shall in any event be announced during the meeting and the minutes of the meeting shall record the declared conflict of interest and the steps taken to deal with the situation with regard to the Committee's deliberations and decisions.

3. Similarly, the Chair will hand over his/her responsibility to the Vice Chair whenever he/she has a role conflict and the Minutes of the meeting shall record the declared conflict of interest and the steps taken to deal with the situation with regard to the Committee's deliberations and decisions.

VIII Evaluation and Improvement

A. Quality Improvement

1. All members of the Committee and the Secretariat are charged with scrutinizing the operations of the Committee in order to identify problems and to offer suggestions for improving the quality of the Committee's work.

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

3. Suggestions requiring formal changes in these SOPs shall be considered under section IX, subsection B below.

B. Independent Evaluation

1. The Secretariat shall arrange for the work of the Committee and Secretariat to be evaluated periodically, at least once in three years, by one or more persons who are knowledgeable about research ethics and the functioning of ethics review committees, provided such evaluators are not members of the Committee and are not in a supervisory or subordinate role to the Secretary or any Committee member.

2. The evaluator(s) should be given complete access to the records of the Committee and Secretariat. They may attend one or more meetings of the Committee as authorized observers and may interview members of the Committee as well as responsible WPRO staff member and Principal Investigators whose research proposals have been reviewed by the Committee during the period under review.

3. The evaluator(s) should endeavor to compare the operations of the Committee - in terms of the quality of its work, the efficiency and effectiveness with which the Secretariat and the Committee carry out their functions, and relationship between the resources available for the work and the workload - to recognized standards or benchmarks for ethical review of research with human participants.

4. The conclusions of the evaluator(s) shall be submitted to the Chair and Secretary, with a copy to the Regional Director, for appropriate action.

IX Adoption and Amendment of the SOP

A. Adoption of SOPs

The SOPs will be approved by Regional Director, Western Pacific Regional Office for adoption by WPRO-ERC. These will be available publically on the WPRO external website under 'health research' web page. These SOPs will supersede any other publications in this regard including the provisions mentioned in WPRO Manual, Part XV, section 2, paragraphs 10-120.

B. Amending SOPs

Any member of WPRO-ERC and secretariat can propose an amendment to these SOPs. The proposed amendment shall be submitted in writing to the Secretariat to be placed on the agenda of the next available Committee meeting for consideration and possible adoption by a majority of the Committee members present and voting. The amendment shall come into effect once approved by the Regional Director.

Glossary

Adverse events: Undesirable and unintended consequences of, or reactions to, procedures experienced by the research participant/ subject

Annual Report: An annual synoptic document that outlines and anlayzes activities, especially summarizing the research proposals reviewed over the last year.

Beneficence: Ethical obligation to maximize benefits and to minimize harms (CIOMS)

Clinical trial: Any research study that prospectively assigns human participants or group of humans to one or more health-related interventions to evaluate the effect on pre-defined 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 of International Organization of Medical Sciences (CIOMS): An international, non-governmental, 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 ethical conduct of research, among other activities. CIOMS promulgated guidelines entitled "International Ethical Guidelines for Biomedical Research Involving Human Subjects" for the first time in 1982, revised in 1993 and 2002, designed to be of use, particularly in low-resource countries, in defining national policies on the ethics of biomedical research, applying ethical standards in local circumstances, and establishing or redefining adequate mechanisms for ethical

review of research involving human subjects. The latest version published in 2002 supersedes that of 1993 and consists of a statement of general ethical principles, a preamble and 21 guidelines which address issues including informed consent, standards for external review, recruitment of participants, and more. Website: http://www.cioms.ch/

Declaration of Helsinki: Adopted in 1964 by the 18th World Medical Assembly (WMA) at Helsinki, Finland as a set of ethical principles for medical research involving human subjects, including research on identifiable human material and data. The original guidelines have been revised six times since then with the latest revision in 2008 by the 59th WMA General Assembly for Physicians conducting biomedical research. The declaration outlines clinical trial procedures required to ensure patient safety, consent and ethical committee review in human subjects. The declaration of Helsinki can be found at http://www.wma.net/en/30publications/10policies/b3/17c.pdf (last accessed on October 12, 2010).

