

**Operational Guidelines
for
Ethics Committees That
Review Biomedical Research**



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TABLE OF CONTENTS

PREFACE	v
1 OBJECTIVE	1
2 THE ROLE OF AN EC	1
3 ESTABLISHING A SYSTEM OF ETHICAL REVIEW	2
4 CONSTITUTING AN EC	2
4.1 <i>Membership Requirements</i>	3
4.2 <i>Terms of Appointment</i>	4
4.3 <i>Conditions of Appointment</i>	4
4.4 <i>Offices</i>	5
4.5 <i>Quorum Requirements</i>	5
4.6 <i>Independent Consultants</i>	5
4.7 <i>Education for EC Members</i>	6
5 SUBMITTING AN APPLICATION	6
5.1 <i>Application</i>	6
5.2 <i>Application Requirements</i>	6
5.3 <i>Documentation</i>	7
6 REVIEW	9
6.1 <i>Meeting Requirements</i>	9
6.2 <i>Elements of the Review</i>	10
6.3 <i>Expedited Review</i>	13
7 DECISION-MAKING	14
8 COMMUNICATING A DECISION	15
9 FOLLOW-UP	16
10 DOCUMENTATION AND ARCHIVING	18
GLOSSARY	21
SUPPORTING DOCUMENTS	23
COMMITTEES	25
BACKGROUND	29

PREFACE

The ethical and scientific standards for carrying out biomedical research on human subjects have been developed and established in international guidelines, including the Declaration of Helsinki, the CIOMS International Ethical Guidelines for Biomedical Research Involving Human Subjects, and the WHO and ICH Guidelines for Good Clinical Practice. Compliance with these guidelines helps to ensure that the dignity, rights, safety, and well-being of research participants are promoted and that the results of the investigations are credible.

All international guidelines require the ethical and scientific review of biomedical research alongside informed consent and the appropriate protection of those unable to consent as essential measures to protect the individual person and the communities who participate in research. For the purposes of these Guidelines, biomedical research includes research on pharmaceuticals, medical devices, medical radiation and imaging, surgical procedures, medical records, and biological samples, as well as epidemiological, social, and psychological investigations.

These Guidelines are intended to facilitate and support ethical review in all countries around the world. They are based on a close examination of the requirements for ethical review as established in international guidelines, as well as on an evaluation of existing practices of ethical review in countries around the world. They do not, however, purport to replace the need for national and local guidelines for the ethical review of biomedical research, nor do they intend to supersede national laws and regulations.

The majority of biomedical research has been predominantly motivated by concern for the benefit of already privileged communities. This is reflected by the fact that the WHO estimates that 90% of the resources devoted to research and development on medical problems are applied to diseases causing less than 10% of the present global suffering. The establishment of international guidelines that assist in strengthening the capacity for the ethical review of biomedical research in all countries contributes to redressing this imbalance.

1 OBJECTIVE

The objective of these Guidelines is to contribute to the development of quality and consistency in the ethical review of biomedical research. The Guidelines are intended to complement existing laws, regulations, and practices, and to serve as a basis upon which ethics committees (ECs) can develop their own specific written procedures for their functions in biomedical research. In this regard, the Guidelines establish an international standard for ensuring quality in ethical review. The Guidelines should be used by national and local bodies in developing, evaluating, and progressively refining standard operating procedures for the ethical review of biomedical research.

2 THE ROLE OF AN EC

The purpose of an EC in reviewing biomedical research is to contribute to safeguarding the dignity, rights, safety, and well-being of all actual or potential research participants. A cardinal principle of research involving human participants is ‘respect for the dignity of persons’. The goals of research, while important, should never be permitted to override the health, well-being, and care of research participants. ECs should also take into consideration the principle of justice. Justice requires that the benefits and burdens of research be distributed fairly among all groups and classes in society, taking into account age, gender, economic status, culture, and ethnic considerations.

