

# **National Ethical Guidelines For Health Research in Nepal**

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## FOREWORD

Advances in science and medicine including molecular biology, genetics, immunology and informatics have over the last few decades contributed significantly towards the improvement " of the health status Of people all over the world. Newer drugs, vaccines, and new technologies in diagnostic and therapeutic interventions are being developed constantly. Such new techniques/procedures first need to be tried on select group of human participants under close observation before they can be approved for use by the general population. The scientific community thus has the dual responsibility of promoting science and medicine as well as protecting the dignity, rights, safety and well being of research participants.

Ethics in health research, though practiced for many years in developed countries, is just beginning to emerge as an important issue in developing countries, including Nepal. Nepal Health Research Council (NHRC) is the apical body in the country entrusted with the responsibility of promoting quality health research of high ethical standards.

In order to meet this responsibility and to arrive at a national consensus NHRC decided to develop ethical guidelines for health research through a National Consultative Meeting. This meeting was held in 12-15 November 2000 and was attended by over 36 national participants, which included research scientists and representatives from Ministry of Health, National Planning Commission, NGO's, INGO's, RONAST, Universities and Research Institutions.

The Consultative Meeting was carried out as a joint activity of NHRC and the Rockefeller Foundation through the International Award for Capacity Strengthening of the Health Research Network in Nepal. The World Health Organization (WHO/SEARQ) provided technical support by providing three resource persons. I wish to express my sincere thanks to organizations, resource persons and participants for their invaluable contribution. *The Ethical Guidelines* that has been developed has incorporated (a) the principles of ethical requirements as outlined in the International Guidelines of CIOMS, Declaration of Helsinki, WHO/ISH guideline for Good Clinical Practice and (b) recommendations from the consultative meeting, while also taking into consideration the socio-cultural milieu of Nepal.

The document is divided into three sections. Section A discusses 'general principles of ethics including beneficence, justice, informed consent, voluntaries and confidentiality. Section B contains operational guidelines for ERBs, which describes their roles and responsibilities, composition and the process of review of research proposals. Section C includes checklists for assessing (a) informed consent, (b) scientific merit of research proposals, (c) ethical questions and (d) operational aspects of ERBs.

It is our sincere hope that the present Guidelines will serve as a useful document for NHRC, the Ethical Review Boards and research scientists in the country in addressing the ethical dimensions of health research.

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# National Ethical Guidelines For Health Research in Nepal

## *Preface*

The Nepal Health Research Council (NHRC) was created by an Act of Parliament in 1991 with the specific purpose of 'promoting scientific study and quality research in health in Nepal'. The development of the National Ethical Guidelines for Health Research is a further step taken by NHRC to promote health research in Nepal. The purpose of these Guidelines is to assist the NHRC Ethical Review Board in the fulfillment of its obligation to promote and protect the dignity, rights, safety and well being of all research participants and to fulfill its duties to the health research community in Nepal.

The ethical and scientific standards for carrying out biomedical research on human participants have been developed and established in international guidelines. These include the *Declaration of Helsinki* of the World Medical Association (WMA), the *International Ethical Guidelines for Biomedical Research Involving Human Subjects* of the Council of International Organizations of Medical Sciences (CIOMS), and the Guidelines for Good Clinical Practice produced by the World Health Organization.

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 psychological investigations.

In preparing these National Ethical Guidelines for Health Research in Nepal, NHRC has acted to establish national guidelines in agreement with the values and principles of the international community, while taking into account substantial and operational considerations described in the ethical guidelines and regulations in other countries, including those in India, the United States, member countries of the European Union, and South Africa. In addition, these Guidelines have been developed during a National Consultative Meeting on the Development of Ethical Guidelines organized by NHRC in 1215 November 2000. This meeting, was supported by the WHO and international experts, and involved extensive international consultations.

These Guidelines present basic ethical principles for health research and framework considerations for ethical review and informed consent in Nepal. They serve as a guide to decision making on health research within NHRC and as a general reference point for researchers and all other Ethical Review Boards in Nepal.

## Section A

### Ethical Principles For Health Research Involving Human Participants

#### 1. Introduction

The word *ethics* is derived from the Greek word 'ethos', which means 'character', 'disposition', or 'a fundamental outlook influencing behavior related to customs and moral values of the people'. Aristotle described ethics as moderation in the choice between extremes or as the decision of the prudent person. In our societies today, ethics refers to issues, problems, judgments, and types of behavior related to morality, social justice, human rights, as well as social and professional responsibility. In biomedical research, ethics concerns itself primarily with the promotion and safeguarding of the dignity, rights and well being of research participants.

#### 2. Historical Background

Codes of medical ethics are to be found as far back as Babylon with Hammurabi's "Code of Law" (Babylon, 1790 BC), Agnivesa's "Charaka Samhita" (the Indian subcontinent, 800 BC to 400 AD), and the Hippocratic Oath (Greece, 600 BC). Recorded writings on medical ethics are to be found even earlier in the ancient writings of Egyptian, Arabic, and Greek scientists and philosophers. More recently, in the West the concept of just moral propriety in medicine was propounded by Thomas Hobbs in 1651 and that of medical humanism by John Gregory in the 18th Century. Thomas Percival came up with the concept of bio-ethics and legislation aspects of ethics related behaviour.

In 1946 the International Health Conference meeting in New York adopted the constitutional structure of the World Health Organization (WHO), which formally came into existence in 1948. This constitution reiterated the responsibilities of government and health professionals for promoting and protecting the health of individuals and populations.

As the key organization responsible for health within the structure of the United Nations, the WHO promotes the *Universal Bill of Human Rights* composed of the *Universal Declaration of Human Rights* (1948), the *International Covenant of Economic, Social and Cultural Rights* (1966, ratified in 1976), and the *International Covenant on Civil and Political Rights* (1966). These three instruments define and describe basic human rights and fundamental freedoms. They form the nucleus of an interlocking set of international conventions, resolutions, and declarations intent on promoting the rights and freedoms of persons through law. The *Universal Declaration on Human Rights* is supported and promoted by the NHRC in all its activities.