Guideline 14 (CIOMS, 2002): "Before undertaking research involving children, the investigator must ensure that: the research might not equally well be carried out with adults; the purpose of research is to obtain knowledge relevant to the health needs of children; a parent or legal representative of each child has given permission; the agreement (assent) of each child has been obtained to the extent of the child's capabilities; and a child's refusal to participate or continue in the research will be respected".

Guideline 16 (CIOMS, 2002): " Investigators, sponsors or ethical review committees should not exclude women of reproductive age from biomedical research. The potential for becoming pregnant during a study should not, in itself, be used as a reason for precluding or limiting participation. However, a thorough discussion of risks to the pregnant woman and to her fetus is a prerequisite for the woman s ability to make a rational decision to enrol in a clinical study. In this discussion, if participation in the research might be hazardous to a fetus or a woman if she becomes pregnant, the sponsors/ investigators should guarantee the prospective subject a pregnancy test and access to effective contraceptive methods before the research commences. Where such access is not possible, for legal or religious reasons, investigators should not recruit for such possibly hazardous research women who might become pregnant".

Guideline 17 (CIOMS, 2002): "Pregnant women should be presumed to be eligible for participation in biomedical research. Investigators and ethical review committees should ensure that prospective subjects who are pregnant are adequately informed about the risks and benefits to themselves, their pregnancies, the fetus and their subsequent offspring, and to their fertility. Research in this population should be performed only if it is relevant to the particular health needs of a pregnant woman or her fetus, or to the health needs of pregnant women in general, and, when appropriate, if it is supported by reliable evidence from animal experiments, particularly as to risks of teratogenicity and mutagenicity".

Individually identifiable information: Data records or biological materials that contain or are linked to a personal identifier (such as a person's name or a patient number) either directly or through a code, even when the key to the code is held by someone other than the investigator, whereas records or materials are considered *unidentifiable* when they lack any personal identifiers (such as samples taken from repositories that do not possess information on the individuals from whom the samples originated, or records that have been "anonymized" by the removal of any information, including any code, that could link them to any particular person).

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 (Clinical trials or intervention trials) that prospectively assign human participants or group of human participants to one or more health-related interventions to evaluate the effects on health outcomes. Website: http://www.who.int/ictrp/en/ [last accessed on October 12, 2010]

Legally authorized representative: An individual, or a judicial or other body with the authority under applicable law to give permission for participation in research of a person who lacks the capacity to decide whether to consent for him or herself.

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

Principal Investigator (PI): The lead scientist for a particularly well-defined social science, biomedical, behavioural, or

epidemiological research project; responsible and accountable for the appropriate conduct of the research.

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

Regional Director: An elected chief-executive of Western Pacific Regional Office of WHO who controls and governs the affairs of the Western Pacific Regional office of WHO.

Research: Any social science, biomedical, behavioural, or epidemiological activity that entails systematic collection or analysis of data with the intent to generate new generalizable knowledge.

Research *involving human participants* (sometimes termed "human subjects") when human beings

i) are exposed to intervention, manipulation, observation, or other interaction with investigators either directly or through alteration of their environment; or

ii) become individually identifiable through investigators' collection, preparation, or use of medical or other records or of biological material from human beings.

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

Research Proposal: A document written for the purpose of obtaining funding for a research project, and in addition to including the research protocol, also includes information on the investigators (e.g., their CVs and institutional affiliation), approvals from various relevant organizations and persons, budgets, dissemination plans, etc.

Research Protocol: A document describing in detail how a research study is to be conducted in practice, including the study design and methodology, data analysis plan, and a budget. A research protocol is part of a research proposal.

Responsible WPRO staff Member: A staff member of WPRO responsible for representing WPRO's involvement in the research (e.g. contracting with investigators to implement such a project, or who have provided direct technical or logistical support to such investigators) and liaising with external parties on matters involving a specific research proposal.

Private information: Individually identifiable data that have been provided by a person, or obtained through observation of or interaction with a person, under circumstances in which the person could reasonably have believed either that the data (such as contained in medical records) would not be made public or shared with others, or that the data were not being recorded.

