National Bioethics Committee (NBC)

Standard Operating Procedures (SOPs)

PAKISTAN MEDICAL RESEARCH COUNCIL

Standard Operating Procedures (SOPs) for National Bioethics Committee (NBC)

1. INTRODUCTION

NBC is an approved body by the Ministry of Health, Government of Pakistan and it has been notified in The Gazette of Pakistan, dated January 28, 2004. It has the major role of an advisory body dealing with all aspects of bioethics in the health sector in Pakistan. To play this role, the Committee would:

- Promote and facilitate ethical health services delivery, health research and health education.
- Be an umbrella body linked with the Ethics Review Committee in various organizations / institutions e.g. PMDC, Medical Colleges / universities, Good Clinical Practice (GCP) Committee of Ministry of Health etc.

It is an independent functioning committee for defining the operating procedures and transparency of the process.

Two major sub-committees of NBC are envisaged:

- Research Ethics Committee (REC): To address ethics in health research.
- Medical Ethics Committee (MEC): To address ethics in medical practice and education.

Section 1:

1.1 SOPs for Research Ethics Committee (REC)

Membership:

The REC will comprise 13 members excluding the Chairperson and Secretary NBC. Eight members will be selected from the NBC, and the remaining 5 members will be co-opted. The REC will have researchers, academicians, lawyer, religious scholar, Journalist etc. The Chairman of the REC will be selected from the REC.

The PMRC will provide the Secretariat for the REC.

1.2 SOPs for Medical (Services) Ethics Committee (MEC)

Membership:

The MEC will comprise 15 members excluding the Chairperson and Secretary NBC. There will be 5 existing members of NBC and 4 co-opted members from PMDC to this committee. The Chairman will be selected from among the members of MEC.

PMDC will provide the secretariat.

1.3 Institutional Review Board (IRB):

IRBs for both REC and MEC at the regional level will be established. Memberships for IRBs (REC) and IRBs (MEC) will be decided by the two sub-committees on REC and MEC. These IRBs will coordinate on various ethical issues referred to bring into the notice with respective REC and MEC. A mechanism will be established at regional level that if a case is to be referred then there should be legal body, which can be contacted, and things are brought in their knowledge.

Dr. Sohail will develop procedural system / mechanism. Mr. Shaukat will prepare a draft with the input from few members and will forward to Dr. Sohail.

2. OBJECTIVES

The objectives of these SOPs are to contribute to the development of quality and consistency in the ethical review of biomedical research. The SOPs are intended to complement existing laws, regulations, and practices, and to serve as a basis upon which National Bioethics Committee (NBC) can develop their own specific written procedures for their functions in biomedical research. The SOPs should be used for evaluating and progressively refining SOPs for the ethical review of biomedical research.

3. THE ROLE OF NBC

The purpose of an NBC 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.** NBC 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, ethnic and religious considerations. NBC should provide independent, competent, and timely review of the ethics of proposed studies. In their composition, procedures, and decision-making, NBC needs to have independence from political, institutional, professional, and market influences. NBC is responsible for carrying out the review of proposed research before the commencement of the research. It also needs to ensure that there is regular evaluation of the ethics of ongoing studies that received a positive decision.

4. ESTABLISHING A SYSTEM OF ETHICAL REVIEW

NBC and ethical review systems should 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. 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 may need to be established at the regional, national, and local levels ensure high to competence in biomedical review while also guaranteeing input from all levels of the community.

Funding: Funding resources for the administrative working of NBC. One source of funding will be generated through reviewing of research proposals:

1. For sponsored research a fee of Rs 10,000 will be charged /or should be determined according to the project funding.
2. For national research proposal a fee of Rs 2000 be charged /or should be determined according to the project funding.
3. For an expedited review; national proposal will be charged for Rs 5000/ and sponsored studies will be charged Rs 20,000.
4. Ministry of health will also be asked to provide annual funding for the NBC secretariat.

4 (a). *Membership Requirements* & Terms of Appointment

Membership of NBC would be multidisciplinary, multi-Sectoral and pleuristic in nature. It is proposed to have 20-21 members. 90% of the members should be regular while 10% should be co-opted as per need on specific subjects. Members will be from both sexes and of a wide age range. There will be representation

from all provinces of Pakistan. PMRC, PMDC, and. CPSP will have ex-officio permanent representation on the committee. Members would also include various categories of stakeholders like legal experts, religious scholars and judiciary.

