

# **National Ethical Guidelines for Health Research in Nepal 2022**



**Nepal Health Research Council (NHRC)  
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## **Foreword**

### **Message from the NHRC**

It is indeed a great pleasure and privilege for NHRC to be able to revise a document entitled 'National Ethical Guidelines for Health Research in Nepal.' NHRC is currently exploring new ideas to overcome the challenges confronting health research. We hope this guideline builds on these very initiatives. NHRC has always been at the fore front of standards setting for ethics in health research. The council published the Ethical Guidelines in 2001, which underwent further revisions in 2011, 2019 and 2022.

National Ethical Guidelines for Health Research 2022 is an outcome of in-depth discussions and debates with the experts, involving diverse stakeholders, NHRC secretariat, Ethical Review Board (ERB) chairperson, former chairperson, and members. We believe NHRC's revised ethical guidelines will be acknowledged and used as a reference by the researchers in Nepal and beyond. This revised version of the guidelines has addressed many emerging ethical issues keeping in view the social, economic, cultural, legal and religious aspects of Nepal. The revised version of the guidelines also aims at sensitizing the government authority, health care institutions, policy makers, planners, research institutions and social scientists of Nepal on ethical obligations and best practices.

We expect that the researchers will be able to gain enhanced clarity about ERB of NHRC requirements, and an understanding of the standard templates, checklists for submission and monitoring compliance need. With the concerted efforts and collaboration of Government, private, public and other relevant organizations, we believe that our goal of preparing National Ethical Guidelines will ultimately result in the development of sound ethical practices in Nepal. We are confident that the government, health care institutions, and individuals will contribute to the guidelines' success.

We would like to express our sincere gratitude to NHRC Executive Committee Member specially to Prof. Dr. Mohan Raj Sharma, Prof. Dr. Prakash Ghimire, former ERB Chairperson (2018-2021), ERB Members, ERB secretariat, Prof. Dr. Mohan Raj Sharma and who have contributed to the development and completion of National Ethical Guidelines for Health Research in Nepal 2022. We'd also like to thank USAID's Suaahara II Program for helping us in editing the guideline.

**Dr. Pradip Gyanwali**  
**Member Secretary, NHRC**

**Prof. Dr. Gehanath Baral**  
**Chairperson, NHRC**

## **Preface**

Nepal Health Research Council (NHRC) has been entrusted and mandated with the responsibility of promoting quality health research in the country. NHRC Act, 1991 and its by-laws have mandated NHRC to publish, disseminate and implement guidelines to make health research scientifically and ethically sound. NHRC has taken steps with the contributions from experts to develop and update the ethical guidelines in different time periods.

NHRC has developed and published a variety of Guidelines including National Ethical Guidelines for Health Research in Nepal-2001 (first edition) and 2011 (second edition), National Health Care Waste Management Guidelines-2002, Ethical Guidelines for the Care and Use of Animals in Health Research-2005, National Guidelines on Clinical Trials with the Use of Pharmaceutical Products-2005, and Guidelines for Institutional Review Committees (IRC)-2005 and 2016.

Realizing the need for timely revision to incorporate newer developments in medicine, science and technology, NHRC executive committee formed a team of ERB members and secretariat staffs to update the existing version of the Ethical Review Guideline in 2018. The current version of the guidelines has attempted to address new concepts, guideline topics and recommendations in medicine, science and technology. The guideline has specific separate sections on basic and general ethical principles, responsible conduct of research, ethical review procedure, informed consent process, vulnerability, clinical trials, public health research, social and behavioral science research, human genetic testing, bio-banking, and research involving experimental animals and insect vectors. This guideline is based on basic principles of Nuremberg Code, the World Medical Association (WMA) Declaration of Helsinki, the Council of International Organization of Medical Sciences (CIOMS), International Ethical Guidelines for Biomedical Research Involving Human Subjects and the World Health Organization (WHO), International Conference on Harmonization (ICH) Guidelines for Good Clinical Practice (GCP).

This revised version of Ethical Guidelines has envisioned separate standard operating procedures (SOPs) for each component including functioning of the Ethical Review Board (ERB), review process and reviewer's roles and responsibilities, and Material Transfer Agreement (MTA) for transferring biological materials addressing intellectual property rights of the research organizations/researchers within the country. This document also incorporates section on the conceptualization of and strategies to mitigate conflict of interest for the reviewers/ERB members, while performing their assigned duties; separate sections on requirements for externally funded research; monitoring of ethical conduct of research; bio repository; animal handling; research using genetic materials/embryos; and research during emergencies.

ERB expects all the researchers and institutions involved in health research to familiarize themselves with and adhere to the principles and guidelines as laid down in this document. Finally, ERB acknowledges the contribution of subject experts, former NHRC Chairperson Prof. Dr. Anjani Kumar Jha, ERB chairperson and members, and all who have directly and indirectly contributed to the completion of this guideline.

**Prof. Dr. Ramesh Kant Adhikari**

**ERB Chair, NHRC**

## Abbreviations

AE	Adverse Events
AMR	Antimicrobial Resistance
BA	Bioavailability
BE	Bioequivalence
CIOMS	Council of International Organizations of Medical Sciences
CoI	Conflict of Interest
COPE	Committee on Publication Ethics
CTR	Clinical Trial Registration
CV	Curriculum Vitae
DDA	Department of Drug Administration
DSMB	Data Safety and Monitoring Board
DTA	Data Transfer Agreement
E-consent	Electronic Informed Consent
EC	Ethics Committee
ERB	Ethical Review Board
FERCAP	Forum for Ethical Review Committees in the Asian and Western Pacific Region
GCP	Good Clinical Practice
GDPR	General Data Protection Regulation
GIS	Geographical Information System
GCLP	Good Clinical Laboratory Practice
GMP	Good Manufacturing Practice
GoN	Government of Nepal
HIV	Human Immunodeficiency Virus
ICD	Informed Consent Document
ICF	Informed Consent Form
ICH	International Conference on Harmonization
ICMJE	International Committee of Medical Journal Editors
ICMR	Indian Council of Medical Research
IMP	Investigational Medicine Product
IP	Investigational Product
IPR	Intellectual Property Rights
IRB	Institutional Review Board
IRC	Institutional Review Committee
LAR	Legally Authorized Representative
LGBT	Lesbian, Gay, Bisexual, and Transgender
MoHP	Ministry of Health and Population
MTA	Material Transfer Agreement
NHRC	Nepal Health Research Council
PI	Principal Investigator

PIS	Participant Information Sheet
QA	Quality Assurance
QC	Quality Control
RNA	Ribonucleic acid
SAE	Serious Adverse Events
SOP	Standard Operating Procedure
TB	Tuberculosis
TSC	Trial Steering Committee
ToR	Terms of Reference
UN	United Nations
WAME	World Association of Medical Editors
WHO	World Health Organization
WMA	World Medical Association

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## **Section1. Introduction**

Nepal Health Research Council (NHRC) has developed Ethical Guidelines for Health Research 2022' for the use of researchers, reviewers, research sponsors and regulatory authorities to ensure that the proposed studies involving human subjects are ethically justifiable and conform to the internationally accepted ethical principles. The main goal of the guidelines is to protect the rights and the dignity of the research participants as well as to ensure essential research of high social and scientific value. NHRC's Ethical Guidelines for Health Research is cognizant of and based on national, regional, and international guidelines and research practices.

### **1.1 Historical background**

Nepal Medical Research Committee (NMRC) was established on April 15, 1982 under Ministry of Health as the first regulatory body for health research in Nepal. Nearly a decade after being involved in regulating Health Research in the country, an Act of Parliament established (NHRC) on 12 April, 1991 as an autonomous institution of the Government of Nepal. NHRC is primarily tasked to promote and coordinate health research to improve the health status of Nepalese people. Ministry of Health and Population (MoHP) is designated as a line ministry for reporting for the NHRC.

In 1995, the first NHRC's 'Ethical Guidelines' was published, which was revised in 2001 as 'National Ethical Guidelines for Health Research in Nepal.' Since then, the NHRC has been organizing workshops and consultative meetings on research ethics regularly in order to educate researchers as well as understand their difficulties in following the global ethical norms and standards. In 2005, 'Ethical Guidelines for the Care and Use of Animals in Health Research in Nepal' and 'National Guidelines on Clinical Trials with the Use of Pharmaceutical Products' were published. The senior researchers' consultations in 2008 recommended updating of the 'National Ethical Guidelines-2001' and related documents. 'National Ethical Guidelines 2001' was reviewed, revised and published in 2011 as 'National Ethical Guidelines for Health Research in Nepal and Standard Operating Procedure (SOP).'

Given the country's major political and socio-cultural changes in last decade and subsequent division of responsibilities among federal and provincial government, some ethical issues were raised demanding revision of the Ethical Guidelines of 2011, which eventually led to the development of 'National Ethical Guidelines for Health Research in Nepal-2019.' The Ethical Review Board (ERB) of NHRC was accredited by Forum for Ethical Review Committees in the Asian and Western Pacific Region (FERCAP) in 2019. The recommendation of the FERCAP was that the national guidelines should be in alignment with the practices endorsed by FERCAP. In addition, there was also growing concern regarding the exigency to address the newer areas of research such as research in public health emergencies, bio-banking, animal experimentation etc. Similarly, the need for the transparency of informed consent process was equally felt in order to protect the welfare, rights and safety of research subjects. Likewise, the formation and functioning of Institutional Review Committees (IRCs) and their

(SOPs) were also missing in the former ethical guidelines. All these issues mentioned above have been addressed by the ‘National Ethical Guidelines for Health Research in Nepal 2022.’

## **1.2 Scope of the Guidelines**

National Ethical Guidelines for Health Research in Nepal 2022 have been developed to assist researchers, sponsors, reviewers, regulatory authorities and beneficiaries of research outcomes. The document underscores legal and ethical issues as well as standard procedures that the researchers are required to consider while undertaking ethically sound and justifiable health research in Nepal.

The guidelines provided in the document are applicable to all types of health research in Nepal involving human beings, their biological specimens, health related data and experimental animals.

Overall, the document offers ethical guidelines and rules on broad range of topics for:

- Researchers while developing research proposals;
- Ethics committee and reviewers while reviewing research proposals for approval, monitoring of ongoing research and dissemination and utilization of research funding;
- Sponsors while approving, funding and utilizing the findings from research;
- Regulatory authorities while reviewing the proposals and monitoring the research process to assess the comprehensiveness of their guidelines.
- Policy makers to review the research funding and possible use of research funding in policies and programs.

## **Section2. Ethical Principles**

Autonomy, beneficence, nonmaleficence and justice are four ethical principles fundamental to research that involves human subjects. These internationally accepted four ethical principles are also the cornerstones of ethically valid health research. In addition to these four ethical principles, being respectful of research participants' environment is equally important to safeguard their wellbeing as well as the community's dignity.

### **2.1 Basic Ethical Principles**

Evaluation of proposals in health research in Nepal requires the incorporation of fundamental ethical principles namely autonomy, beneficence and nonmaleficence, justice, and respect for environment.

#### **a) Respect for the Autonomy of Participants**

- The researcher should respect participants' autonomy throughout the research process. This principle of autonomy is based on the premise that an individual participant, when fully informed of involvement, benefits, and possible harm/in convenience of research activities, can independently decide on a correct course of action i.e. whether to participate or refuse to participate in a research activity. The basic requirements to ensure research participants' autonomy include their right to decide what is best for her/him.
- Researchers must safeguard the interests of individuals with impaired or diminished autonomy and ensure that the vulnerable persons are protected against any harm, abuse, or exploitation.
- Respect for human rights and human dignity should take precedence not withstanding the scientific value of research. Practices that violate human dignity should be prohibited or halted immediately.
- Provisions for human subjects' autonomy in health research should be implemented primarily through the process of 'Informed Consent.'

#### **b) Beneficence and Nonmaleficence**

Beneficence refers to the ethical obligation to maximize benefits and to minimize possible harms to individual participants. This ethical principle requires that all health research proposals/projects be reviewed in the light of potential benefits and risks on the human subjects and their environment. This does not prevent the participation of volunteers in health research. However, in all cases, health research should promote the wellbeing of human subjects as upheld by the principle of nonmaleficence (do no harm).

#### **c) Justice**

Justice requires individuals in similar circumstances be treated equally, and the differences between persons due to circumstances should be acknowledged and addressed. For example, individuals with similar health complaints should be treated equally. Likewise, justice requires an equitable distribution of the burdens and benefits of research participation. Differences in such distribution are justifiable only if they are based on morally relevant distinctions

between individuals, as reflected in cases where it is essential to ensure the protection of the rights and welfare of vulnerable persons.

The principle of justice incorporates an ethical obligation to protect the rights and welfare of vulnerable participants, or participants, who are exposed to vulnerable situations. People in vulnerable situations include those who are unable to express or protect their interests fully or partially. People in vulnerable situations are deemed to lack capacity to **give** consent adequately and/or ability to obtain quality and effective health care. These individuals could also be juniors or subordinate members of a hierarchical group or legally incompetent. Thus, special provision is mandatory for the protection of the rights and welfare of all participants in vulnerable situation. Vulnerabilities should be seen broadly in terms of individuals' adaptive capacity, exposure, and sensitivity which may at times be determined by their economic status, position as migrants, age, gender etc.

#### **d) Respect for the Environment**

This principle requires researchers to be sensitive towards community (e.g. adopting culturally and environmentally appropriate approach) while undertaking health research. This principle is reinforced by the World Medical Association (WMA) declaration of Helsinki, which focuses on special precautions for the protection of the environment while conducting research. Every researcher is accountable for protection of social, cultural and natural environment and historical heritage of communities and societies, as well as biodiversity. This includes commitments to ensure proper and safe disposal of any hazardous waste, and left over investigational products (IP) from laboratory/clinical/field research; should return to the sponsor according to standard guidelines and notify to ERB.

In addition to above mentioned four core ethical principles, health research involving human subjects should also incorporate general (extension of core principles) ethical principles as outlined in Section 2.2.

### **2.2 General Ethical Principles**

**(i) Principle of essentiality:** With due consideration to all the options within the existing knowledge, the use of human participants in health research is justifiable only when it is inevitably indispensable for the advancement of knowledge that is valuable for the research subjects, community, environment etc. Essentiality of proposed research should be assessed by the competent Ethical Review Board/Institutional Review Committee.

**(ii) Principle of voluntariness:** Research participants' right to make decisions as to whether or not to participate in the research should be respected. In other words, research participants are free to withdraw from the research at any time without being penalized. Documented (written/visual/audio) informed consent guarantees that the rights of participants are protected.

**(iii) Principle of non-exploitation:** Principle of non-exploitation ensures that the research

participants are not subject to exploitation or any kind of abuse. Appropriate precautions are required to be in place to safeguard the rights, well-being and safety of vulnerable individuals.

**(iv) Principle of social responsibility:** Health research needs to be planned and conducted in such a way that it does not destroy the social fabric of communities. The research outcome must also benefit the community/society as a whole.

**(v) Principle of ensuring privacy and confidentiality:** Researchers are required to maintain privacy of the participants. Identity and records of the participants should be kept confidential, and access to such information should be limited to authorized individuals only. However, privacy of certain information such as suicidal ideation, homicidal tendency, risky behavior of participants with positive status of infectious diseases (HIV, TB, Influenza, COVID-19 etc.) can be breached only in consultation with the ERB and judicial bodies(if necessary). In other words, breach of privacy and confidentiality is justified only when supported by valid scientific or legal reasons, wherein individuals' right to life is considered to be more important than the research participants' right to privacy and confidentiality.

**(vi) Principle of risk minimization:** During the research process, all stakeholders (researchers, ERB/IRC members, regulators, sponsors etc.) should identify the potential risks and take precautionary steps either to eliminate or minimize risks. In addition, any kind of inconvenience or distress experienced by the research subjects should be met with fair compensation.

**(vii) Principle of benefit maximization:** During the research process, researcher should take decision that works in the best interests of the research participants. This principle of benefit maximization maintains that the researcher should take steps to maximize possible benefits to the research participants and the society.

**(viii) Principle of professional competence:** Health research involving human subjects should be conducted by qualified (in terms of education, training and experience) and competent persons, who can plan, conduct and monitor the research process with due consideration to research ethics.

**(ix) Principle of institutional arrangements:** Institution(s), where the proposed health research will be carried out, should ensure research governance which also includes capacity to make sound institutional arrangements (e.g. provision of essential infrastructures, including storage of the IP, human resources, funds, opportunities for training etc.) for high quality research.