ECs should provide independent, competent, and timely review of the ethics of proposed studies. In their composition, procedures, and decision-making, ECs need to have independence from political, institutional, professional, and market influences. They need similarly to demonstrate competence and efficiency in their work.

ECs are responsible for carrying out the review of proposed research before the commencement of the research. They also need to ensure that there is regular evaluation of the ethics of ongoing studies that received a positive decision.

ECs are responsible for acting in the full interest of potential research participants and concerned communities, taking into account the interests and needs of the researchers, and having due regard for the requirements of relevant regulatory agencies and applicable laws.

3 ESTABLISHING A SYSTEM OF ETHICAL REVIEW

Countries, institutions, and communities should strive to develop ECs and ethical review systems that ensure the broadest possible coverage of protection for potential research participants and contribute to the highest attainable quality in the science and ethics of biomedical research. States should promote, as appropriate, the establishment of ECs at the national, institutional, and local levels that are independent, multi-disciplinary, multi-sectorial, and pluralistic in nature. ECs require administrative and financial support.

Procedures need to be established for relating various levels of review in order to ensure consistency and facilitate cooperation. Mechanism for cooperation and communication need to be developed between national committees and institutional and local committees. These mechanisms should ensure clear and efficient communication. They should also promote the development of ethical review within a country as well as the ongoing education of members of ethics committees. In addition, procedures need to be established for the review of biomedical research protocols carried out at more than one site in a country or in more than one country. A network of ethical review should be established at the regional, national, and local levels that ensures the highest competence in biomedical review while also guaranteeing input from all levels of the community.

4 CONSTITUTING AN EC

ECs should be constituted to ensure the competent review and evaluation of all ethical aspects of the research projects they receive and

to ensure that their tasks can be executed free from bias and influence that could affect their independence.

ECs should be multidisciplinary and multi-sectorial in composition, including relevant scientific expertise, balanced age and gender distribution, and laypersons representing the interests and the concerns of the community.

ECs should be established in accordance with the applicable laws and regulations of the country and in accordance with the values and principles of the communities they serve.

ECs should establish publicly available standard operating procedures that state the authority under which the committee is established, the functions and duties of the EC, membership requirements, the terms of appointment, the conditions of appointment, the offices, the structure of the secretariat, internal procedures, and the quorum requirements. ECs should act in accordance with their written operating procedures.

It may be helpful to summarize the activities of the EC in a regular (annual) report.

4.1 Membership Requirements

Clear procedures for identifying or recruiting potential EC members should be established. A statement should be drawn up of the requirements for candidacy that includes an outline of the duties and responsibilities of EC members.

Membership requirements should be established that include the following:

- 4.1.1 the name or description of the party responsible for making appointments;
- 4.1.2 the procedure for selecting members, including the method for appointing a member (e.g., by consensus, by majority vote, by direct appointment);

- 4.1.3 conflicts of interest should be avoided when making appointments, but where unavoidable there should be transparency with regard to such interests.

A rotation system for membership should be considered that allows for continuity, the development and maintenance of expertise within the EC, and the regular input of fresh ideas and approaches.

4.2 Terms of Appointment

Terms of appointment should be established that include the following:

- 4.2.1 the duration of an appointment,
- 4.2.2 the policy for the renewal of an appointment,
- 4.2.3 the disqualification procedure,
- 4.2.4 the resignation procedure,
- 4.2.5 the replacement procedure.

4.3 Conditions of Appointment

A statement of the conditions of appointment should be drawn up that includes the following:

- 4.3.1 a member should be willing to publicize his/her full name, profession, and affiliation;
- 4.3.2 all reimbursement for work and expenses, if any, within or related to an EC should be recorded and made available to the public upon request;
- 4.3.3 a member should sign a confidentiality agreement regarding meeting deliberations, applications, information on research participants, and related matters; in addition, all EC administrative staff should sign a similar confidentiality agreement.

