

The WHO Research Ethics Review Committee

Rules of Procedure

(Version 2, w.e.f. 1st January 2011)

(Revised from Version dated 6th of May 2004)

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Abbreviations

WHO: World Health Organization

ERC: Research Ethics Review Committee

PMDS: Performance Management and Development System

REC: Any research ethics committee other than the WHO ERC

IRB: Institutional review Board

CIOMS: Council for International Organizations of Medical Sciences

I. Purpose of the Document

These Rules of Procedure (hereinafter "Rules") have been adopted by the WHO Research Ethics Review Committee (hereinafter "the Committee" or "ERC") pursuant to WHO Manual Part XV, section 2, paragraphs 70-90 , and are intended to provide a framework within which the Committee will carry out its activities.

II. *The Role of the Committee*

A. *The Role*

1. The role of the Committee is to provide ethics review, in accordance with the provisions set forth in WHO Manual XV.2.70-90 and as hereinafter specified in these Rules, of all research projects involving human participants that are funded or otherwise supported by WHO.

2. *Research* is defined as any social science, biomedical, behavioural, or epidemiological activity that entails systematic collection or analysis of data, with the intent to develop or contribute to generalizable knowledge. Generalizable knowledge consists of theories, principles or relationships, or the accumulation of information on which they are based, that can be corroborated by accepted scientific methods of observation and inference.

3. *Human participants (sometimes termed “human subjects”)* are defined as human beings (i) whose biological material or medical or other records are collected or used by investigators’ and/or (ii) who are exposed to manipulation, intervention, observation, or other interaction with investigators either directly or through alteration of their environment as part of a research activity.

B. *WHO Support*

1. In determining what constitutes "WHO support" so as to require a project to be submitted to review by the Committee as provided in paragraph II (A) above, the following shall apply:

The expertise of WHO staff is a valuable resource globally for officials and researchers working to improve public health and it is appropriate for WHO staff to provide review and technical advice for a research proposal and/or study protocol involving human participants developed outside the Organization; however, when doing so, staff should keep in mind that the proposal is considered to have been supported by WHO within the meaning of WHO Manual XV.2.80 and these Rules and must be submitted to the ERC unless:

(a) The review provided by the WHO staff member(s) was limited to advice regarding only some portions, and not all, of the research project (*e.g.*, where their advice was sought on a particular technical matter);

(b) The investigators developing the project are neither WHO employees nor expected to be under contract to the Organization to develop the research proposal or carry out the research; and

(c) The WHO staff have informed the investigator in writing that the project has not been formally reviewed by WHO and the technical advice provided by WHO staff does not constitute endorsement of, or support for, the research project by WHO and should not be construed or portrayed to anyone as WHO support or approval.

III. Membership

A. Members

1. The Committee shall consist of 27 members: Chair, and 13 members and 13 paired alternates, from among which two vice-Chairs will be appointed. Members and alternates shall have equal status, and responsibilities and, except as may be indicated otherwise by the context in which the term occurs, both being included in the term "Member and/or Members" in these Rules. Depending on the context the term "Members" in these Rules may also include references to the Chair.

(a) Members shall be appointed by the Director-General for an initial term of three years, renewable for a maximum of two consecutive terms;

(b) All Members, including those who are WHO staff members, shall serve in an individual capacity and not as official representatives of, respectively, their relevant bodies and any unit or programme of the Organization. WHO staff who are Members of ERC (including the Chair and Vice-Chairs) shall not receive compensation specifically for serving on the Committee. The contribution of WHO staff to the ERC shall be included in the Performance Management and Development System (PMDS);

(c) Upon accepting an invitation by the Director-General to join the ERC, Members shall submit to the Director-General a signed declaration of acceptance to abide by these Rules of Procedures;

(d) It shall be incumbent upon the Members to undergo training in research ethics offered or recommended by the ERC Secretariat (the "Secretariat"). This will consist of an on-line training course to be completed before joining the Committee, and workshops organized or recommended by the Secretariat;

(e) It shall be incumbent upon the Members to keep abreast of research ethics issues that emerge in global health research;

(f) Service on the Committee shall be reported in the ERC Annual Report;

(g) Membership of WHO staff members shall be drawn from all clusters within the Organization, overall membership shall be gender balanced, and shall include persons with experience in and knowledge of all WHO regions and from the full range of disciplines (including, but not limited to, medical, behavioural and social-sciences, public health, epidemiology and other relevant disciplines) relevant to the work of the Committee;

(h) There shall be at least one Member-Alternate pair on the Committee which is not technically qualified in the field of health;

(i) There shall be at least one Member-Alternate pair on the Committee which is not employed by WHO. These Members shall be known as "non-affiliated members". Non-affiliated members shall be designated as WHO temporary advisors while engaged in ERC activities, through arrangements made by the Secretariat with the appropriate services of the Organization.

B. Appointment of Members

1. Members shall be appointed based on:

(a) their willingness to commit the time required to fulfil their duties on the ERC; and

(b) either their expert knowledge in medicine, science, or another field, as appropriate; or their knowledge of research ethics, or for the Member-Alternate pair not technically qualified in health or research ethics, their commitment to contributing to the ethical conduct of WHO sponsored health research.

2. In so far as necessary, membership terms may be set for periods of less than a full term to achieve a balanced staggering of membership turnover.

3. Decisions about reappointments should be guided by the objective of not having more than 20% of the Committee consist of new Members in any given year.

4. Members who find that they are unable to fulfil the responsibilities expected may resign by notifying the Chair.

5. Notwithstanding their term of appointment, the service of WHO staff on the Committee shall in any event end when their employment terminates. However, in the case of WHO staff members on temporary appointments, breaks between contracts of up to 31 days shall not be considered termination of appointment for the purposes of this Rule, although during such breaks they shall not perform functions for the Committee.

6. Each Member-Alternate pair shall between them attend at least 80% of all scheduled Committee meetings. Each Member shall attend at least 40% of the meetings.

7. To ensure the independence of the Committee and the ability of its Members to exercise their judgement concerning matters coming before the Committee, they may only be removed from the Committee by the Director-General in the event of:

- (a) failure to attend two consecutive meetings for which they had previously committed, without providing an acceptable explanation to the Secretariat prior to the meetings;
- (b) failure to attend at least 40% of the 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;¹ or
- (d) flagrant departure from the Rules of the Committee.

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

¹ If a member who is not absent on duty travel or leave and who has not reviewed two or more proposals in the prior two months declines three consecutive requests to perform an expedited review, the Chair may discuss with the member how the member proposes to discharge his or her responsibilities on the Committee or if the member wishes to resign.

IV. Chair and Vice-Chair

A. Appointment

1. The Director-General shall appoint a Chair, and two Vice Chairs of the Committee from among its Members.

2. The persons appointed as Chair and Vice-Chairs should have experience in the design and review of research involving human participants and knowledge of the relevant ethical standards.