**(x) Principle of transparency and accountability:** Transparency and accountability are two important ethical considerations to be incorporated in health research. In health research involving human subjects, researchers are ethically obliged to bring their work into the



public domain through dissemination of database, reports and publications while equally protecting their research subjects' right to privacy. Stakeholders (researchers, ERB/IRC members, regulators, sponsors etc.) involved in particular research should disclose any existing CoI and manage it properly. Besides, researchers should maintain impartiality, sincerity, justice and transparency while conducting health research in order to ensure accountability. Valuable sources of information such as records and notes should be preserved for the specified period of time for any possible external inspection/audit or other purposes.

**(xi) Principle of totality of responsibility:** All stakeholders (researchers, ERB/IRC members, regulators, sponsors, etc.) involved in health research, should be fully accountable for their engagements as they are bound directly or indirectly with national ethical guidelines and related protocols.

**(xii) Principle of environmental protection:** Researchers are ethically obliged to ensure that their work does not violate the existing guidelines and protocols pertaining to environmental protection. In other words, researchers should ensure that the protection of environment and resources is taken into consideration throughout their search process.

**(xiii) Principle of dissemination of research findings:** Researchers are ethically obliged to bring their research findings or, any further research (conducted using the same research findings) into the public domain through publications. The research findings should be shared with the local stakeholders, preferably through publication in local scientific journals. If the researcher plans to publish a scientific paper in an internationally acclaimed indexed journal, a summary of a research paper must be published in the local scientific journal. Publications resulting from the research should be subject to such rights as are available to the researcher and her/his associates as determined by the laws(s) in force at that time.

Overall, individual researcher or the research team is required to abide by 4 core and 13 general ethical principles (as mentioned above) while undertaking health research in Nepal.

## **Section 3. Responsible Conduct of Health Research**

Researchers have a significant role and responsibility to prevent possible scientific fraud and research misconduct. Researchers are guided by the standard ethical norms, values and relevant laws. Research teams are expected to maintain high ethical standards and fundamental values of research. The Responsible Conduct of Research (RCR) needs to address:

- Social values of research;
- Policies and priorities that influence health research;
- Issues that emerge during research planning and conduction;
- Professional, legal, and moral responsibilities of researchers, sponsors and institutions;
- Research monitoring, reviewing, and reporting;
- Authorships in research publications;
- Handling of scientific fraud and research misconduct; and
- Clinical trials registration (if needed);
- Collaboration and networking.

Academic/Research institutions should establish a research department within their institution to facilitate and manage research, grants, and all aspects of (RCR). Any health research involving human participants must obtain ethical approval from the ethics committees approved by NHRC. IRCs are allowed to review and approve research carried out within the institute as per the latest Ethical Guideline published by NHRC.

### **3.1 Social Values of Research**

It is the responsibility of the researcher to make sure that the research topic holds adequate social values in accordance with the prevalent norms and standards. While considering social values, the following issues need to be addressed:

- Relevance to the needs of the people/society/community/country where the study is to be conducted;
- In compliance with the contemporary ethical norms and standards; and
- Sensitivity and responsiveness to the locals' socio-cultural and ethnic values.

### **3.2. Policies and Priorities that Influence Health Research**

Health research must be guided by National Health Policy of Government of Nepal, National Health Research Strategies published by NHRC, and National Health Research Policy and priority areas set by NHRC. Researcher and research institution should develop SOP based on ethical guidelines of NHRC for the protection of human participants' rights and well-being. Researchers should also follow all the existing policies and guidelines for the safety and welfare of animals used in health research.

### **3.3 Issues that Emerge during Research Planning and Conduction**

To avoid or mitigate the possible CoI at every step of research (e.g. designing, site selection, ethical review, participant enrollment/follow up, data collection & interpretation, etc.), research institutes should develop and follow clear policies, strategies and SOPs.

### **3.3.1. Identifying, Mitigating and Managing Conflict of Interest**

**(a) At the level of researchers:** Researcher must identify and disclose if there is any financial and/or non-financial conflict between the interests of the researcher and the interests of those bodies representing the ethical oversight. Researcher should also express his/her commitment to time and resource investment in conducting the research.

**(b) At the level of reviewers:** Reviewer should declare CoI during review process if any of his/her close friends, family members and/or students have submitted the research proposal for obtaining research grants and approval. Reviewer should declare CoI if any of his/her close friends, family members and/or students are directly or indirectly involved in the research study.

**(c) At the level of research institutions:** Institution must declare CoI during research process and develop SOP to manage and mitigate CoI, if any. It should be communicated in a transparent way. Particularly when the institutions like NHRC are involved in research implementation, CoI should not interfere in any process of the ethical review, implementation monitoring, data analysis and recommendation to the government for policy making. The process of managing CoI should be clearly documented in the SOP.

**(d) At the level of ECs:** ERB members must declare their CoI (if any) and take appropriate actions to recuse themselves from the review and decision-making process on the protocol(s) related to their CoI; and, follow directives from the ERB.

### **3.3.2. Data Acquisition, Management, Sharing and Ownership**

- Researchers are ethically obliged to use ‘cultural by sensitive approach’ while dealing with their research subjects. In other words, researchers should be mindful of participants’ socio-cultural context while collecting information. In addition, since certain information requires informed consent or prior permission, researchers should have knowledge about the process, method and the whereabouts of obtaining informed consent. Given the importance of reliability of information in research ethics, it is equally important for the researchers to exhibit ‘research competence’ in acquiring credible information. Hence, researchers’ qualification and training hold a paramount importance. Researchers should also have an understanding of key issues, key concepts and the importance of data protection. For data protection, researchers should refer to European Union's General Data Protection Regulation (GDPR), 2018, and Nepal's Privacy Act, 2075 (2018), and the National Civil (Code) Act, 2017 (2074) of Nepal. Researchers should be able to develop research protocols, tools and SOPs as well. Research information and findings should accurately be recorded, interpreted, and reported by the researchers to ensure reliability of information.
- Collected data should be archived and analyzed (appropriately) using appropriate software.

The analyzed findings should be reported to IRC/ERB and concerned authorities, as required. Research roles and responsibilities framework should be clearly outlined. Moreover, researchers should clarify about the ownership and publication rights relating to research data before data collection starts. Memorandum of Understanding (MoU) (if needed) should also be signed between investigators and institutions or sponsors in advance. This also applies to any biological samples collected/stored during the study period to achieve the study objectives.

- Appropriate precautions should be taken to avoid or reduce the risk of damage, loss or theft, fire, flood, and other disastrous events. Data/biological sample files should properly be archived and stored in a secured place along with the creation of back-up system.
- Researchers should be aware of serious ethical challenges confronting ‘protection of data’ while processing and analyzing information involving human subjects such as:
  - (a) Any personal information or identifiers such as ethnic origin, political opinions, religious or ideological conviction, union membership, sexual orientation, biological samples, health status etc., and unique identification such as genetic and biometric data;
  - (b) Personal data of children, pregnant women, persons with disabilities, vulnerable people, and those who have not given their consent to participate in the study;
  - (c) Data processing procedures and methods that potentially risk violating research participants’ rights and freedoms;
  - (d) Large-scale personal data processing, large-scale systematic surveillance of a publicly accessible area, and merging and analyzing multiple data sets;
  - (e) Data fabrication and falsification i.e., research misconduct;
  - (f) Inaccurate data collection, management, or analysis which lead to skewed results that are used by others; and
  - (g) Domestic (from one institution to another) and/or international (from one country to another) transfer of data.
- Given the potential risks of abuse of data, researcher should be familiar with data protection measures that include:
  - (a) Anonymization of personal data;
  - (b) Data minimization i.e., collection of required data (sufficient enough to fulfill the study objectives); and
  - (c) Use of appropriate software or techniques or service providers (as per the resources available) for data storage and archival.
- If the data processing methods risk violating rights and freedoms of research participants, such risks must be disclosed during the process of obtaining informed consent. Without obtaining prior permission/approval from there Levant authorities such as ERB of NHRC or IRCs of the institutions (where proposed study is to be carried out), it is unethical to collect data for certain types of study such as:
  - (a) Health research involving human subjects;
  - (b) Health research involving experiments on animals;
  - (c) Biological specimen collection;
  - (d) Use of data sets from the bio-samples stored in the bio-bank for future research;
  - (e) Data from hospital/medical/police records, some institutions/library, databases and

archives;

(f) Photographs, recorded messages and notes; and

(g) Other copyrighted or patented processes or materials.

- Research protocols, tools and SOPs must be prepared, and research data and results should accurately be recorded, interpreted, and reported. If required, research protocols or tools should be modified to fit into the local context of Nepal.
- Data governance mechanism should be in place. If projects are conducted with international collaboration where sample require transferring, there should be a backup storage of samples in the country.
- Data sharing/ dissemination plan (when, how and with whom) should be mentioned in the research proposal, which should be approved by the competent ethical review committee before implementation.
- All cleaned data related to international collaboration should be submitted to Nepal Health Research Council/Concerned organization in a standard format after publication in Journal or as a report.
- Research team should include at least one statistician or who has adequate knowledge and experience on study design, data management, and statistical analysis.

### **3.4 Professional, Legal and Moral Responsibilities of Researchers and Sponsors**

Study team (that conducts the research), sponsor (that funds the research) and institution (where the research is conducted) should take respective professional, legal, and moral responsibilities to follow ethical principles and guidelines. Researchers involved in a collaborative study should work in tandem throughout the research process, right from the early stage of proposal development to the completion of the study. Same study protocol and SOPs signed and dated by National and International PI, should be followed in each site in case of multi-centric studies. Sponsor should uphold unbiased contract negotiation. While conducting collaborative research, a clear mechanism should be established for benefit sharing. There should also be a regulatory mechanism that discourages the use of unauthorized bio-specimens, data, and human resources.

Sponsor should also have provisions for capacity building of the institution/research team/local community involved in the study.

#### **3.4.1 Roles and Responsibilities of the Researchers/Investigators**

National Ethical Guidelines for Health Research in Nepal 2022 defines researcher or investigator as an individual or group of individuals who conceptualizes, initiates, and conducts a study. The ‘Principal Investigator’ is an individual or the leader of a group of individuals who initiates and takes full responsibility of health research being conducted. If there is more than one such individual, they may be called co-principal investigators/co-investigators. Co-Investigators (Co-Is) are individuals who make significant contributions, but are not fully responsible for and/or have full authority of the project. All investigators share common responsibilities of protecting the rights and welfare of the research participants

and ensuring credibility of data. However, despite sharing common ethical responsibilities and obligations, investigators perform their respective tasks based on clear delegation of responsibilities from the principal investigator.

**Investigator's Roles and Responsibilities:**

**Qualifications:** Investigators should-

1. Be qualified by education, training, and experience to assume responsibility for the proposed study.
2. Provide evidence of qualifications through up-to-date curriculum vitae and/or other relevant documentation requested by the ERB.
3. Ensure the selection of and maintain a list of appropriately qualified persons (co-investigators and research staff) to whom she/he has delegated duties related to the study.

**Adequate resources:** Investigators should-

1. Assume responsibility for assessing and ensuring the availability of adequate resources including human resource, funding, facilities, equipment and supplies. In doing so she/he should:
2. Have available an adequate number of qualified staff and adequate facilities for the foreseen duration of the study.
3. Provide training to the research team in order to ensure adherence to appropriate safety procedure and protocol. In case of clinical trials, training on Good Clinical Practices (GCP)/Good Clinical Laboratory Practice (GCLP)/General Data Protection Regulation (GDPR) (valid for 3 years) should be provided.
4. Arrange for a Site Initiation Visit to ensure that the appropriate infrastructure and resources are in place in case of clinical trials.
5. Demonstrate (e.g., based on retrospective data) a potential for recruiting the required number of suitable subjects within the agreed recruitment period.
6. Have sufficient time to properly conduct and complete the study within the agreed time frame.

**Medical care of study participants:** A qualified physician or appropriate health worker (e.g. dentist, psychologist, etc.) who is an investigator should be responsible for all study-related medical decisions during the duration of the study. In doing so she/he:

1. Should ensure that adequate medical care is provided to a study participant for any adverse events
2. Inform a subject when medical care is needed for inter current illness (es) of which the investigator becomes aware.

**Communication with ERB:** The investigator is responsible for-

1. Development of the proposal in the prescribed format of the ERB, through online portal.
2. Applying and obtaining ethical approval from the ERB following the submission of all the required documents.
3. Disclosing and documenting all the financial and non-financial (COI) also ensuring

good practice and documentation of the mitigation measures where there is any possibility of COI.

4. Informing the ERB/IRC and the sponsor, should she/he terminate or suspend a study along with a detailed written explanation of the termination or suspension.
5. Adhering to existing national and international law/regulations/guidelines.

#### **Compliance with study protocol**

1. Using the ERB approved version of the documents i.e. protocols, SOP, informed consent documents, data collection tools, etc. for the implementation of the research
2. Conducting research within a specified timeline as mentioned in the ERB approval letter and approved protocol
3. Submitting an amendment request and obtaining ERB approval if any changes are required in the original approved protocol before its implementation.

#### **Investigational products**

1. For studies using investigational products (IP), responsibility for their accountability rests with the investigator/institution. Investigators should:
2. Maintain an IP accountability log
3. Ensure IP is stored as specified by the sponsor's protocol and in accordance with regulatory requirements
4. Ensure IP is used only in accordance with the approved protocol.
5. Plan for returning to the sponsor or alternative disposition (destruction/disposal) of unused IP using an SOP, especially developed for the purpose
6. Informed consent of study participants
7. The investigator should comply with the applicable regulatory requirement(s) in obtaining and documenting informed consent as outlined in the section 5.
8. The investigator should have the ERB's written approval of the written informed consent form and any other written information to be provided to study participants. This also applies to any revision of content in the consent form and written information.
9. In emergency situations, when prior consent of the subject is not possible, the consent of the participant's legally acceptable representative, if present, should be requested. When prior consent of the subject is not possible, and the subject's legally acceptable representative is not available, enrolment of the participant should require measures described in the protocol, with documented approval by the IRB/IEC, to protect the rights, safety and well-being of the subject and to ensure compliance with applicable regulatory requirements. The participant or the legally acceptable representative should be informed about the study as soon as possible and consent to continue and other consent as appropriate should be requested.

#### **Records and reports:**

The investigator should-

1. Maintain adequate and accurate study records and source documents that include all pertinent observations on each of the study site's participants

2. Take measures to prevent accidental or premature destruction of study related documents
3. Retain study related documents for a period of at least 5 years after the end of study. These documents should be retained for a longer period however if required by the applicable regulatory requirements or by an agreement with the sponsor. It is the responsibility of the sponsor to inform the investigator as to when these documents no longer need to be retained.
4. Provide direct access upon request of the ERB/IRC, or regulatory authority all study related records.
5. Submit written summaries of the progress of the study, especially in the case of clinical trials, to the ERB annually, or more frequently, if requested by the ERB.
6. Submit a review report at least one month prior to the expiry of timeline of the study as stated in the approval letter from NHRC. This should be accompanied by an application for approval to continue the study.
7. Submit a written report to the ERB upon completion of the study.
8. Report all serious adverse events (SAEs) immediately to the sponsor and ERB except for those SAEs that the protocol identifies as not needing immediate reporting. The immediate reports should be followed promptly by detailed, written reports. The immediate and follow-up reports should identify participants by unique code numbers rather than by the subjects' names, personal identification numbers, and/or addresses. The investigator should also comply with the applicable regulatory requirement(s) related to the reporting of unexpected serious adverse drug reactions to the regulatory authority (ies) and the ERB.
9. For reported deaths, supply the sponsor and the ERB/IRC with any additional requested information (e.g., autopsy reports and terminal medical reports).
10. Take accountability for the content of all study related documents submitted to the ERB in addition to ensuring all documents are submitted in timely manner.

*Note: Verbal/oral consent should only be taken in exceptional cases, with precise and reasonable explanations, and only with prior ERB approval.*

### **3.4.2 Roles and Responsibilities of the Sponsor**

1. Sponsor in the document refers to individual/company, institution or organization who takes responsibility for the initiation, management and/or financing of a clinical trial. The role of sponsor is initiating the research including the protocol development. In general, sponsor should:
2. Ensure that the ethical and technical competent research is receiving the support;
3. Ensure that study site is ready in terms of infrastructure, human resources, logistics and supply before the initiation of the study. Monitor the study before, during and after the completion of the research activities.
4. Ensure that the release of fund to carry out the research is timely and regular;
5. Justify the inclusion of vulnerable groups in the proposal and make provisions to safe guard them;
6. Justify the exclusion of some specific participants (if any);



7. Facilitate monitoring by ERB and ensure that the Quality Assurance (QA) and Quality Control (QC) procedures are in place;
8. Ensure that the research participants and the study team are well protected especially when the study is on sensitive topics;
9. Select investigator(s), ensure availability of study site(s), and assure relevant qualification of the study team to conduct the study;
10. Develop, maintain, modify, and ensure the availability of research support systems and tools; and
11. Avoid exerting influence on research design, data collection, data analysis and publication of research findings.

