A brief background to this document

Numerous international guidelines, most notably the Declaration of Helsinki and the CIOMS guidelines, outline principles and expectations for ethical research conduct. Other documents also describe procedures that RECs should have in place to ensure sound functioning and quality. In November 2009, WHO convened an "informal consultation" that included research ethics experts from each of the WHO regions, representatives from key stakeholder organizations and key departments from WHO. The consultation focused on ***norms and standards for RECs*** recognizing that member states may also find it useful to have a set of global *standards* available to help define what quality functioning means for the ***review of ethics of health related research***, and against which member states and RECs might measure their own performance. The experts recommended that WHO should take the lead in developing "new" standards for research ethics committees that build upon what already exists. The set of guidelines published by TDR-WHO in 2000 (Operational Guidelines for Ethic Committees that Review Biomedical Research) that is still widely used in the field, and has been used by over 100 countries and republished in multiple languages should be updated, but that drafting should go further to articulate ***standards*** that delineate what is required as a minimum for committees to meet a globally agreed upon standard in at least the core elements of ethical review, operations, their independence and governance.

The attached document "**Standards and Operational Guidance for Ethics Review of Health-Related Research with Human Participants"** is an outcome of that recommendation.

The standards for RECs outlined in this document are more specific than the broad ethical guidelines for research, outlining in some detail the benchmarks for the research ethics system, for the research ethics committees (how they are established, what procedures and standards they follow in conducting reviews, and how they are governed and administered), for the supporting secretariats of RECs, and also for researchers that submit proposals for an ethics review.

This document has been modified following a peer review by the expert group that met in November 2009, and additional experts who could not attend the 2009 meeting, as well as by the participants of the 10th World Congress of Bioethics (held in Singapore in July 2010), and been modified to include Standards not only for research ethics committees, but for the entire research ethics review system. WHO is now circulating this document for a wider, global peer review and we look forward to receiving back specific recommendations for modifications/ amendments/ changes. ***Please follow the following instructions when you provide your comments.***

1. Please be specific in your comments, and provide the ***specific language*** that you would like used. Do not send in broad recommendations such as "the text could be more succinct", or "the 3rd paragraph of the second standard does not go far enough".
2. Use line numbers to indicate where you wish the changes to happen, for example,

   "Line 166, should be made more specific. Replace 'Committees should be large enough to ensure a robust discussion of protocols' by 'Committees should have at the minimum 7 members to ensure a robust discussion of protocols' " or that

   "Lines 170-172 could be modified as follows: ……."
3. Please send in your comments either as an e-mail or as an attachment to an e-mail to ERCStandards@who.int. Please do not send your comments to any specific WHO staff members.

Please note that the last date for receiving back comments on this document is 4th of February 2011

Standards and Operational Guidance for Ethics Review of Health-Related Research with Human Participants

Draft document
For discussion only

9 December 2010

We would like to acknowledge the contributions of all the experts who provided valuable comments on the first version of this document.

NOT FOR CIRCULATION

PREFACE

This document was developed for individuals and organizations involved in health-related research with human beings, including biomedical, behavioural, social science, and epidemiological research. Throughout this document, the term "research" is meant to include and refer to all of these activities. In particular, this document is intended to provide guidance to the Research Ethics Committees (RECs) on which organizations rely to review and oversee such research, as well as to the investigators who design and carry out the research.

Ethics guidance for research involving human participants has been developed and disseminated by numerous organizations and agencies at the international, regional and national levels over the past fifty years. Examples of key guidelines are set forth in Appendix I. Adherence to these guidelines helps to promote the ethical conduct of research and enhance and protect the rights and well-being of research participants and communities.

A core component of all contemporary research ethics guidelines is that research should be subject to prior ethical review by a competent REC. Such review is intended to ensure that the ethical principles and practices put forward in the guidelines will be followed in the proposed research, including that the study is scientifically valid, that risks of harm are minimized to the extent reasonably possible, that the potential benefits outweigh the risks of harm, that selection and recruitment of study participants are equitable and fair, that, with narrow exceptions, participants or their representatives provide voluntary informed consent, and that the research does not significantly compromise the health, rights, well-being, or care of research participants and/or their communities.

In 2000, the UNDP/World Bank/WHO Special Programme for Research and Training in Tropical Diseases (TDR) published *Operational Guidelines for Ethics Committees that Review Biomedical Research*, in response to requests from collaborating researchers throughout the world. These guidelines were reviewed by multiple experts, stakeholders, researchers, and organizations, including officials of the African Malaria Vaccine Testing Network, Council of Europe, National Institutes of Health (USA), the International Conference on Harmonization, and the World Medical Association. Since 2000, the guidelines have been translated into more than 25 languages, widely disseminated, and used by RECs in more than 100 countries.