3. Appointment as Chair and Vice-Chairs should be for an initial term of two years, renewable for a maximum of two consecutive terms or for the duration of the membership, whichever is shorter.

B. Responsibilities

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

- (a) Preside at meetings of the Committee;
- (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 Director-General the Committee's advice on matters related to the ethics of research involving human participants and to the activities and responsibilities of the Committee;
- (e) Approve the Annual Report on the work of the Committee and the Secretariat;
- (f) Work with and provide general direction to the Secretary of the Committee ("Secretary") regarding the operation of the Committee and the Secretariat; and
- (g) Recommend to the Director-General possible new Members, endeavouring to ensure appropriate balance of expertise, gender, geography and cross-cluster involvement.

2. The Chair and the Vice-Chairs, shall among themselves, develop a schedule of their availability, and inform the Secretariat accordingly. The Secretariat shall keep a roster of availability for

the Chair and the Vice-Chairs, and ensure that at any given time, only one person is designated to carry out the function of the Chair, and that this information is available to the entire Committee.

3. The Chair will hand over the responsibility of the office to the Vice-Chair whenever proposals from the Chair are being reviewed or discussed, or if he/she has been involved in the development of a proposal. Similarly, the Vice-Chairs shall not act as the Chair if their proposals are being reviewed or discussed or if he/she has been involved in the development of a proposal.

4. The Chair and Vice-Chairs shall meet periodically to discuss and resolve administrative and policy issues related to Committee work.

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

V. The Committee Secretariat

The Secretary shall be a WHO official designated by the Director-General. The Secretary shall be assisted by such additional technically qualified and administrative staff as is required to fulfil the function of the Secretariat.

A. Responsibilities of the Secretary and the Secretariat

1. In addition to such other functions as are provided in these Rules, the Secretary shall ensure that the Secretariat operates in an efficient, accountable, and transparent manner, specifically by:

(a) Liaising with the Chair and the Members on policy issues relating to the ERC and the protection of the rights and interests of human participants in research funded or otherwise supported by WHO; and

(b) Ensuring any administrative assistance that may be needed by the Chair and Members in carrying out the Committee's functions.

2. The Secretariat, under the leadership of the Secretary shall:

(a) Certify, on behalf of the Organization, which research proposals have been duly approved by the Committee in accordance with these Rules;

(b) Maintain a registry of WHO research projects involving Human Participants submitted for Committee review ("Register");

(c) Undertake a preliminary review of all submitted proposals to assess whether the proposal is complete in all respects as specified in Appendix 1, and if not, to liaise with the WHO staff member responsible for each research proposal ("WHO responsible staff member") in order to bring it up to the required standard;

(d) Ensure that all necessary reviews of new research proposals, and continuing review of all previously approved research proposals, are carried out promptly by the Committee and at such intervals and in such a manner as is specified in these Rules or as is otherwise directed by the Committee;

(e) Ensure that timelines for the review of submitted materials are provided to the technical units;

(f) Organize ERC meetings and promptly inform the WHO responsible staff member reviewed by the ERC of the Committee's disposition of the proposal;

- (g) Draft annual reports, and such other reports as may be required, regarding the work of the Secretariat and of the Committee;
- (h) Work with the Chair and other officials to obtain for WHO such approvals, evaluations, or accreditation of its research ethics review processes as are necessary and appropriate;
- (i) Maintain the following documentation:
 - (i) A copy of these Rules;
 - (ii) An up-to-date list of all ERC Members with their terms of service, titles, and curricula 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 ERC meetings and decisions, and such additional detailed records as the Committee may require;
 - (iv) The Register, which shall document the current status of all research proposals submitted to the Committee (*e.g.*, whether exempt from review, approved, awaiting changes before action, or not approved);
 - (v) Information relating to any other research ethics committees ("RECs") that have reviewed proposals also reviewed by ERC; and
 - (vi) Copies of all research proposals submitted to ERC, including comments from any scientific or technical bodies and RECs that reviewed any such proposal.
- (j) Retain all project-related documentation for a period of five years after the closure of the project, and all Secretariat-related documentation (meeting agenda, minutes of meetings, annual reports, reports etc.) for a period of ten years, unless otherwise advised by the Records and Archive Department of WHO;
- (k) Make readily available information to WHO staff about ERC, including its standards, rules, procedures, activities (*e.g.*, meeting times, educational programmes, etc.) and disposition of proposals; and
- (l) Make readily available to WHO staff information and educational materials and training on ethical issues related to human research, including particularly ethical issues in international health research.

VI. ERC Meetings

A. Frequency

1. Meetings of the Committee generally shall be convened and organized by the Secretariat once a month, or more often, depending upon the workload.

2. The Secretariat shall provide the Members with at least one week's notice of all meetings, together with a copy of the proposed agenda and required meeting materials. Special meetings may be called on shorter notice by the Chair.

B. Attendance

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

2. 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 member(s) to attend if possible.

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 WHO responsible staff member (or in his/her absence such other person(s) designated by the WHO 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, of other UN agencies and bodies 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 persons may attend those portions of the meeting at which the proposal is being reviewed and participate in the discussion thereof or may be asked to submit written comments related to a

proposal. These persons shall depart from the meeting before the Committee reaches its decision on the proposal.

6. In the interest of transparency and improving the wider understanding of the work of the ERC, the Chair may, after consultations with the Committee (or with the Vice-Chairs), invite or allow a limited number of individuals to be observers at the ERC meetings - provided that confidentiality and conflict of interest requirements are fulfilled. Invitations shall be issued on an ad hoc basis and may be renewed, where appropriate, after consideration by the Committee. Observers may attend the entire meeting to which they have been invited to, but may not take part in discussions, unless explicitly invited by the Committee to do so. The Chair, after consultations with the Committee, may decide to request the invited observers to leave 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 WHO staff are bound to respect such confidentiality. Non-affiliated members of the Committee must sign a confidentiality agreement regarding the Committee's work. The Chair shall provide a reminder of the requirement for confidentiality at the beginning of each meeting or otherwise as necessary, including the fact that they may only discuss the information with other Members (including non-affiliated members who have signed the confidentiality agreement).

2. All persons invited to any ERC meeting, or asked to provide written comments related to a particular proposal, must sign a confidentiality agreement 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 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.

4. All communications about committee decisions, meeting discussions, and review outcomes shall be made only by the Chair and /or the Secretariat, on behalf of the Committee.

5. 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 or about specific committee reviewers.

D. Quorum

Except as otherwise provided in these Rules, a majority of the Members must be present to constitute a quorum for the conduct of business. Such a quorum for any Committee meeting shall be 8 Members, none of whom shall belong to the same pair - as only one person within each member-alternate pair may be counted towards quorum, and at least one of whom is a non-affiliated member. This does not apply to the pair of the Vice-Chairs should one of them act as Chair . Representatives of the Office of the Legal Counsel, members of the Secretariat, and other persons do not count towards the quorum.