### **3.5 Research Reporting**

1. Submission of final report by sponsor/ Principal Investigator to ERB/IRC within 3 months of completion of the study is mandatory. The research report should be in a standard format as available in online system. It should also contain information in accordance with the study objectives, with clear scientific analysis assuring transparency and credibility.
2. Upon submission of the final report, ERB/NHRC should arrange review of the report by the subject expert within two weeks with due attention to maintaining confidentiality, integrity and honesty. The reviewer should provide the feedbacks and comments within four weeks. Researcher or sponsor may be asked to present the revised reports with incorporated feedbacks/comments within a month to subject experts, NHRC, MOHP and other relevant people with similar research interests.
3. Researchers should duly acknowledge the contributors in the report.
4. Investigators should follow international and national requirements and guidelines, including National Ethical Guideline and ICMJE Guideline when publicizing the raw or analyzed data.

### **3.6 Authorships in Research Publications**

1. Research institution should follow the authorship policies and guidelines of International Committee of Medical Journal Editors (ICMJE), Committee on Publication Ethics (COPE) and World Association of Medical Editors (WAME).
2. The authorship should be defined before the start of writing the research article. No one should be offered or should accept gift authorship without substantially contributing to the research process or writing of the article.
3. The principal author should do most of the research work related to the manuscript submitted for the publication. For the fulfillment of authorship criteria, all efforts should be made to provide the researchers an opportunity for authorship based on national and international guidelines of ICMJE/COPE/WAME. While doing so, one should also adhere to rules and regulations of the university/institution.

### **3.7 Handling of Research Misconduct**

Research misconduct may occur due to fabrication, falsification, and plagiarism of the data. ERB/IRC should institute fair investigation of the complaints/claims for misconduct through formation of specific committee with reference to its ToR, to investigate the misconduct and suggest appropriate mitigation measures. This process should take priority based on the risks associated with and/or sensitivity of the misconduct. It may be on the same day (however, not later than a month) of misconduct being reported by an individual/institution or broadcast by the media.

### **3.8 Clinical Trials Registration**

Clinical trials involving human participants such as trials of vaccines, drugs, herbal products, complementary medicine products, medical device, surgical procedures, alternative medicine procedure, etc. and public health intervention involving clinical procedures should be registered in the WHO accredited clinical trial registries. Researchers should provide its registration number to the ERB while submitting the proposal for ethical approval.

In addition to ethical approval from ERB, permission from national regulatory authority (DDA permission as per Drug Act 1978) needs to be obtained before implementation of the trial.

### **3.9 Collaboration and Networking in Research**

Collaboration and networking can be done with colleagues/experts/institution to conduct multi-centric research. Such collaboration may entail sharing of tools & techniques, research products, sample, specimens etc.; following the same SOPs; co-owning copyright of research materials and research data, final product of the study, publication etc.; management of CoI; and commercialization of the results/products by the collaborating centers.

All parties involved in MoU should provide detailed information on the nature of collaboration prior to submitting the MoU to ERB/IRC for review and Ethical approval of the proposal.

**3.9.1 Externally Sponsored Research:** Externally sponsored research should fulfill following conditions-

- 1) Research should be based on local needs and priorities.
- 2) Researcher should be aware of and sensitive towards the locals' socio-cultural, religious and environmental norms and values.
- 3) Researcher should provide scientific evidence-based rationale for the selection of study site in Nepal. Sponsor should also provide evidences that the same research cannot be carried out in the sponsor's country due to lack of disease burden of same scale as in Nepal.
- 4) Researcher should submit ethical approval of the responsible IRB in the sponsoring

country.

- 5) The proposal should contain information on how the proposed research would significantly contribute to the enhancement of the research capacity in Nepal.
- 6) Research process should be transparent and ensure a high ethical standard, as approved by the competent EC.
- 7) Sponsors should ensure research participants of insurance/compensation in context of research involving more than minimal risks.
- 8) If the biological specimens need to be transferred to a laboratory outside Nepal, a MoU or MTA should clearly address IPR, roles, responsibilities and obligations of each partner organizations/investigators including publication roles, data confidentiality, and post-study benefit sharing. The ERB should evaluate the feasibility of the testing in the country's laboratories along with its risk and benefits on a case-by-case basis before granting a permit to transport biological specimens to another country. Once approved, a letter of transfer approval could be issued for facilitation of custom clearance/courier clearance in line with International Air Transport Association Guideline.

### **3.9.2 Institutional Research Arrangements**

Any research activity should only be started after ensuring appropriate institutional arrangements. Such institutional arrangements should be ensured before applying for the ethical review of the study. An effective institutional arrangement includes involvement of competent researchers and support staff; formation of an organizational set up according to the requirement of the research; assurance of research participants' safety; protection of confidentiality of data; effective dissemination of research findings; etc. Institutional arrangements also involve providing secure place for the preservation and archiving of research materials, data and reports. Institutions undertaking a collaborative study should also follow the same standard of the protocol and procedures. The research conducted in any institution should obtain no objection letter from the institution. In case of investigator-initiated trial, a commitment letter from the institution for the management of AE/SAE should be obtained/provided.

### **3.9.3 Special Considerations in Collaborative Research**

1. Any changes in partnership should be approved by the ERB before initiation of the study.
2. For international collaborative research, there should be one Nepalese PI and site Co-Principal Investigators relevant to the research project. Also, Nepalese PI should take all the legal, technical and ethical responsibilities of the project in Nepal.
3. International collaborators should strengthen their institutional capacity in terms of human capital and infrastructure.

## **Section 4. Ethical Issues in Health Research**

Ethical challenges are inevitable in health research on account of various reasons, including the involvement of human subjects. Some of the key ethical challenges confronting health research include ensuring safety and well-being of the participants, markedly the vulnerable groups; effective assessment of risks and benefits; maintaining transparency, privacy, and confidentiality; compensating and paying participants for their time; managing CoI; collection, storage and transfer of samples; promoting fair and equitable benefit sharing; etc. In addition to ensuring participants' safety and benefit, the research team should also improve their efficiency/capacity in conducting research.

### **4.1 Research Involving Vulnerable Populations**

Vulnerable populations are those who are relatively (or absolutely) incapable of protecting their own interests. More formally, they may have insufficient power, intelligence, education, resources, strength, or other needed attributes to protect their own interests. Moreover, a researcher may consider the selected individual as vulnerable provided that he/she has following characteristics.

1. Person's autonomy is compromised or the person is incompetent of making a voluntary informed decision for himself/herself. For example, individual who is unconscious, or differently abled.
2. Person is able to provide informed consent, but his/her understanding is compromised because of the circumstances, unjustifiable influence (such as intimidation from the third party), anticipation of benefits etc.
3. Person is susceptible to exploitation due to his/her disadvantaged position relating to his/her social, economic and political settings.

Although there are many methods of assessing vulnerability, ERB takes into consideration individuals' social status and physical condition to assess vulnerability. However, status of an individual's vulnerability is subject to change in accordance with the changes in his/her social status/environment, or physical attributes/conditions.

#### **Social Status**

1. Refugees, immigrants, migrant workers, sex workers, slum dwellers, orphans, homeless etc.;
2. Women and sexual minorities such as lesbian, gay, bisexual, transgender etc.;
3. Individuals who are at the lower echelons of hierarchical structures such as prisoners, public forces (armies, armed forces, police forces), students, employees, etc.

#### **Participant's Condition:**

Children (minors or individuals under the legal age of consent, i.e. less than 18 years); elderly; pregnant and lactating women; differently abled person; juvenile delinquents under legal trial; victims of traumatic events, disease outbreak, natural disasters and conflict; individuals with mental illness or cognitive impairment; individuals with a life-threatening

illness or condition(e.g., cancer, HIV/AIDS, etc.) or terminally ill persons, and individuals who have poor decision-making powers/poor access to healthcare.

*Note: This list of vulnerable population is not exhaustive, and in case of uncertainty, the Ethical Review Board/Institutional Review Committee may decide whether or not research participant meets the criteria for vulnerability.*

If vulnerable populations are to be included in research, researcher/institution is required to follow specific procedures and ethical obligations to protect such research participants. In other words, research team must ensure that the additional steps will be taken to protect the rights, dignity, safety and well-being of vulnerable participants. Researcher must capacitate vulnerable individuals in order to enable them to make decisions regarding whether or not to participate in the health research. If vulnerable individuals lack the ability to consent, a legally authorized representative (LAR) must be involved in decision making procedure. Throughout the process, researcher should ensure that the privacy and confidentiality of vulnerable population are maintained to safeguard their rights, safety and well-being.

#### **4.1.1 Additional Safeguards/Protection Mechanisms**

Vulnerable populations are at high risk of being manipulated or easily affected by the external factors and circumstances. Therefore, when recruiting vulnerable individuals as research participants, additional precaution should be taken to avoid putting vulnerable population at even greater risk of abuse, exploitation, etc., or situation where vulnerable individuals are likely to undermine their voluntariness and well-being. Key points to be considered to ensure protection for vulnerable population include:

1. Inclusion of vulnerable population in the study must be justified;
2. Assessment of benefits and risks;
3. Risk mitigation strategies should be outlined;
4. Ensuring absence of coercion, force, threat, undue influence etc.;
5. Assured incentives for participation;
6. Information about the research, benefits, risks and alternatives (if any) should be communicated in the language prospective participants understand;
7. Any possibility of CoI between the vulnerable participant and LAR should be addressed.
8. Efforts to address issues where participants may be susceptible to discrimination and stigmatization must be ensured; and
9. Support system to deal with associated medical and social problems of research participants should be in place.

#### **4.1.2 Research Involving Children**

If a research question can be answered with adults as participants, research should not involve children. Research involving children should be carried out only after taking informed consent from their parents or LAR and, assent from the child if applicable. Conditions in which Health Research can be carried out with children:

1. For the disease which is only seen in children
2. The information that cannot be obtained by alternative means
3. Health issues, that are significantly different for adults and children
4. Instances where adverse effects of drugs/vaccines need to be checked or investigated in children; and
5. In cases, where drug delivery formulations are required to follow precise, safe, and age-appropriate route of administration.

*Note: This list of conditions is not exhaustive. Ethics Committees shall ensure that the research with children is ethically justified.*

#### **4.1.3 Research Involving Pregnant and Lactating Women**

Interventional research involving pregnant women and lactating mothers should not be carried out unless the study is related to their physiological condition, and the required information cannot be generated from other means.

Justification for inclusion of pregnant and lactating women in the clinical trials needs to be provided. Similarly, for some groups of women, informed consent can be challenging because of socio-cultural reasons. In such cases, with due respect to the woman's autonomy, the researcher must also follow the requirements of local cultural practices so as not to disturb the harmony in the household/family/community.

Researchers should provide with proper justification for inclusion of pregnant and lactating women in the clinical trials e.g. trials designed to test the safety and efficacy of a drug for reducing perinatal transmission of Human Immunodeficiency Virus (HIV) infection from mother to child, trial of a device for detecting fetal abnormalities etc.

Women of reproductive age should be informed of the probable risk to the fetus if they become pregnant during the period of their recruitment in the clinical trials. In such circumstances, researchers need to advise these women to use an effective contraceptive method and talk about the options available in case of failure of contraception. In case of unexpected pregnancy, they should not be automatically removed from the clinical trial unless there is evidence showing potential harm to the fetus. However, even though clinical trials were to be harmless for the pregnant women, they must be offered the option to withdraw or continue to participate in the trial. If women agree to continue with the trial, researchers and sponsors should monitor such women participants comprehensively and offer the required support to the women for a certain time period.

#### **4.1.4 Research involving Sexual Minorities and Sex Workers**

Sexual minorities and sex workers may face violence, stigmatization, discrimination, etc. Hence, research involving such population is challenging in itself. Given the unique nature of challenges, it is important for the researcher to be responsible and respectful in ensuring that their research participants' rights and well-being will be safeguarded without any

compromises. Moreover, research participants should be assured that the research practices and the outcomes will not further reinforce discrimination or the stigmatization of already vulnerable population.

#### **4.1.5 Research Involving Tribal and Indigenous Population**

Research targeting tribal and indigenous population is justified only if it is precise, diagnostic, therapeutic and protective in nature, with suitable benefits to the tribal and indigenous population. For any research that utilizes tribal/indigenous knowledge that has potential for commercialization, the details should be mentioned in the proposal as well as shared with the tribal groups through community engagements. However, gatekeeper consent should be obtained prior to approaching research subjects for community engagements.

#### **4.1.6 Research Involving Individuals with Mental Illness or Cognitive Impairment**

Research involving individuals with mental illness or cognitive impairments should be carried out only when the study is related to their condition, and the required information cannot be generated from other means.

#### **4.1.7 Research Involving Members of a Group within a Hierarchical structure**

For members of such group, additional safeguard mechanism should be ensured so that their participation is free of coercion.

#### **4.1.8 Research Involving Terminally Ill Persons**

Persons, who are in search of new interventions after having exhausted all available therapies, may be ready to provide consent for any new intervention that is not yet validated. In such circumstances, there should be appropriate consent procedures and the ERB should carefully review the recruitment procedures of such persons during the research process. There should be a process of additional monitoring to detect any adverse events at an early stage. If the new intervention is beneficial to the persons, the ERB should carefully review post-trial access to the medication.

### **4.2 Assessment of Risks and Benefits**

Risk refers to the situation that involves exposure to harm or danger. In health research, risk refers to chance or probability that a person will be harmed or experience an adverse health effect because of the participation in the research. Participants who are vulnerable are comparatively at higher risk than the non-vulnerable participants. Investigators/sponsors should incorporate risk and benefit assessment matrix in the submitted protocol. ERB/IRC should evaluate the proposed risk benefit matrix/information. ERB/IRC may grant approval for the trial on human subjects once it is convinced that the benefits of trial outweigh the risks. If there is any risk, mitigation measures should be incorporated by the researcher/sponsor. The document classifies different categories of risk in health research as

outlined in Box 1.

### BOX 1. Risk Categorization and its Descriptions

Types of Risk	Descriptions
<b>Less than minimal risk</b>	Probability of harm or discomfort anticipated in the research is nil or not expected. For example, research on anonymous or non-identified data/samples, data available in the public domain, meta-analysis, etc.
<b>Minimal risk</b>	Probability of harm or discomfort anticipated in there search is not greater than the one encountered in normal everyday activities performed by an average healthy individual or general population or, during the performance of routine tests where occurrence of serious harm or an adverse event (AE) is unlikely. Examples include research involving routine questioning or history taking, observing, obtaining body fluids, hair, saliva, urine etc., without invasive intervention.
<b>Minor increase over minimal risk or Low risk</b>	Increment in probability of harm or discomfort is slightly more than the minimal risk threshold. This may be present in the situations such as routine research on children and adolescents; research on persons in capable of giving consent; use of minimally invasive procedures that might cause no more than brief pain or tenderness, small bruises or scars, or very slight temporary distress, such as drawing a small sample of blood for testing; trying a new diagnostic technique in pregnant and breastfeeding women, etc. Such research should have a social value. Use of personal identifiable data in research also poses indirect risks such as social risks ( <i>stigma, work place discrimination, loss of respect, disclosure to family, isolation, etc.</i> ), economic risk (loss of employment), psychological harm ( <i>if the research is sensitive in nature and the participants risk being stigmatized if it is known that they are on the study, e.g.an HIV study</i> ) and discomfort. .
<b>High risk or more than minimal risk</b>	Probability of harm or discomfort anticipated in the research is invasive and greater than minimal risk. Examples include research involving any interventional study. E.g. using a drug, device or invasive procedure such as lumbar puncture, lung or liver biopsy, endoscopic procedure, intravenous sedation for diagnostic procedures, etc.

Source: ICMR, 2017, *National Ethical Guidelines for Biomedical and Health Research involving Human Participants*, Page 6.

Benefits to the participants refer to any sort of favorable outcome (direct or indirect) of the research. The participation in a research process should be of potential benefit to the participant or to his or her community or the population in general. Sometimes, benefits are commonly presented as available only during the study, which means the benefits end when the research is completed. The duration of any benefit associated or derived from the research participation must be clear to the potential participants beforehand. Benefits include the potential for better treatment, either immediately or in the future, and financial benefits in terms of compensation for being on the study and free or reduced price of the health care. Special attention is needed in determining how benefits are presented in individuals with limited access to health care services. Offering free health care to individuals, who would otherwise not have access to it, is a powerful incentive to participate in a research study and is potentially coercive. Researchers are responsible for ensuring that potential participants'



decisions are not clouded by the promise of health care or a potentially better (but unproven) new treatment. ERB should carefully review this. The risk/benefit ratio must be in favor of benefits and the researcher must demonstrate that all efforts have been made to minimize the risks and maximize the benefits. However, making precise judgments about the risk/benefit 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 collection, and assessment of information about all aspects of the research should be done, and alternatives should systematically be considered.