In November 2009, WHO organized a consultation of key experts in Geneva, including researchers, ethicists, members and chairs of ethics committees, and representatives of international organizations[1] to discuss what additional guidance, if any, is needed by RECs globally, given that RECs continue to be quite variable in terms of their experience, training, capacity, institutional support, human and financial resources, and expertise. Based on experience from the field, participants concluded that the 2000 *Operational Guidelines* have been an invaluable resource but need to be updated and strengthened. The meeting also

[1] Attendees included representatives from UNESCO, the World Medical Association (WMA), Council for International Organization of Medical Sciences (CIOMS), the Council of Europe (CoE), the Nuffield Council on Bioethics, the Wellcome Trust, Council on Health Research for Development (COHRED), and Program for Appropriate Technology in Health (PATH) and REC members or staff persons from Botswana, Brazil, China, India, Morocco, and Uganda.

recognized that Member States may find it useful to have a set of global standards for high quality decision-makiong against which RECs might measure their own performance. The meeting participants recommended that the World Health Organization coordinate efforts to draft standards for RECs and to revise the 2000 *Operational Guidelines* to describe specific procedures to meet the standards.

STANDARDS AND OPERATIONAL GUIDELINES: In this document, the term "standards" is used to delineate general principles and norms that all research ethics systems are expected to follow. Standards are intended to help RECs achieve high quality performance and to provide a common language that establishes specific outcomes or characteristics against which achievements can be benchmarked. The standards put forward in this document do not represent new ideas for REC functioning. Rather, they are based on requirements for RECs delineated in existing international guidance documents. Accompanying the standards are a series of "operational guidance" points, which reflect commonly-used strategies for implementing and fulfilling each of the standards. . While the standards apply equally to all settings in which research is conducted, the applicability of the operational guidelines may vary based on the local context of a study.

The standards and guidelines in this document are similar to the 2000 *Operational Guidelines*, but they have been streamlined to avoid redundancy with other international ethical guidance documents. Their purpose is to highlight important considerations relevant to the ethical review of research, not to take a substantive position on how specific ethical dilemmas should be resolved.

This document is intended to complement existing laws, regulations, and practices and to serve as a basis upon which RECs can develop their own specific practices and written procedures. It is not intended to replace the need for national and local guidelines for the ethical review of research involving human beings, nor to supersede national laws and regulations. Indeed, it is hoped that this document may be useful to those charged with drafting national, local, and institutional regulations and policies.

I. The Research Ethics System

Standard 1

Relevant legal authorities ensure that ethics review of health-related research is supported by an adequate legal framework that is consistent with the standards set forth in this document, that research ethics committees adequate to provide review of all health-related research exist at the national, subnational, and/or institutional levels, and that an appropriate and sustainable system is in place to monitor the quality and effectiveness of research ethics review.

While this document focuses primarily on standards and guidelines for RECs, unless attention is given to the larger system of human research protections of which RECs are a part, these committees may become isolated or be unable to perform efficiently or effectively, despite their best intentions. A systems approach means that

1. RECs operate under explicit legal authority. All research with human participants is subject to the oversight of an REC (although specific categories of research may be exempted from REC review or subject to expedited review, as allowed by national laws and regulations that are consistent with international guidelines).
2. RECs are part of larger research participant protection programs that also include training for REC members and investigators and mechanisms to ensure that RECs work efficiently and effectively. National governments have the primary responsibility for ensuring that RECs are subject to adequate oversight.
3. Procedures exist to ensure clear and efficient communication, harmonization of standards, networking, and cooperation among national committees and between different levels of committees, as applicable. In addition, procedures exist for the coordinated review of multi-site research, whether within a country or in more than one country.
4. Mechanisms exist to ensure that RECs' activities are coordinated with national regulatory authorities' oversight of drugs and medical devices.
5. Mechanisms are in place for obtaining community input into the ethics review system.
6. A system exists for registration of RECs that operate in the country.

Institutional, national, and regional committees
Different approaches to ethics review exist in different countries. In some countries, review may occur only at institutional level, in others at both a national and institutional level, and in still others at a regional level. Further, differences exist in the way that various committees communicate with each other.

Having a good systems approach and clear rules of how the various RECs within a country interact with each other can greatly facilitate the conduct of international health research.