E. Meeting Records

Minutes shall be recorded by the Secretariat for all meetings and shall be submitted to the Chair, and subsequently to the Committee for approval.

VII. Submission of Research Proposals

A. Basic Requirement

In order to ensure that appropriate ethics review has occurred for all research involving human participants that meets the requirements of these Rules and that is funded or otherwise supported by WHO, the WHO responsible staff member, working in close collaboration with the Principal Investigator, shall submit the proposal for such research to the Secretariat, in accordance with the documentation requirements of Appendix 1.

B. Conformance with Applicable Requirements

Before submitting a research proposal to the Secretariat, the WHO responsible staff member shall ensure that:

1. Such research has been previously reviewed and approved by a scientific review committee, panel or group that is external to WHO and whose entire membership is independent from the research project team;
2. Such research conforms not only to the ethics requirements established by ERC but also to those of any other applicable ethics review body convened by the Organization, if any;
3. Such research has been authorized by the relevant health authorities in the country where the research will be conducted when so required by the country concerned; if such authorization has not yet been granted, an explanation is provided concerning the reasons for the delay of such a granting and if and when such authorization approval will be forthcoming;
4. Such research has been submitted for review to at least one ethics committee in the country in which the research will be undertaken with the understanding that the country-level committee shall take responsibility for ensuring that all locally-relevant ethics standards and other local requirements are being followed. The ERC shall review but not grant final approval of a research proposal until a copy of the approval by the designated local ethics committee has been provided;

5. It shall be the responsibility of the Principal Investigator to identify any other relevant committees that also need to approve the proposal in a given setting according to local and institutional requirements. Any such local requirements shall be brought to the attention of the Secretariat when the proposal is submitted to the ERC, and a copy of these approvals provided;

6. The Principal Investigator and the institution under whose auspices the research will be conducted have formally committed to safeguard the rights and welfare of the research participants in accordance with international ethics requirements, in addition to all local and national ethics and legal requirements, to conform to the standards for research ethics adopted by the Committee, to adhere to the obligations of Principal Investigators as specified in these Rules and to adhere to other requirements as may be made by the Committee in granting approval.

C. Manner of Submissions

1. The WHO responsible staff member or unit should provide all documentation for review in a manner indicated by the Secretariat through the WHO intranet and the internet.

2. With each research proposal submitted to the Committee, the WHO responsible staff member shall submit the following cover documents:

- (a) A brief memorandum using the template provided by the Secretariat, which
 - (i) explains the purpose of the research;
 - (ii) reports the outcome of peer review by a scientific body (such as a funding agency or a WHO scientific and technical advisory committee) and whether the comments from the scientific review group have been incorporated into the proposal or are attached thereto;
 - (iii) reports all significant previous decisions by other institutional review boards or RECs or regulatory authorities including any that rejected the research proposal or that required it to be modified (with an explanation of the reasons given for such decisions and any changes made in the proposal as a result); and
 - (iv) provides information on submission or approval of the project by the relevant local ethics committee(s).

(b) 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), and if not, an explanation for any missing documentation, as well as information on when such documentation will be made available to the Committee.

VIII. Review of Research Proposals

A. Standards for Review

1. The evaluation of research proposals by the ERC shall be guided by the *World Medical Association Declaration of Helsinki - Ethical Principles for Medical Research Involving Human Subjects (2008)*, 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, from time to time, officially recognize other statements on research ethics or formulate its own standards for particular topics in addition those contained in these documents.

2. The principal considerations for ERC review will usually be whether the proposal exhibits a favourable balance of benefits to risks, whether the risks to participants and others have been minimized, whether participants will be fairly selected, whether potential participants are so situated as to be able to make a free and competent decision, and whether the information provided to potential participants about the research project is in its nature and form such as to permit them to make an informed decision about whether to participate.

3. In determining the balance of benefits to risks, the Committee may consider the nature (including the adequacy) of any scientific review of the proposal, but the existence of such prior review does not preclude raising questions about the design and, when appropriate, asking for further information, requesting modifications in the design, or not approving the proposal, since a research project involving human participants that lacks scientific merit is inherently unethical. The Committee shall also review the plans for dissemination of the outcome of the research to ensure that the research results are disseminated to the research participants and other concerned stakeholders in an appropriate manner.

4. The Secretariat shall take appropriate steps to make the standards employed by the ERC in reviewing research known and accessible to WHO staff and to investigators who conduct research involving human participants funded or otherwise supported by WHO.

B. Procedure for Review

1. Before a research proposal can be reviewed on its merits, all necessary materials (as specified in section VII.C and appendix 1) must have been submitted to the Secretariat.

2. All new proposals for research involving human participants funded or otherwise supported by the WHO as well as all amendments (see Section VIII.G) shall, unless they are determined to be exempt from ERC review as provided in section VIII.B.3 below, be subject to an initial review in accordance with the standards for review set forth in section VIII.A. Such review shall be in the form of an expedited review, if determined to be eligible as provided in section VIII.B.4 below, or a review by the Committee as provided in section VIII.B.5 below.

3. Exemption from Review

(a) A research proposal may be exempted from review by the Committee when:

(i) it does not involve human participants according to the definition outlined in these Rules;

(ii) 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 by the investigator or any member of the research team;

(iii) public officials are interviewed in their official capacity on issues that are in the public domain;

(iv) the data for the study are generated by observation of public behaviour;

or

(v) the relevant activity is limited to public health surveillance or evaluation of health programmes carried out pursuant to statutory or regulatory requirements.

(b) If the Secretariat and the Chair both find that a proposal is exempt from review by the Committee in accordance with the criteria set forth in subparagraph (a) above, the research proposal shall be classified as "exempt from ERC review", an appropriate notation shall be made in the Register, and the WHO responsible staff member shall be notified accordingly. 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.

(c) If the WHO responsible staff member considers that the activity supported by him/her qualifies for an exemption from ERC review, he/she should use the procedure for requesting an exemption, as indicated on the ERC intranet and internet sites.

(d) If the Secretariat and Chair cannot agree whether a research proposal qualifies as exempt from review, the proposal shall be categorized as eligible for expedited review as provided in VIII.B.4 below, and reviewed accordingly, and the WHO responsible staff member shall be informed as per these Rules.

4. Expedited Review

(a) A research proposal is eligible for an expedited review when:

(i) it will expose research participants to no more than minimal risk i.e. the level of risk to which it will expose participants is no greater than that encountered by people involved in their normal daily activities, such as working at home, in an office, or on a farm, attending school, or undergoing a routine health examination.