United Nations Convention on the Elimination of all forms of Discrimination against women: see http://www.un.org/womenwatch/daw/cedaw/ as accessed on October 21, 2010

United Nations Convention on the Rights of the Child: see http://www2.ohchr.org/english/law/crc.htm as accessed on October 21, 2010.

WHO Funded Research: Research conducted by the investigator(s) under a contract with WHO , which provides, or serves as a conduit for, direct financial support for research project.

WHO supported Research: Research activities in which WHO staff organize and coordinate the research, participate significantly in the design of the research, or provide significant review of, or technical advice on, the research project as a whole, but not when

i) WHO staff have provided technical advice only on portions of a research project;

ii) the investigators developing the project and seeking the advice are neither employed under a contract with WHO to develop the research proposal or carry out the research; and

iii) the WHO staff have notified those investigators in writing that the project has not been formally reviewed by WHO and the technical advice provided by WHO staff do not constitute endorsement of, or support for, the research

project by WHO and should not be construed or portrayed as such.

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. Website: http:// www.who.int/rpc/research_ethics/erc/eng

Annex 1: Recommended format for research proposal for financial support from WPRO/WHO

I. Summary Sheet And Checklist Of Required Documents

1		Principal Investigator Prof/Dr/Mr/Ms. FAMILY NAME (SURNAME): FIRST NAME: OTHER NAMES:
	1.1	Title of post, position or appointment presently held by principal investigator
	1.2	Complete postal address: Email:
2		Institution responsible for the research proposed Name and address (including website address, if any)
3		Title of health research proposed (should be brief, precise and informative to workers outside your field)
	3.1	Objectives of research proposed (clearly and concisely list specific objectives of the proposed study)
	3.2	Duration of research from preparations for field work till analysis and compilation of final research results From (date): To (date): Total (years):
	3.3	Funds required (US$)
	3.4	Any conflict of interest by research institute/PI/funding source declared Yes____ No_____

4	4.1	Informed consent documentation included in the proposal Yes____ No_____
	4.2	Questionnaires for collection of data included in the proposal Yes____ No_____
	4.3	If the study design involves a clinical trial, proof of Registration in a database linked to Search Portal of International Clinical Trial Register Platform of WHO is attached Yes____ No_____ Not a clinical trial____
5	5.1	Institutional and national ethical clearance Name and contact details of the local ERC/IRB/ERB in the country of research where the proposal has been reviewed/ submitted: Name of local ERC/IRB: Contact details including email address:
	5.2	Institutional/national ethical clearance enclosed Proposal under review by institutional/national ERC Yes____ No_____ (proof of submission to local ERC enclosed)
6		Approval of national Ministry of Health or national Medical Research Council (or equivalent body) National approval document enclosed Yes____ No_____
7		Institutional endorsement (can be attached as a separate document also) Head of Institution Title:_____ Name: _____ Date: _____ (print) Signature:
8		Curriculum Vitae of Principal Investigator attached Yes____ No_____
9		Applicant's signature Date: Signature:

II. Recommended Format For Research Protocol

_____

Title of research:

_____

1. Statement of the problem
2. Relevance of the problem to national or local health objectives
3. Field(s) of application of the proposed research results
   (a) Potential users of research results
   (b) Plan for dissemination of research results
   (c) Plan for utilization of research results
4. Review of literature and other existing information
5. Statement of research objectives
6. Statement of research hypotheses, if any
7. Research design
   7.1 Key research design (e.g. experimental study, cross-sectional survey, facility survey, etc)
   7.2 Research setting (country, district, province etc) and study population (age groups, women, men, etc)
   7.3 Sampling design, sample size, and use of controls (if applicable)
   7.4 Study instrument(s)
   7.5 Plans for fieldwork for collecting data
   7.6 Data analysis plan including description of key outcome indicators proposed to be measured in the research
8. Ethical considerations
   8.1 Assessment of risk to research participants
   8.2 Information Sheet for Research participants
   8.3 Informed consent certificate
9. Timeline for research implementation
10. Budget (use attached Section III. Budget Sheet)