Types of research studies
RECs may review different types of research studies, including the following:

- clinical trials
- interviews, survey, and focus research
- research with biological samples
- studies involving medical records or other personal information
- research of health care systems
- quality improvement research

RECs should be familiar with the different methodologies and ethical considerations that apply to each type of proposal they review.

II. STANDARDS AND GUIDANCE FOR ENTITIES THAT ESTABLISH RECS

Standard 2

The research ethics committee (REC) is appointed according to a charter or other document that establishes the manner in which members will be appointed. The appointing official ensures that the REC has a multidisciplinary and multisectorial membership, that its composition is not limited to one gender, that it reflects the social and cultural diversity of the communities from which research participants are most likely to be drawn, and that it includes individuals with backgrounds relevant to the areas of research the committee is most likely to review. Committee members recognize the limitations of their knowledge and seek external input when necessary, particularly in relation to research that involves participants whose life experiences may differ significantly from those of the committee members.

The entity establishing the REC takes the following factors into consideration when appointing members:

1. Members with scientific expertise relevant to the types of research that the committee is most likely to review are essential, as are members with backgrounds in the social sciences, law, ethics, and the humanities, as well as lay members whose primary role is to understand the communities from which participants are likely to be drawn.
2. Members whose primary background is not in science or research should be appointed in sufficient numbers to ensure that they feel comfortable voicing their views.
3. In order to enhance independence, committee membership should include members who are not affiliated with the organization that sponsors or conducts the research reviewed by the REC (see also Standard 4).
4. Committees should be large enough to ensure a robust discussion of protocols.

Standard 3

The entity establishing the REC supports it with adequate resources, including staffing, facilities, and financial resources to allow the REC to carry out its responsibilities.

As integral parts of a health research institution or health system, an REC receives

1. support staff adequate in number and training to carry out the REC's responsibilities

2. adequate resources for the staff to fulfil its assigned functions, including office space and equipment and supplies (e.g., computers, stationery, telephones, photocopying machines) to conduct administrative business, to store all committee files, and to keep documents secure

3. access to appropriate space for the committee to meet and adequate means for members to communicate as needed between meetings

4. adequate financial resources to permit the committee to produce high quality work

5. if determined necessary by the REC, resources necessary to compensate REC members, unless they are already being compensated for their time and effort on the REC through other means

6. any other resources, as needed, to ensure committee independence (both financial and technical) from other parts of any organization that sponsors or conducts the research the REC reviews.

Standard 4

Policies governing the REC ensure independence of the REC's operations and decision-making from influence by anyone who sponsors, conducts, or hosts the research it reviews. Such policies provide at a minimum that REC members remove themselves from the review of any protocol in which they or a close family member has a conflict of interest.

To ensure that the REC cannot be pressured to approve or disapprove particular protocols, the charter, bylaws, policies and/or procedural rules of the REC provide that

1. the REC's membership includes sufficient number of persons with no connection to the organization that sponsors or conducts the research under review to ensure its independence

2. the REC's policies specify that its decision-making process is free from bias or influence

3. investigators and funders may attend an REC meeting to answer questions about their research protocols and associated documents, but they are not present when the REC discusses their studies or reaches decisions about them

4. senior decision-makers of the entity creating the REC, or of any organization that sponsors or conducts the research reviewed by the REC (such as the director of an institution), do not serve as members of the REC

5. members disclose relevant interests so that any conflicts can be managed as appropriate.

Standard 5

Training on the ethical aspects of health-related research with human beings, how ethical considerations apply to different types of research, and how the REC conducts its review of research is provided to REC members when they join the committee and periodically during their committee service.

The training provided to REC members, either directly by the appointing entity or through cooperative arrangements with other RECs and/or organizations that provide education on research ethics, focuses on

1. the role and responsibilities of the REC, and the REC's relationship with other relevant entities, according to relevant international guidelines (e.g., GCP)
2. the full range of ethical considerations relevant to research with human participants
3. how such ethical considerations apply to different types of research
4. basic aspects of research methodology and design (for members who lack such background)
5. how different scientific designs and objectives may affect the ethics of a research study
6. the various approaches for recognizing and resolving the tensions that can arise among different ethical considerations and modes of ethical reasoning
7. using resources prudently to maximize committee members' training opportunities.

Standard 6

Mechanisms exist to make REC operations transparent, accountable, consistent, and of high quality.

The entity establishing the REC employs reliable means to evaluate whether the staff and members routinely follow the REC's policies, rules and SOPs[2] with special attention to whether the ethical considerations articulated in international guidelines and national standards are being considered and applied consistently and coherently.