Ethics related to health and biomedical research is a more recent phenomenon. The first international document on this is the Nuremberg Code in 1947. This initiated the development of a series of international declarations, conventions, and covenants related to ethics in health, healthcare, and research. The most prominent of these documents today are the WMA *Declaration of Helsinki*, the CIOMS *International Ethical Guidelines for Biomedical Research Involving Human Subjects*, and the WHO and the ICH Guidelines for Good Clinical Practice.

### **3. Definition of Research Involving Human Participants**

The term "research" refers to a set of activities designed to develop or to contribute to generalizable knowledge consisting of theories, principles, or relationships, or the accumulation of information on which they are based, that can be corroborated by accepted scientific methods of observation and inference. Health research includes medical and behavioural studies related to human health. 'Biomedical' research refers to Research related, directly or indirectly, to the advancement of medicine. 'Clinical' research refers to any study of which one or more of the components is diagnostic, prophylactic, or therapeutic in nature and is applied to human participants.

Research involving human participants may involve physical, chemical, psychological, or social interventions, or it may be strictly observational or historical in its methodology. The study of existing records or generated records containing biomedical or other information, or of tissue samples or biological material, about individuals that may or may not be identifiable, is also to be understood as research involving human participants.

#### **Research involving human participants includes:**

- 3.1 Studies of physiological, biochemical, or pathological processes.
- 3.2 Studies of responses to physical, chemical, genetic, psychological, or social interventions.
- 3.3 Controlled trials of diagnostic, preventive, or therapeutic methods or measures in persons, designed to demonstrate a specific generalized response to these measures against a background of individual biological variation.
- 3.4 Studies designed to determine the consequences for individuals and communities of specific preventive or therapeutic measures.
- 3.5 Studied concerning human health-related behaviour in variety of circumstances and environments.
- 3.6 Studies in which environmental factors are manipulated in a way that could affect incidentally exposed individuals; for example, exposure to toxic chemicals, radiation, or pathogenic organisms or agents (or the absence of these); also psycho-social challenges or deprivations, and the implementation of health policy or management options influencing the environment of the participants should be considered as research involving human participants.
- 3.7 Epidemiological or observational studies aimed at exploring the distribution and determinants or risk factors of health-related events or problems in a specified population and geographic area in order to prevent, control, and/or manage health problems and/or promote healthy or environment-friendly behaviour.

### **4. Ethical Principles for Health and Biomedical Research**

Four basic ethical principles form the basis for the ethical evaluation of health and biomedical research process. These principles are respect for the dignity of persons, beneficence (non-maleficence), justice, and respect for the environment.

#### **4.1 Respect for the dignity of persons**

The obligation to respect the dignity of persons in all activities of health and biomedical research is the cornerstone of research ethics. This requires specific attention to the following:

- Respect for the autonomy of persons, promoting the essential freedom in decision making attributable to persons based on their moral and rational dignity and their capacity for self-determination.
- The active protection of persons with impaired or diminished autonomy, requiring those who are dependent or vulnerable be afforded security against harm or abuse.
- No research should prevail over respect for human rights, fundamental freedoms and human dignity, and that practices contrary to human dignity should be prohibited.

For research involving human participants, the respect for persons is promoted primarily through the informed consent process.

#### **4.2 Beneficence (non-maleficence)**

Beneficence is the obligation to maximise possible benefits and to minimise possible harm or wrongs. This requires that all health and biomedical research projects be preceded by a careful assessment of the potential risks and burdens in comparison with the potential benefits to the prospective research participants and their communities. This does not preclude the participation of healthy volunteers in research. However, in all cases the research should promote the health of the population represented.

Beneficence also requires that the researchers are qualified to carry out the proposed research and that they are committed to promoting and protecting the health of the participants and their communities. Beneficence proscribes the deliberate infliction of harm on persons.

#### **4.3 Justice**

Justice requires that persons in similar circumstances be treated alike and that differences between persons due to circumstances be acknowledged and addressed. In the context of health and biomedical research, justice requires that persons having similar health complaints or threats be treated equally.

Justice also requires the equitable distribution of the burdens and benefits of research. Differences in such distribution are justifiable only if they are based on morally relevant distinctions between persons, or example, in cases where it is necessary to ensure the protection of the rights and welfare of vulnerable persons.

The protection of persons in vulnerable situations is of special importance. Persons in vulnerable situations are those who are unable to express fully or protect fully their own interests owing to such impediments as a lack of capacity to consent fully, an inability to obtain alternative means, of medical care and/or other health necessities, or because they are a junior or subordinate member of a hierarchical group. Accordingly, special provisions must be made for the protection of the rights and welfare of all persons in vulnerable situations.

#### **4.4 Respect for the Environment**

Respect for the environment requires that health and biomedical research 'is undertaken within a context of respect for the social, cultural, and natural heritage of a society. This fundamental ethical principle is re-enforced by the Declaration of Helsinki, which stresses the special precautions that must be exercised for the protection of the environment in the conduct of research. In view of the increasing world movement for the protection of the environment, every researcher is responsible for a moral engagement to protect the social, cultural and natural heritage of societies and communities where they undertake research. This responsibility includes a commitment:

- To ensure the proper and safe disposal of biologically hazardous waste from laboratory, clinical or field research.
- To safeguard the cultural, including religious and linguistic, heritage of communities and persons.
- To treat with respect and caution the biologic and genetic heritage of people. This requires respecting the principles of informed consent and confidentiality of genetic data. (Individuals should be fully informed of the foreseen uses of the collected data or research. The confidentiality of the data collected for the purpose of research should be effectively guaranteed. Every use of material or information should comply with the requirements of confidentiality and informed consent of the person involved.)
- To prevent any damage or degradation of the natural environment caused by the implementation, conduct or products or research.
- To treat with respect domestic and wild animals in the context of research and with regard to the effects of the conduct or outcome of research.