4.4 Offices

ECs should establish clearly defined offices for the good functioning of ethical review. A statement is required of the officers within the EC (e.g., chairperson, secretary), the requirements for holding each office, the terms and conditions of each office, and the duties and responsibilities of each office (e.g., agenda, minutes, notification of decisions). Clear procedures for selecting or appointing officers should be established.

In addition to the EC officers, an EC should have adequate support staff for carrying out its responsibilities.

4.5 Quorum Requirements

ECs should establish specific quorum requirements for reviewing and deciding on an application. These requirements should include:

- 4.5.1 the minimum number of members required to compose a quorum (e.g., more than half the members);
- 4.5.2 the professional qualifications requirements (e.g., physician, lawyer, statistician, paramedical, layperson) and the distribution of those requirements over 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.

4.6 Independent Consultants

ECs may call upon, or establish a standing list of, independent consultants who may provide special expertise to the EC on proposed research protocols. These consultants may be specialists in ethical or legal aspects, specific diseases or methodologies, or they may be representatives of communities, patients, or special interest groups. Terms of reference for independent consultants should be established.

4.7 Education for EC Members

EC members have a need for initial and continued education regarding the ethics and science of biomedical research. The conditions of appointment should state the provisions available for EC members to receive introductory training in the work of an EC as well as ongoing opportunities for enhancing their capacity for ethical review. These conditions should also include the requirements or expectations regarding the initial and continuing education of EC members. This education may be linked to co-operative arrangements with other ECs in the area, the country, and the region, as well as other opportunities for the initial and continued training of EC members.

5 SUBMITTING AN APPLICATION

ECs are responsible for establishing well-defined requirements for submitting an application for review of a biomedical research project. These requirements should be readily available to prospective applicants.

5.1 Application

An application for review of the ethics of proposed biomedical research should be submitted by a qualified researcher responsible for the ethical and scientific conduct of the research.

5.2 Application Requirements

The requirements for the submission of a research project for ethical review should be clearly described in an application procedure. These requirements should include the following:

- 5.2.1 the name(s) and address(es) of the EC secretariat or member(s) to whom the application material is to be submitted;
- 5.2.2 the application form(s);

- 5.2.3 the format for submission;
- 5.2.4 the documentation (see 5.3);
- 5.2.5 the language(s) in which (core) documents are to be submitted;
- 5.2.6 the number of copies to be submitted;
- 5.2.7 the deadlines for submission of the application in relation to review dates;
- 5.2.8 the means by which applications will be acknowledged, including the communication of the incompleteness of an application;
- 5.2.9 the expected time for notification of the decision following review;
- 5.2.10 the time frame to be followed in cases where the EC requests supplementary information or changes to documents from the applicant;
- 5.2.11 the fee structure, if any, for reviewing an application;
- 5.2.12 the application procedure for amendments to the protocol, the recruitment material, the potential research participant information, or the informed consent form.

5.3 Documentation

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

- 5.3.1 signed and dated application form;
- 5.3.2 the protocol of the proposed research (clearly identified and dated), together with supporting documents and annexes;
- 5.3.3 a summary (as far as possible in non-technical language),

- synopsis, or diagrammatic representation ('flowchart') of the protocol;
- 5.3.4 a description (usually included in the protocol) of the ethical considerations involved in the research;
 - 5.3.5 case report forms, diary cards, and other questionnaires intended for research participants;
 - 5.3.6 when the research involves a study product (such as a pharmaceutical or 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);
 - 5.3.7 investigator(s)'s curriculum vitae (updated, signed, and dated);
 - 5.3.8 material to be used (including advertisements) for the recruitment of potential research participants;
 - 5.3.9 a description of the process used to obtain and document consent;
 - 5.3.10 written and other forms of information for potential research participants (clearly identified and dated) in the language(s) understood by the potential research participants and, when required, in other languages;
 - 5.3.11 informed consent form (clearly identified and dated) in the language(s) understood by the potential research participants and, when required, in other languages;
 - 5.3.12 a statement describing any compensation for study participation (including expenses and access to medical care) to be given to research participants;

- 5.3.13 a description of the arrangements for indemnity, if applicable;
- 5.3.14 a description of the arrangements for insurance coverage for research participants, if applicable;
- 5.3.15 a statement of agreement to comply with ethical principles set out in relevant guidelines;
- 5.3.16 all significant previous decisions (e.g., those leading to a negative decision or modified protocol) by other ECs or regulatory authorities for the proposed study (whether in the same location or elsewhere) and an indication of modification(s) to the protocol made on that account. The reasons for previous negative decisions should be provided.