[2] SOPs—"standard operating procedures"—consist of the processes established for the everyday operations of an REC, to allow routine tasks to be delegated to staff with confidence that they will be handled efficiently and predictably. Each SOP is a written set of instructions detailing all steps and activities relevant to a particular task (e.g., how research protocols are logged into the REC system; how the staff is to assess the completeness of research protocols before they are distributed to reviewers; the manner and timing of notifying investigators about the outcome of the REC's review; etc.). SOPs are distinct from the REC's policies (regarding, for example, the mandate and composition of the REC, the authority to appoint and remove members and chair, quorum for conducting business, management of conflicts of interest, and so forth), as well as from the rules under which it conducts its meetings; such policies and rules are usually set forth in the charter, bylaws or "Terms of Reference" of the REC.

1. Such evaluations are conducted at regular, pre-defined intervals, using a pre-defined format by knowledgeable and unbiased persons; internal assessments are supplemented periodically by independent external evaluations.

2. The entity establishing the REC is committed to consider and, when appropriate, follow up on the findings and recommendations of the internal and external evaluations.

3. The results of the evaluation are of a type that can aid the REC in reviewing its practice and appraising performance (rather than apportioning blame) while also assuring the public that research proposals are being review according to established standards.

4. Researchers, research participants, and other interested parties should have a means of lodging complaints about the REC; such complaints should be reviewed by an entity other than the REC itself, and appropriate follow-up actions should be taken.

III. STANDARDS AND GUIDANCE FOR MEMBERS OF THE RESEARCH ETHICS COMMITTEE

The primary task of an REC is the review of research proposals and their supporting documents. Approval or disapproval is based on the *ethical acceptability* of the research, including its social value and scientific validity, an acceptable ratio of potential benefits to risks of harm for the participants and their communities, the minimization of risks of harm, adequate informed consent procedures (including cultural appropriateness and mechanisms to ensure voluntariness), measures to ensure protection of vulnerable populations, fair procedures for selection of participants, and fair benefits for study populations. Reviews take into account any prior scientific reviews and applicable laws.

Standard 7

The REC bases its decisions about research protocols on a coherent and consistent application of the ethical principles articulated in international guidance documents and human rights instruments, as well as any national laws or policies consistent with those principles. The REC makes clear the specific ethical guidelines on which it relies in making decisions and makes them readily available to researchers and the public.

To aid it in determining the ethical acceptability of research protocols, an REC may utilize a checklist to ensure that all relevant criteria are considered during review and that, as a general rule, similar protocols are treated similarly. When an REC determines that an approach it has taken to a particular ethical issue in the past is no longer appropriate, it provides an explicit rationale for its change in position.

As articulated in more detail in international ethics guidelines and the research regulations of a number of nations, key criteria include, but are not limited, to the following:

1. Scientific Design and Conduct of the Study

Research is ethically acceptable only if it is scientifically valid. Research that is not valid exposes research participants to risks of harm without any possibility of scientific benefit. RECs should have documentation from a prior scientific review, or must themselves determine that the research methods are scientifically sound, and should examine the ethical implications of the chosen research design or strategy. The REC should also assess how the study will be conducted, the adequacy of provisions made for monitoring and auditing, as well as the adequacy of the study site (e.g., available staff and facilities for emergency procedures).

2. Risks and Potential Benefits

In ethically acceptable research, risks have been minimized (both by preventing potential harms and minimizing their negative impacts should they occur) and are reasonable in relation to the potential benefits of the study. The nature of the risks may differ according to the type of research to be conducted, and members of RECs should be aware that risks may occur in different dimensions (e.g. physical, social, financial, or psychological), all of which require serious consideration. Further, harm may occur either at an individual level or at the population level.

3. Selection of study population and recruitment of research participants

Ethically acceptable research ensures that no group or class of persons bears more than its fair share of the burdens of participation in research. Similarly, no group should be deprived of its fair share of the benefits of research; these benefits include the direct benefits of participation (if any) as well as the new knowledge that the research is designed to yield. Thus, one question for research ethics review to consider is whether the population that will bear the risks of participating in research is likely to benefit from the knowledge derived from the research.

4. Inducements, financial benefits, and financial costs

It is considered ethically acceptable and appropriate to reimburse participants for any costs associated with participation, including transportation, childcare, or lost wages. Many RECs also believe it is ethically acceptable to pay participants for their time. However, payments should not be so large, or free medical care so extensive, as to induce prospective participants to consent to participate in the research against their better judgment or to compromise their understanding of the research ("undue inducement").