(ii) minor changes are planned in research that has been previously approved by the ERC and where proposed changes do not create more than minimal risks;

(iii) an additional research centre is to be added to a project previously approved on a multi-centre basis, such that ERC review is limited to ensuring that the necessary local review and approval has taken place.

(b) If the Secretariat and the Chair (or the Committee, pursuant to the process described in VIII.C.7-9 below) determine that a proposal is eligible for expedited review in accordance with the criteria set forth in VIII.B. 3d or 4a (i) above, the research proposal shall then be reviewed on its merits by two members of the ERC independently. The reviewers shall be identified by the Secretariat based upon relevant knowledge and availability to evaluate the proposal and such other criteria as may be determined by the Committee.

(c) A proposal that is eligible for expedited review in accordance with the criteria set forth in 4a (ii and iii) above may be reviewed by the Chair on behalf of the Committee. Following the review of a research proposal, the Chair shall provide an outcome of using either option VIII.C.1 (i) or (ii).

(d) Following the review of a research proposal, the two reviewers shall recommend an outcome using one of the options provided in VIII.C.1 (i), (ii) and (iii), or those provided in points (f) and (g) below.

(e) The recommendations of the two reviewers except in case of (f) and (g) below shall be discussed by the Secretariat with the Chair. Based on their recommendations, the Chair, on behalf of the Committee shall make a determination of the outcome of the review and the Secretariat shall communicate this decision to the WHO responsible staff member as a comprehensive summary assessment as per Section VIII C. The identity of the two reviewers shall not be divulged and the notification to the WHO responsible staff member shall be done on behalf of the ERC. Such notification shall include a reminder that any material changes in the design or execution of the activity in question must be approved pursuant to these Rules prior to implementation.

(f) If either of the two reviewers, based on their review, determine that the proposal poses **more than** minimal risk to the research participants or that it involves participants who have diminished autonomy and/or who are not capable of giving informed consent, the Secretariat shall submit the proposal for a Committee Review at the next available meeting, as described in section VIII B.5 below, and notify the responsible staff member accordingly. Explicit justification for making that determination should be provided by the reviewer(s), in writing.

(g) If either of the two reviewers make a determination that the proposal is ethically unacceptable, and recommend that it be Rejected, the Secretariat shall submit the proposal for a Committee Review at the next available meeting, as described in section VIII B.5 below and notify the responsible staff member accordingly. No proposal shall be Rejected based on an expedited review.

(h) Notwithstanding the above, a research proposal shall be submitted for Committee review, as provided in VIII.B.5 below, whenever required by the terms of any grant, donation or other arrangement for the provision of funds for the research concerned.

5. Review by the Committee

(a) All proposals for research involving human participants funded or otherwise supported by WHO that are neither determined to be exempt from ERC review, nor approved by expedited review in accordance with these Rules shall be subject to a review by the Committee at a convened meeting.

(b) Research that involves persons with diminished autonomy and/or who are not capable of giving informed consent must be submitted to the Committee for review and cannot be approved through an expedited review process.

(c) The Committee shall perform such review in a conscientious and expeditious manner and shall in each case determine whether to approve, request modifications, or disapprove the proposal.

(d) In reaching decisions about research proposals, Members must exercise their judgment in applying the applicable ethical standards for review to the facts of each case, including what they know about the circumstances and conditions under which the research will be conducted.

(e) 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”. Such primary reviewers shall summarize the proposal at the Committee meeting and provide their opinions on relevant ethical considerations, 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 WHO responsible staff member at the ERC meeting would be desirable, he/she should promptly notify the Secretariat, who shall then attempt to obtain the needed information.

(f) 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.

(g) Following a discussion of a proposal, the Committee shall provide an outcome of the discussion using any one of the options provided under section VIII.C1 below.

6. Accelerated Review

(a) As a public health organization, WHO may often need to carry out research in the context of public health emergencies such as the investigation of a disease outbreak or a disaster relief operation. The standards and procedures for review of these proposals shall be guided by Sections VIII.A. 1-4 and VIII.B.1-5; however, recognizing the urgency of the situation, the Secretariat shall ensure that the review of such research proposals is conducted in an accelerated manner, including convening a special ERC meeting, if required. The procedure of review in such a case is described under Section VIII.E.3 below (Review of Special Categories of Proposals)

C. *Outcome of Review and Reporting the Outcome of Review*

1. The outcome of the review of a research proposal, notwithstanding the procedure followed for carrying it out, must be in accordance with one of the following actions:

(i) ***Approved as submitted***: means that the proposal is approved and no modifications are required.

(ii) ***Not approved; requires amendments and/or clarifications***. This means that final approval is contingent upon an adequate response by the Principal Investigator, to the satisfaction of the reviewers or the Chair on behalf of the ERC.

(iii) ***Not approved; requires additional information and/or rewriting***. This means that the revised version of the proposal should be re-submitted by the WHO responsible staff member as a new submission to the ERC for re-review by Committee.

(iv) ***Rejected***. This means that the proposal is ethically unacceptable, and may not be approved by the ERC. The Principal Investigator may submit a new proposal that takes into consideration the ethical issues raised by the Committee.

2. Except as otherwise provided in these Rules, decisions on review of proposals shall be taken by consensus². When consensus cannot be reached, the Chair may ask the Committee to vote, by a show of hands. In case of voting, decisions on review of proposal shall be taken by two-thirds majority of the Members present and voting.

3. A copy of the final approved version of the proposal and the informed consent forms shall be retained by the Secretariat.

4. The outcome of a review, whether on an expedited basis, accelerated or by the Committee, shall be communicated by the Secretariat to the WHO responsible staff member in writing, together with an explanation of the reasons for the decision. If, following a Committee review, a proposal is rejected, the explanation shall include the ethical principles underlying the decision.

5. If a proposal is "rejected", the Chair shall provide an opportunity to the WHO responsible staff member to appeal the decision in writing. When the Chair considers it is warranted on the basis of the information provided by the WHO responsible staff member, she/he may decide to have the decision of rejection of that proposal reconsidered by the Committee at its next meeting.

6. Notwithstanding the action chosen, among those listed above, for conducting the final review of a proposal that requires amendments and/or clarifications, the Secretariat shall, upon a final approval of the proposal, have the approval signed by the Chair of the Committee.

7. At each meeting of the Committee, the Secretariat shall provide the Committee with a summary report on the outcome of all research proposals since the previous meeting, as well as a summary report on all proposals which were determined to be eligible for expedited review or to be exempt from review. At that time, any Member may request a re-assessment of the proposals that were deemed to be exempt from review or eligible for expedited review.

8. When such a request has been made, the Secretariat shall immediately notify the WHO responsible 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 of the Committee's review.

9. If the Committee decides to override the determination made by the Chair and the Secretariat in either VIII.B.3 (b) or VIII.B.4 (b), it shall then determine the type of review the proposal shall undergo.