Relevant risks and benefits should clearly be spelled out in the proposal and informed consent document. When research involves significant risk, there should be an extra justification of such risk, and ERB should review this aspect and record it in the ERB meeting report. ERB should ensure a favorable balance of benefits and risks and assess the plans for decreasing the risks or, mitigating the effects before approving the proposal. If there are any altered risks in the study, the ERB should also assess such risks during ‘continuing review process’.

### **4.3 Privacy and Confidentiality**

Protection of confidential information provided by the participants and the community should be ensured to protect the individuals’ right and to avoid stigmatization and/or discrimination. It may not be possible to keep participants’ identity confidential in certain situation such as compelling scientific and legal requirements, where disclosures could be made with the permission of ERB (Box 2).

Researcher should not publish any information or photographs that may disclose the participant’s identity without obtaining his/her fully understood/informed consent.

#### **4.3.1 Data Privacy and Security**

When the research-based data is outsourced or shared for commercial gain, data privacy, data security, and possibility of legal liability should be safeguarded. There should be a mechanism (like data auditing by NHRC) to detect misuse of research-based datasets.

Research data sets whether in paper or in electronic format should be stored, without compromising security. Appropriate measures to be adopted for the protection of participants’ privacy and confidentiality, are outlined in Box2.

### **BOX 2. Measures for Protecting Participants' Privacy and Confidentiality**

1. Ensure physical safety and security of the involved devices and computer servers (Firewalls, etc.).
2. Take data security measures such as password protection, etc.
3. Provide differential and role-based controlled access to data elements for members of the research team.
4. Ensure use of data encryption when data is transferred from one location/device to another.
5. Ensure compliance with national regulations such as Nepal Statistical Act-2015 BS and

#### **4.4 Equitable Distribution**

The selection of research participants should be such that there is fair distribution of the burden and benefits of participation among population groups (geographical differences, ethnicity, socio-economic status, etc.) as far as possible. There should be specific criteria for participants' selection and efforts must be taken to guarantee that participants are not exploited or over-sampled during their search process.

#### **4.5 Compensation and Payment**

Provisions to reasonably compensate the participants for any harm including compensating for the participants' effort and time should be ensured. The information on such compensation should be communicated to the participants through informed consent document.

##### **4.5.1 Payment for Participation**

Research participants need to be reimbursed for expenses such as travel cost, foods, lost wages and other compensations where applicable. The research participants should not be required to pay for any expenses incurred beyond routine clinical care and for research related investigations, interventions or related therapy. If participants will be offered free medical care for non-research-related conditions during the study period, whether such ancillary care amounts to undue inducement, needs to be reviewed. Sometimes, research participants may also receive extra medical facilities at no cost. When consent is given on behalf of a participant by the LAR, payment should not become an undue inducement.

##### **4.5.2 Compensation for Research-related Harm**

Participants in research, who suffer direct psychological, physical, social, legal or economic harm as a result of their participation, are entitled to financial or other assistance after due evaluation, to compensate them equitably for any temporary or permanent damage. Dependents of the participants are entitled to financial compensation in the event of death.

1. The researcher is responsible for reporting all SAEs to the ERB within 48 hours. SAEs can be reported by on-line ERB platform or e-mail or fax communication (including non-working days). Trial should be halted until further notice in case of a series of SAEs. It is also necessary to submit a report on how the SAE was related to the research within two weeks of its onset.
2. After receiving the SAE report, the ERB is responsible for (i) reviewing the SAEs associated with the research; and (ii) suggesting the kind of support to be provided to the participant's if required.

3. It is the responsibility of the sponsor to incorporate insurance coverage or provision for possible compensation for research related injury or harm. All the adverse events (AE) should be documented and reported.

**Note:** *In investigator-initiated research, the investigator/institution where the research is conducted becomes the sponsor.*

#### **4.6 Qualification of the Researchers**

The researcher conducting the study should have relevant qualifications, experiences in related field, relevant number of publications, education and training (on research methodology and research ethics). In case of clinical trials, training on GCP is required.

Criteria for PI for the studies having more than minimal risk, multi-centric, externally funded collaborative and national level:

1. Master's degree in a subject related to the field of research with relevant experience of having worked as a principal investigator; or worked as a co-investigator in a minimum of two researches and one publication in a scientific journal.
2. Bachelor degree related to the field of research with relevant experience of having worked as a co-investigator in a minimum of three researches and two publications in a scientific journal.
3. In case of academic thesis, there should be a competent supervisor in a team.
4. Investigator shall be involved in up to five researches as PI at a time (not exceeding three in trials), as PI should have sufficient time to properly conduct and complete the study within the agreed time.

#### **4.7 Transparency and Conflict of Interest**

Transparency is fundamental to ethical research. And, registration is the first step towards research transparency. Research transparency requires researchers to follow mechanisms that enable them to effectively inform participants and the public about the study procedures and research outcomes. There should also be a provision for making data available for further/future research if applicable

Besides study procedures and research outcomes, researchers are also required to declare COI if any. Failure to disclose the same is liable to result in corrective actions or punitive measures. In case of suspension of the study, researcher should inform such a decision to the ERB at the earliest.

#### **4.8 Data/Bio-sample Collection, Storage, Biosecurity, Transfer and Bio-banking**

Investigator should ensure compliance with relevant standards for personnel information confidentiality. Investigators are also required to follow data safety regulations/guidelines for biosafety& bio-security to ensure that the collection, testing, archiving and transportation of the

bio-samples and data are done in conjunction with the safety guidelines and ethical standards.

#### **4.8.1 Data Collection, Storage, Security and Transfer**

It is always important to define tools/sources of primary and secondary data collection. Primary data collection tools comprise observations, questionnaire, pro-forma, personal interview, experiments, survey, etc., whereas secondary data collection tools include journal articles, internal records, government/non-government publications, books, websites, etc. Once data is collected, researchers must explain how such data will be stored and what storage medium (paper or electronic based) will be adopted. Even after processing/analyzing the data, researcher needs to set the storage retention period.

The study proposal should have details of measures to be taken to secure research-based data in the field, laboratory and office settings. There are wide ranging measures to secure research-based data which include physical security of equipment (if any); digital security mechanisms, such as system, program and file pass-wording; file cabinet security process, e.g. lock & key that can only be accessed by the authorized person; data storage and back-up plan, etc. Failure to address security issues in health research may be considered as breaching the research ethics.

While accessing the sensitive data from the medical records of the people living/suffering with TB/leprosy/HIV/AIDS/Cancer, etc., and also police records of people involved in accidents, alcoholism, prostitution, criminal proceedings for any offense, drug abuse, etc., the researcher needs to obtain official permission from the concerned authority. The researcher is also expected to meet ethical requirements in handling of such records, from retrieving of data to its incorporation in report and publication.

Data Transfer Agreement (DTA) between the host and the collaborating institution(s) must be submitted to the concerned authority. Prior approval is required to ship any data outside the country even for valid scientific reason. Breaching of the code is punishable in line with the Data Act and Privacy Act 2018 of Nepal. On transferring the data, a copy of such data should be stored in the host institution in Nepal, making it accessible to the authorized persons or investigating authorities, when required.

***Note:** GoN's Privacy Act, 2018 is applicable in providing guidelines on the protection of privacy during data storing and transfer process.*

#### **4.8.2 Biological Specimen Collection, Storage, Security and Bio-banking**

Biological specimens may be any biological materials from human beings (whole blood, cord blood, dried blood spots, serum, naso-pharyngeal swabs, sperm, semen, tumor cells, embryos, urine, hair, tissues, organs, cerebrospinal fluids, etc.) or extracted products from the biological materials (DNA, RNA, Genes, Proteins, etc.). Researchers need to mention quantity, quality, and frequency of collection of such samples from each participant, with a

strong rationale for the minimal amount and frequency.

The proposal should have clear explanation on how, when and where such biological specimens will be stored/processed with power back up plan and coding (bar/manual coding) strategy. Proposal should clearly mention about biosafety and biosecurity, physical security, including access control provision and assurances for maintaining standards in accordance with applicable guidelines/rules/laws. Failure to address above mentioned points may not be considered ethically competent.

In collaborative studies, part of the study is under taken within the country, while advanced study (in case of non-availability of tests) may be allowed by ERB to be carried out in advanced labs abroad on valid grounds. In such circumstances, researcher should store duplicate biological specimens in Nepal for at least 5 years upon the completion of the study.

The biological specimens are precious resources, which could be stored in a bio-bank for an extended period of time. Such long-term storage enables long-term future research (when broad consent is obtained from the participants).

#### **4.8.2.1 Biobank and Types of Biological Specimens**

Biobanks can store biological specimens such as whole blood, cord blood, dried blood spots, serum, sperm, semen, tumor cells, embryos, urine, hair, tissues, organs, cerebrospinal fluids, DNA, RNA, etc. All the ethical issues concerning bio-banking viz. ownership, access, benefit sharing etc., should be addressed with greater responsibility. If researchers would like to conduct any further study with the stored bio-samples, researcher must obtain prior ethical approval from the ERB and may also need to obtain individual's informed consent, if personnel identifiers are required. When personnel identifiers are not used, only ERB approval (based on bio-bank agreement of confidentiality and anonymity of the samples) should be obtained prior to conduct the study.

#### **BOX 3. Types of biological specimens stored by biobanks:**

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<b>Anonymous or unidentified</b>	No identifiers are present from the start, or if collected, are not maintained. Such samples are received by biobanks without any identifier sand supplied to researchers.		
<b>Anonymized</b>	This involves systematic de-identification, reversible or irreversible; Link of samples/data to personal identity is reversibly or irreversibly cut.		
	<b>Coded or reversibly anonymized:</b>  There is an indirect link of sample/data to the participant’s identity with restricted access. This link could be re-linked if required; therefore, it may also be termed reversible anonymization.	<b>Irreversibly anonymized:</b>  Link to the participant's identity is removed and cannot be re-linked.	
<b>Identifiable</b>	A direct link of sample/data to the participant’s identity exists.		
<b>Source:</b> ICMR, 2017, National Ethical Guidelines for Biomedical and Health Research involving Human Participants, Page129.			

#### 4.8.2.2 Key Aspects in Maintaining Confidentiality and Privacy of Donors Related to Biological Specimens and /or Data

The procedure of anonymization minimizes the connection between the identifiers and the stored sample by delinking the person from her/his biological material. Maintaining confidentiality of data and respecting ethnic identity are of prime importance; especially in population based genetic studies. More precautions should be sought when the research pertains to stigmatizing diseases. When data pertains to public health research, it may be dealt with in the manner described in section 7.5.

#### 4.8.2.3 Biological Specimen Transfer

When the study involves the transfer of biological samples to other countries, there should be a strong justification for such transfer in the research proposal, particularly if the tests are available in country's laboratories. ERB through expert reviewer will evaluate the justification on non-availability of the tests/labs performing such specialized tests with specified standards in the country. Based on expert members' recommendations, ERB may approve transferring only processed bio-samples/extracted products (e.g. DNA, RNA, serum, plasma etc.) to non-commercial laboratories, for specific purposes (e.g. quality assurance). However, for academic collaboration with non-commercial interest (e.g. Nepali PhD student working in advanced country lab, collecting and analyzing specimens from Nepal for his/her degree purpose) may request for ERB's approval for transferring such human biological samples. ERB may approve transfer of biological samples based on the documentation of such non-commercial academic collaboration.

**Note:** Shipping of biological specimens from Nepal to other countries requires that the specified criteria and requirements are met in compliance with existing laws, rules, regulations (including protection of country's bio-diversity and genetic materials) etc.

Research involving exchange of biological materials/specimens between collaborating institution(s) must sign the MTA and/or MoU with clear information on the purpose, quality, quantity, confidentiality, data sharing and publication policy, IPR, benefit sharing, post analysis reporting mechanism, handling of the left-over bio-samples, bio-safety and bio-security norms, etc.

#### **4.9 Research Benefits Sharing**

If the research is about development of a product (e.g. drug, vaccine, device etc.), researchers must identify the ways (resources, infrastructure and technical assistance) to ensure availability of the product to the research participants, and/or, to the community from where participants are enrolled.

Sometimes, benefits of the study may not be direct. Community people may be indirectly benefitted through the establishment of health facilities or schools, or by the provision of education on good health practices. Participants will not be able to receive any feedback on individual data if the findings are in an aggregate form. So, such data must be discussed with the community, especially when the study involves vulnerable populations.

In the condition where participants are in a condition not prepared to utilize the research outcome, researcher needs to prepare an enabling environment or develop an appropriate mechanism (wherever possible) to communicate their findings. Sometimes, participants would like to have an aggregate report of all the results of the study which could become a shared benefit for the community. In this condition, study team may put all the results in publicly accessible website.

If possible, investigators and sponsors should attempt to continue to offer beneficial interventions (which were part of the research initiative) even after the completion of research i.e. Until the local administrative and social support system are restored and are capable enough to provide regular services.

If researcher thinks that the data and/or biological materials have possible commercial value, this must clearly be highlighted in the informed consent form with clarity about benefit sharing. This form must explain whether donors, their families, or communities would receive any benefits (financial or non-financial) by having access to the tests, products, or discoveries resulting from the study.

## **Section5. Informed Consent Process in Health Research**

Informed consent is a process by which prospective participants are approached by the researcher before the enrollment. It is the responsibility of the researcher to inform the prospective participant about the aims and objectives of the research, participant's roles and responsibilities, research procedures, potential benefits and risks of such participation, etc. After communicating information in the best way a participant can understand, it is the responsibility of the researcher again to allow the prospective participant to be fully involved in the decision-making process. The researcher must also ensure that the prospective participant has fully understood the information provided. Adequate time should be given to the participant to comprehend the process. The researcher has to clearly emphasize that the participant is being asked for permission to participate in the study voluntarily and hence, is very much entitled to withdraw from the study any time without any prejudice. The participant should also be assured that the refusal to participate will not affect the way he/she is getting treatment now or in future. Research details should be outlined in the Informed Consent Document (ICD) in the manner and language the prospective participant can easily understand. Sufficient time should be provided to him or her to think and take decision on whether to participate or not to participate.

### **5.1 Requisites**

It is mandatory to document voluntary informed consent before commencement of research involving human participants. It is also necessary to maintain privacy and confidentiality of the participant's personal information during all stages of the study. General requirements for Informed Consent in health research have been outlined as follows.

1. The prospective participant must be provided with detailed information on the research subject elaborate enough to make a fully informed decision. Such detailed information may include potential risks and benefits, nature of involvement, discomfort, compensation for time, travel, and lost wages, etc. Participants should be medically competent to give a valid, well-informed and voluntary consent. Some of the legal and ethical considerations of informed consent are mentioned as follows.
2. Consent to participate in the research should be voluntary, without any pressure, coercion, and/or any undue inducements.
3. Written informed consent must be obtained from the participants above the age of 18 years.
4. For children above 12 years and under 18 years, in addition to LAR's written consent, a written assent must be obtained from the participating child. The assent form shall be written in simple language which is understandable by a child.
5. For children above 7 years and under 12 years, in addition to LAR's written consent, a verbal assent is required. The entire process of obtaining informed consent should be recorded in audio/video and, well documented in written form.
6. In case of children below 7 years old, researcher is required to obtain written informed consent from parents or LAR (assent not required).



7. The prospective research participant must be given sufficient time to read and comprehend research-related information and, weigh risks and benefits of the study before providing voluntary consent on research participation. The prospective participant should also be allowed to ask clarification from the research team and/or discuss with family and friends if he/she has any fear or doubt about the research.
8. The child's refusal to participate or continue in the research should be respected.
9. The age of the child should be determined by child's birth certificate/ school record or competent documentary evidence.
10. In case of elderly (who is not in mental/physical state of taking self-decision or is not capable of providing voluntary informed consent) and individuals with impaired cognitive functions/mental disability, the consent of LAR must be obtained.

## **5.2 Information**

Participants should be given sufficient information about the proposed research, including information on procedures, purpose, risks/discomforts, anticipated benefits, alternative procedures etc. Participant should also be provided with a statement that clearly mentions about participants' right to question and withdraw from the research any time without any penalty. Information about the research should be provided in the best way and the language that research subjects are able to understand.