6 REVIEW

All properly submitted applications should be reviewed in a timely fashion and according to an established review procedure.

6.1 Meeting Requirements

ECs should meet regularly on scheduled dates that are announced in advance. The meeting requirements should include the following:

- 6.1.1 meetings should be planned in accordance with the needs of the workload;
- 6.1.2 EC members should be given enough time in advance of the meeting to review the relevant documents;
- 6.1.3 meetings should be minuted; there should be an approval procedure for the minutes;
- 6.1.4 the applicant, sponsor, and/or investigator may be invited to present the proposal or elaborate on specific issues;

- 6.1.5 independent consultants may be invited to the meeting or to provide written comments, subject to applicable confidentiality agreements.

6.2 Elements of the Review

The primary task of an EC lies in the review of research proposals and their supporting documents, with special attention given to the informed consent process, documentation, and the suitability and feasibility of the protocol. ECs need to take into account prior scientific reviews, if any, and the requirements of applicable laws and regulations. The following should be considered, as applicable:

6.2.1 Scientific Design and Conduct of the Study

- 6.2.1.1 the appropriateness of the study design in relation to the objectives of the study, the statistical methodology (including sample size calculation), and the potential for reaching sound conclusions with the smallest number of research participants;
- 6.2.1.2 the justification of predictable risks and inconveniences weighed against the anticipated benefits for the research participants and the concerned communities;
- 6.2.1.3 the justification for the use of control arms;
- 6.2.1.4 criteria for prematurely withdrawing research participants;
- 6.2.1.5 criteria for suspending or terminating the research as a whole;
- 6.2.1.6 the adequacy of provisions made for monitoring and auditing the conduct of the research, including the constitution of a data safety monitoring board (DSMB);
- 6.2.1.7 the adequacy of the site, including the supporting staff, available facilities, and emergency procedures;
- 6.2.1.8 the manner in which the results of the research will be reported and published;

6.2.2 *Recruitment of Research Participants*

- 6.2.2.1 the characteristics of the population from which the research participants will be drawn (including gender, age, literacy, culture, economic status, and ethnicity);
- 6.2.2.2 the means by which initial contact and recruitment is to be conducted;
- 6.2.2.3 the means by which full information is to be conveyed to potential research participants or their representatives;
- 6.2.2.4 inclusion criteria for research participants;
- 6.2.2.5 exclusion criteria for research participants;

6.2.3 *Care and Protection of Research Participants*

- 6.2.3.1 the suitability of the investigator(s)'s qualifications and experience for the proposed study;
- 6.2.3.2 any plans to withdraw or withhold standard therapies for the purpose of the research, and the justification for such action;
- 6.2.3.3 the medical care to be provided to research participants during and after the course of the research;
- 6.2.3.4 the adequacy of medical supervision and psycho-social support for the research participants;
- 6.2.3.5 steps to be taken if research participants voluntarily withdraw during the course of the research;
- 6.2.3.6 the criteria for extended access to, the emergency use of, and/or the compassionate use of study products;
- 6.2.3.7 the arrangements, if appropriate, for informing the research participant's general practitioner (family doctor), including procedures for seeking the participant's consent to do so;
- 6.2.3.8 a description of any plans to make the study product available to the research participants following the research;