D. Continuing Review of Approved Studies

1. Ongoing projects must be reviewed annually, 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 participants have been recruited. When the Committee determines that continuing review of an approved project should occur more frequently than once per year, or determines that continuing review should occur after the accrual of a specified number of participants, this decision should be communicated to the WHO responsible staff member.

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. In this context, such an expedited review may be carried out by the Chair, on behalf of the Committee.

3. If any substantive changes have been made in the protocol or consent documents, the continuing review shall be conducted in the same manner as provided in section VIII.B.2.

² Consensus is defined as absence of assertion of an objection

4. If the WHO responsible staff member fails to adhere to the obligations to submit reports on the progress of approved projects provided in these Rules, the Committee shall – unless it considers circumstances warrant otherwise - withdraw its approval of the project.

5. Should the process of review lead to a withdrawal of approval from a previously approved study, this determination shall be immediately communicated to the WHO responsible 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 WHO responsible staff member shall promptly report back to the ERC concerning the date in which the enrolment of new participants was halted and the manner in which the research project is dealing with the follow up of previously enrolled participants.

6. In some cases, follow up with participants will be required even where a protocol is halted, in order to maximize safety of participants. This might be where it would be unsafe to discontinue an ongoing intervention, or where an alternate intervention must be provided in place of the one being tested, where serious test results must be provided, where additional safety monitoring is in the best interest of the participants, or to inform participants of the halting of the study. Any such follow up plans for an otherwise halted study must be described in detail to the ERC.

E. Review of Special Categories of Proposals

1. *Multi-site research* is research conducted by a group of one or more investigators using the same overall research plan at several different research sites. Data are pooled for analyses to accomplish the specific aims of the study, and results are disseminated jointly by the investigators. Review of multisite research studies require review in the same manner as any other research funded or supported by WHO that involves human participants, but the multisite nature of such projects can lead to two variations in the process of approval:

(a) When WHO is the lead agency funding or organizing the research, an expedited review process may be utilized to add new sites to an approved research proposal

(i) Once the ERC has approved the main protocol, the review and approval of additional research sites for the same project can be undertaken on an expedited basis, but each proposed new site shall be given a new ID in the Register, with a notation that it is derivative of a particular protocol;

(ii) In such a situation, expedited review will be limited to determining whether the research proposal remains unchanged from the main protocol; whether any variations in the local circumstances (in terms of the characteristics of the population, the setting, the local manifestation or nature of the disease or treatment thereof, etc.) could adversely affect the benefit-risk ratio, the minimization of risk, or the validity of informed consent; and whether any necessary translation of information and documentation has been prepared in an adequate and culturally appropriate fashion. In this context, such an expedited review may be conducted by the Chair, on behalf of the Committee;

(iii). If, in light of this assessment, the Chair is of the opinion that an additional research-site may be added under the proposal, the extension of the project to that site will be recorded in the Register as "approved" and will be reported to the WHO responsible staff member and to the Committee. If the Chair makes a determination that the benefit-risk ratio is adversely affected, the proposal will be submitted for review by the Committee, and the responsible WHO staff member shall be so informed.

(b) When WHO staff or persons under contract with WHO are involved in only one or a few sites of a multisite study being led by scientists unaffiliated with the Organization and when another institutional review board (IRB) or REC 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 IRB or REC 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 WHO involvement in the study;

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

(iii) The WHO responsible staff member shall submit to the Secretariat the results of the review by the lead ethics review board (including any explanations, requirements, or other comments);

(iv) If the primary reviewers report that the quality of the review process and conclusion of the lead ethics review board satisfy the standards used by the Committee, the Committee may approve the protocol without discussing all the points usually considered in a review of proposals, but it is also free to decide that the proposal or a particular aspect of the proposal does not meet WHO's requirements and is therefore

'rejected', or that factors particular to the research sites for which WHO is responsible require alterations in the protocol, consent materials, etc.

2. *Nested Studies*: Any study which is part of another, i.e., "nested" within another study, shall be considered in the same way as any other research project, and shall be subject to the procedures and criteria for review as set forth in these Rules. However, together with the documentation indicated in Appendix 1, the WHO responsible staff member shall also submit the protocol for the main study. While the main protocol does not need to be formally reviewed by the Committee, the Committee should be satisfied with the ethical aspects of the main study and have documentation of the ethical approval of the main study before considering approving the nested study.

3. *Research conducted in the context of public health emergencies*: Research studies that are to be conducted in the context of public health emergencies, such as the investigation of a disease outbreak, or during a disaster relief operation, may require review on an urgent basis. The proposal shall be subject to the standards and procedures for review as set forth in these Rules, however, the procedure for Committee Review may be modified depending upon the nature of the emergency. In cases where the proposal warrants a Committee Review, as set out in these Rules (Section VIII.B.5 above), the Secretariat shall endeavour to conduct an accelerated review, by calling a special meeting of the ERC. If however, the quorum for the conduct of business provided in VI.D is not reached, the Chairperson may decide, depending upon the nature of the circumstances that the proposal be reviewed by a minimum of 3 members attending the special meeting of the ERC.

(a) The outcome of such a review, to be provided using one of the options provided under section VIII.C.1 above, shall be communicated to the WHO responsible staff member as quickly as possible;

(b) The proposal and the outcome of the review shall however be presented by the Secretariat at the next Committee Meeting for information. At this time any Member may make additional recommendations. When such recommendations have been made, the Secretariat shall immediately notify the WHO responsible staff member to incorporate these additional recommendations in to the approved protocol;

(c) Notwithstanding the availability of this review procedure, the Secretariat shall work in collaboration with the concerned WHO departments, and encourage the development of protocol templates that may be pre-reviewed by the Committee as per these Rules, such that any new protocol based on a pre-reviewed protocol may be reviewed by an expedited review.

F. Timelines for Review and response

1. Once the proposal is complete and ready to be reviewed, the Secretariat shall ensure that the WHO responsible staff member receives a review outcome within the stipulated time frame as follows:

- (a) Exemption from ERC review: within 5 working days;
- (b) Expedited Review: within 15 working days;
- (c) Committee Review: within 30 working days except where the WHO responsible staff member requests an Accelerated review;
- (d) Accelerated Review: within 7-15 working days.

2. It is incumbent upon the WHO responsible staff member to respond to the queries of the Secretariat or the review outcome provided by the ERC within a reasonable time-frame.

3. The Secretariat shall send reminders to the WHO responsible staff member once a month for three months after submitting a query or the review outcome, after which, if no response is obtained, the project shall be deemed closed before approval, and the WHO responsible staff member must re-start the process for review.