The tenure of membership would be for **5 years** (50 % will be replaced after 2.5 years) if a member does not attend three consecutive meetings the member will be replaced. The provision of renewal for another term will be one time on the same basis.

Clear procedures for identifying or recruiting potential NBC members should be established. A statement should be drawn up of the requirements for candidate that includes an outline of the duties and responsibilities of NBC members. Membership requirements should be established that include the following:

a) The core working group of NBC headed by Chairman would be responsible for making appointments.
b) The members should preferably be appointed through consensus or at least through majority vote.
c) Conflicts of interest should be avoided while making appointments.
d) A rotation system for membership should be considered continuity, the development and maintenance of expertise within the NBC, and for regular input of fresh ideas and approaches e.g., 50% members retiring at every 2.5 year term.
e) Members desirous of resigning from the membership should apply in writing with plausible reasons for resignation. Such application(s) will be considered in the next NBC meeting.
f) Replacement of the resigned (or deceased) member will be made by the NBC from the same discipline.

4 (b). *Conditions of Appointment*

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

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

4(c). *Offices*

The following structure of the office / office holders is envisaged:

- Patrons: Minister of Health and Health Secretary, Government of Pakistan will be the Patrons of NBC. Their advice and guidance will be sought from time to time especially on policy issues and international liaison.
- Chairman: Director-General Health, Government of Pakistan. He/she will chair the meetings of the main body of NBC especially when policy decisions are foreseen.
- Secretary : Executive Director, PMRC will act as the secretary and will coordinate day to day activities of NBC and be responsible for calling the meetings, formulating the agenda and keeping the records of the minutes.

4(d). *Secretariat*

PMRC will provide the secretariat for NBC. Adequate support staff for the functioning of NBC will be provided to carry out its functions. Secretariat will be responsible for arranging regular meetings of the Committee and implementations of the decisions and recommendations.

4(e). *Quorum Requirements*

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

a) The minimum number of members required to compose a quorum would be at least 50% of the invitees.

b) No quorum should consist entirely of members of the one profession. The 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(f). *Independent Consultants*

NBC may call upon, or establish a standing list of, independent consultants who may provide special expertise to the NBC 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 need to be established.

4(g). *Education for NBC Members*

NBC 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 NBC members to receive introductory training in the work of an NBC 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 NBC members. This education may be linked to co-operative arrangements with other NBC in the area, the country, and the region, as well as other opportunities for the initial and continued training of NBC members.

4(h). *Finances*

- PMRC will bear the cost of maintenance of the secretariat from its own budget with the support from Ministry of Health.
- A fee to be charged from research proposal presented for ethical clearance. PMRC will maintain the accounts. The fee should be charged up front i.e. before review and is meant for administrative cost and is in not related to the outcome of the review. See under **Funding**.

- The Chairman (DGH) will make efforts to secure funds from WHO EMRO through WHO-Government of Pakistan Joint Review Mission.

5. PROCEDURE FOR SUBMITTING AN APPLICATION

NBC is 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(a). *Application*

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

5(b). *Application Requirements*

The requirements for the submission of a research project for ethical review should include the following:

a) The application should be submitted to Secretary, NBC.
b) The application form(s);
c) The format for submission;
d) The documentation (see 5c);
e) Two (2) original applications and 1 soft copy should be submitted along with copies, at least as many as there are members.
f) The receipt of applications will be acknowledged by NBC including the communication of the incompleteness of an application within 2 weeks of the receiving the application.
g) The notification of the decision following review within 6-8 weeks in case of complete application
h) In case of incomplete applications NBC requests supplementary information or changes to documents from the applicant within two weeks.
I) The fee structure for reviewing an application. (see under funding).
j) The application procedure for amendments to the protocol, the recruitment material, the potential research participant information, or the informed consent form.