- 6.2.3.9 a description of any financial costs to research participants;
- 6.2.3.10 the rewards and compensations for research participants (including money, services, and/or gifts);
- 6.2.3.11 the provisions for compensation/treatment in the case of the injury/disability/death of a research participant attributable to participation in the research;
- 6.2.3.12 the insurance and indemnity arrangements;
- 6.2.4 *Protection of Research Participant Confidentiality*
 - 6.2.4.1 a description of the persons who will have access to personal data of the research participants, including medical records and biological samples;
 - 6.2.4.2 the measures taken to ensure the confidentiality and security of personal information concerning research participants;
- 6.2.5 *Informed Consent Process*
 - 6.2.5.1 a full description of the process for obtaining informed consent, including the identification of those responsible for obtaining consent;
 - 6.2.5.2 the adequacy, completeness, and understandability of written and oral information to be given to the research participants, and, when appropriate, their legally acceptable representative(s);
 - 6.2.5.3 clear justification for the intention to include in the research individuals who cannot consent, and a full account of the arrangements for obtaining consent or authorization for the participation of such individuals;
 - 6.2.5.4 assurances that research participants will receive information that becomes available during the course of the research relevant to their participation (including their rights, safety, and well-being);

6.2.5.5 the provisions made for receiving and responding to queries and complaints from research participants or their representatives during the course of a research project;

6.2.6 *Community Considerations*

6.2.6.1 the impact and relevance of the research on the local community and on the concerned communities from which the research participants are drawn;

6.2.6.2 the steps taken to consult with the concerned communities during the course of designing the research;

6.2.6.3 the influence of the community on the consent of individuals;

6.2.6.4 proposed community consultation during the course of the research;

6.2.6.5 the extent to which the research contributes to capacity building, such as the enhancement of local healthcare, research, and the ability to respond to public health needs;

6.2.6.6 a description of the availability and affordability of any successful study product to the concerned communities following the research;

6.2.6.7 the manner in which the results of the research will be made available to the research participants and the concerned communities.

6.3 *Expedited Review*

ECs should establish procedures for the expedited review of research proposals. These procedures should specify the following:

6.3.1 the nature of the applications, amendments, and other considerations that will be eligible for expedited review;

6.3.2 the quorum requirement(s) for expedited review;

- 6.3.3 the status of decisions (e.g., subject to confirmation by full EC or not).

7 DECISION-MAKING

In making decisions on applications for the ethical review of biomedical research, an EC should take the following into consideration:

- 7.1 a member should withdraw from the meeting for the decision procedure concerning an application where there arises a conflict of interest; the conflict of interest should be indicated to the chairperson prior to the review of the application and recorded in the minutes;
- 7.2 a decision may only be taken when sufficient time has been allowed for review and discussion of an application in the absence of non-members (e.g., the investigator, representatives of the sponsor, independent consultants) from the meeting, with the exception of EC staff;
- 7.3 decisions should only be made at meetings where a quorum (as stipulated in the EC's written operating procedures) is present;
- 7.4 the documents required for a full review of the application should be complete and the relevant elements mentioned above (see 6.2) should be considered before a decision is made;
- 7.5 only members who participate in the review should participate in the decision;
- 7.6 there should be a predefined method for arriving at a decision (e.g., by consensus, by vote); it is recommended that decisions be arrived at through consensus, where possible; when a consensus appears unlikely, it is recommended that the EC vote;

- 7.7 advice that is non-binding may be appended to the decision;
- 7.8 in cases of conditional decisions, clear suggestions for revision and the procedure for having the application re-reviewed should be specified;
- 7.9 a negative decision on an application should be supported by clearly stated reasons.