## **5.3 Comprehension**

It is the researcher's responsibility to ascertain that the participants have comprehended the information. If a research participant is not capable of comprehending the information, the proxy consent of LAR should be taken. One of the ways to ensure that the participant has comprehended the information is by giving the information in a language that he/she can easily understand.

## **5.4 Voluntariness**

Informed consent is valid only if it is given voluntarily. Therefore, there should not be coercion of any form or undue inducements while obtaining informed consent from the research subject.

## **5.5 Process for Obtaining an Informed Consent**

To obtain an informed consent, following aspects must be considered:

- (i) **Obtaining consent from participants:** Prior to obtaining informed consent from the participant, it is important that an individual who obtains informed consent should be able to explain the entire research process, including risk/benefits, obligations, discomforts etc., to the prospective participant. It is also worth estimating time for obtaining consent from the participants. To avoid undue influence, informed consent should not be obtained by the health practitioner that the participant has been consulting for the treatment. Instead, informed consent should be taken by someone (for instance, assisting nurse or research assistant) who is not the investigator and has no conflict of interest in the research.

Similarly, in case of vulnerable population (e.g. Uniformed personnel, prison inmates etc.) who are bound in a hierarchical relationship (reflecting power differences), consent should not be obtained by someone, who already has an undue influence over the participant. Undue influence and coercion are some of the barriers to obtaining truly informed consent.

**(ii) Coercion, inducement and informed consent**

The consent form should clearly indicate that the prospective participants agreeing to participate in the study voluntarily, without coercion or undue inducements. Efforts to manipulate potential research into consenting through coercion/intimidation or undue inducements (e.g. offering large amount of money, inappropriate gifts etc.) should be avoided. In addition, an individual, who has upper hand in his/her relationship with the prospective participant, should not be asked to obtain consent from the research subject. Consent must also be taken to use biological specimen (collected for routine diagnostic purpose) for which the participants have had to pay for.

**(iii) Deception and informed consent**

Any consent obtained through deception (e.g. incomplete disclosure, misleading information, etc.) cannot be considered a fully informed consent. During the process of obtaining informed consent, it is important for the researcher not to withhold from the prospective participants any information about the research that the research subject is entitled to know. Obtaining consent from the prospective participant through incomplete disclosure, false promises of benefits (to the participant and/or community), stonewalling, etc. are considered to be against the research ethics. Deception or incomplete disclosure is only justified under circumstances, where ‘incomplete disclosure’ is indispensable to conducting a research of essential value. However, the researcher should follow review committee’s directives while opting for non-disclosure of information to the prospective participant. In addition, consent form should also specify beforehand that some information is being deliberately withheld from the participant and s/he will be debriefed at the end of the study. Examples- psychological research.

**(iv) Language:** Consent should be written in a language which participants can comprehend. In collaborative research, consent may be written in local language and English.

**(v) Information required in the consent document:** The consent document should start with a statement that it is a research study in order to distinguish it from routine clinical care. It then should be followed by other statements mentioned as follows.

- a. The nature of the study, whether investigational drugs/vaccine/devices/products, etc. are being used or procedures being performed; or if information seeking through questionnaires or interviews is used;
- b. Objectives and methodology of the study;
- c. Estimated number of participants to be enrolled, expected duration of the study and frequency of participant’s involvement;
- d. A statement that the participation is voluntary and the participant can withdraw from the study at any time without explanation, penalty, fear and/or loss of benefits;
- e. A statement on exactly what is expected from the research participant, and direct or

- indirect benefits to the participant and community;
- f. Type, amount, frequency of collection and period of storage of biological specimens/data and possible use of stored biological specimens/data in future or, to be used for secondary purposes including sharing with others (if any);
- g. The risks, discomforts, and inconveniences associated with the study, e.g. risk of further stigmatization of individuals living with HIV resulting from their participation in the study;
- h. A statement suggesting that all records will be kept confidential. However, it should also mention whether it is possible or not to guarantee absolute confidentiality. If absolute confidentiality is not possible, explain why. Also, explain the extent to which the confidentiality of participants' information will be protected. In case of breach of confidentiality, state the possible consequences;
- i. A statement clarifying any re-imbursement/compensation/provision of management of AE or SAE/free treatment/incidental expenses/insurance coverage for the participants depending on the type of study;
- j. A statement on the post-research benefit sharing, if research on biological specimens and/or data has scope for product commercialization;
- k. A statement indicating that the participant has understood all the information in the consent form, is willing to participate in the study, and may leave the study at any time without any obstruction to his/her regular treatments;
- l. Contact details (name and address including telephone numbers and e-mails) of responsible person(s) of the research team (usually PI) and NHRC/ERB secretariat focal person for any complaints/queries related to the study; and
- m. Signature space for the research participant, LAR, Researcher (if required) and the date and place.

## **5.6 E-consent**

Electronic informed consent (E-consent) uses electronic formats (online, SMS, video, audio, etc.), which can be used to generate information related to the study and also to document the consent using digital signatures. E-consent must contain all elements of the informed consent, as mentioned in section 5.5. E-consent could also be taken during public health emergencies including disease outbreaks, where taking consent in person by the researchers is not possible or feasible.

All the contents of the E-consent, the process of generating information, the documentation of the E-consent including electronic signatures, the mechanisms of maintaining privacy/confidentiality and security of information, and the data use policies must be reviewed and approved by the ERB before starting the study. The process must be supervised by the PI or the designee.

## **5.7 Re-consent: Re-consent needs to be obtained in following situations-**

1. Discovery of new information related to the study, which may affect participants or

has implications to participants or may influence the risk benefit ratio;

2. A participant enrolled using the consent of LAR, regains the ability to consent for him/herself. For example, a researcher might have to obtain a re-consent when an unconscious participant suddenly gains consciousness during the trial; when a participant, who lacked medical competence, becomes medically competent; and when a child turns into a competent adult during the longitudinal trial; etc.)
3. Study requires extension for a long-term follow-up;
4. Modification in research methods, duration of participation, treatment modality, and study sites which may impact participant's decision on whether or not to continue participating in the study. Besides, re-consent should also be obtained if there is probability of revelation of participant's identity through publications or data presentation; and
5. In some cases, additional re-consent of partner/spouse may also be required. Examples of scenarios, where re-consent is taken, have been discussed in the Box 3.

#### **BOX 4: Examples of Scenarios where Re-consent is taken**

**Secondary or extended use of stored samples/dataset:** In such an instance, one of the preliminary considerations for ERB must be to identify the circumstances under which the research requires re-use of collected identifiable biological material to generate the data or utilize the pre-existing identifiable dataset. This must also include review of the informed consent obtained originally to see if re-consent is warranted. There may be situations where consent would be impossible or impracticable to obtain for such research, in which case the research may be done only after independent evaluation by ERB (Declaration of Helsinki, October 2013).

**Pediatric donors:** In longitudinal studies, once the child donor attains the legal age of consent, a re-consent should be sought for the storage and use of her/his tissue or sample. In pediatric bio-banks or bio-banks with pediatric samples it is important to address the issue of children reaching legal age of consent. Sometimes re-contact may lead to withdrawal, resulting in limited data analysis. This may lead to bias or it could evoke emotional distress about past research. On the other hand, re-consent may give the participant the power to agree. A bio-bank should decide the policy it would like to adopt for re-contact.

**Source:** ICMR, 2017, National Ethical Guidelines for Biomedical and Health Research involving Human Participants.

### **5.8 Waiver of the Consent**

For certain conditions, as mentioned in the Box 5, the ERB/IRC may consider granting waiver of consent, if the researcher applies for a waiver and the request for waiver is justified scientifically and ethically, based on ERB/IRC evaluation. The waiver request may be made if the research involves less than minimal risk to participants and the waiver will not adversely affect the rights and welfare of the participants. However, the researcher must justify waiver request by providing an explanation of why obtaining signed consent would add additional risk to the research participants. In addition to justifying waiver request, the researcher is also required to provide alternative provisions/options for informing prospective participants about the research details. Conditions for granting waiver of consent are

discussed in the Box 5.

### **BOX 5. Conditions for granting Waiver of Consent**

1. Research cannot practically be carried out without the waiver and the waiver is scientifically and ethically justified;
2. Retrospective studies, where the participants are de-identified or cannot be contacted;
3. Research on anonymized biological samples/data;
4. Research on data available in the public domain; Research during humanitarian emergencies and disasters, when the participant may not be in a position to give consent. However, attempts should be made to obtain the participant's consent at the earliest possible dates even after the collection of information from participants is complete.

**Source:** ICMR, 2017, National Ethical Guidelines for Biomedical and Health Research involving Human Participants.

Conditions that are applied for waiver of informed consent in adults may also apply for waiver of assent in children. Waiver of assent may be allowed when the available intervention is anticipated to benefit the child but would be possible only if the child participates in the study. However, this condition may be accepted only in exceptional cases where all forms of assent have failed but, the LAR provides the consent. In such circumstances, ERB/IRC approval should be obtained.

### **5.9 Obtaining consent in Special Situations**

In certain conditions, investigators need to take consent from group leader, community leader, Legally Authorized Representative (LAR) etc. as described below:

- (a) **Consent from Gatekeepers:** Sometimes, on behalf of a group, permission of the gatekeepers who are usually the head or leader of the political/social/cultural/professional group may be obtained. The process of obtaining gatekeeper consent should be recorded in audio, visual and/or written forms. Obtaining gatekeeper consent is applicable during the time of natural disasters, where the participants are not mentally ready to provide informed consent. Besides, gatekeeper consent is also obtained while studying tribal or isolated indigenous groups, where tribal members are suspicious of the outsiders and, are also, hesitant to share their culturally sensitive information with the strangers.
- (b) **Community Consent:** In certain population groups (for e.g. ethnic minorities, marginalized populations, mobile migrants, etc.), who are incapable of protecting their own interests because of their limited exposure to the outside world, some participants may not be able participate in the research without community's consent. In such situations, community's consent is required. When permission is obtained from an organization that represents the community, the quorum required for representation in such a committee must be met i.e. the number of members required to be present while giving the consent. However, even after taking the community's consent, individual consent must

also be obtained.

**(c) Consent from Vulnerable Groups:** Vulnerable persons are those individuals who are relatively or absolutely incapable of protecting their own interests for reasons such as disability; environmental burdens; social injustice; lack of power, understanding or ability to communicate; and/or, being in a situation that prevents them from working in their best interests. The common characteristics of the vulnerable groups and the example of vulnerable populations are provided in detail in section 4.1. If vulnerable populations are to be included in research, all stakeholders must ensure that the additional protections are in place to safeguard the dignity, rights, safety and well-being of these individuals. Because of their inability to consent, LAR must be involved in decision making. Also, since vulnerable people are at an increased risk of being further marginalized or discriminated, measures must be taken to safeguard vulnerable participants' privacy and confidentiality.

When the participants cannot sign, a thumb impression must be obtained. The researcher, who administers the consent form, must also sign and date the consent form. In the case of institutionalized individuals, in addition to individual/LAR consent, institutional permission to conduct the research should be obtained from the head of the institution.

In some types of research, the partner/spouse of the prospective research participant may be required to give their consent as well; whereas in genetic research, other members of the family may become involved as secondary participants if their details are recorded as a part of the family history. If information about the secondary participants is identifiable, their informed consent will also be required.

In case of illiterate participant-the consent process should be witnessed by an impartial witness (who is not a relative of the participant and is also not associated with the research) without any CoI. Such impartial witness could be the other patient in the ward who is not the part of the study, staff from the social service department, and/or counselor. The witness, however, should be alliterate person who can read the participant information sheet (PIS) and informed consent form (ICF). The witness should also be able to understand the language of the prospective participant so that he/she can read as well as communicate the information to the participant or LAR effectively for them to make an informed decision.

## **5.10 Consent for Studies using Deception**

Deception refers to intentional misleading of subjects or the withholding of full information about the nature of the experiment. Investigators may mislead or omit information about the purpose of the research, the role of the researcher, or what procedures in the study are experimental. Deception is defined as an untrue falsehood or is the act of lying to or tricking someone. Every deception, according to Whaley, is comprised of two parts: dissimulation (covert, hiding what is real) and simulation (overt, showing the false). An example of deception is when you tell someone you are 30 years' old when you are actually 40.

Deception is allowed only when alternative procedures are unavailable and when participants are debriefed at the end of the study. Although deception is not permissible, approval should be taken from the ERB/IRC in circumstances where some information requires to be withheld for validation until the completion of the study. A two-step procedure may be required comprising an initial consent and a debriefing after participation. In such instances, an attempt should be made to debrief the participants/communities after completion of the research. However, the deception cannot conceal a real risk or danger to participants.

Researcher should not include the data, if on debriefing; the participants refuse to allow the use of their data. These types of research may carefully be reviewed by the ERB/IRC before implementation and the possibility of unjustified deception, undue influence and intimidation should be avoided at all costs.

### **5.11 Procedures after the Consent Process**

After obtaining the consent, the participant should be provided with a copy of PIS and signed ICF. If they are not willing to take the copies, the reason for their reluctance should be noted. The original PIS and ICF should be archived as per the guideline.

### **5.12 Documentation of the Consent**

Documentation of the informed consent process is an important task. The signed informed consent form or consent from the LAR must be documented and safely archived. In all cases, the investigators must ensure that the privacy of the participant and confidentiality of related data are maintained.

## **Section 6. Ethical Review Process**

NHRC established under the act of the parliament in 1991, is mandated to review, approve, and monitor the research involving human participants and ensure social and scientific value of the study and its ethical conduct. Accordingly, all the research proposals involving human participants need to be reviewed and approved by ERB/NHRC or IRC. As per "NHRC Act, if a person or organization who intends to do research works on health after the commencement of this Act has to obtain permission of the Council (section 11, "Requirement of approval to do health related research"). If any person or organization does a research work without obtaining approval pursuant to Section 11 or does not observe the direction given by the Council in doing research work after obtaining approval, the Council may warn such person or organization or restrict such research work for a certain period of time (NHRC Act section 12, "Special powers of Council").

### **6.1 Formation and Terms of Reference of Ethical Review Board (ERB)**

An Ethical Review Board (ERB) is formed by the Executive Committee of NHRC with an objective to review, approve and monitor health research involving human participation. The membership and terms of reference are periodically reviewed by the NHRC Executive Committee. The process of formation of ERB, tenure of its chairman and members, working procedure, process of maintaining confidentiality and avoiding conflict of interest and/or, measures to manage CoI (if present) are outlined as follows:

#### **6.1.1 Formation of the ERB**

1. ERB is formed under the provision of NHRC Act, section 10.
2. A name list of prospective candidates, interested in the membership of ERB, is prepared by the member secretary of the NHRC. The list has to be prepared before the appointment deadline. The proposal for the new chairperson for ERB along with the name list of candidates for board members is then submitted to the NHRC executive committee. NHRC executive committee selects the chair and the members of ERB based on candidates' academic qualification, experience in conducting research, past contributions to the research ethics committee, integrity, non-partiality, independence, and decision-making capacity.
3. Modality of the selection of the ERB members and its composition should be endorsed by the Executive Committee of NHRC.
4. NHRC should prepare a roster of experts representing different areas in health science (Physician, Surgeon, Bio-medical scientist, Public Health expert, Social scientist, Legal expert for selection of chair and members.
5. NHRC Executive Committee selects 11 to 15 members including the chair, affiliated and non-affiliated members. A balance of experience and gender is maintained in the



process.

6. Member Secretary of NHRC will function as the Member Secretary for ERB. However, in the absence of the NHRC Member Secretary or when NHRC Member Secretary becomes Executive Chief of the organization, Chief of Ethical Review Monitoring and Evaluation Section shall be the acting Member Secretary for ERB.
7. The tenure of the ERB members will be of three years.
8. Standard Operating Procedures (SOP) provides the details on the process of selection of ERB members and the chair and its procedure.

## **6.1.2 Appointment of the ERB Chair/Members and Conditions of Appointment**

### **6.1.2.1 Appointment of the ERB Chair/Members**

With the approval from the NHRC executive committee, NHRC executive chief will appoint the ERB chair, affiliated and non-affiliated members, which will be notified to the respective appointees by an appointment letter. ERB chair shall be an independent senior health professional not affiliated with NHRC. The tenure of appointment will be of three years which could be extended for one more term, based on the performance and need of the organization. ERB members including the chair's term will not be extended for a third consecutive term.