5(c). *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,
a) Signed and dated application form;
b) The protocol of the proposed research (clearly identified and dated), together with supporting documents and annexure;
c) A summary (as far as possible in non-technical language), synopsis, or diagrammatic representation ('flowchart') of the protocol;
d) A description (usually included in the protocol) of the ethical considerations involved in the research;
e) Case report forms, diary cards, and other questionnaires intended for research participants;
f) 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);
g) Investigator(s)'s curriculum vitae (updated, signed, and dated);
h) Material to be used (including advertisements) for the recruitment of potential research participants;
i) A description of the process used to obtain and document consent;

j) 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;
k) Informed consent form (clearly identified and dated) in the language(s) understood by the potential research participants and, when required, in other languages;
l) A statement describing any compensation for study participation (including expenses and access to medical care) to be given to research participants;
m) A description of the arrangements for indemnity, if applicable;
n) A description of the arrangements for insurance coverage for research participants, if applicable;
o) A statement of agreement to comply with ethical principles set out in relevant guidelines;
p) All significant previous decisions (e.g., those leading to a negative decision or modified protocol) by other NBC 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(a). *Meeting Requirements*

NBC should have two meetings per years, Sub-committees will meet quarterly and IRB will have monthly meetings on scheduled dates that are announced in advance. The meeting requirements should include the following:

a) Meetings should be planned in accordance with the needs of the workload;
b) NBC members should be given enough time, **4-weeks,** in advance of the meeting to review the relevant documents. Expedited review will charge extra. Maximum three months period will be given for reviewing of Research Proposal.
c) Meetings should be documented; there should be an approval procedure for the minutes;
d) The applicant, sponsor, and/or investigator may be invited to present the proposal or elaborate on specific issues;
e) Independent consultants may be invited to the meeting or to provide written comments, subject to applicable confidentiality agreements.

6(b). *Elements of the Review*

The primary task of an NBC 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. NBC needs to take into account prior scientific reviews, if any, and the requirements of applicable laws and regulations. The following should be considered, as applicable:

I. *Scientific Design and Conduct of the Study*

a) 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;
b) The justification of predictable risks and inconveniences weighed against the anticipated benefits for the research participants and the concerned communities;
c) The justification for the use of control arms;
d) Criteria for prematurely withdrawing research participants;
e) Criteria for suspending or terminating the research as a whole;
f) The adequacy of provisions made for monitoring and auditing the conduct of the research, including the constitution of a data safety monitoring board (DSMB);
g) The adequacy of the site, including the supporting staff, available facilities, and emergency procedures;
h) The manner in which the results of the research will be reported and published;

II. Recruitment of Research Participants

a) The characteristics of the population from which the research participants will be drawn (including gender, age, literacy, culture, economic status, and ethnicity);
b) The means by which initial contact and recruitment is to be conducted;
c) The means by which full information is to be conveyed to potential research participants or their representatives;
d) Inclusion criteria for research participants;
e) Exclusion criteria for research participants;

III. Care and Protection of Research Participants

a) The suitability of the investigator(s)'s qualification and experience for the proposed study;
b) Any plans to withdraw or withhold standard therapies for the purpose of the research, and the justification for such action;

c) The medical care to be provided to research participants during and after the course of the research;
d) The adequacy of medical supervision and psycho-social support for the research participants;
e) Steps to be taken if research participants voluntarily with-draw during the course of the research;
f) The criteria for extended access to, the emergency use of, and/or the compassionate use of study products;
g) 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;
h) A description of any plans to make the study product available to the research participants following the research;
i) A description of any financial costs to research participants;
j) The rewards and compensations for research participants (including money, services, and/or gifts);
k) The provisions for compensation/treatment in the case of the injury/disability/death of a research participant attributable to participation in the research;
l) The insurance and indemnity arrangements;

IV. Protection of Research Participant Confidentiality

a) A description of the persons who will have access to personal data of the research participants, including medical records and biological samples;

b) The measures taken to ensure the confidentiality and security of personal information concerning research participants;

V. Informed Consent Process

a) A full description of the process for obtaining informed consent, including the identification of those responsible for obtaining consent;
b) 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);
c) 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;
d) Assurances that research participants will receive information that becomes available during the course of the re-search relevant to their participation (including their rights, safety, and well-being);
e) The provisions made for receiving and responding to queries and complaints from research participants or their representatives during the course of a research project;