8 COMMUNICATING A DECISION

A decision should be communicated in writing to the applicant according to EC procedures, preferably within two weeks' time of the meeting at which the decision was made. The communication of the decision should include, but is not limited to, the following:

- 8.1 the exact title of the research proposal reviewed;
- 8.2 the clear identification of the protocol of the proposed research or amendment, date and version number (if applicable). on which the decision is based;
- 8.3 the names and (where possible) specific identification numbers (version numbers/dates) of the documents reviewed, including the potential research participant information sheet/material and informed consent form;
- 8.4 the name and title of the applicant;
- 8.5 the name of the site(s);
- 8.6 the date and place of the decision;
- 8.7 the name of the EC taking the decision;
- 8.8 a clear statement of the decision reached;
- 8.9 any advice by the EC;

- 8.10 in the case of a conditional decision, any requirements by the EC, including suggestions for revision and the procedure for having the application re-reviewed;
- 8.11 in the case of a positive decision, a statement of the responsibilities of the applicant; for example, confirmation of the acceptance of any requirements imposed by the EC; submission of progress report(s); the need to notify the EC in cases of protocol amendments (other than amendments involving only logistical or administrative aspects of the study); the need to notify the EC in the case of amendments to the recruitment material, the potential research participant information, or the informed consent form; the need to report serious and unexpected adverse events related to the conduct of the study; the need to report unforeseen circumstances, the termination of the study, or significant decisions by other ECs; the information the EC expects to receive in order to perform ongoing review; the final summary or final report;
- 8.12 the schedule/plan of ongoing review by the EC;
- 8.13 in the case of a negative decision, clearly stated reason(s) for the negative decision;
- 8.14 signature (dated) of the chairperson (or other authorized person) of the EC.

9 FOLLOW-UP

ECs should establish a follow-up procedure for following the progress of all studies for which a positive decision has been reached, from the time the decision was taken until the termination of the research. The ongoing lines of communication between the EC and the applicant should be clearly specified. The follow-up procedure should take the following into consideration:

- 9.1 the quorum requirements, the review procedure, and the communication procedure for follow-up reviews, which may vary from the requirements and procedures for the initial decision on an application;
- 9.2 the follow-up review intervals should be determined by the nature and the events of research projects, though each protocol should undergo a follow-up review at least once a year;
- 9.3 the following instances or events require the follow-up review of a study:
 - a. any protocol amendment likely to affect the rights, safety, and/or well-being of the research participants or the conduct of the study;
 - b. serious and unexpected adverse events related to the conduct of the study or study product, and the response taken by investigators, sponsors, and regulatory agencies;
 - c. any event or new information that may affect the benefit/risk ratio of the study;
- 9.4 a decision of a follow-up review should be issued and communicated to the applicant, indicating a modification, suspension, or termination of the EC's original decision or confirmation that the decision is still valid;
- 9.5 in the case of the premature suspension/termination of a study, the applicant should notify the EC of the reasons for suspension/termination; a summary of results obtained in a study prematurely suspended/terminated should be communicated to the EC;
- 9.6 ECs should receive notification from the applicant at the time of the completion of a study;

- 9.7 ECs should receive a copy of the final summary or final report of a study.

10 DOCUMENTATION AND ARCHIVING

All documentation and communication of an EC should be dated, filed, and archived according to written procedures. A statement is required defining the access and retrieval procedure (including authorized persons) for the various documents, files, and archives.

It is recommended that documents be archived for a minimum period of 3 years following the completion of a study.

Documents that should be filed and archived include, but are not limited to,

- 10.1 the constitution, written standard operating procedures of the EC, and regular (annual) reports;
- 10.2 the curriculum vitae of all EC members;
- 10.3 a record of all income and expenses of the EC, including allowances and reimbursements made to the secretariat and EC members;
- 10.4 the published guidelines for submission established by the EC;
- 10.5 the agenda of the EC meetings;
- 10.6 the minutes of the EC meetings;
- 10.7 one copy of all materials submitted by an applicant;
- 10.8 the correspondence by EC members with applicants or concerned parties regarding application, decision, and follow-up;
- 10.9 a copy of the decision and any advice or requirements sent to an applicant;

- 10.10 all written documentation received during the follow-up;
- 10.11 the notification of the completion, premature suspension, or premature termination of a study;
- 10.12 the final summary or final report of the study.