G. Continuing Oversight

1. The Organization's obligation to ensure continuing oversight of approved research projects, which it funds or otherwise supports, creates responsibilities for the WHO responsible staff member and for the Committee beyond the obligation to perform continuing reviews, as detailed below.

2. Principal Investigators shall inform the WHO responsible staff member of any proposed changes to an approved research proposal prior to implementation of those changes, and these shall be immediately reported by the WHO responsible staff member to the Committee.

- (a) When the Secretariat receives a report of proposed changes to the previously approved protocol or consent documentation of a research project, a determination shall be made by the Chair and Secretariat in accordance with VIII.B.4 (a) and VIII.B.5 (a) whether the

proposed changes should be subject to an expedited review or a review by the Committee in accordance with these Rules.

(b) Pending the Committee's decision, which it shall endeavour 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 adverse events assessed as being related to the research that occur to participants during their participation in any approved research project, and all protocol violations shall be immediately reported by the Principal Investigator to the WHO responsible staff member as well as to any other persons, relevant ethics review bodies, funding agencies or other bodies with whom such information must be filed pursuant to national regulations and terms and conditions covered in the protocol and agreed by WHO. The WHO responsible staff member must promptly convey such reports to the Secretariat, including the feedback from other review bodies.

(a) The Chair 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 a decision to re-review the project is made, the Chair has the discretion to suspend approval and require that recruitment not be continued pending the re- review

(c) If the Chair determines that such re-review should occur, it shall take place as soon as possible (including through a special Committee meeting, if required by the circumstances).

(d) The results of the re-review will be promptly conveyed to the WHO responsible staff member.

(e) It shall remain the obligation of the WHO responsible staff member, rather than of the Committee, to ensure that serious adverse event reports, as well as the determinations reached by the Committee in a re-review, are filed with all appropriate persons and bodies, pursuant to terms and conditions agreed by WHO.

4. It is the duty of the WHO responsible staff member to report when projects have been completed or discontinued and to submit a final report on the study to the Secretariat. A notation shall be made in the Register accordingly.

5. A project is eligible to be 'Closed' with the ERC when

- (a) all initial and follow up contacts with research participants have been completed;
- and
- (b) all study related activities have been completed.

6. If the Principal Investigator believes that both conditions VIII.G.5 (a) and (b) above have been satisfied, then the 'ERC Closure Form' should be completed and submitted to the Secretariat. When a signed letter from the Secretariat has been received by the Principal Investigator, the project can be considered “closed” and continuing reviews are no longer required. However, data analysis and report writing may continue after a study has been “closed” for purposes of ERC review.

7. The Principal Investigator may keep the data they collected, including identifiable data, for future, further analysis, if such proposal has already been approved by the ERC. The confidentiality of such data should be honoured as described in the research proposal.

IX. Conflicts of Interest

A. The Commitment to avoid real and perceived Conflicts of Interest

The avoidance of conflicts of interest, or avoidance of the appearance such conflicts, is important to ensure both the quality and credibility of research ethics review. WHO therefore takes seriously the need to take steps to avoid both conflicts of interest and the appearance of conflicts of interest for investigators, WHO staff members, Committee Members and the Secretariat.

B. Investigators

1. All investigators involved in a research proposals submitted for review shall complete the form *WHO Declaration of Interests for Experts* ("DOI"). The WHO responsible staff member shall certify to the Secretariat that all DOI and other required forms have been completed. In addition, the WHO responsible staff member shall transmit to the Secretariat a copy of the minutes (or memo to file) of the meeting during which the DOI Forms were reviewed and assessed. In accordance with the WHO Guidelines for Declaration of Interests, such minutes (or memo to file) must be approved by the Director or Coordinator of the unit concerned. The Secretariat shall make available to the Committee such minutes (or memo to file) and may request additional clarifications in this regard.

2. The Committee shall pay careful attention to the content of such minutes (or memo to file) and shall approve a research proposal only if it concludes that the Principal Investigator, who will conduct the research, does not have any material conflict of interest or that such interest is not sufficient to compromise 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.)

(a) 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.

(b) For cases in which an interest is revealed, but it is not so material as to warrant not approving the project, the Committee shall determine what description of such interest, should be included in the information provided to prospective participants and shall ensure that the consent documentation also includes an appropriate disclosure.

C. WHO Staff and Temporary Advisors: Financial Conflicts

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. WHO officers and WHO responsible staff members on the Committee and Secretariat are bound by Staff Rule 110.7.1 to inform the Director-General of any interest they, as well as their spouses and dependent children, may have in any entity that has a commercial interest in 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 project submitted to the Committee, all such staff members shall also inform the Secretariat. 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.

3. Members having reported a financial conflict of interest 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.

4. Similarly, the Chair will hand over his/her responsibility to one of the Vice Chair whenever such conflicts of interest occur to the Chair 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.

D. WHO Staff and Temporary Advisors: Role Conflicts

A Member who is also a WHO responsible staff member for a proposal under review or is connected closely to a proposal (such as being on the same team as the responsible staff member submitting the proposal or being in a supervisory position with the submitting responsible staff member,

or if he/she has been involved in the development of a proposal) would have a conflict of interest if he or she participated in the ethics review of the proposal.

1. When asked to perform an expedited review or to be a primary reviewer, a Member with such a conflict shall disclose it and decline to undertake the review.

2. Members having reported a 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 at the meeting before the commencement of the relevant discussion 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 one of the Vice Chair whenever such conflicts of interest occur to the Chair 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 decision

X. Evaluation and Improvement

A. Quality Assurance of the work of the ERC

1. All Members 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 and procedures of the Committee's work.

2. Such suggestions should typically be presented to the Chair, who will review the suggestions and consult with the Secretariat. If they conclude that the suggestions would improve the functioning of the Committee, the Secretariat shall either place the suggestions 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 Rules shall be considered under section XI.B below.

4. The Secretariat shall arrange for the work of the Committee and Secretariat to be evaluated every five years by one or more external, independent persons who are knowledgeable about research ethics and the functioning of ethics review committees.

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

6. The evaluator(s) should endeavour 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.

7. The conclusions of the evaluator(s) shall be submitted to the Chair and Secretary for appropriate action, and a copy submitted to the Director-General.

8. Two years prior to a planned external evaluation, the Secretariat shall have the work of the Committee and the Secretariat evaluated by the Internal Oversight Services (IOS) of the Organization. The conclusions of the IOS shall be submitted to the Chair and Secretary for appropriate action, and a copy submitted to the Director-General.

B. Annual Report

1. At the conclusion of each year of work, the Secretary shall prepare an Annual Report, which shall be subject to approval by the Chair.