VI. Community Considerations

a) The impact and relevance of the research on the local community and on the concerned communities from which the research participants are drawn;
b) The steps taken to consult with the concerned communities during the course of designing the research. The members of the NBC can be nominated by the Chairman to participate in the deliberations of national and international meetings/conferences on the subject of the ethics of health research.
c) The influence of the community on the consent of individuals;
d) Proposed community consultation during the course of the research;
e) The extent to which the research contributes to capacity building, such as the enhancement of local healthcare, re-search, and the ability to respond to public health needs;
f) A description of the availability and affordability of any successful study product to the concerned communities following the research;
g) The manner in which the results of the research will be made available to the research participants and the concerned communities.

6(c). *Expedited Review*

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

a) The nature of the applications, amendments, and other considerations that will be eligible for expedited review;
b) The quorum requirement(s) for expedited review;
c) The status of decisions (e.g., subject to confirmation by full NBC or not).

7. DECISION-MAKING

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

a) 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;
b) 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 NBC staff;

c) Decisions should only be made at meetings where a required quorum (as stipulated earlier) is present;
e) The documents required for a full review of the application should be complete and the relevant elements mentioned above should be considered before a decision is made;
f) Only members who participate in the review should participate in the decision;
g) 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 NBC vote;
g) Advices that are non-binding may be appended to the decision;
h) In cases of conditional decisions, clear suggestions for revision and the procedure for having the application reviewed should be specified;
i) 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 NBC 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:

a) The exact title of the research proposal reviewed;
b) The clear identification of the protocol of the proposed research or amendment, date and version number (if applicable), on which the decision is based;
c) 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;
d) The name and title of the applicant;
e) The name of the site(s);
f) The date and place of the decision;
g) A clear statement of the decision reached;
h) Any advice by the NBC;
i) In the case of a conditional decision, any requirements by the NBC, including suggestions for revision and the procedure for having the application re-reviewed;
j) 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 NBC; submission of progress report(s); the need to notify the NBC in cases of protocol amendments (other than amendments involving only logistical or administrative aspects of the study); the need to notify the NBC in the case of amendments to the recruitment material, the potential re-search 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 NBC; the information the NBC expects to receive in order to perform ongoing review; the final summary or final report;

k) The schedule/plan of ongoing review by the NBC;

l) In the case of a negative decision, clearly stated reason(s) for the negative decision;

m) Signatures (dated) of the chairperson (or other authorized person) of the NBC.

9. FOLLOW-UP

NBC 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 NBC and the applicant should be clearly specified. The follow-up procedure should take the following into consideration:

a) 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;

b) 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;

c) The following instances or events require the follow-up review of a study:

    1. Any protocol 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, and the response taken by investigators, sponsors, and regulatory agencies;
    3. Any event or new information that may affect the benefit/risk ratio of the study;

d) A decision of a follow-up review should be issued and communicated to the applicant, indicating a modification, suspension, or termination of the NBC's original decision or confirmation that the decision is still valid;

e) In the case of the premature suspension/termination of a study, the applicant should notify the NBC of the reasons for suspension/termination; a summary of results obtained in a study prematurely suspended/terminated should be communicated to the NBC;

f) NBC should receive notification from the applicant at the time of the completion of a study;

g) NBC should receive a copy of the final summary or final report of a study.

h) NBC Secretariat will generate an annual report of the projects approved

and the status of the progress of the projects. The recipients of the report will be all members of the NBC and the concerned institutions.

10. DOCUMENTATION AND ARCHIVING

All documentation and communication of an NBC 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,

a) The constitution, written standard operating procedures of the NBC, and regular (annual) reports;
b) The curriculum vitae of all NBC members;
c) A record of all income and expenses of the NBC, including allowances and reimbursements made to the secretariat and NBC members;
d) The published guidelines for submission established by the NBC;
e) The agenda of the NBC meetings;
f) The minutes of the NBC meetings;
g) One copy of all materials submitted by an applicant;
h) The correspondence by NBC members with applicants or concerned parties regarding application, decision, and follow-up;
i) A copy of the decision and any advice or requirements sent to an applicant;
j) All written documentation received during the follow-up;
k) The notification of the completion, premature suspension, or premature termination of a study;
l) The final summary or final report of the study.