III. Recommended Format for presenting Budget

		ITEM	Amount (US $)
1	PERSONNEL (allowances to be paid)		
	1.1	Professional scientific Staff (name and functional title)	
	1.2	Technical staff (name and functional title)	
	1.3	Other staff (name and functional title)	
	Subtotal		
2.	MAJOR EQUIPMENT (over US$500)		
	(include specifications, shipment and freight insurance costs; comment on local provision for maintenance/service		
	Subtotal		
3	SUPPLIES		
	3.1	Chemicals	
	3.2	Glassware	
	3.3	Minor equipment (less than US$500 each)	
	3.4	Animals	
	3.5	Other supplies	
	3.6	Operating cost (specify maintenance of equipment, gasoline, etc)	
	Subtotal		
4.	TRAVEL (specify domestic and international)		
	Subtotal		
5.	DATA ANALYSIS COST		
	Subtotal		
6.	COST OF DISSEMINATION OF RESULTS		
	Subtotal		
7.	MISCELLANEOUS EXPENDITURES		
	Subtotal		
8.	SUMMARY		
	(1) Personnel		
	(2) Major equipment		
	(3) Supplies		
	(4) Travel		
	(5) Data analysis cost		
	(6) Cost of dissemination of results		
	(7) Miscellaneous expenses		
	TOTAL		

Annex 2: Additional documents (or information) to be included in a research proposal (where applicable), for submission to WPRO-ERC for review

In addition to the items required in section IV-B for all research proposals involving human participants, the responsible WPRO staff member shall submit additional information that may be helpful in the review process, such as

1. An explanation of how the research is relevant to the health needs of the population in which it will be conducted and how it is consistent with the research agenda of the country where it will be conducted, or, in the absence of such relevance or consistency, a justification for why it is appropriate to conduct the research in that country;
2. A copy of any instruments being used to collect data, such as questionnaires that will be administered, including translations into the local language;
3. Detailed information about how biological materials or other data from the research will be collected, preserved, transported, and stored, as well as the conditions under which such items will be released in the future to persons outside the present research project, and a copy of the information that will be provided to participants about such future use and whether, and if so how, their consent will be sought before such use outside the present project would occur, and whether they will or will not be provided with information derived from such future studies;
4. A description of the plans that have been made, and any formal agreements that have been negotiated with representatives of the participant population or officials of the country where the research will occur, to continue to provide any drug, device, vaccine, or other product being tested, or any other service, to any participants who are benefiting from such intervention at the conclusion of their participation in the research, or a justification for the absence of such plans;
5. A description of the plans that have been made, and any formal agreements that have been negotiated with officials of the country where the research will occur (or with any agency providing services to the members of the population from which participants will be drawn or to residents of that country) to make any drug, device, vaccine, or other product being tested, or any other service, available at an affordable cost to the population or residents once such drug, device, vaccine or other product has been approved for use by the relevant authorities, or a justification for the absence of such plans;
6. Complete information on the regulatory status of any drug, vaccine, or device being studied, including an adequate summary of all safety, pharmacological, pharmaceutical, and toxicological data available on the product and of the clinical experience to date; and

7. Where the research involves a risk of injury (such as research on an infectious agent or research involving venepuncture) a description of the means that will be used to avoid or minimize risks to the investigator and other persons conducting the research;
8. Where the research involves an infectious agent or a vaccine, a description of any risk to persons who are not directly involved in the research but who might be exposed to risk through contact with participants or otherwise;
9. A description of the arrangements that have been put in place to address any needs that will arise should harm occur to the persons conducting the research or to other persons who might be harmed in the foreseeable future;
10. Details concerning any Data Safety and Monitoring Board (DSMB) or comparable body that will be established to oversee the research, including information on who will appoint the DSMB, to whom it will report (including the circumstances for which it will provide specified information to the WPRO-ERC), and the decision rules it will utilize in deciding or recommending that the research should be altered or halted.