5 Protection of Research Participants' Privacy and Confidentiality

Unauthorized invasions of privacy and breaches of confidentiality are disrespectful to participants and can lead to feelings of loss of control or embarrassment, as well as tangible harms such as social stigma, rejection by families or communities, or lost opportunities such as employment or housing. RECs should therefore examine the precautions taken to safeguard participants' privacy and confidentiality.

6. Informed Consent Process

The ethical foundation of informed consent is the principle of respect for persons. Competent individuals are entitled to choose freely whether to participate in research, and they are able to do so only if they adequately understand what the research entails. Decisions for children or adults who lack the mental capacity to provide informed consent should be made by an authorized surrogate decision-maker.

RECs should examine the process through which informed consent will occur, as well as the information that will be provided. RECs may waive the requirement of informed consent only when doing so is consistent with international guidelines and national standards.

7. Community Considerations

Research has impacts not only on the individuals who join but also on the communities where research occurs and/or to whom findings can be linked. Duties to respect and protect communities require examining and minimizing any negative effects on communities such as stigma or draining of local capacity, and promoting, as relevant, positive effects on communities including those related to health effects or capacity development. Researchers should actively engage with communities in decision making about the design and conduct of research (including the informed consent process), while being sensitive to and respecting the communities' cultural, traditional and religious practices.

Standard 8

Decisions on research protocols designated for full REC review are based on a thorough and inclusive process of discussion and deliberation by members of the REC. Protocols involving no more than minimal risk to research subjects may be reviewed on an expedited basis by just one or more members (rather than the full committee), if the REC has established written procedures permitting such a procedure.

1. During meetings of the REC, members engage in discussions to elicit all concerns and opinions related to the protocols under consideration. The committee's established rules ensure that discussions are respectful of all opinions and allow for varied beliefs to be aired. The REC Chair fosters a respectful and inclusive tone and allows adequate time for deliberation (which includes only REC members and staff, without consultants, investigators, funders, or others directly associated with the proposal in question) before a decision is reached on each protocol.

2. Decisions are made only by those who were present during the entire discussion of a protocol.

3. When possible decisions are arrived at through consensus. When a consensus appears unlikely, the REC decides by taking a vote. A pre-defined method determines when votes will be taken and how many favourable votes will be needed for a proposal to be approved.

IV. STANDARDS AND GUIDANCE FOR THE SECRETARIAT, STAFF, AND ADMINISTRATION OF THE REC

Standard 9

Written policies specify the REC's membership, committee governance, review procedures, decision-making, communications, follow-up, monitoring, documentation and archiving, training, and quality assurance.

The entity that creates the REC has a responsibility to establish the necessary policies to govern the REC. The REC adopts its rules of procedure and, with the secretariat/staff, promulgates comprehensive, written SOPs, which are distributed to all committee members and made publicly available. To ensure efficient operation, the policies, rules and SOPs are reviewed periodically in light of ongoing assessment of performance and outcomes to determine if any revisions are needed.

RECs' policies and rules typically address the following topics:

1. Membership of the Committee

    a. Authority for appointment of committee members, specifying the name or description of the party responsible for making appointments and the procedures for

        i. selecting and appointing the REC chair and members, including the method by which new members are selected (e.g., by consensus or majority vote of existing members, by direct appointment of the Chair or other official)

        ii. managing conflicts of interest in making appointments (see Standard 4).

    b. Terms of appointment, including

        i. the duration of an appointment
        ii. the policy for the renewal of an appointment
        iii. the disqualification procedure
        iv. the resignation procedure
        v. the replacement procedure.

    Staggered, finite terms of appointment should be considered, allowing continuity of some members when other members are newly appointed. Having limited terms also promotes the development of research ethics expertise and greater knowledge of REC procedures among the larger community of individuals who may rotate through committee service, and allows for input of fresh ideas and approaches to committee deliberations.

c. Conditions of appointment, including

i. whether members receive any reimbursement for travel expenses and/or lost wages

ii. that such reimbursements, if any, shall be recorded and made available to the public

iii. that REC members shall sign confidentiality agreements regarding sensitive aspects of protocols, meeting deliberations and related matters (e.g., information about trade secrets or personal information about research participants).

2 Committee Governance

The REC's policies and procedures define how the REC will establish its offices (e.g. Chair, Vice-Chairs) for the good functioning of ethical review. The Chair is someone respectful of divergent views, able to encourage and help achieve consensus, and with the time to prepare adequately for meetings. The Chair is not a person who has a supervisory relationship with other members of the committee.

Terms of reference are established for officers that outline

a. procedures for selecting and appointing officers
b. the requirements for holding the office
c. the terms and conditions of each office
d. the duties, responsibilities, and authority of each office (e.g., running the meeting, setting the agenda, notifying applicants of decisions).