GLOSSARY

The definitions provided within this glossary apply to terms as they are used in these Guidelines. The terms may have different meanings in other contexts.

advice

Non-binding considerations adjoined to a decision intended to provide ethical assistance to those involved in the research.

applicant

A qualified researcher undertaking the scientific and ethical responsibility for a research project, either on his/her own behalf or on behalf of an organization/firm, seeking a decision from an ethics committee through formal application.

community

A community is a group of people understood as having a certain identity due to the sharing of common interests or to a shared proximity. A community may be identified as a group of people living in the same village, town, or country and, thus, sharing geographical proximity. A community may be otherwise identified as a group of people sharing a common set of values, a common set of interests, or a common disease.

conflict of interest

A conflict of interest arises when a member (or members) of the EC holds interests with respect to specific applications for review that may jeopardize his/her (their) ability to provide a free and independent evaluation of the research focused on the protection of the research participants. Conflicts of interests may arise when an EC member has financial, material, institutional, or social ties to the research.

decision

The response, (either positive, conditional or negative), by an EC to an application following the review in which the position of the EC on the ethical validity of the proposed study is stated.

investigator

A qualified scientist who undertakes scientific and ethical responsibility, either on his/her own behalf or on behalf of an organization/firm, for the ethical and scientific integrity of a research project at a specific site or group of sites. In some instances a coordinating or principal investigator may be appointed as the responsible leader of a team of subinvestigators.

protocol

A document that provides the background, rationale, and objective(s) of a biomedical research project and describes its design, methodology, and organization, including ethical and statistical considerations. Some of these considerations may be provided in other documents referred to in the protocol.

protocol amendment

A written description of a change to, or formal clarification of, a protocol.

requirements

In the context of decisions, requirements are binding elements that express ethical considerations whose implementation the ethics committee requires or views as obligatory in pursuing the research.

research participant

An individual who participates in a biomedical research project, either as the direct recipient of an intervention (e.g., study product or invasive procedure), as a control, or through observation. The individual may be a healthy person who volunteers to participate in the research, or a person with a condition unrelated to the research carried out who volunteers to participate, or a person (usually a patient) whose condition is relevant to the use of the study product or questions being investigated.

sponsor

An individual, company, institution, or organization that takes responsibility for the initiation, management, and/or financing of a research project.

SUPPORTING DOCUMENTS

Council for International Organizations of Medical Sciences (CIOMS), in collaboration with the World Health Organization (WHO). *International Ethical Guidelines for Biomedical Research Involving Human Subjects*. Geneva 1993.

Council for International Organizations of Medical Sciences (CIOMS). *International Guidelines for Ethical Review of Epidemiological Studies*. Geneva 1991.

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World Health Organization (WHO). Guidelines for Good Clinical Practice (GCP) for Trials on Pharmaceutical Products. Annex 3 of *The Use of Essential Drugs*. Sixth Report of the WHO Expert Committee. Geneva: World Health Organization, 1995: 97-137.

World Medical Association, *Declaration of Helsinki: Recommendations Guiding Physicians in Biomedical Research Involving Human Subjects*. Adopted by the 18th World Medical Assembly, Helsinki, Finland, June 1964. Amended by the 29th World Medical Assembly, Tokyo, Japan, October 1975; the 35th World Medical

Assembly, Venice, Italy, October 1983; the 41st World Medical Assembly, Hong Kong, September 1989; and the 48th General Assembly, Somerset West, Republic of South Africa, October 1996.

World Medical Association, *Declaration of Lisbon on the Rights of the Patient*. Adopted by the 34th World Medical Assembly, Lisbon, Portugal, September/October 1981 and amended by the 47th General Assembly, Bali, Indonesia, September 1995.