2. The Annual Report shall include:

(a) A listing of the composition of the Committee and their department or outside affiliation;

(b) A description of the Committee's activities, accomplishments, and any particular difficulties experienced;

(c) A summary of the recommendations and conclusions of the independent evaluator(s) if such an evaluation has occurred;

(d) Recommendations for improvement that have been, are being, or should be considered by the Committee, including any that would require a change in the Committee's terms of reference as set forth in the WHO Manual;

(e) Tables summarizing the proposals exempted from review and reviewed by expedited and Committee review, by WHO clusters, departments, and regions, and by topics; and

(f) A table summarizing the contributions of Members, including the number of proposals reviewed by each Member during the past year; and

(g) A table summarizing the professional development activities related to their role as Members.

3. The Secretary shall submit the Annual Report to the Director-General within the first quarter of the following year. The Secretary shall also file the report with such other persons (such as research sponsors) as may be required and post it on the Committee's intranet page.

XI. Adoption and Amendment of the Rules of Procedure

A. Manual

The terms of reference for ERC are set forth in the WHO Manual, Part XV, Section 2. paragraphs 70-90.

B. Rules of Procedure

The Committee may adopt such Rules of procedure as it deems necessary, consistent with its terms of reference, subject to approval by the Director-General. Any amendment proposed by a member of the Committee shall be submitted in writing to the Secretariat, who shall submit it to the Legal Counsel for clearance. Once cleared by the Legal Counsel, it shall be placed on the agenda of the next available Committee meeting for consideration and possible adoption by a majority of the Members present and voting. The amendment shall come into effect once approved by the Director-General.

Appendix 1: Items to be included in a Research Proposal submitted to ERC for review

A. Required Information

In addition to the cover documents, the documentation submitted with a research proposal to ERC shall, at a minimum, include:

1. A research protocol - as part of the research proposal - that includes the following, as relevant:

(a) The scientific design of the study, including the questions being addressed or other objectives, and the medical, scientific, and statistical methods being used, sufficient to permit a technically qualified person to determine whether the study can answer the stated questions or meet the stated objectives;

(b) 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;

(c) Specification of the population(s) in which the research will be conducted and the methods by which members of the population will be identified for inclusion in, or exclusion from, the study, including sufficient information to permit a reviewer to determine whether the methods used are scientifically justified and ethically fair;

(d) Description and justification of the research design, including any division of the participants into two or more groups who will be subjected to different procedures or receive different treatment, especially when one or more of the groups will receive no intervention or a placebo;

(e) A description of the gender considerations relevant to the project, including a discussion on how gender issues are being considered during key stages of the proposal development and implementation e.g. during participant recruitment, risk-benefit analysis, data analysis, etc.;

(f) An explanation of the benefits that the research will likely produce, whether to research participants, members of the population from which participants will be drawn, other populations, or to basic or applied scientific knowledge;

(g) A description of physical, social, psychological and economic risks to both individuals and communities;

(h) Specification of any circumstances or characteristics that might render participants especially vulnerable to harm or to risk of exploitation (including factors that would render their consent uninformed or involuntary) and of the steps that will be taken to overcome, ameliorate, or be responsive to such vulnerabilities;

(i) A detailed description of the steps that will be taken to minimize the risks to participants, physically (including provisions to address injuries or medical emergencies should they occur or to minimize the likelihood of serious adverse events occurring through eligibility criteria), psychologically (including any counselling or other services), and socially or economically (including steps taken to protect the confidentiality of information obtained from or about participants, to prevent dissemination of identifiable data regarding participants without their consent, and to protect participants from social or economic discrimination or stigmatization should information from the research be disclosed to persons outside the research project);

(j) Details on how the study will be monitored, including details concerning any Data and Safety 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 relevant ethics committees including the WHO ERC), and the decision rules it will utilize in deciding or recommending that the research should be altered or halted;

(k) A description of the arrangements (including immediate medical or other assistance and compensation for medical expenses, lost income, or the like) that will be available to compensate any harm that occurs to research participants;

(l) The amount and type of incentives, in terms of money, goods, or medical services, that will be offered to participants, uniformly or selectively, as well as any treatment or compensation that will be provided participants who are injured in the course of the research, with an explanation of what will constitute a covered injury and how such coverage will be determined;

(m) Any information that will be provided to participants, verbally and/or in writing, following their participation, including a description of the categories of information that will be provided or offered such as the general findings or conclusions of the research, the individualized results of any tests or other procedures undergone by the participants, etc.;

(n) The statistical or other rules (such as the occurrence at a specified rate of particular serious adverse events) that will determine whether the study will be halted before accruing the full complement of participants specified in the protocol, with specification of the

role that anyone other than the investigators such as a DSMB will play in making such a determination;

2. Curriculum vitae of the investigators and co-investigators submitting the proposal;

3. A detailed budget;

4. Timeline for the project activities, enrolment, analysis, and completion;

5. Reports on the outcome of any review of the scientific, technical, or medical aspects of the research proposal by individuals or groups other than the staff of the responsible WHO unit (such as a peer review committee of the sponsoring agency or a WHO scientific and technical advisory committee);

6. Copies of all materials (recruitment materials, advertisements, flyers, consent documents, information brochures, and the like) to be provided to participants concerning the research prior to their decision on whether to enrol (such information being provided in English and, when appropriate to the research site, also in the participants' native language(s), accompanied by a "back translation" prepared by someone skilled in interpretation and not directly involved in the research); if oral consent will be used, a copy of disclosure information provided to participants must also be provided to the Committee for review;

7. A copy of any instruments being used to collect data, such as questionnaires that will be administered, including translations into the local language;

8. Detailed information about how biological materials or other data from the research will be collected, preserved, transported, and stored, as well as which of those pieces include identifiable vs. non-identifiable data, and 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;

9. Documentation that the proposal has been reviewed and approved by the appropriate IRBs or RECs for the site(s) where the research will be conducted, or in the absence thereof, an explanation of when such review will occur;

10. A description of the plans that have been made, and any formal agreements that have been negotiated with representatives of the participant population, officials of the country where the research will occur, or donor organizations or companies, 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 to participants in a placebo or control group if the intervention is demonstrated to be effective, or a justification for the absence of such plans;

11. 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) or with donor organizations or companies 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;

12. 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.

B. Additional Elements

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

1. The processes for (and, if already completed, the outcomes of) consultation with the communities where the research will be conducted or with other bodies that represent the study population;

2. Information on the ways in which the research will contribute to capacity-building in the country or among the population where it will be conducted;

3. 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;

4. 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;

5. 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;

6. 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;

7. Any information on the capacity of the persons who will conduct the research and the organization or institution where it will be implemented (such as special training, certification, or facilities) as well as any relevant information on the capacity of the group(s) providing ethics review of the research proposal at the institutional, local, regional or national level.

Purpose

The purpose of this glossary is to aid WHO staff and investigators conducting research funded or otherwise supported by WHO to understand which activities are subject to review by the ERC as well as the concepts used by the Committee in such review. This glossary is not intended to supplant or substitute for the processes set forth elsewhere in these Rules but merely to explain the meaning of terms.