11. 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 NBEC 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 NBC member has financial, material, institutional, or social ties to the research.

Decision
The response, (positive, conditional or negative), by an NBC to an application following the review in which the position of the NBC 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 sub-investigators.

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 a research project.

12. Additional Readings

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

- Council of Europe. *Convention for the Protection of Human Rights and Dignity of the Human Being with Regard to the Application of Biology and Medicine: Convention on Human Rights and Biomedicin*e.

- Department of Health, Education, and Welfare, Office of the Secretary, Protection of Human Subjects. *Belmont Report: Ethical Principles and Guidelines for the Protection of Human Subjects of Re-search. Report of the National Committee for the Protection of Human Subjects of Biomedical and Behavioral Researc*h.

- International Conference on Harmonization of Technical Requirements for the Registration of Pharmaceuticals for Human Use (ICH). *Note for Guidance on Good Clinical Practice*

- World Health Organization (WHO). Guidelines for Good Clinical Practice (GCP) for Trials on Pharmaceutical Products.

- World Medical Association, *Declaration of Helsinki: Recommendations Guiding Physicians in Biomedical Research Involving Human Subject*s.

Ethical principles and benchmarks for multinational clinical research.
(What Makes Clinical Research in Developing Countries Ethical? The Benchmarks of Ethical Research Ezekiel J. Emanuel, David Wendler, Jack Killen, and Christine Grady The Journal of Infectious Diseases 2004; 189:930–7)

Principles	**Benchmarks**
Collaborative partnership	Develop partnerships with researchers, makers of health policies, and the community. Involve partners in sharing responsibilities for determining the importance of health problem, assessing the value of research, planning, conducting, and overseeing research, and integrating research into the health-care system. Respect the community's values, culture, traditions, and social practices.

	Develop the capacity for researchers, makers of health policies, and the community to become full and equal partners in the research enterprise.
	Ensure that recruited participants and communities receive benefits from the conduct and results of research.
	Share fairly financial and other rewards of the research.
Social value	Specify the beneficiaries of the research-who.
	Assess the importance of the health problems being investigated and the prospective value of the research for each of the beneficiaries—what.
	Enhance the value of the research for each of the beneficiaries through dissemination of knowledge, product development, long-term research collaboration, and/or health system improvements. Prevent supplanting the extant health system infrastructure and services.
Scientific validity	Ensure that the scientific design of the research realizes social value for the primary beneficiaries of the research.
	Ensure that the scientific design realizes the scientific objectives while guaranteeing research participants the health-care interventions to which they are entitled.
	Ensure that the research study is feasible within the social, political, and cultural context or with sustainable improvements in the local health-care and physical infrastructure.
Fair selection of study Population	Select the study population to ensure scientific validity of the research.

	Select the study population to minimize the risks of the research and enhance other principles, especially collaborative partnership and social value. Identify and protect vulnerable populations.
Favorable risk-benefit ratio	Assess the potential risks and benefits of the research to the study population in the context of its health risks. Assess the risk-benefit ratio by comparing the net risks of the research project with the potential benefits derived from collaborative partnership, social value, and respect for study populations.
Independent review	Ensure public accountability through reviews mandated by laws and regulations. Ensure public accountability through transparency and reviews by other international and nongovernmental bodies, as appropriate. Ensure independence and competence of the reviews.
Informed consent	Involve the community in establishing recruitment procedures and incentives. Disclose information in culturally and linguistically appropriate formats. Implement supplementary community and familial consent procedures where culturally appropriate. Obtain consent in culturally and linguistically appropriate formats. Ensure the freedom to refuse or withdraw. Respect for recruited participants and study communities

Develop and implement procedures to protect the confidentiality of recruited and enrolled participants.

Ensure that participants know they can withdraw without penalty.

Provide enrolled participants with information that arises in the course of the research study.

Monitor and develop interventions for medical conditions, including research-related injuries, for enrolled participants' at least as good as existing local norms. Inform participants and the study community of the results of the research.