3 Independent Consultants

SOPs define the circumstances under which RECs may call upon independent consultants to provide special expertise to the REC on specific research protocols, populations, or topics. Such consultants could include experts in ethics, law, or specific diseases or methodologies, or they might be representatives of communities, patients, or other groups relevant to deliberations about specific protocols. The SOPs requires terms of reference for independent consultants and clarifies that, because consultants are not members of the REC, they do not have any voting or decision making authority.

4 Submissions, Documents Required for Review, Review Procedures and Decision-Making

a. Submission procedures

The SOPs describes the requirements for submitting an application for review, including the forms that be completed and the documents that must be submitted. Submission requirements and required forms should be readily available to prospective applicants. Application instructions generally include the following:

i. the name(s) and address(es) of the REC secretariat, offices, or member(s) to whom the application material should be submitted

ii. all written documentation to be submitted as part of the application

iii. the format for submission

iv. the language(s) in which (core) documents are to be submitted

v. the number of copies to be submitted

vi. the deadlines for submission of the application in relation to review dates

vii. the means by which applications will be acknowledged and by which notices about the incompleteness of an application will be communicated

viii. the expected time for notification of the decision following review

ix. the time frame to be followed in cases where the REC requests supplementary information or changes to documents from the applicant

x. the fee structure, if any, for reviewing an application

xi. the application procedure for amendments to the proposal, the recruitment material, the prospective research participant information, or the informed consent form

xii. a check list for the above procedures.

b. Documents required for review

All documentation required for a thorough and complete review of the proposed research should be submitted by the applicant. As applicable, this may include, but is not limited to

i. signed and dated application form, including signatures of listed co-applicants and institutional officials (e.g. heads of departments) where relevant

ii. the protocol for the proposed research, clearly identified and dated, together with supporting documents and annexes

iii. a project summary or synopsis in non-technical language

iv. a description (which may be included in the proposal) of the ethical considerations in the proposed research, including specifically how the study addresses ethical considerations relevant to the committee's review

vi. background information on previous research in the same area that justifies the conduct of this project

vii. when the research involves an experimental product (such as a pharmaceutical or medical device under investigation), an adequate summary of all safety, pharmacological, pharmaceutical, and toxicological data available on the study product, together with a summary of clinical experience with the study product to date (e.g., recent investigator's brochure, published data, a summary of the product's characteristics)

viii. investigator's current curriculum vitae

ix. all data collection forms to be used in the research, including but not limited to case report forms, diary cards, questionnaires, interview schedules, etc.

x. all forms, documents, advertisements, and the like to be used in recruitment of potential participants

xi. a detailed description of the recruitment process and strategies

xii. informed consent form(s) in languages and at a reading level appropriate for the potential research participants

xiii. a description of the process that will be used to obtain informed consent

xiv. a statement describing any remuneration or other benefits to be provided to study participants, including reimbursement of expenses and access to medical care

xv. a description of arrangements for insurance coverage for research participants, if applicable

xvi. disclosure of all previous decisions (including those leading to a negative decision or modified proposal) by other RECs or regulatory authorities for the proposed study, whether in the same location or elsewhere, and indication of the reasons for previous negative decisions and modification(s) to the proposal made on that account

xvii. a statement of the investigators' agreement to comply with ethical principles set out in relevant guidelines.

c. Review Procedures

The REC's policies specify the process by which the REC will decide which proposals should be reviewed by the full convened committee and which proposals may be reviewed through an expedited procedure. The SOPs address who will have the responsibility of making this determination, as well as the number of reviewers required for expedited review and how those reviewers will be selected.

d. REC meetings

RECs meet regularly as a committee on dates that are announced in advance. The SOPs describe the process for setting up meetings, circulating documentation for the meetings, inviting non-members of the REC, approving the meeting minutes, and any related process issues. The following issues are outlined in the SOPs:

i. the frequency of meetings, which should be based on committee workload and regular enough to avoid undue delays in approving research

ii. the maximum timeframe for review after receipt of applications

iii. mechanisms to ensure that REC members receive all relevant documents in advance of the meetings with enough time to adequately review meeting materials

iii. standards and procedures for inviting the researcher and/or sponsor of a particular proposal to present or comment on the proposal in question or on specific issues that relate to it during the meeting, at the discretion of the committee; this practice may be implemented routinely or on an as-needed basis

iv. standards and procedures for inviting independent consultants to the meeting or to provide written comments

v. standards and procedures for taking and approving meeting minutes.