## **5. Informed Consent**

For all bio-medical research involving human participants, the investigators must obtain the informed consent of the prospective participants or in the case of an individual who is not capable of giving informed consent, the proxy consent of a properly authorized representative.

The informed consent process can be analyzed as having three components:

### **5.1 Information**

The research participants should be given sufficient information of the proposed research including information on the research procedures, their purpose, risks and discomforts and anticipated benefits, alternative procedures, and a statement offering the participant the opportunity to ask questions and to withdraw any time from the research without any fear of negative consequences.

A special problem of consent arises when informing participants of some pertinent aspect of research that is likely to impair the validity of the research. Such circumstances should be discussed with the ERB who will then decide on the matter.

### **5.2 Comprehension**

It is the investigators' responsibility to ascertain that the research participant is competent and has comprehended the information. If the research participant is not capable of comprehending the information or is incompetent, the proxy consent of a properly authorized representative is necessary.

It is necessary to adapt the presentation of the information to the participants' capacities in a language the participants can understand. Necessary attention and sensitivity should be given to cultural particularities.

### **5.3 Voluntariness**

Informed consent is valid only if it is given voluntarily. Therefore there should be no coercion in the form of any threat or undue influence in the form of excessive, unwarranted, inappropriate, or improper award.

When the research design involves no more than minimal risk, that is, risk that is no more likely and not greater than that attached to routine medical or psychological examination, and it is not practical to obtain informed consent from each participant, the Ethical Review Board may waive some or all of the elements of informed consent.

Even though the legal guardian of a child or a person with a mental disorder gives the actual consent for participation in research, whenever possible, the assent of the child or the person with a mental disorder, to the extent possible, has to be obtained.

### **5.4 Assessment of Risks and Benefits**

The principle of beneficence requires that the research be justified on the basis of a favourable risk/benefit assessment. The term "risk" refers to a possibility that harm may occur. The term "benefit" in research refers to something of a positive value related to health or welfare. The most likely types of harm to research participants are physical pain or injury or psychological effects. However, other kinds of harm must not be overlooked which include legal, social, and economic. Benefits may also be of the corresponding types.

Making precise judgments about the risk/benefits ratio is difficult in most instances as only rarely can quantitative techniques be available to judge research proposals. Therefore systematic, non-arbitrary analysis of risks and benefits should be adopted as far as possible. For this purpose, thorough accumulation and assessment of information about all aspects of the research should be done, and alternatives should be considered systematically.

**In assessing the justifiability of research, consideration of the following is the minimum:**

- a) It should be judged whether the use of human participants is in fact necessary at

- all.
- b) Brutal or inhumane treatment of human participants is never justified.
- c) Risks should be reduced to those necessary to achieve the research objectives.
- d) When research involves significant risk, extraordinary insistence on the justification of risk is necessary.
- e) When vulnerable populations are involved in research, the necessity of involving them should be clearly demonstrated.
- f) Relevant risks and benefits should be clearly and thoroughly spelled out in the documents used in the informed consent process.

## **5.5 Selection of Research Participants**

The principle of justice requires that there be fair procedures and outcome in the selection of research participants. Individual justice in the selection of participants requires that researchers exhibit fairness. Thus they should not offer potentially beneficial research only to some patients who are in their favour or select only "undesirable" persons for risky research. Social justice requires that distinction be drawn between classes of participants that ought and ought not to participate in any particular kind of research. Thus, it is a matter of social justice that there is an order of preference in the selection of classes of participants (e.g. institutionalized mentally infirmed or prisoners may be involved as research participants, if at all, only on certain conditions). Special attention should be taken in research involving medical students and soldiers because of their potentially vulnerable situation.

In accordance with this principle, a new drug or appliance developed elsewhere can only be tested in the Nepalese population after a Phase 1 trial' has been conducted elsewhere.

*Prisoners* must not be made subjects of intervention' research that involves more than minimal risk, as the consent given by them may not be given voluntarily or may have been unduly influenced by expectations of reward. Other types of research involving prisoners will be reviewed by the full ERB.

*Pregnant and nursing women* should not be subjects of any clinical trails except those that .are designed to protect or advance the health of pregnant or nursing women or fetuses or nursing infants and for which they are the only suitable participants.

*Children* cannot be considered mini-adults, and therefore any new drug intended for use in children has to be studied in children for its rational and scientific use. However, before undertaking research in children, in addition to the action under "Informed consent", it has to be ensured that:

- a) Children will not be involved in research that might be carried out equally well in adults.
- b) The purpose of the research is to obtain knowledge relevant to the health needs of children.

Before undertaking research in mentally disadvantaged persons, in addition to the section under "Informed consent" it has to be ensured that:

- a) Such, research cannot be carried out satisfactorily in persons in full possession of their mental faculties (i.e. persons capable of consent).
- b) The purpose of the research is to obtain knowledge relevant to the health needs of persons with mental disorders.

## **6. Best Research Practices**

Research involving human participants should be carried out by qualified, competent, and responsible investigators according to a research proposal (protocol) that clearly identifies the purpose, questions and methodology of the study. The proposal should be scientifically and ethically appraised by one or more suitably and legally constituted review bodies, independent of the investigators. The implementation of the research should follow best research practices including internationally accepted Good Clinical Practice Guidelines, Good Laboratory Practice Guidelines, and Good Manufacturing Practice Guidelines.

Data should be handled, processed, and analysed by competent, and qualified persons led by qualified health professionals. Ethical responsibility of managers/handlers of data for data safety, confidentiality, and prevention of misuse should be strictly upheld.