Operational Guidelines for Ethics Committees Reviewing Biomedical Research

UNDP/World Bank/WHO
Special Programme for Research & Training
in Tropical Diseases
(TDR)

Committees

International Working Party

Solomon Benatar, South Africa

Chifumbe Chintu, Zambia

Francis P. Crawley, Belgium (Chairman)

Dafna Feinholz, Mexico

Christine Grady, USA

Dirceau Greco, Brazil

Hakima Himmich, Morocco

Andrew Kitua, Tanzania

Olga Kubar, Russia

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Reidar Lie, Norway

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BACKGROUND

The *Operational Guidelines for Ethics Committees That Review Biomedical Research* is the result of a wide international consultation begun in August 1999 at A Seminar on the Ethical Review of Clinical Research in Asian & Western Pacific Countries organized by TDR WHO in Chiang Mai, Thailand. The participants at the seminar expressed a need for international guidance on the constitution and operation of ethics committees.

The first draft of these *Guidelines* was discussed at a workshop for members of African Ethical Review Committees organized by TDR WHO and the African Malaria Vaccine Testing Network in Arusha, Tanzania, on 5 November 1999. The draft was subsequently presented to an Interim Meeting of the Forum for Ethical Review Committees in the Asian & Western Pacific Regions (FERCAP) in Bethesda, MD, USA, on 9 November 1999. It was also distributed for consultation at the Global Forum for Bioethics in Research organized by the NIH and WHO in Bethesda on 7-10 November 1999. Following these initial consultations the *Guidelines* were redrafted and widely distributed for comment.

Further development of these *Guidelines* was carried out under the auspices of a Secretariat composed of representatives from WHO, UNAIDS, CIOMS, UNESCO, and the WMA. Responsibility for drafting these *Guidelines* was given to an International Drafting Committee of 14 experts from various continents representing a wide range of disciplines in biomedical research and bioethics. The consultation process was carried out through representatives from the African Malaria Vaccine Testing Network, Council of Europe, European Commission, European Medicines Evaluation Agency, National Institutes of Health (USA), Food & Drug Administration (USA), Office for Protection from Research Risks (USA), Centers for Disease Control and Prevention (USA), National Council on Ethics in Human Research (Canada), Faculty of Pharmaceutical Medicine (United Kingdom), European Organization for Research

& Treatment of Cancer, International Federation of Pharmaceutical Physicians, Foundation Marcel Mérieux, International Federation of Pharmaceutical Manufacturers' Associations, International Conference on Harmonization, and European Forum for Good Clinical Practice. In addition, the draft text was widely distributed to organizations of ethics committees in Europe and the United States as well as to experts in the field of biomedical research ethics. On 2 January 2000 a new draft was prepared and distributed to the members of the Drafting Working Party, the Secretariat, and the Consultation Partners as well as to other parties who had commented or expressed an interest.

Following on the reception of a wide range of detailed comments from around the world, the text was then widely discussed at a Meeting on Guidelines and Standard Operating Procedures for Ethical Review Committees held in Bangkok on 10-12 January 2000. Participants in this meeting were drawn from the regions of Africa, Asia, Latin America, North America, and Europe, from international organizations, (including WHO, UNAIDS, UNESCO, CIOMS, EFGCP, and IFPMA), and from universities and research institutions. A final deliberation took place at a Drafting Meeting held on 13 January 2000 in Bangkok. Following the Drafting Meeting a final set of comments were solicited and integrated into the final document.

The purpose of this wide consultative process was to ensure extensive input while fostering the sharing of knowledge from developing and developed countries alongside organizations and institutions with varying degrees of experience and expertise. This process also help to prepare for the dissemination of the final text through an international process of capacity building that would strengthen national and local infrastructures for ethical review throughout the world.

The Operational Guidelines for Ethics Committees That Review Biomedical Research are proposed by the WHO and CIOMS as a support for improving the organization, quality, and standards of

ethical review around the world. These *Guidelines* take into account current practices while suggesting guidance for a harmonized state-of-the-art approach.

Comments and suggestions on all aspects of these guidelines are welcome for consideration in future revisions of this document. Please correspond with:

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