Annex 3: Examples of guidelines and templates of informed consent forms

- World Health Organization. Informed consent form templates. Accessed on 12 October 2010 at http://www.who.int/rpc/research_ethics/informed_consent/en/
- Code of Federal Regulations, Title 45, Public Welfare, Department of Health and Human Services (HHS), U.S. Government. Last visited on September 20, 2010 at http://www.hhs.gov/ohrp/humansubjects/guidance/45cfr46.htm

Other templates

- World Health Organization. WHO-ERC guide for principal investigators. Accessed on October 26, 2010. http://www.who.int/rpc/research_ethics/Guide%20for%20PIs.doc

Annex 4: WPRO-ERC Protocol Review standards [adapted from National Institutes of Health, USA and WHO-ERC review standards]

Minimum regulatory requirements for WPRO-ERC review, discussion, documentation in the meeting minutes

Regulatory Review Requirement	Suggested question for WPRO-ERC discussion
1. The proposed research design is scientifically sound and will not unnecessarily expose human research participants to risk	a) Is the hypothesis or research question clear? Is it clearly stated? b) Is the study design appropriate to prove the hypothesis or answer the research question? c) Will the research contribute to generalizable knowledge and is it worth exposing human research participants to risk?
2. Risks to the participants are reasonable in relation to anticipated benefits, it any, to the participants and the importance of knowledge that may reasonably be expected to result.	a) What does the WPRO-ERC consider the level of risk to be? (See risk assessment guide on back of form). b) What does PI consider the level of risk/discomfort/inconvenience to be? c) Is there prospect of direct benefit to human research participants(see benefit assessment guide below)
3. Participant selection is equitable	a) Who is to be enrolled? Men? Women? Ethnic Minorities? Children (rationale for inclusion/ exclusion addressed)? Seriously ill patients? Healthy volunteers? b) Are these research participants appropriate for the protocol?
4. Additional safeguards required for subjects likely to be vulnerable to coercion or undue influence.	a) Are appropriate protection in place for vulnerable participants, e.g. pregnant women, socially or economically disadvantaged, decisionally impaired, subjects in special situations e.g. doc-patient relationship making them more vulnerable?

Regulatory Review Requirement	Suggested question for WPRO-ERC discussion
5. Informed consent is obtained from research subjects or their legally authorized representative (s).	a) Is the informed consent document include all the required elements? b) Is the consent document understandable to participants? c) Who will obtain the consent (PI, nurse, other?) & in what setting? d) Is WPRO-ERC requested to waive or alter any informed consent requirements?
6. Risks to the subjects are minimised?	a) Does the research design minimize risks to subjects? b) Would use of a data and safety monitoring board or other research oversight process enhance subject safety.
7. Subject privacy and confidentiality are maximized.	a) Will personally-identifiable research data be protected to the extent possible from access or use? b) Are any special privacy and confidentiality issues properly addressed, e.g. use of genetic information?

Risk/Benefit Assessment

Risk: Minimal risk means that the probability and magnitude of harm or discomfort anticipated in the research are not greater in and of themselves than those ordinarily encountered in the daily life or during the performance of routine physical or psychological examination or tests.

Check appropriate risk category:

1._____ The research involves no more than minimal risk to subject.

2._____ The research involves more than minimal risk to subjects.

- o The risk(s) represents a minor increase over minimal risk, OR
- o The risk(s) represents more than a minor increase over minimal risk.

Benefit: A research benefit is considered to be something of a health-related, psychosocial, or other value to an individual research subject, or something that will contribute to the acquisition of generalizable knowledge. Money or other compensation for participation in research is not considered to be a benefit, but rather compensation for research-related inconveniences.

Check appropriate benefit category(ies):

1._____ no prospect of direct benefit to individual participants, but likely to yield generalizable knowledge about the participants' disorder or condition.

2._____ no prospect of direct benefit to individual participants, but likely to yield generalizable knowledge to further society's understanding or the disorder or condition under study; or

3._____ the research involves the prospect of direct benefit to individual participants

Annex 5: Format for all WPRO-ERC minutes

(The order in which agenda items are reviewed is at the discretion of WPRO-ERC Chair)

Minutes of the WPRO-ERC Meeting Held on (date)

Members present: (indicate who is a non-scientist, non-WPRO affiliated etc.)	_____	(Chair)	_____
	_____		_____
	_____		_____
	_____		_____
	_____		_____
	_____		_____
	_____		_____
	_____		_____
	_____		_____
	_____		_____
Members Absent	_____		_____
	_____		_____
	_____		_____
	_____		_____
	_____		_____
	_____		_____
Guests: (include affiliation)	_____		_____
	_____		_____
	_____		_____

The meeting convened at --:-- (a.m./p.m.) with a quorum present.