## **7. Externally Sponsored Research**

The following conditions have to be considered before external sponsors can undertake research among the Nepalese people:

- a) The research is preferably responsive to the health needs and priorities of Nepal as well" as being sensitive to the existing culture and social values.
- b) The research cannot be carried out reasonably well in the sponsors' country.
- c) The research protocol has the approval of an Ethical Review Board/Institutional Review Board of the country of the sponsor.
- d) The sponsor should -consider means in which the research capability of Nepal can be strengthened and other means of compensating the community.
- e) The research process should be transparent.
- f) External sponsors should apply insurance to research participants in health research that Involves more than minimal risk.
- g) In case. it is necessary to transfer biological samples abroad, a memorandum of understanding has to be signed by the sponsor and NHRC defining clearly the purpose for the transfer, the material that is being transferred, ownership of intellectual property rights, and. provisions for privacy protection.
- h) The proposal has to be approved by NHRC.

## Section B

### The Ethical Review Board The authority under which the Ethical Review Board is established

The NHRC Ethical Review Board (ERB) is established as per the Nepal Health Research Council Act, 1991. Section 6, Functions, Duties, and Rights of the Council. NHRC can permit the establishment of other ERBs and will provide the assistance for such ERBs to be established. These ERBs must follow the guidelines of NHRC.

#### **1. Role Duty, and Responsibility of the Ethical Review Board**

- 1.1 The Ethical Review Board is a Board established to oversee all medical research involving human participants. No such research can be conducted in Nepal without the review and approval of the NHRC ERB or a duly approved ERB. The NHRC has the role, duty, and responsibility to approve and register other ERBs.
- 1.2 The purpose of the ERB is to safeguard the rights, dignity, safety and the well being of all potential research participants. The ERB should ensure the full review and evaluation of all ethical aspects of the research project they receive. The tasks of the ERB should be executed free from bias and influence. Everything should be done to ensure the safety and well being of an individual involved in research.
- 1.3 The ERB is legally viewed as the protector of the scientific quality and ethical standards of all health research and has the authority to do whatever is necessary to enforce those standards. It has the duty to investigate all research projects before they are carried out and to make sure they follow all ethical guidelines.
- 1.4 The ERB has the authority to demand research protocol modifications. The ERB has the authority to enforce and monitor all informed consent or patients' rights issues and to suspend or stop any research that present problems. The ERB serves as the conscience of the scientific research community and the protector of the human participants.
- 1.5 The ERB should provide independent, competent, and timely review of the ethics of proposed studies. The ERB is responsible for reviewing the proposed research before the beginning of any health research in Nepal. The ERB should also be involved in the on-going evaluation of research projects that are approved by the ERB.
- 1.6 The ERB is 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.

## **2. Membership of the Ethical Review Board**

### **2.1 The Executive Board (EB) of NHRC determines membership of the ERB.**

- 2.1.1 When a person is required for the ERB a name (or names) will be submitted by the Member-Secretary to the EB along with an explanation as to why this person is being nominated to be a member of the ERB. After presentation and discussion, the members of the (EB) will vote on this person's nomination to the ERB.
- 2.1.2 Institutions authorized by NHRC to have an ERB may constitute one of the following procedures laid out therein. The Board must be approved by NHRC.

### **2.2 Conditions of appointment to the Ethical Review Board include:**

- 2.2.1 A member should provide his/her full name, profession, and affiliation.
- 2.2.2 All ERB members should be capable of making an adequate time commitment.
- 2.2.3 All ERB members should consider all ERB deliberations as strictly confidential.
- 2.2.4 All expenses, if any, within or related to the ERB should be duly recorded.

### **2.3 Constituting an Ethical Review Board.**

The Executive Board for NHRC has identified the following criteria as guiding principles for appointing personnel to the Ethical Review Board.

- 2.3.1 The Ethical Review Board is made up of individuals who are appointed by the Executive Board. The members of the ERB should represent the various interests of the research community. Members of the ERB should be multi-disciplinary and multi-sartorial in composition, including relevant scientific expertise, balanced age and gender distribution and laypersons representing the interests and concerns of the community. The ERB shall not consist entirely of members of one profession. The ERB shall include at least one member whose primary concerns are scientific areas, and at least one member whose primary concerns are in non-scientific areas.
- 2.3.2 The NHRC Ethical Review Board shall have at least six and a maximum of eleven members with varying backgrounds to promote complete and adequate review of research activities.
- 2.3.3 The members of the ERB should have sensitivity to such issues as community attitudes, and the committee shall be able to ascertain the acceptability of proposed research in terms of institutional commitments and regulations, applicable law, and standards of professional conduct and practice.
- 2.3.4 If the ERB reviews medical research that involves a vulnerable category of participants, such as children, prisoners, pregnant women, or handicapped or mentally disabled persons, consideration shall be given to the inclusion of one or more individuals who are knowledgeable about and experienced in working with

these participants.

- 2.3.5 No ERB may have a member participate in the review of any health research proposal in which the member has a conflicting interest, except to provide information requested by the NHRC Ethical Review Board.
- 2.3.6 All the members of the ERB have a need for on-going education regarding ethics and health research.

## **2.4 Ethical Review Board Meetings**

- 2.4.1 The NHRC Ethical Review Board meets every two months. The meetings are announced well in advance. The members of the ERB should be give sufficient time to review the relevant documents for the meeting.
- 2.4.2 Minutes should be taken for each meeting, and minute from the previous meeting should be approved.
- 2.4.3 The researcher, independent consultants, and others may be invited to an ERB meeting, as circumstances require. The presence of the researcher or independent consultant should be in order to assist the ERB to reach a conclusion and help them with additional information, clarification, etc, but that none of them will be involved in the final decision (either consensus or voting). It is understood that all matters discussed in the ERB are confidential.
- 2.4.4 At all the meetings sufficient time should be given to allow for the full review and discussion of an application. Only members who participate in the review at the meeting should participate in the decision.