### **6.1.2.2 Conditions of Appointment**

ERB members shall be appointed under the following conditions:

1. If he/she completely agrees to make his/her profile public, as the member of ERB;
2. If he/she is able to read meticulously, understand what constitutes a conflict of interest for ERB members and declare CoI, if any;
3. If he/she signs a confidentiality agreement regarding ERB meetings, discussions, and research proposals applied for ethical review.
4. If he/she agrees that the remunerations paid to him/her in course of ERB work will be recorded and made available to the public on request;
5. If he/she provides recent CV and relevant training certificate(s) related to health research ethics, GCP, GCLP, etc. (as applicable), etc; and
6. If he/she is aware of relevant national laws, NHRC guidelines and regulations and, is also ready to abide by these laws, guidelines and regulations.

## **6.1.3 Qualification of the ERB Chair/Members:**

### **6.1.3.1 Chairperson**

ERB chair is a senior and well-respected person with post graduate qualification in health-related sciences, with significant research experience, as evidenced by his/her original research publications in international/national peer reviewed indexed Journals. ERB chair should be trained in research methods, research ethics and, GCP/GCLP with prior experience

of serving as an IRC or ERB chair/member. Given ERB Chair's roles and responsibilities, ERB chair should be independent and simultaneously exhibit ethical leadership ability.

#### **6.1.3.2 Member-Secretary**

NHRC Member Secretary will be the Member Secretary of the ERB. When NHRC Member Secretary assumes the role of Executive Chief of the organization, Chief of Ethical Review M & E Section shall be the acting Member Secretary for ERB, to minimize possible CoI for executive chief.

#### **6.1.3.3 ERB Members**

A person is considered eligible for the membership of ERB, if s/he has post graduate qualification in health-related sciences (basic bio-medical/clinical/public health) with knowledge and experience in ethical conduct of the health research. In addition, a person with a post-graduate degree in law and legal experience in health sector, and a sociology/anthropology post-graduate with experience related to social health research can be the ERB members. Each member should be self-motivated to maintain basic ethical principles including autonomy, independence and impartiality, fairness, and justice, etc. ERB should have members representing each of the following experts:

- Clinicians (MD)
- Basic & Bio-medical scientists (MD/PhD)
- Allied Health Professionals
- Public Health experts/ Epidemiologist / Biostatisticians (MPH/MD/PhD)
- Social scientists or Ethicist (MA/PhD)
- Legal (LLM/LLB)

***Note:** For some specific research related to ethnic/vulnerable communities, a lay person should be included as an invited member of ERB, based on the nature of the proposal, to represent community concerns on benefits/risks and socio-cultural barriers. Lay person should be a literate person to be selected from the public or community, who has not pursued a health science related career in the last five years but has been involved in social and community welfare activities. Such member may be a representative of the community from where the research participants will be taken. Such person must be aware of the local language, culture and moral values of the community.*

#### **6.1.4 Disqualification, Resignation, Cancellation, and Renewal of the ERB Chair/Members**

1. If an ERB member is found acting in contrary to, or breaching the conditions of

appointment, he/she may be disqualified by the NHRC Executive Committee. Legal prosecution against a member shall also lead to that member's disqualification. If any member—including ERB chair does not attend three consecutive ERB meetings without prior notice with valid reasons, he/she shall be disqualified as a member of ERB.

2. ERB chair or a member may resign from his/her position by submitting a letter of resignation to the member secretary. Member secretary shall forward this to the chairperson and executive chief of NHRC. Executive chief shall forward this to Executive Committee of NHRC. On acceptance of his/her resignation by the Executive Committee, he/she will no longer be a chair/member of ERB.
3. NHRC Executive Committee has the right to replace the ERB chair/members in case of their resignation/disqualification and sudden death. While replacing ERB chair/member for the remaining tenure, NHRC Executive Committee shall follow the same procedure mentioned in the conditions of appointment of new ERB chair/member. Such appointment should have to be done as early as possible and not later than three months.
4. If ERB chair/member is nominated as a member in executive committee of NHRC, the existing membership in ERB will automatically be cancelled.
5. At least 50 percent of the existing ERB should be retained in a new ERB to maintain continuity of experience and institutional memory. Appointments of ERB chair/member should not exceed two consecutive terms.
6. The appointment letter for ERB Chair/Member should clearly specify the following:
  - a. Subject area representing specific roles and responsibilities for each member of the committee;
  - b. Duration of appointment; and
  - c. Conditions of appointment.

#### **6.1.5 Responsibilities of Ethical Review Board:** The ERB is responsible to-

1. Ensure the protection of rights, dignity, safety, and well-being of the participants and, monitor the compliance of implementation process in line with the national and international guidelines. This is achieved through proposal review, monitoring of the implementation of approved research protocols, and, review of non-compliance and final reports;
2. Recommend appropriate compensation package for research related injuries based on scientific evidence and requirements;
3. Provide constructive feedback with a view point to help approve or disapprove the submitted research proposal;
4. Maintain confidentiality of all the documents at different steps starting from submission to review, feedback, monitoring, approval, reports review and, writing of ERB minutes;
5. Facilitate the researchers in conducting research in compliance with the ethical guidelines, rules, and regulations. Facilitation should also include making researchers aware about the importance of respecting the local culture and traditions of the

- community where the study is conducted;
6. Organize periodic/annual review meeting/workshop/training programs for IRCs;
  7. Interact with proposal reviewers on the ethical and technical review process and invite them in the ERB meeting if required;
  8. Organize joint review meeting if the study is multi-centric in nature among institutions that have their own IRC;
  9. Organize reviewers' training periodically for ethical and technical review process; and
  10. Monitor approved studies to ensure that the research is conducted in accordance with the approved protocols.

**Special conditions z:** *In order to carry out its roles, ERB needs to function regularly, even in the absence of NHRC executive committee. In such a condition, ERB chair and members are mandated to function as per assigned ToR in the appointed tenure.*

## **6.2 Office of the ERB Secretariat and its Functions and Responsibilities**

### **6.2.1 Office of ERB Secretariat**

1. NHRC should set up a separate ERB secretariat office with necessary administrative and resources support such as phone, internet, photocopy machine, scanner, printer, computers, file cabinets, desks, chairs, projector, meeting tables, shredder, online proposal submission and review portal and its data base management system, etc.
2. NHRC should assign an appropriately qualified (in terms of academic qualification, training and experience in research ethics) senior officer as the chief of the ERB secretariat to support ERB Chair and, member secretary in coordinating all the activities including organization of ERB meetings, monitoring and oversight of the implementation and, investigation of complaints. ERB secretariat should have adequate number of qualified and trained staffs in different areas of health research.
3. The names of ERB chair, member-secretary and members should be displayed in front of the ERB office and NHRC website. Their duties and responsibilities should clearly be stated and documented in the ERB office.
4. NHRC should allocate adequate financial provision for effective functioning of ERB and strengthening of the capacity of the secretariat and ERB members, utilizing the revenues generated through proposal review.

### **6.2.2 Functions and Responsibilities of ERB Secretariat**

The ERB secretariat should work in close coordination with ERB chair, ERB member-secretary and executive chief of NHRC, and is responsible to:

1. Develop a roster of subject specific expert reviewers with approval from ERB, whose review service could be obtained by the ERB/NHRC and could also be invited for meetings either virtually or in person;
2. Collect and archive CVs, confidentiality agreements and CoI from ERB chair, member-secretary, members, and reviewers;
3. Validate the financial section of the proposal in line with the grant agreement for payment of ethical review processing fee;

4. Maintain the electronic data base of the proposals, archiving and tracking procedures, including preliminary screening and verification of the submitted proposals as per the checklist;
5. Prepare, maintain, and distribute proposals to primary and technical reviewers. Communicate with the reviewers and investigators, for clarifications, responses; revision until the final approved proposal is archived;
6. Prepare the meeting agenda in consultation with ERB Chair and member-secretary, communicate with the ERB chair/member secretary/members and, coordinate/organize ERB and expedited review committee meetings regularly;
7. Prepare and present the summary of the proposals (Title, PI, Sponsor, Site, Risk assessment Matrix, etc.) for discussion in the ERB and expedited review sub-committee meetings;
8. Draft the meeting minutes, share with members, member-secretary and, chair for review/revision/editing and final approval. The final minute should be signed by Chief of the ERB secretariat, Member Secretary and ERB Chair before further communication;
9. Prepare the decision letter according to the approved minute. Obtain signature from member secretary/executive chief of NHRC/any designated officer of NHRC and, communicate the decision to the researcher. If NHRC authority is the applicant for obtaining ethical approval from ERB, decision letter should be signed by ERB chair;
10. Organize ERB documentation, communication and archiving;
11. Plan and organize monitoring site visit of the ongoing studies;
12. Update and share relevant and contemporary ethical issues to the ERB;
13. Facilitate to organize meetings/workshops/trainings related to research ethics capacity building and IRC periodic review;
14. Carry out the additional responsibilities given by ERB chair/member-secretary and NHRC chief executive;
15. Organize IRC accreditation sub-committee meetings and inspection visits for accreditation of IRCs; and
16. Organize the complaint handling meeting and communicate with members and concerned stakeholders.

### **6.2.3 Capacity building of ERB and its Secretariat**

NHRC should conduct regular training programs related to research ethics for ERB members, ERB secretariat and IRC members at least twice a year. Such training programs will provide opportunities for hands-on experience of reviewing the research proposals and responsible conduct of research. ERB members and ERB secretariat staffs should be oriented with the ethics related guidelines and SOPs, upon appointment annually and whenever there is any update/revision.

### **6.3 Submission and Review Procedures**

ERB secretariat is responsible for managing proposal submission, review, feedback and approval process through an online submission portal and maintaining the archival database. Investigators planning to conduct health research in Nepal should submit their research proposals through online ERB portal (<http://erb.nhrc.gov.np> or <http://nhrc.gov.np/erb>) for ethical review and approval.

### **6.3.1 Application Submission**

Principal Investigator or an assigned team member should submit the proposal attaching all the administrative and technical documents as mentioned below. The Investigator should first register with their details. Upon successful registration, automatic email will be sent to the investigators with login details. With this login details (username and password), the investigators can enter into researcher login portal.

#### ***The administrative and technical documents to be submitted:***

1. Dated cover letter signed by the Principal Investigator, mentioning that he/she has sufficient expertise to conduct the research and will take full responsibility of the research from recruitment to the completion of research;
2. Informed Consent Document (ICD) in Nepali and English, as a separate copy (if required). In addition, this can include a translation copy, in a local language if relevant;
3. Document with clear information on any compensation to be given to the research participant (e.g. any transportation costs, food, free health care or insurance coverage etc.);
4. In case of interventional study, institutional acceptance letter indicating that the institute is a collaborating partner and any SAE/AE during the course of research will be managed by the institute;
5. Sponsors grant agreement;
6. IRB approval from other collaborating institutes if it is a multi-national and multi-centric study;
7. A signed statement by the researcher stating that he/she will abide by the ethical principles of research; and
8. A declaration of the CoI and its mitigation measures, as applicable.

Only those applications fulfilling the requirements will be accepted for review and further process. Incomplete submission will not be processed further. Upon successful completion of submission of the required documents including proposal, an auto generated acknowledgment email containing proposal registration number (for future follow up) will be sent to the researchers. Verification email will be automatically sent by the online portal, which needs to be verified by the prospective investigators, for further processing. For any additional documents required during the review process, the researcher will be notified by the ERB secretariat. Process and list of documents required for applying online proposal submission could be accessed in Annex – II.

### **6.3.2 Elements of the Review Process**

Once the research proposal is submitted and screened for completeness of reference documents by the ERB secretariat, primary and technical reviewers will be assigned in consultation with ERB chair and/or member secretary, based on technical expertise and experience in research ethics. Review will be based on the provided checklist. Secretariat will coordinate communication of the feedback/revision between the reviewer and the investigators maintaining confidentiality and mitigating CoI. Upon completion of review and revision of the proposal, the proposal in consultation with ERB chair and/member secretary will be further processed depending on the category of risk. It will be reviewed in the Expedited Review Subcommittee or by the full ERB (Section 4, Box 1).

#### ***Basic requirements of review process***

1. Relevant Qualification (academic degrees, training and experience) of the PI and other investigators in subject area of the research in line with national rules and regulations;
2. Infrastructure (human resources, equipment, bio-safety/data safety and supplies) and other facilities in the institutions (if any);
3. Description of the population from which the research participants will be drawn;
4. Assessment of possible risks, inconveniences, and anticipated benefits of the research to the participants;
5. Clearly articulated rationale and justification for exclusion and inclusion in the study;
6. Provisions for Data Safety Monitoring Board (DSMB)/Data Safety Monitoring Committee (if relevant for the study). For any trials, the formation and functioning charter of DSMB needs to be evaluated;
7. Provision of insurance or indemnity to the participants in case of adverse drug reaction and or adverse events (if relevant for the study);
8. Mechanism for reporting and management of any adverse drug reaction and/or adverse event (if relevant for the study);
9. Plan for dissemination or publication of research results; and
10. Assurance of the availability of research product for the use of the participants and the community/country, if relevant.

### **6.3.3 Joint Review**

Joint review shall be organized for the multi-centric studies being conducted in institutions which have IRCs. This is initiated to increase institutional ownership, reduce the additional burden to IRCs and monitoring implementation process. In such studies, ERB shall call on relevant IRC representatives to attend the meeting and provide their opinion for decision making.

### **6.3.4 Exemption from Review**

Researchers can apply for exemption from review in certain situations. Based on the risk categorization, ERB secretariat will put forward the proposal to Expedited Subcommittee review meeting for necessary decision.

#### ***Conditions for exemption from review:***

1. Research which involves accessing and analyzing data available in public domain;
2. Research on anonymous or non-identified data/samples;
3. Observation of public behavior when information is recorded without any link and disclosure of the person under observation; and
4. Quality assurance and quality control audits in the institution.

### **6.3.5 Expedited Review**

Expedited Review Sub-committee (consisting of affiliated and non-affiliated members) shall be formed by Executive Chief of the NHRC. ERB chair will be the coordinator and others will be the members of the sub-committee. Emphasis will be laid on balancing gender and discipline while forming the Expedited Review Sub-committee. The Expedited Review Sub-committee's recommendations are put forward to ERB for final approval. Expedited Review Sub-committee only reviews proposals which are grouped into 'less than minimal' and/or 'minimal risk' category. Proposals, which are grouped into 'higher risk' category, are sent to ERB to decide upon further actions on approval process as per SOP. Urgent implementation of the protocols during public health emergencies and disasters, requiring fast track approval may also be considered for expedited review as per below procedure:

1. Secretariat prepares the list of proposals for Expedited Review Sub-Committee meeting in consultation with Member Secretary and Expedited Review Sub-Committee Coordinator.
2. Secretariat prepares and presents the summary of the proposals (Title, PI, Sponsor, Site, Risk assessment, etc.) for discussion in the Expedited Review Sub-committee meetings.
3. Secretariat drafts meeting minutes and submits it for review/editing and approval by Expedited Review Sub-Committee coordinator.
4. Secretariat prepares a list of proposals approved by the Expedited Review Sub-Committee meeting and forwards them to ERB full board meeting for endorsement.

### **6.3.6 Re-submitted Proposal Review**

For proposal requiring major revision, researcher may re-submit the proposals according to the decision of the ERB. The re-submitted proposal with major revisions will follow the same process which is used for a new proposal.



### **6.3.7 Review of Amendment of the Approved Proposal**

The researcher should submit a request for amendment through online portal and get approval within valid timeline before its implementation. Minor revisions on approved proposal shall be cleared through Expedited Review Sub-Committee meeting process; however, major revision shall be reviewed by the full board. The rationale and justification for amendment should be scientifically strong, without deviating much from the main objective and methodology of the approved proposal.

### **6.3.8 Review of the Final Report**

The researcher should submit his/her final report upon completion of the study through the online ERB portal. The report will be reviewed by the relevant Secretariat staff, and expert member of the ERB or the subject expert (as applicable), before issuing an acknowledgement letter.

## **6.4 ERB Meetings**

ERB meetings shall be organized at regular intervals, based on the number of proposals and urgency in conducting the research, which requires swift review and approval. ERB Member-Secretary or chief of the ERB secretariat in consultation with the ERB Chair will organize the meetings. The followings points should be considered for organizing ERB meeting:

1. Agenda for the meeting needs to be shared with the members at least a day before the meeting.
2. If ERB feels it necessary, the PI or co-investigator or study team members as mentioned in the research proposal can be invited to the meeting to present the proposal or elaborate on specific issues of the proposal in the meeting. However, the study team member shall not participate in the decision-making process.
3. ERB meeting will be considered valid only if the quorum (>51%) is fulfilled.
4. The ERB member(s) should declare their CoI, if any, before the meeting. The chair should institute appropriate management or mitigation measures to address the declared CoI. In case of adoption of CoI management measures, the member, who declares CoI, may be asked to leave the ERB meeting while the specific proposal is being discussed. He/she also may not be a part of decision-making process. The Secretariat should ensure the quorum requirement in each proposal is discussion.
5. The related subject experts could be invited in the meeting for expert opinion about the proposal (if required) and their opinions should be recorded in the minute. However, the final decision is made by ERB members, after evaluating the proposal and incorporating opinions of the invited expert.
6. The ERB can allow virtual presentation of the proposal by the researcher(s), if needed.
7. The decisions and procedures of the meeting should be recorded in the meeting minute.