In relation to research with human participants as defined under Section II.A of these Rules, **intervention** includes both invasive and non-invasive physical procedures (such as venepuncture, surgery, administration of medication, weight and blood pressure measures, or physical examination); **manipulation** includes changes to the physical, clinical, social, psychological, informational or other circumstances in which a person lives or receives services; **observation** includes viewing, listening to, or otherwise studying people or their actions or behaviour; and **interaction** includes communication or other interpersonal contact between investigator and participant (such as through interviews or questionnaires; this may be in person, by telephone, in writing, or electronically).

The **WHO responsible staff member and/or unit** include the individual employee and/or administrative unit of the organization that have designed a research project that involves human participants, and who have contracted with investigators to implement such a project, or who have provided direct technical or logistic support to such investigators.

A **Principal Investigator** is the person who leads a social science, biomedical, behavioural, or epidemiological research project. The principal investigator has primary responsibility for adherence to the study protocol and training of all research staff on the project to ensure that all staff also adhere to the protocol and are in compliance with ethical norms and guidelines as relevant to the conduct of the study. An **investigator** is a social, biomedical, behavioural, or epidemiological researcher who collaborates in the conduct of such a project.

A **research proposal** is 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 CV and institutional affiliation), approvals from various relevant organizations and persons, budgets, dissemination plans.

A **research protocol** is the document describing the research study in detail.

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 by anyone to any particular person).

A serious adverse event is an event that is associated with death, admission to hospital, prolongation of a hospital stay, persistent or significant disability or incapacity, or is otherwise life-threatening in connection with a clinical trial. Serious adverse events can also occur in the context of other types of research studies (including social sciences and behavioral studies) and include but are not limited to suicide, confidentiality breach with expected serious consequences, loss of employment, loss of insurance, severe emotional distress requiring treatment etc.

An unexpected adverse event is an adverse event that was not anticipated, and usually

- is not listed in the informed consent and/or research protocol
- has an increased severity from that which is described and expected
- Occurs at greater frequency than that which is described and expected

An unexpected event should be classified as serious if it meets the definition of serious, otherwise it should be classified as non-serious.

PART XV: INDIVIDUAL PROGRAMME ACTIVITIES

Section 2: Research Collaboration and Training

WHO RESEARCH ETHICS REVIEW COMMITTEE (ERC)

70. In order to fulfil WHO's responsibilities and oversee its involvement in research involving human participants, the Director-General has established a WHO Research Ethics Review Committee (ERC or the Committee) to provide an ethical review of research involving human participants funded or otherwise supported by WHO, and has designated a WHO staff member as Secretary to the Committee (the Secretary). Equivalent committees, and secretaries, may be established in Regional Offices and WHO Centers and Agencies where warranted by the Organization's involvement at the regional level in research involving human participants. In the absence of an equivalent committee at the regional level or of WHO Centers and Agencies functioning in accordance with these provisions, all research proposals involving human participants shall be submitted to ERC as provided herein.
- 70.1. The Committee's function shall be to provide ethical review of research projects involving human participants funded or otherwise supported by WHO and to approve, reject, or modify research proposals submitted to it. The Committee shall be guided by the Declaration of Helsinki, the CIOMS International Ethical Guidelines for Biomedical Research Involving Human Subjects, and supplemented by other internationally accepted statements of ethical guidance adopted by the Committee. The Committee may also consider and provide advice to the Organization on any matter of general policy relating to ethical aspects of research involving human participants. The Committee shall, subject to approval by the Director-General, adopt such rules and procedures as are necessary and consistent with these terms of reference. It shall hold such meetings as are required to fulfil its responsibilities.
- 70.2. The Committee shall consist of members appointed by the Director-General, including a Chair and two Vice-Chairs. Membership of the Committee shall consist of WHO staff members, including at least one person not being technically qualified in medicine or public health, as well as at least one person not employed by WHO. Members shall be

appointed for terms of three years, renewable for a maximum of two consecutive terms . Members should be drawn from all clusters within the Organization, should include both males and females, and should include persons with experience in and knowledge of all WHO regions and from the full range of scientific, medical and other disciplines relevant to the work of the Committee. Additional persons, either WHO staff members or outside experts may be co-opted by the Chariot provide the Committee with relevant expertise as necessary.

70.3 The Secretary's function shall be to provide administrative support to the Committee.

80. All research proposals involving human participants which are foreseen to be funded or otherwise supported by WHO shall be submitted to the Committee for review. All research involving human participants funded or supported by WHO shall conform to the requirements set forth in the ERC operating rules and procedures. No research involving human participants shall be funded or otherwise supported or endorsed by WHO until it has been reviewed and approved by the Committee. Consequently, the responsible WHO unit may not commence or allow others to commence such research until notified by the Secretary that the research has been approved.

80.1. For this purpose, research shall be defined as “any social science, biomedical, behavioural, or epidemiological activity that entails systematic collection or analysis of data, with the intent to develop or contribute to generalizable knowledge. Generalizable knowledge consists of theories, principles or relationships, or the accumulation of information on which they are based, that can be corroborated by accepted scientific methods of observation and inference”, and human participants shall be defined as human beings whose biological material or medical or other records are collected or used by investigators' and/or (ii) who are exposed to manipulation, intervention, observation, or other interaction with investigators either directly or through alteration of their environment as part of a research activity.

80.2. Before submitting to the Secretary a research proposal for review by the Committee, the WHO staff member responsible for the research shall ensure that:

80.2.1 The proposal conforms to the ethical requirements established by ERC and by any other applicable ethical review body convened by the Organization;

80.2.2 Such research has been authorized by the relevant health authorities in all the countries where the research will be undertaken and conforms to national ethical and legal requirements of such countries, when so required in the countries concerned;

80.2.3 Such research has been approved by an appropriate research ethics committee at the institutional or national level which will be responsible for ensuring that the ethical principles involved and any other relevant requirements are followed carefully; and

80.2.4 The Principal Investigator and the Institution under whose auspices the research will be conducted have agreed to safeguard the rights and welfare of the research participants in accordance with all local and national ethical and legal requirements and the standards for research ethics adopted by ERC.

90. Any changes to approved research proposals which might in any way be reasonably considered to alter the balance of risk and benefits or otherwise have ethical implications on the research shall be reported and resubmitted to the ERC and to any other applicable ethical review body having previously reviewed the research proposal. The Committee shall also be notified immediately, through the Secretary, of any serious or unexpected adverse event that was not identified in the research proposal and of any development in the project which suggests that the research exposes participants to any risk not foreseen in the research proposal.

90.1. The responsible WHO staff member for each research project approved by ERC shall submit a progress report to ERC on an annual basis, highlighting any developments in the project that might have ethical implications.