## **2.5 The Quorum**

**The quorum required for an ERB meeting is 50 percent or more of the total ERB membership.**

## **2.6 Members' Attendance at Ethical Review Board Meetings**

The ERB will conduct meetings on a regular basis. If a member of the ERB missed three consecutive meetings, this could be considered grounds for disqualification from the ERB.

## **2.7 Duration of Appointment to the Ethical Review Board**

The duration of the appointment to the ERB is for a period of three years. This can be renewed, with the approval of the EB, for another three years. If there is change, 50 percent of the members should be retained. Membership in the ERB should be staggered so that ERB members do not leave the ERB ail at the same time.

## **2.8 Disqualification from the Ethical Review Board**

If a member of the Ethical Review Board is deemed not to have adhered to the guidelines and policies as outlined in this document the following disqualification procedure may be enacted:

What is being striven for here is justice and due process:

- 2.8.1 A sealed and confidential letter will be submitted to the Chairman of the ERB that clearly states the reasons why a member of the Ethical Review Board is being suggested for disqualification from the ERB. The one submitting it must sign the letter.
- 2.8.2 Upon reception of this letter the Chairman of the ERB will review the letter and determine that it is authentic. He will then call in the one who wrote the letter to verify its contents. After this the Chairman will then call in the person suggested for disqualification and with him review the submitted letter. He will then give the person suggested for disqualification the opportunity to respond in writing to the submitted letter.
- 2.8.3 Two choices are now available to the person suggested for disqualification. The first choice is that he can submit a letter of resignation to the Chairperson of the Ethical Review Board and follow the resignation procedure.
- 2.8.4 The second choice is that after submission of his written response to the Chairman, the Chairman of the ERB presents the case to the members of the ERB for their review and final decision. A decision will be reached by voting of the ERB members taken at 50 percent plus 1. The final decision of the ERB will be submitted to the individual suggested for disqualification as well as to the individual who submitted the letter suggesting the disqualification.

*It is understood that such matters are highly confidential and all attempts should be made for due process*

## **2.9 Resignation Procedure from the Ethical Review Board**

At any time a member of the Ethical Review Board can submit his/her letter of resignation to the Chairperson of the ERB. The ERB Chairman then submits this letter as well as his recommendation to the Chairman of the EB. The Chairman of the EB presents the resignation letter and attached letter from the Chairperson of the ERB to the members of the EB for their final decision. The final decision from the EB is communicated by the Chairman of the EB to the Chairperson of the ERB who then communicates the decision to the individual who originally submitted the resignation letter.

## **3. Criteria for NHRC Ethical Review Board Approval of a Research Proposal**

In order to approve health research all of the following requirements must be satisfied:

### **3.1 Risks to subjects are minimized:**

1. Using procedures which are consistent with sound research design, and which do not expose participants to risks and
  2. Using procedures already being performed on the participants for diagnostic or treatment purposes.
- 3.2 Risks to subjects are reasonable in relation to anticipated benefits. In evaluating the risks and benefits, the ERB should consider only those risks and benefits that may result from the research.
  - 3.3 Selection of participants is equitable. In making this assessment, the ERB should take into account the purpose of the research, and the setting in which the research will be conducted. The ERB shall be particularly cognizant of the special problems of research involving the vulnerable population of the Nepalese society including children, prisoners, pregnant women, mentally disabled persons, or economically or educationally disadvantaged people. If the research involves primarily the vulnerable population additional safeguards should be included in the research to protect the rights and welfare of these people.
  - 3.4 Informed consent will be sought and properly documented from each prospective research participant or the participant's legally authorized representative.
  - 3.5 When required, the research plan makes adequate provision for monitoring the data collected, to ensure the safety of subjects.
  - 3.6 When appropriate, there are adequate provisions to protect the privacy of participants, and to maintain the confidentiality of data.
  - 3.7 There is a mechanism for compensation in case of injury.
  - 3.8 It is clear to the research participant that he/she can withdraw from the research at any time without fear of any action.
  - 3.9 The ERB should receive a written notice from the researcher upon the completion of the research as well as a final summary or full report of the research study.

#### **4. Decision Making Process of the Ethical Review Board**

- 4.1 The ERB will attempt to arrive at all *decisions through consensus*. When consensus is unlikely or not possible, it is recommended that a vote be taken.
- 4.2 In cases of *needed revision*, clear suggestions for revision and the procedure for having the application re-submitted for review should be stated.
- 4.3 A *negative decision* should be supported by reasons that are clearly stated.

#### **5. Communicating Decision from the ERB**

- 5.1 The NHRC Ethical Review Board shall *notify the researcher in writing of its decision to approve or disapprove the proposed research activity, or of modifications required to secure ERB approval of the research activity*. This should be accomplished within two weeks of the meeting.
- 5.2
- 5.3 If the ERB decides to *disapprove a research activity*, it shall include in its written notification a clear statement of the reasons for its decision, and give the researcher an opportunity to respond in person or in writing.
- 5.4 In the case of a *positive decision*, the ERB sends information regarding the responsibilities of the applicant such as: confirmation of the acceptance of any requirements imposed by the ERB; submission of progress report(s); the need to notify the ERB in cases of protocol amendments (Other than amendments involving only logistical or administrative aspects of the study); the need to notify the ERB in the case of amendments to the recruitment material, the potential research participant information, the informed consent form; the need to report serious and unexpected adverse events related to the conduct of the study, or significant decisions by other ERBs, and the information the ERB expects to receive in order to perform ongoing review and the final report.