e. Deliberation and decision making

Procedures for deliberation and decision making are clearly established and describe

i. the ethical guidelines on which the REC will rely to make its decisions

ii. the manner in which the protocol will be presented to the committee for discussion

iii. the process by which the protocol will be discussed, including who may remain in the room during discussions

iv. quorum requirements for making a decision

v. the predefined method for arriving at a decision and who may take part in decision making

vi. clear options for decision outcomes, including approval, conditional approval, a request to revise and resubmit, or disapproval; criteria for each outcome should be described, as should any specific follow up procedures associated with each option, including specific procedures for re-review, as applicable

Committee correspondence must make clear to the applicant that no research with human participants can commence before the REC's concerns have been satisfied and full approval has been granted.

f. Quorum Requirements

Specific quorum requirements for reviewing and making decisions or taking actions on a research proposal are clearly established in the SOPs, including

1. the minimum number of members required to compose a quorum (e.g., half of the members, or a simple majority)

2. the distribution of committee composition requirements across the quorum; no quorum should consist entirely of members of one profession or one gender; a quorum should include at least one member whose primary area of expertise is in a non-scientific area, and at least one member who is independent of the institution/research site.

5 Communicating a Decision

SOPs describe procedures for communicating the decisions of the REC. SOPs outline the maximum amount of time between the decision about the proposal and when the applicant is informed. The communication of the decision includes, but is not limited to, the following:

1. Specific identifying information about the proposal, including

i. the exact title of the research proposal reviewed

ii. clear identification of the proposal or amendment, date and version number (if applicable) on which the decision is based

iii. the names and (where possible) specific identification numbers (version numbers/dates) of the documents reviewed, including the research participant information sheet/material and informed consent form

iv. the name and title of the applicant or sponsor

v. the name of the site(s)
vi. the date and place of the decision
vii. the name of the REC making the decision

2. A clear statement of the decision reached

1) In the case of a positive decision,

i. any significant ethical issues that were discussed during the meeting, and the resolution of those issues

i. the fact that approval is given only for the proposal as accepted by the REC, and compliance is expected

ii. the duration for which the approval is valid, and the procedures to be followed to renew the approval at the end of that period.

iii. a statement of the responsibilities of the applicant; for example,

- confirmation of the acceptance by the researchers of the requirements imposed by the REC
- submission of progress report(s) at predefined intervals
- the need to seek further prior approval from the REC in cases of proposal amendments or deviations (other than logistical or administrative changes that may be made without permission of the REC, as authorized by local law and REC policies)
- the need to seek further prior approval from the REC in the case of amendments to the recruitment material, the prospective research participant information, or the informed consent form
- the need to report serious and unexpected adverse events related to the conduct of the study or unanticipated problems involving risks of harm to the participants or others
- the information the REC expects to receive in order to perform ongoing reviews
- the need to notify the REC when a study is completed and to provide a final report.

2) In the case of a conditional decision, any requirements by the REC, including suggestions for revision and the procedure for having the application re-reviewed

3) In the case of a negative decision, clearly stated reasons related specifically to ethical considerations

4) Advice or suggestions that are non-binding may be appended to the decision but should clearly be marked as advice separate from any stipulations or determinations of the REC.

3. Signature (dated) of the chairperson (or other authorized person) of the REC

4. RECs must determine and include in their procedures whether an appeals procedure is available. If allowed, SOPs should address the process for appeals. If appeals will be allowed, the SOPs should outline what materials must be submitted and to whom, and who will be the ultimate decision maker.

6. Follow-Up Reviews and Monitoring of Proposals

SOPs describe the process by which RECs will follow up the progress of all approved studies, from the time the approval decision is taken until the termination of the research. The procedure for follow up review take the following into consideration:

1. the review procedure, quorum requirements, and communication procedure for follow-up reviews, which may vary from requirements and procedures for the initial review of the application

2. the intervals for follow-up reviews, which should be determined by the nature of the research protocol but should generally be at least once a year

3. circumstances that will trigger follow-up reviews in addition to those that are regularly scheduled, including the following:

    1) any proposal amendment likely to affect the rights, safety, and/or well-being of the research participants or the conduct of the study
    2) serious and unexpected adverse events related to the conduct of the study or study product
    3) any event or new information that might affect the potential benefits or risks of harm involved in the study
    4) decisions made by a DSMB or regulatory authorities to suspend a study in whole or in part.