1. MINUTES OF THE MEETING HELD ON (DATE). (The minutes must be voted on and any changes documented.)
2. ANNOUNCEMENTS
3. INITIAL REVIEWS.

A. Principal Investigator:

Protocol Title:

Protocol summary:

(a) Discussion:

General discussion:

Specific discussions: (include the following headings)

- Scientific design (discuss and note that Institute pre-scientific review has been done)
- Risks/benefits (assign a level of risk here or at the time of the WPRO-ERC decision and vote, [(d) below] consistent with page 2, WPRO-ERC Protocol Review Standards form.
- Subject selection (discuss populations to be studied & recruitment

plan)

- Additional safeguards for vulnerable subjects
- Minimization of risks to subjects
- Privacy & confidentiality.
- Consent document (document that all required elements are present)
- Additional considerations (e.g. multi-center research; collaborative research; nested study. State if these considerations do not apply)

(b) Stipulations (number the stipulations)

(c) Recommendations (number the recommendations)

(d) IRB Decision and Vote: State whether the vote is unanimous; if not, state how many members voted for, against or abstained. Document in or attach to the minutes the reason(s) for the minority opinion(s).

If the protocol is approved with stipulations and/or recommendations, the minutes must state whether the WPRO-ERC votes that the stipulations and/or recommendations are to be reviewed by the Chair, by secretariat, by a subcommittee of the WPRO-ERC, or by the full WPRO-ERC.

B., C., etc. (Follow same format as above for additional new protocols)

4. CONTINUING REVIEWS OR Re-review of proposals submitted earlier either due to proposed AMENDMENTS or otherwise

A. Principal Investigator:

Title and type of expedited action:

Date approved by WPRO-ERC Chair or designee:

Description of expedited action: (Expedited actions must be listed separately in the minutes. The Chair should provide a brief explanation of any expedited actions. A vote is not required but the WPRO-ERC has the prerogative to discuss, rescind or amend expedited actions.)

B., C. etc. (List additional expedited actions following the above format

5. CONTINUING REVIEWS (it is useful for the primary or secondary reviewer or the WPRO-ERC secretariat to have the entire protocol file available for reference at the meeting)

A. Principal Investigator:

Protocol Title:

Protocol Number:

Expiration Date:

Protocol Summary (if not provided in discussion at (a) below):

(a) Discussion:

(b) Stipulations (number the stipulations)

(c) Recommendations (number the recommendations)

(d) WPRO-ERC Decision and Vote (Include WPRO-ERC reaffirmation of the level of risk or establishment of a new risk level consistent with the Protocol Review Standards form, page 2)

B., C. etc. (Follow the same format as above for additional continuing reviews)

6. AMENDMENTS to a research proposal approved earlier

A. Principal Investigator:

Protocol Title:

Protocol Number:

Expiration Date:

Description of the amendment:

(a) Discussion:

(b) Stipulations (number the stipulations)

(c) Recommendations (number the recommendations)

(d) WPRO-ERC Decision and Vote (include a statement indicating whether or not the protocol's level of risk is altered by the amendment)

B., C. etc. (Follow the same format as above for additional amendments)

7. REPORT OF ADVERSE EVENT(S)

Principal Investigator:

Protocol Title:

Protocol Number:

Date of Adverse Event(s):

Description of the adverse event(s):

Document WPRO-ERC's acknowledgement of receipt of the adverse event report(s) and discussion. Discussion of serious adverse events occurring on an protocol should include immediate actions taken as a result of the event by the PI; recommendations for further actions, if any, by the WPRO-ERC (e.g., suspension of subject accrual, etc.), and any necessary recommendations for further reporting (RD, WR, etc)

If the adverse events are reported from non-WPRO sites for the WPRO-ERC's information only, and no action is required on the WPRO-ERC's part, acknowledgement of the report(s) should be documented.

8. INFORMATION ITEMS

(a)

(b)

9. ADJOURNMENT The meeting adjourned at --:-- (a.m./p.m.).

Annex 6: Declaration of Helsinki (2008)

Annex 7: International guidelines for biomedical research involving human subjects (CIOMs, 2002) : copyright permission sought from CIOMs.