#### **6. On-Going Review by the Ethical Review Board**

- 6.1 The NHRC Ethical Review Board shall conduct continuing review and monitoring of all approved health research at intervals appropriate to the degree of risk, and shall have authority to observe or have a third party observe the consent process and the research.
  - 6.1.1 The ERB has a right to monitor approved studies.
  - 6.1.2 A fee for the ethical review should be included in the protocol.
  - 6.1.3 The following instances or events require the follow-up review of a study:
    - 6.2.1 Any protocol amendment likely to affect the rights, safety, and/or well being of the research participants or the conduct of the study.
    - 6.2.2 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.

- 6.2.3 Any event or new information that may affect the benefit/risk ratio of the study.
  - 6.2.4 A decision of a follow-up review should be issued and communicated to the researcher, indicating a modification, suspension, or termination of the ERB's original decision or confirmation that the decision is still valid.
- 6.3 Proposals should have a statement stating the mode of monitoring.

## **7. Suspension or Termination of an Approved Research**

- 7.1 The NHRC Ethical Review Board shall have the authority to suspend or terminate approval of health research that is not being conducted in accordance with the ERBs requirements, or that has been associated with unexpected serious harm to participants.
- 7.2 Any suspension or termination of approval shall include a statement of the reasons for the ERBs action, and shall be reported promptly to the researcher.
- 7.3 If a researcher decides to terminate the research, he/she should notify the ERB of this decision and provide the reasons. A summary report of the study should be submitted to the ERB.
- 7.4 In the case of a suspended or terminated research study the ERB can recommend that appropriate action be taken by NHRC.
- 7.5 In the case of a suspended or terminated clinical trial any treatment initiated during the trial, if appropriate, should be continued as proposed by the ERB.

## **8. Independent consultation**

The NHRC Ethical Review Board may call upon or establish a standing list of independent consultants who may provide special expertise to the ERB 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.

## **9. Co-operation with Other Ethical Review Boards**

Health research may involve more than one institution. In the conduct of co-operative health research projects, each ERB is responsible for safeguarding the rights and welfare of human participants. With the approval of the NHRC Ethical Review Board, an institution participating in a co-operative project may enter into a joint review arrangement, rely upon the review of another qualified ERB., or make similar arrangements for avoiding duplication of effort. Terms of reference for the procedure should be formulated beforehand.

## **10. Office/Officers of the Ethical Review Board**

The ERB will have clearly defined officers that include a chairperson and a member-secretary. The chairperson's responsibilities include: calling of the meetings, setting the agenda, notification of decisions. The Secretary's responsibilities include: keeping the minutes of all the meetings, maintaining the ERB files and co-ordinating all correspondence.

## **11. Ethical Review Board Records/Secretarial Reporting**

The NHRC Ethical Review Board shall *prepare and maintain adequate documentation* of ERB activities, including the following:

- 11.1 Copies of all research proposals reviewed, including the approved sample consent documents, progress reports submitted by investigators, and reports of injuries to participants.
- 11.2 Minutes of ERB meetings, which shall indicate the attendance at the meeting, actions taken by the ERB, the vote on these actions, including the number of members voting for, against, and abstaining; the basis for requiring changes in a or disapproving research and a written summary of the discussion of issues and their resolutions.
- 11.3 Records of continuing review activities.
- 11.4 Copies of all correspondence between the NHRC Ethical Review Board and the researchers. This includes a copy of any decision and any advice or requirement sent to researchers.
- 11.5 An up-to-date list of NHRC Ethical Review Board members.
- 11.6 Written procedures for the NHRC Ethical Review Board.
- 11.7 The CV s of all ERB members.
- 11.8 Record of all income and expenses of the ERB.
- 11.9 A record of the notification of the completion, or premature suspension or termination of a study.
- 11.10 Final summary and/or final reports of all suspended/terminated or completed research studies.

These records shall be retained in an *active file for at least three years*, and records relating to research that is conducted shall be retained for at least three years after completion of the research. All records shall be accessible for inspection by authorized personnel.

## **12. Expedited Review Procedures**

Research activities involving no risk or minimal risk, and in which the only involvement of human subjects will be in one or more of the following categories, may be reviewed by the NHRC Ethical Review Board through the expedited review procedure.

Therefore in order to expedite the health research review process in such cases as noted below the Chairman of the ERB or a person designated by him/her can expedite the decision making process as indicated by the ERB.

- 12.1 Collection of hair and nail clippings, in a non-disfiguring manner; deciduous teeth, and permanent teeth if patient care indicates a need for extraction.
- 12.2 Collection of excreta and external secretions, including sweat, uncannulated saliva, placenta removed 'at delivery and amniotic fluid at the time of rupture of the membrane prior to or during labour.
- 12.3 Recording of data from subjects 18 years of age or older, using non-invasive procedures routinely employed in clinical practice. This includes the use of physical sensors that are applied either to the surface of the body or at a distance, and do not involve input of matter or significant amounts of energy into the subject, or an invasion of the participants' privacy. It also includes such procedures as weighing, testing sensory acuity, electrocardiography, electroencephalography, thermography, and detection of naturally occurring radioactivity, diagnostic echography, and eletroretinography.
- 12.4 Voice recordings made for research purposes, such as investigations of speech defects.
- 12.5 Moderate exercise by healthy volunteers.
- 12.6 The study of existing data, documents, records, pathological specimens, or diagnostic specimens.
- 12.7 Research on individual or group behaviour or characteristics of individuals, such as studies of perception, cognition, game theory, or test development, where the investigator does not manipulate subjects' behaviour, and the research will not involve stress to subjects.
- 12.8 Serious outbreaks of disease and similar emergency situations.

### **13. Information Researchers Provide to the ERB**

Some specific information the researcher needs to provide to the Ethical Review Board:

- 13.1 Professional *qualifications* and stated research experience as evidenced by research publications.
- 13.2 *Research Protocol* that includes addresses, title of the research, purpose of the research, reasons why human participants are required (or not required) for the research, sponsor of the search, results of previous related research, justification for use of any special/vulnerable participant population, study design, the descriptions of procedures to be performed and the previsions for managing adverse reactions. The- institution of affiliation of the Principal Investigator (PI) and the institution where the research is being conducted as well as addresses, and concurrence of the institution, if applicable.
- 13.3 The *informed consent document*. Details of the consent procedure should be given including the language difficulties, the procedures for documentation of informed consent, the procedures for obtaining consent from any minors, and the

use of witnesses or translators.