4. a decision resulting from a follow up review should be issued and communicated to the applicant, indicating either that the original decision is still valid or that there has been a modification, suspension, or termination of the REC's original decision

5. in the case of the premature suspension/termination of a study by any party other than the REC, the applicant should notify the REC of the reasons for suspension/termination; a summary of any results obtained in a study prematurely suspended/terminated should be communicated to the REC, as well as how information on the suspension of the study will be communicated to participants and any plans for providing follow up care to the participants.

Documentation and Archiving

All of the REC's documentation and communication is dated, filed, and archived according to the committee's written procedures. Records may be kept either in hard copy or electronically. In either case, sufficient safeguards are established (e.g., locked cabinets for hard copy files, password protection and encryption for electronic files) to maintain confidentiality. Staff are sufficiently trained to understand their responsibilities related to record keeping, retrieval, and confidentiality. Procedures outline who is authorized to access committee files and documents.

a. Committee-related documents.

Committee-related documents that should be filed and archived include, but are not limited to

(1) any documents formally establishing the REC
(2) the REC's standard operating procedures
(3) the published guidelines for submission established by the REC

(4) annual reports summarizing REC activities; such reports will promote transparency and will help raise awareness of the REC within its institution or jurisdiction, as well as serving as an ongoing reminder of the resources necessary to run the committee
(5) the curriculum vitae of all REC members
(6) record of all income and expenses of the REC, including allowances and reimbursements made to the secretariat and REC members and for what purposes
(7) agendas of the REC meetings
(8) minutes of the REC meetings.

b. Proposal-Related Documents

All documents and materials related to the review of specific study proposals should be filed. Committee procedures should specify length of time documents must be archived. Such policies should be consistent with any relevant local laws or institutional policies. These include but are not limited to:

1. one copy of all materials submitted by an applicant
2. any correspondence by the REC with applicants or concerned parties regarding applications, decisions, and follow-up
3. a copy of initial and follow up decisions and any advice or requirements sent to an applicant
4. all written documentation received during the follow-up, including any advice or requirements sent to the applicant
5. the notification of the completion, premature suspension, or premature termination of a study

VI. STANDARDS AND GUIDANCE FOR RESEARCHERS

Standard 10

Research is performed by persons with scientific and clinical qualifications appropriate to the project, who are familiar with the ethical standards applicable to their research, who submit the necessary applications and protocols to an REC to review, and who carry out the research in compliance with the requirements established by the REC.

1. Submitting an Application

1. An application for review of the ethics of proposed biomedical research should be submitted by a qualified researcher, who is directly responsible for the ethical and scientific conduct of the research. In certain jurisdictions, the sponsor of a clinical trial is responsible for submitting the research proposal to the REC.

2. Student proposals should be submitted under the responsibility of a qualified advisor/faculty member involved in the oversight of the student's work or be in the student's name, co-signed by the qualified faculty supervisor.

3. All documentation required for a thorough and complete review of the ethics of proposed research should be submitted, as specified in the REC's standard operating procedures.

2. Conduct of Research

1. The research should be conducted in compliance with the proposal approved by the REC.

2. No deviation or changes should be made to the approved proposal, or in following it, without prior approval of the REC, except where immediate action is necessary to avoid harm to the research participant(s). In such a case, the REC should be informed promptly of the changes/deviations made, and the justification for doing so.

3. The REC should be informed of any changes at the research site that significantly affect the conduct of the trial, and/or increase the risks of harm to participants (for example closing down of a health facility at the research site or other impediments to obtaining access to health care that was originally available).

3. Safety Reporting

1. All serious adverse events as defined in the proposal and any unexpected adverse events should be promptly reported to the REC as described in the proposal, and according to the procedures established by the REC.

2. Any recommendations provided by the REC in response to such reporting should be immediately implemented.

4. Ongoing Reporting and Follow-up

1. In the case of the early suspension/termination of a study, the applicant should notify the REC of the reasons for suspension/termination; provide a summary of results obtained prior to prematurely suspending or terminating the study; and describe the manner by which enrolled participants will be notified of the suspension or termination and the plans for care and follow-up plan for the participants.

Researchers should inform the RECs when a study is completed or cancelled.

4. If the REC terminates or suspends its approval, the investigator should inform the institution under whose authority the research is being conducted, the sponsor of the research, and any other applicable organizations.

5. Information to research participants

The investigators have an obligation to keep the research participants and their communities informed of the progress of research at suitable time frames in a simple and non-technical language. Notification is particularly important when

1. the research study is modified, suspended, terminated or cancelled;
2. any changes occur in the context of the research study that alter the potential benefits or risks
3. the research project is completed.

743 PARTICIPANTS to the WHO Consultation on Norms and Standards for Research Ethics Review Committees
744 – November 2009

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