8. Attendance sheet should record the name of all those who are present and absent in the meeting.
9. The meeting minute of the previous meeting, recommendations of expedited review sub-committee and, proposals for review exemption should be shared and approved by the full board meeting.
10. ERB minutes should be drafted by secretariat and, verified and approved by both Member-secretary and ERB Chair.

#### 6.4.1 Quorum requirements for ERB

1. At least 51% ERB members must be present to form a quorum in order to make a valid decision.
2. The quorum should include medical and non-medical and, technical and/or non-technical, affiliated and non- affiliated members.
3. Presence of members representing only one gender does not constitute a quorum.
4. The proposed proposal under discussion should have been reviewed by at least one ERB member or subject expert.
5. No decision is valid without fulfillment of the quorum.
6. Invited expert should not be counted in meeting quorum requirement.

#### 6.5 Decision Making

The ERB must consider the following while making a decision about the research proposal:

1. ERB meeting has met quorum requirements.
2. Normally, decisions can be taken by consensus; if consensus is not possible, the voting process can be initiated.
3. All ERB members present during the meeting have the right to express their opinion or vote to decide.
4. Decision must be taken either by consensus or majority votes and should be recorded. A dissenting view or opinion (if any) should be recorded with reasons.
5. If any member has CoI related to a particular proposal, he/she should declare CoI in advance. Anyone, who declares CoI, will not be the part of decision-making process.
6. The ERB can **fully approve** (to start the study as presented, with no changes required) or, **approve** with minor modification (requiring minor changes/corrections to the item(s) noted at the convened meeting; to be followed-up by the ERB Chair and Member Secretary after the researcher makes changes/corrections/modifications as per the suggestions). ERB can ask for the **resubmission of** the proposal (requiring major changes/corrections to the items and full committee review of the materials) or, **completely disapprove** the proposal (rejecting the study, stating the reason for disapproval).
7. Reason for the proposal disapproval will be clearly stated and communicated to the researcher.

**Note:** *If the Board votes not to approve the study and if the investigator wishes to appeal this decision, he or she may do so by contacting NHRC Executive, through ERB*

*secretariat or directly within 35 working days from the date of receiving the letter.*

## **6.6 Communicating a Decision**

On behalf of the ERB, ERB secretariat will communicate its decision to the applicant in a written form through online systems within two weeks of the ERB meeting. ERB should give initial decision within 6 to 8 weeks of the submission of the proposal.

**Note:** *Application will not be entertained and put on a pending list if the researcher investigator does not respond to the queries from the secretariat for more than 3 months. Such studies will be permanently closed and the researcher(s) will have to reapply with a new protocol for further processing.*

***The communication of the decision includes, but is not limited to the following information:***

1. The exact title of the research proposal reviewed;
2. The clear registration number of the protocol of the proposed research or amendment, date, and version number (if applicable) on which the decision is based,
3. The names and where possible, specific identification numbers (version numbers/dates) of the documents reviewed, including the potential research participant information sheet/material and informed consent form;
4. The name and title of the applicant;
5. The date of the decision;
6. A clear statement of the decision reached; and
7. Any advice, suggestion, and recommendation by the ERB.

## **6.7 Continuing Review**

Approved ongoing research with more than one-year study duration should be reviewed regularly, at least once a year. For that, ERB can establish a follow-up procedure (continuing review) to keep itself updated with the progress of all approved research (right from the approval of the research to its completion). The researcher should apply for continuing review at least one month before the expiry date. The communication for continuing review will be entertained if initiated before the expiry date and will be valid if only applied within the approval time. The follow-up review intervals shall be determined by the risk category, nature, and the research proposal review schedule.

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

1. Any protocol amendment,
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. A decision of a follow-up review can be issued and communicated to the applicant, indicating a modification, suspension, or termination of the ERB's original decision or confirmation that the decision is still valid; and

4. In case of the premature suspension/termination of a study, the applicant should notify the ERB of the reasons for the suspension/termination, including the submission (to the ERB) of a summary of results obtained from a study prematurely suspended/terminated.

***The procedure for continued review takes the following aspects into consideration:***

1. Documents to be reviewed such as progress reports, safety reports(if any),technical audit reports (if any),final reports, etc.;
2. Experiences of the research participants (e.g. independent observation of the discussion being held during informed consent taking process, independent surveys of participant's experiences etc.); and
3. Notification from the applicant with regard to suspension/premature termination or completion of the study.

## **6.8 Site Monitoring Visit**

ERB secretariat (in consultation with ERB Member Secretary and ERB Chair) prepares the list of proposals for monitoring visit and forms a team including ERB member, subject expert, and secretariat.

## **6.9 Documentation and Archiving**

All documents including administrative and technical documents should be archived. Administrative documents include ERB members' nomination decision by the NHRC executive committee, name lists of ERB members, appointment letters, CV and CoI declaration letter of the ERB members and secretariat staffs, registration and accreditation, academic certificates, training records, international and national guidelines, ERB agenda and minutes. ERB secretariat should archive all communications with members and reviewers and/or experts along with the technical documents, including copies of the proposal submitted by an applicant; ERB decision letters; amendment; SAE/AE report; safety reports; protocol deviation and violation report; continuing review report; site monitoring visit report; documents received during follow-up; progress and final reports; complaints; audit reports; signed CoI form of the researcher; and, other required documents submitted by the researchers as per the checklist. The records should be kept in an appropriate storage electronic/hard copy. An authorized officer of ERB secretariat should sufficiently be trained to understand their responsibilities related to record keeping, retrieval, and maintaining confidentiality.

ERB secretariat should inform the researcher/research organization that the research-based data (filled questionnaire/pro-forma/electronically filled data set, etc.), filled informed consent forms, collected bio-samples (back-up) and other related documents should be archived for at least five years (or more for some cases) period after the completion of the study.

## **Section 7. Specific Requirements for Specialized Research:**

There are some specific requirements that investigators and sponsor need to fulfill in conducting specialized types of research, e.g. clinical trials of drugs, vaccines and devices, synthetic biology, radioactive materials, X-rays, bioavailability, bioequivalence, public health, social and behavioral science, human genetics, humanitarian emergency, disaster, stem cell research and, use of animals in health research. While conducting different phases of clinical trial, the investigator and sponsor must adhere to and comply with the international GCP guidelines along with the followings:

### **7.i. Human resources and infrastructure**

For conducting clinical trial qualified human resources with clinical trial experience should be available. Similarly, infrastructure like laboratory, equipment, devices, space for ICF and intervention and other prerequisite work should be ensured. These should be in line with international guidelines for conducting different phases of clinical trials. Before initiation of the trial, investigator should submit the site verification report to ERB.

### **7.ii. Contract Research Organization (CRO)**

There should be a qualified local CRO for planning, developing and implementing the clinical trial as per the protocol.

### **7.iii. Declaration of conflict of interest and mitigation measures:**

Investigators (principal and co-investigators), sponsors and the implementing institution involved in clinical trial should declare CoI, wherein statement of declaration of the trial product should be used only for research purpose without any direct/indirect financial benefit to the investigators and implementing institutions. It should also clearly mention that the investigators will ethically perform professional duties maintaining equity to all whether they are participants or not.

### **7.iv. Insurance, Indemnity and Medical Coverage of the Participants**

Clinical trials sometime may pose threats to the participants. In order to mitigate the harmful effects of the trial, the sponsor of the study together with principal investigator should clearly mention the benefits and possible harms of the participation in the informed consent document. And, if there is any harm, details about the compensation/insurance policies, provisions and coverage should be outlined. In addition, the role of the implementing institution (undertaking the research project) in case management related to trial effect should also be clearly stated. The sponsor, research implementing institution and the investigator should submit insurance policy clearly mentioning what will be covered by the insurance and what not, how the insurance claim will be approved and what will be the role of investigators and participants in insurance coverage approval process.

#### **7.v. Independent Data and Safety Monitoring Board (DSMB)**

Sponsors of the study should form an independent Data and Safety Monitoring Board (DSMB) before initiating the trial. DSMB should consist of independent subject experts (representing different research subject areas) such as clinicians, bio-statisticians, and, epidemiologist with prior DSMB experience representing the country where the study is being implemented. For international multi-centric trials with research sites in many countries, it should have at least one DSMB member representing Nepal. However, it would be preferable to have national DSMB. PI should submit a DSMB charter with clarity on DSMB members' roles and responsibilities outlined as follows.

1. Interim review of the trial's progress including updated figures on recruitment, data quality, adherence to protocol treatment and follow-up, and main outcomes and safety data;
2. Monitor evidence for treatment induced harm (e.g. toxicity, SAEs and ADRs, deaths, etc.);
3. Monitor evidence for treatment differences in the main efficacy outcome measures;
4. Assess the impact and relevance of external evidence;
5. Decide whether to recommend continuation of participants' recruitment in trial or, termination of trial (for everyone/some treatment groups/some participant subgroups);
6. Decide whether trial should be stopped earlier;
7. Assess data quality, including completeness (and by so doing, encourage collection of high-quality data);
8. Maintain confidentiality of all trial information;
9. Monitor recruitment figures and losses to follow-up;
10. Monitor compliance with the protocol by participants and investigators;
11. Monitor planned sample size assumptions, preferably with regards to:
  - a) A priori assumption about the control arm outcome; and/or
  - b) Emerging differences in clinically relevant subgroups, rather than on un-blinded differences between treatment groups.
12. Suggest additional data analyses if necessary;
13. Advise on protocol modifications (e.g. on inclusion criteria, trial endpoints, or sample size) proposed by investigators or sponsors; and
14. Monitor continuing appropriateness of patient information.

#### **7.vi. Trial Steering Committee**

Sponsor of the study should form an independent Trial Steering Committee (TSC) consisting of independent subject experts representing from different research subject areas (not directly involved in the trial other than as a member of the TSC). Representative from Ministry of Health and Population, Department of Drug Administration and Nepal Health Research Council can also be the member of the TSC.

The role of the TSC is to provide overall supervision for the trial to ensure that the trial is conducted to the rigorous standards set out in the Medical Research Council's (MRC) Guidelines for Good Clinical Practice. Particularly, the TSC should concentrate on the

progress of the trial, adherence to the protocol, patient safety and the consideration of new information.

## **7.vii. Community Engagement**

Before the initiation of the trial, the investigator should clearly mention how the community engagement will be done. The detailed procedure should be described in the protocol and report of the community engagement should be submitted to ERB during the implementation of the trial.

### **7.1 Clinical Trials of Investigational Products (Drugs, Vaccines, Devices and other Investigational Products in Traditional Medicine)**

Clinical trials are experimental and usually well designed, where the investigational products (IP) (modern allopathic medicines/vaccines/devices or traditional ayurvedic/alternative medicine products or procedures) related intervention(s) are done to evaluate the safety and effectiveness of the interventions on participant's health outcomes. Such trials usually involve healthy participants to evaluate the outcomes of the IP. Such IPs could also be used in sick patients for verifying their effects and possible adverse events in establishing their safety, reactogenicity, immunogenicity, and efficacy.

Clinical trials compare the effectiveness of the interventions in test group participants (treated with an investigational product/intervention - IP) versus the control group (receiving placebo or an active comparator). Such investigation will determine and distinguish between the effects of IP and placebo, concomitant treatment, spontaneous change, etc. When using placebo in trial, the participants should be informed and also, be able to comprehend that they are randomized to a test or a placebo group and may receive IP or an inert drug, during the trial period. Placebo group participants should be offered post-trial access to the IP, if found effective in test group participants. During the clinical trial period and even for a longer period, based on the pharmacokinetic properties of the IP, the safety monitoring follow-up and clinical case management of all participants must be ensured by the implementing institution (or through sponsor support). Long-term safety monitoring must be considered based on the pharmaco-kinetic & pharmaco-dynamic properties of the IP.

Clinical trials are classified into Phases I to IV. In certain special conditions like public health emergency(requiring early development and validation of the effects of the IP in different population groups in a very short period for protection/treatment of the population),NHRC may permit even Phase II trial of the IP developed outside Nepal, with sufficient scientific and ethical discussion and justification in ERB full board.

NHRC may only permit Phase-I clinical trial in Nepal where the institutes planning to conduct such trials have sufficient infrastructures and resources in addressing any events related to IP and after effects. In such situation sponsors should develop infrastructures and capacitate human resources as stipulated in international guidelines. It should also comply

with Drug Act-1978. And, investigators institute should produce sufficient evidence of pharmacological, microbiological, toxicological safety of the IP in non-human models.

The ERB should review the evidence of Phase-I and Phase-II results published in peer reviewed international professional journals, showing that the IP is suitable for continuation on to Phase-III, in making decision on the approval of the trial. The Research institute and the Principal investigator proposing to conduct Phase III clinical trial should submit the signed copy of the previously conducted Phase I and II clinical trial documents, clinical trial registration and publications to ERB, for review and approval process. Upon approval of the clinical trial research from NHRC, the implementing institution should obtain IP import license from DDA as per the existing Drug act of the country and report regularly to DDA as per the Drug Act provisions.

An investigator Brochure should be made available with information of its product, intended purpose of use, safety profile, registration and approval from regulatory authority in the manufacturing country, which should clearly show its usefulness, limitations, potential risks/hazards and mitigation measures as applicable.

## **7.2 Clinical Trial involving Vulnerable Participants:**

A clinical trial involving vulnerable populations will only be allowed when strong justification on the need of such a trial in vulnerable population is provided ensuring effective participants' protections measures by the institute implementing the trial. The clinical trial involving vulnerable population must be undertaken with caveats mentioned as follows:

1. Women of childbearing age must be counseled for possible adverse effects of the trial on the pregnant woman and her fetus during the period of study. Women participants also need to use effective contraceptive methods during the period in order not to conceive and mitigate the possible adverse effects of the trial on the fetus.
2. If the study objective is to find new knowledge directly relevant to the fetus, the pregnancy or lactation (like gestational diabetes, pregnancy induced hypertension and HIV), pregnant women and fetuses can be included in the clinical trial, ensuring sufficient participant protection/effect mitigation measures in place.
3. Lactating women should not be encouraged to discontinue nursing for the sake of participation in the study except in the condition where breast-feeding is harmful to the infant. If lactating woman decides to stop breastfeeding, harm of cessation of such breast feeding to the nursing infant should properly be evaluated and effects should be mitigated.
4. Terminally ill patients may be recruited in the clinical trial if their clinician thinks that the IP may be the last hope for cure, or a way to get free treatment for their disease, which may otherwise be beyond their reach. In such cases, the treating doctor should only recommend such treatment if it is helpful to the participants.
5. Clinical trial is permissible in people living with HIV, if the drug under the study cannot be tested in healthy participants due to predictable toxicity of the IP. When a preventive HIV vaccine trial is conducted, it can result in positive serological test and



may create problems for travel and employment. However, this does not indicate any HIV infection. In such cases, the PI should issue a document stating that he/she was a research participant in a HIV vaccine trial and provide explanation for the serological test result.

***Note:** As HIV is a sexually transmitted disease and is potentially life-threatening, the right to life of the sexual partner should be respected over the right to confidentiality of HIV infected person.*

### **7.3 Clinical Trial Involving Devices/Instruments/Implants:**

Clinical trial incorporates use of wide-ranging devices, which may be an instrument, implant, material, etc. Such devices may also be used alone or in combination with another device. Besides, devices can be used both internally and externally, for human beings or animals, and, for one or more than one specific purpose (e.g. treatment, detection, diagnosis, prevention of disease or disorder, monitoring, etc.). Such device trial should be conducted following similar steps of ethical principles as applicable for drugs or vaccines trials and should be considered in the same way as for a new drug/vaccine licensing procedure adopted by the Drug Act 1978. It may not be possible to remove the internal device if the research participant would like to withdraw from a trial after the installation of the device. This should be explained clearly through a comprehensive informed consent document to the participant prior to their enrollment. It is also important to ensure that the participant has fully understood what is being explained to him/her before participating in the trial. When a device is implanted within the human body, its follow-up period would be long enough to find the late onset of its adverse reactions/events.