13.4 *Compensation* to the human subjects for participation in the research, any compensation for injured research participants, provisions for protection of participants' privacy, extra cost to participants for participation in the study, extra costs to third party payers because of the participants' participation.

13.5 The ERB and the prospective research subject should know if the researcher stands to gain financially (e.g. through a bounty paid by a drug company) in enrolling a patient.

#### **14. Procedure for Submitting the Proposal**

Procedure for submitting health research proposals to the Ethical Review Board

- 14.1 The principal investigator submits the research proposal along with an abstract and the consent form, as well as other required material, to the Secretary of the Ethical' Review Board at least one month prior-to the meeting of the ERB.
- 14.2 The Secretary of the ERB keeps a record of all submitted research proposals as well as the date of their arrival.
- 14.3 The Secretary submits the recorded research proposal to the Chairperson of the ERB.
- 14.4 The Chairperson of the ERB assigns a submitted research proposal to one Board member for a thorough review. The Chairperson may also assign a person to lead the discussion for each proposal. The member- reviews carefully the proposal and relates this to the consent form. The member evaluates .the research proposal for ethics, scientific merit, and the adequacy of the consent form. The member is then responsible to give a written report of his/her findings at the next ERB meeting.
- 14.5 The Secretary attending the meeting prepares a detailed account of the meeting.
- 14.6 After the meeting, the Chairperson, or a designated member of the ERB, notifies the researcher of the ERB decision.
- 14.7 The study is then -recorded in the health research database.
- 14.8 Timely progress reports as designated by the ERB are submitted to the Chairperson of the ERB by the researcher.
- 14.9 Upon the completion of the study the researcher makes a final report to the ERB.

## Section C

### APPENDICES Appendix I INFORMED CONSENT

**Process and information contained in a consent form may include:**

#### *Informed Consent*

#### **1. Obtaining consent from the subjects:**

It is important to know who will explain the research questions, and get informed consent from the participants. It is essential to determine how much time will be given to this important matter.

#### **2. Is there any coercion or deception?**

The Consent Form must clearly indicate that participants volunteer of their own free will. Is there anything being withheld from the participants at the time the consent is being sought?

#### **3. Information given to a research participant:**

3.1 The Consent Form should be submitted in English and Nepali (or the relevant local language, if appropriate) and should also include the following information:

3.1.1 The nature of the study-whether investigational, in terms of the use of drugs or procedures, or whether information seeking, if questionnaires or interviews are to be used.

3.1.2 The number of study participants.

3.1.3 The purpose/objective of the study.

3.1.4 The expected duration of the study and the frequency of the participant's involvement.

3.1.5 The participant's responsibilities.

3.1.6 A statement that the participation is voluntary.

3.1.7 A statement that the participant can withdraw from the study at any time without giving any reason and without fear.

3.1.8 A statement guaranteeing confidentiality.

3.1.9 A statement on reimbursement of study related expenses.

3.1.10 A statement on exactly what the research subject is expected to do in the research.

**For example: If a blood test, how much blood will be drawn, how many times? If a questionnaire, what are the questions about, how much time will it take to complete it, are any of the questions sensitive? (A copy of the questionnaire should be attached to the proposal.)**

3.1.11 In the case of a clinical trial, the following information should also be included:

- a) The trial treatment and the probability for random assignment to different treatments.
  - b) A detailed explanation of the trial procedures including all invasive procedures.
  - c) The potential or direct benefits (if any) from participation.
  - d) The alternative procedure(s) or treatment(s) that may be available.
  - e) The risks, discomforts, and inconveniences associated with the study.
  - f) The provisions for management of adverse reaction.
  - g) The provision of insurance coverage for any permanent disability or death caused directly by the investigational treatment or procedure.
  - h) That a study participant will be given information that may be relevant to his/ her willingness to continue participation.
  - i) The name and address, including telephone numbers, of the person to be contacted in case of adverse events or for any information related to the trial.
- 3.2 Sentence indicating that the participant has understood all the information in the consent form and is willing to volunteer/participate in the research.
- 3.3 Signature space for the subject, a witness, and the date.

## **APPENDIX II**

### **SCIENTIFIC MERIT OF A HEALTH RESEARCH PROPOSAL**

*The scientific merit of the submitted research proposal will be evaluated on the following criteria:*

- a) Relevance of the study to the national health priorities.
- b) Clearly stated objectives, hypothesis, and conceptual framework.
- c) Methodology suggested is valid for the objectives to be achieved.
- d) Sampling frame and size are adequate to reach the valid conclusions.
- e) Plans for data collection and analysis are adequate and appropriate.
- f) Researcher(s) and the research institution(s) have the capability of conducting the research. This includes submitting CVs of the researcher(s) as well as the necessary documentation from the institution(s).
- g) Plans for supervising and monitoring the data collection and analysis are appropriate.
- h) Mechanism for the dissemination of the findings has been articulated.
- i) Mechanism for the utilization of the study findings by other researchers or by the health system have been specified.
- j) The specific merit of a proposal could include provisions for research involving qualitative methodologies.

## APPENDIX III

### CHECKLIST FOR THE ETHICAL REVIEW OF PROPOSALS

Review of the research proposal for ethical clearance:

Title of the research proposal:

Date of review:

Reviewer:

Issue Under Consideration	Questions related to the main Issues	Yes	No	Remarks
Consent	Provision for informed consent			
	Clarity of the topics to the subjects.			
	Voluntariness of the consent			
	Inducements to participate, monetary or others			
	Unconditional withdrawal allowed?			
	Mechanism for taking consent from minors and disabled			
	Possibility of tricking participants to participants			
Benefits to the Participants	Possibility of intervention (Vaccine, drug or supplementation) being available to the participant population if found effective.			
Application of ethical Principals	Is the study essential to accomplish the goal?			
	Is there no other way to obtain the information?			
	Do the benefits outweigh the risks?			
	Are the risks reasonable and not excessive?			
	Do the researchers have adequate qualifications and competencies?			
Obligations of the sponsors	Assurance of medical services related to research for study participants.			
	Assurance of access to beneficial results to study participants.			
	Reasonable mechanisms for care and compensation in case of injury, resulting from research.			
	Provision of mechanism for capacity building of the national research institutions in the host country.			

## APPEND IV

### CHECKLIST FOR THE FUNCTIONING OF THE ETHICAL REVIEW BOARD

The following is an Ethical Review Board checklist. Review the checklist and provide one of three responses: *Yes response* means that the ERB has a written policy/procedure and it is current. *No response* means that a policy/procedure is lacking and needs to be updated. *N/A response* indicates that the section is not applicable and therefore a policy/procedure is not needed by the ERB.

#### **Does the ERB have written policies or procedures that describe?**

##### 1. The authority of the Ethical Review Board:

- 1.1 The institutional authority under which the ERB is established and empowered.
- 1.2 The definition and purpose of the ERB.
- 1.3 The principles that govern the ERB in assuring that the rights and welfare of the participants are protected.
- 1.4 The type of research proposal that the ERB must review.
- 1.5 The authority of the ERB to approve, disapprove, and modify studies based upon consideration of human participants well defined.
- 1.6 The authority of the ERB to require progress reports from the researchers and to oversee the conduct of the study.
- 1.7 The authority to suspend or terminate approval of a study.
- 1.8 The authority to place restrictions on a research study.
- 1.9 The ERB's relationship to the Executive Board of NHRC.
- 1.10 The ERB's relationship to other committees, departments, ministries, and other institutions.
- 1.11 Meetings of the Ethical Review Board:

#### **2. Membership of the Ethical Review Board:**

- 2.1 Number of members.
- 2.2 Qualification of members.
- 2.3 Diversity of members on the ERB.
- 2.4 Alternate members (if required).

#### **3. Management of the Ethical Review Board:**

- 3.1 The Chairperson (selection and appointment, length of term/service, duties, removal from office.)
- 3.2 The ERB members (selection, and appointment, length of term/service, duties, attendance requirements, removal from the ERB).

- 3.3 Training for the ERB members, orientation, continuing education, reference material.
- 3.4 Compensation of ERB members.
- 3.5 Secretarial/administrative support staff (duties responsibilities).
- 3.6 Resource material (includes meeting area, files space, office equipment).
- 3.7 Conflict of interest policy for ERB members.

#### **4. Meeting of the Ethical Review Board:**

- 4.1 Scheduling of meetings.
- 4.2 Circulating the agenda, time, and place of the meeting.
- 4.3 Circulation of all review material for the meeting.
- 4.4 Criteria for approval.
- 4.5 Decision making policy (consensus, voting, quorum required, no proxy votes by written form or by telephone, prohibition against conflict of interest voting).
- 4.6 Further review/approval of ERB actions by other (override of disapproval is prohibited).

#### **5. Communication from the Ethical Review Board:**

- 5.1 To the researcher for additional information.
- 5.2 To the researcher conveying the ERB decisions.
- 5.3 To the NHRC Board conveying ERB decisions.

#### **6. Appeal of Ethical Review Board Decisions:**

- 6.1 Criteria for appeal.
- 6.2 Person to whom the appeal is addressed.
- 6.3 How an appeal is resolved.

#### **7. Ethical Review Board Record Requirements:**

- 7.1 ERB membership with qualifications.
- 7.2 Written procedures and guidelines.
- 7.3 Minutes of meetings.
- 7.4 Summary of discussions on debated issues.
- 7.5 Record of ERB decisions.
- 7.6 Retention of material reviewed and approved Consent Forms.
- 7.7 All correspondence to and from the ERB.
- 7.8 Budget and account records.

## **8. Functions and Duties of the ERB:**

- 8.1 Procedure for initial and continuing review of a research proposal.
- 8.2 Procedure for reporting to the researcher/institution.
- 8.3 Procedure for determining which research proposals need verification and changes since initial review.
- 8.4 Procedure for ensuring that changes in approved research are not initiated with ERB review and approval except where necessary to eliminate apparent immediate hazards.
- 8.5 Suspension or termination of ERB approval.

## APPENDIX V

### ETHICAL QUESTIONS

#### **Ethically Driving Questions for the Ethical Review Board to consider include:**

- 3.1 What questions does this research answer?
- 3.2 Are those questions relevant to the needs of the country?
- 3.3 Has/ve such research( es) been already conducted in Nepal? Elsewhere?
- 3.4 Has another ERB reviewed this proposed research? If yes, what was their decision?
- 3.5 Is it necessary to involve human subjects for the research?
- 3.6 Whom does the research put at risk?
- 3.7 What are risks? Identify them.
- 3.8 Whom does the research benefit?
- 3.9 Do the participants benefit at all from the study?
- 3.10 Do the participants have any risk from participating in the study? If so, what are those risks?
- 3.11 Do the benefits outweigh any risks?
- 3.12 How is informed consent obtained from the participants, and is the type of informed consent appropriate?
- 3.13 How can the participants opt out of the research once it is started?
- 3.14 Is the research" externally sponsored? If yes, what are the responsibilities of the external sponsor?
- 3.15 Is there 'any transfer of technology involved during the research process?
- 3.16 How are the' sponsors going to strengthen the research capability of the host institution?
- 3.17 Is there going to be transfer, of biological materials?

## Section D

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