Based on the type of medical devices, the levels of risk may range from low to high. For example, use of thermometers/bandage/tongue depressors may put participant at lower risk, and/or the use of hypodermic needles/suction equipment may give low-moderate risk. However, use of lung ventilator/bone fixation plate may put research participant at moderate-high risk, and similarly, heart valves/pacemaker/defibrillator may pose even higher risk.

### **7.4 Surgical Intervention/Trial:**

For conducting a trial that includes a surgical intervention, investigators should provide references for the process and define the most probable difficulties (if any) in the proposal for the ERB to review and perform risk-benefit assessment. Such surgical intervention must be guided by ethical principles applicable to drug trials. Mock surgery must not be incorporated in the design of surgical intervention (trial), except in the situation where researcher can come up with strong scientific reasons for it.

### **7.5 Community Trials**

Community trials are trials carried out at the community level and the intervention is targeted to communities rather than at individuals. The randomization procedure can also be adopted at the community level and the method of such trial is useful for studying disease prevention or public health intervention models, including behavior change interventions. Ethical review

of the community trial proposal may be treated differently, emphasizing more on how specific measures are established to protect the welfare of community members who are not participating in the trial.

## **7.6 Traditional and Complementary Medicine Clinical Trials**

To conduct clinical trials on traditional and complementary medicines developed within the country, each product must go through various pharmacological, toxicological and microbiological testing (heavy metal contamination, toxicity, microbiological testing, etc.) from the recognized laboratory, ensuring the safety of the product. The reports of such testing should be submitted to ERB along with the scientific proposal. In addition to the requirements for clinical trial of allopathic medicine, investigators must follow ‘NHRC Traditional and Complementary Medicine Research Guideline.’

## **7.7 Research in the Area of Synthetic Biology**

Synthetic biology is the field of science that involves application of science, technology and engineering to facilitate and accelerate the design, manufacture and/or, modification of genetic material of living organisms. Investigator should follow ethical and legal aspects pertaining to impacts/potential risks of synthetic biology on biosafety, biosecurity, IPRs, environment (physical and social environment) etc.

Safety provisions in Environmental Protection Act, Biomedical Waste Management Rules, and other relevant laws of the country need to be followed by the researchers working on synthetic biology. Appropriate safety training (like safe handling of the product) must be provided to researchers and staff working in an area of synthetic biology. Their periodic health screening should be done as they are at potential risk of harm from their exposure to occupational health hazards.

Biomaterials have potential for both use and harm. Notwithstanding potential benefits, there are also a number of ethical concerns about synthetic biology vis-à-vis both physical (safety and security) and non-physical harms. To ensure safety, it is important for the researchers involved in synthetic biology to weigh the benefits of research against potential risks. Researchers should also adhere to ethical principles (beneficence, nonmaleficence, equity, justice etc.) while working on synthetic biology. Besides, to avoid misuse of research, researchers are required to work in accordance with the ethical guidelines, policies, regulations and acts pertaining to research on synthetic biology. There also must be effective partnership between policy makers and researchers to generate a secure system.

Biomaterials and biocompatibility testing in a certified laboratory must be done as per the relevant regulatory standards of GoN.

## **7.8 Research in an Area of Radioactive Materials including X-rays**

If the radioactive substance is to be tested in health care, it should be considered in the same way as for a new drug/vaccine in line with Drug-Act 1978 and relevant DDA regulations. Radioactive materials comprise of radioactive isotopes with diagnostic or therapeutic uses. When such materials are used in research, their permissible radiation limits must comply with regulatory authority guidelines, and this exposure must be within acceptable limits. Research site must have obtained authority for storage, handling and dispensing such materials. Only trained researchers with appropriate safe handling training for radioactive materials should be involved in carrying out the study. Radiation workers or any person who has received more than the permissible amount of radiation in the past one year and vulnerable populations (particularly women of childbearing age and children) should be excluded from the study involving radioactive materials or X-rays. Sufficient provisions should be in place for identifying pregnancies and preventing exposure risks to the embryo. Information about possible genetic damage to the off spring must be included in the ICD/ICF.GCLP, Good Manufacturing Practice (GMP) and GCP, should be observed when conducting clinical trials.

## **7.9 Research for Bioavailability and Bioequivalence Study**

Bioavailability (BA) is the measurement of the proportion of the total administered dose of a therapeutically active drug that reaches the systemic circulation and is therefore available at the site of action.

Bioequivalence (BE) is a term used in pharmacokinetics when there are two or more medicinal products (proprietary preparations of a drug), containing the same active substance that needs to be compared in vivo for biological equivalence. These comparative studies are used to assess if the new version (generic) produces the same concentration in the systemic circulation when given to human participants. If two products are said to be bioequivalent, it means that they would be expected to be the same for all intents and purposes.

BE studies are used as surrogates for clinical effectiveness data for generic drugs, where no clinical difference is anticipated between the two products. All bioavailability and bioequivalence studies should be conducted scientifically in compliance with ethical code of conduct described earlier for Phase-I clinical trials. Ethical conduct of BA/BE study requires evaluation of the benefit–risk profile of:

- The reference (comparator) and investigational (generic) product; and
- The study procedures such as indoor stay, fasting, screening, and blood sampling.

BA/BE studies are usually conducted in healthy volunteers. Hence, they have no direct benefit to the participant but may pose risks due to the adverse effects of the drug. Therefore, all safeguards to protect participants must be in place.

The EC must carefully review the recruitment methods, payment for participation and consent procedures.

The volume of blood drawn must be within physiological limits irrespective of study design and the ERB should take precise note on the volume of blood drawn depending on whether the research participant is a healthy adult or a child. The ERB should carefully review the enrollment methods, fee/compensation for participation and informed consent taking process.

### **7.10 Public Health Research**

Defining boundaries between public health practice and research remains a challenge in public health ethics as the purpose or intent of the investigation may overlap. Public health practice involves data collection through surveillance, vital statistics, disease reporting and registries; investigation of outbreaks including contact tracing, use of preventive interventions and health promotion; monitoring and program evaluation; and enforcing of mandatory requirements, such as screening, treatment, immunization, notifying diseases and, sometimes, quarantine depending upon the situation.

By using epidemiological designs, sampling techniques and analysis, some of these activities could create generalizable knowledge, which is the primary intent of research.

Benefits and risks of public health research may influence populations, communities, and the environment, and are not restricted to a person.

ERB should differentiate between public health practice and research in order to determine its role with more clarity. It is also important to ensure that the population-based data from secondary sources do not violate any ethical principles (as mentioned hereunder) of public health research as- Principle of social justice, Principle of reciprocity, Principle of solidarity, and Principle of accountability and transparency.

#### **ERB should consider the followings aspects while reviewing public health research proposals:**

1. Are the objectives of the study scientifically sound and linked to the achievement of public health goals?
2. Is individual written informed consent required?
  - a. If not, is gatekeeper consent/permission sufficient?
  - b. Who is a gatekeeper and how is this decided?
  - c. Is it a two-stage process- initially a gatekeeper consent/permission followed by individual consent?
3. If applicable, is respect for the community applied through community engagement?
  - a. If so, is the methodology appropriate?
4. Which segments of the population are likely beneficiaries?
  - a. What are the expected benefits?
5. Is an individual harm overriding the potentially larger societal benefit?
  - a. If so, is it justified?
  - b. What are the different types of potential harm?
  - c. Who would be harmed?

- d. What, if any, measures can be taken to mitigate/minimize this?
  - e. Is the harm fairly distributed?
  - f. How do societal benefits outweigh individual harm?
6. Is social justice given due consideration while designing, implementing and assessing outcomes of the study?

### **7.11 Implementation Research**

Implementation research facilitates informed decisions about health policies, programs and clinical practices. It is co-designed and co-implemented with end users to understand and encourage uptake of a completed research. Analysis is intended to explain how best to scale an intervention or how to introduce/expand public health innovation, and, how and why a policy works. It is adaptive in nature and builds on operational research and implementation science framework. Implementation research proposal should have clear and accurate pre-defined interventions, delivery mode, outcome measurement and the role of implementers and research participants. ERB needs to understand the flexibility requirement while assessing stakeholder engagements, roles and responsibilities of the investigators to scale-up, advocate, promote uptake, or sustain the public health intervention, and harms to investigating team members related to interventions. ERB needs to ensure that the investigators provide available standard of care and health benefits resulting from the research to the research participants and the results of the study is disseminated at local level, enabling local authorities in designing future health programs/interventions.

### **7.12 Socio-behavioral Research**

Socio-behavioral research include, but are not limited to, anthropology, sociology, psychology, philosophy, political science, economics, history, communications, and education, and is different from public health, bio-medical and clinical research. Many of these research initiatives are relevant in mid to long term for knowledge production, science and society (social equity and intersectionality of populations), providing a deeper understanding of explanatory factors for policymaking.

This kind of study generally focuses on understanding human behavior, the details of symbolic communication of cultures (which includes a group's skills, knowledge, attitudes, values, and motives) and geographical contexts for planning the interventions. ERB should consider the diversity in practices of the societies due to religion, caste, social-class, gender, indigenous groups, and geo-ethnic variations which are important characteristics of society in socio-behavioral research proposals, and the mechanisms to protect vulnerabilities similar to those for public health and biomedical research.

When the researchers plan to observe some technically questionable practices and behavior of the study participants, researchers should not interrupt such practices and behaviors and must document these into their research findings. ERB needs to review investigator's

obligation to not to interrupt social harmony, data sharing and post-research benefits to the research participants on a case-by-case basis. If investigators find some patterns of behaviors such as suicidal tendency or infanticide among research participants, he/she must disclose this information to the relevant persons/authorities to save life or prevent damage intended by the participants. If researcher thinks that they might come up with sensitive incidental findings during research process, he/she needs to mention the method to handle these at individual, family, and community levels in the proposal. When the study is on sensitive topics such as mental health, gender-based violence, social exclusion and discrimination, researchers should be prepared enough to be in contact with support systems such as access to counseling centers, rehabilitation centers, security force protection, etc. In such circumstances, individuals with necessary domain knowledge and experience need to be invited as external subject experts or as the reviewers during ERB meetings, with the viewpoint to providing technical expert advice to ERB in decision making process. ERB members and investigators must have a basic understanding of legal provisions in the related area.

The safety of the study team needs to be taken into consideration especially when the research is being conducted on sensitive topics or in sensitive areas as there would be a possibility of the research team being subjected to disturbing instances while conducting the study. Sponsors and local research institution should take full responsibility for such safety concern.

If researcher would like to conduct a study within communities, he/she should not hire a local person from the same village as an interpreter, to avoid possible conflict of interest. In such cases, interpreter must be from nearby village, so that his/her possible conflict of interest, vulnerability and threat from participants can be mitigated. Research agency must develop SOPs for handling deteriorating/unforeseen situations (trauma, humiliation, and threats of violence) which might happen either to participants or study team members.

For audio/visual recording of research participant's interviews, Investigators must take prior permission from the ERB with justifiable reasons. ERB must review psychological, emotional, social, and informational harm (if any), which might have been resulted from participating in a study.

If research participants feel that they are not autonomous in decision making, informed consent should be obtained only with the permission of spouse/family head/community head/leader/culturally appropriate local authority/health care provider or institution. The consent taking process should respect local cultural customs and practices. However, such permission does not substitute for individual consent unless a waiver has been approved by ERB. In certain situations, where the power differences between investigators and research participants are clearly visible, it would be difficult for the participants to explicitly refuse to participate. Investigators must be sensitive to cultural signs of refusal, such as silence, body language, uncommunicative replies, etc., and should not continue the interview in those cases. ERB may consider these contexts during review process. Sometimes, ERB may waive

the requirement for individual informed consent, if it is convinced that the study is very important for scientific evidence generation for policy making and would not be possible without a waiver, for example, study on harmful practices.

### 7.13 Research on Molecular Genetics

Investigators need to consider following issues while conducting research on molecular genetics:

1. **Genetic test** results may put research participants into psychological stress which may be in the form of anxiety, depression, and sometimes, disruption in family relationships. There may be a possibility of social stigma and discrimination (in schooling, employment, health care, and general insurance). Thus, it is very important to maintain the confidentiality in genetic testing and follow appropriate communication skills during genetic counseling.
2. Investigators and relevant ERB members must keep abreast of emerging genetic/**genomic technologies** including genetic manipulations for known and unknown consequences for the future, so that any emergence of newer ethical concerns and issues could be tackled in due course.
3. Study team should comprise of clinicians, geneticists, genetic counselors, and laboratory personnel.
4. **Genetic testing** among vulnerable participants like children, individuals with mental illness, people with rare diseases, cognitively impaired individuals, etc. should ensure core ethical principles for protection of the participants and ERB should ensure such protection measures in the proposal and its institutional arrangements.
5. **Genetic counseling** should be done only by qualified (in terms of academic qualification, training and experience) personnel with comprehensive information in the language comprehensible/graspable for a lay person. At times, following genetic testing results, a participant may require terminating pregnancy in order to avoid genetically abnormal fetus. In such circumstances, choices must be provided to the family enabling them to come to a decision while disclosing such results during the study period. While communicating such information, there must be the presence of both spouses, and essential precaution should be taken so as not to break families. Such type of counseling should be done with extreme caution and patience, so that participant's psychosocial harm is minimized.
6. Genetic research at times demands collection of family members' details. Such family members will be regarded as secondary participants. Informed consent needs to be obtained if identifiable information is being collected about the secondary participants.
7. Research participants' genetic information is confidential and investigators should not share it with family members without their permission, especially in case where genetic information is about non-paternity, disease carrier status, etc. Sharing such confidential information may at times induce family disputes. Family members' information should be kept confidential from each other by the investigator if they have undergone genetic tests. If clinician/investigator thinks that disclosure of the genetic test is absolutely warranted to provide treatment or counseling, he/she should

first try to take informed consent from the family members, as otherwise the risks of non-disclosure against breach of confidentiality needs to be balanced after the approval from ERB. For example, if a female research participant happens to be diagnosed as a carrier of X-linked or some disease conditions (hemophilia, Huntington's disease, non-syndromic deafness, etc.) affecting the fetus and may transmit such abnormality to the next progeny. It may cause marital conflict once such information is revealed to the husband or other family members, despite the fact that husband himself is a carrier of the autosomal recessive disorder. Thus, suitable counseling must be an integral part of the genetic testing process.

8. **Genetic information** has potential for misuse. E.g. prenatal sex determination is banned by the law to restrict pre-selection of fetal gender. All investigators shall follow the provisions of the relevant guidelines, directives, regulations and law of the country.
9. Knowledge of **genetic information** of an individual/family/community/population/child might be misused by employers/insurers leading to psychosocial harm and discrimination. Therefore, participant's information should not be shared with anyone without obtaining their consent.
10. For **future genetic research**, collected bio-samples can be stored for much longer period after obtaining consent from the research participants. Biological samples from the participants with rare genetic conditions, ethnic groups/tribes/populations on the verge of extinction, and others have huge geographical and cultural value and, can be preserved for future genetic research, upon approval of the same by the ERB.
11. If the investigators discover new gene or product during the research, which could be patented, it should follow country law/regulations and proposed mechanism in the approved proposal.
12. Steps must be taken to safeguard investigators and research participants from possible inducement or coercion when the study is sponsored by commercial companies.
13. The laboratories performing genetic testing should follow standard protocols and should have a legal standing through registration.
14. Extra efforts should be ensured to maintain privacy, confidentiality of the genomic data, in addition to anonymization of the personnel identity.

#### **7.14 Molecular Testing on Biological and Environmental Samples related to Human Health:**

Molecular studies on micro-organism from biological samples (body tissues, biopsy materials, body fluids, etc.) related with human health are included in molecular diagnosis and genomic research. This also includes biomarkers testing in human tissues. Investigators should obtain informed consent from the prospective participants while collecting the specimens, fulfilling standard ICD requirements for further analysis using genetic tools.

When the anonymized specimens/ isolates/tissues are obtained from a repository/hospital, without any direct/indirect linkage with the participant identification (mostly retrospective assessment specimens), there is no need to obtain individual ICD, however



hospital/repository approval for using such specimens needs to be obtained before processing any specimens for study.

### **7.15 Research in Humanitarian Emergencies and Disasters Situations**

Health research might be necessary in humanitarian emergencies and disaster situations, to collect, analyze and recommend scientific evidence-based health response in a timely manner. In such circumstances, utmost care must be taken to protect/minimize harm to vulnerable participants, and in the ethical review processes. Designing health research in such situation is becoming a challenge because of rapidly evolving ethical uncertainties and the role of ERB is very critical for fast-tracking/expediting review process, while ensuring that the research protects the vulnerable participants and does not violate the ethical norms and standards. ERB must determine who could be an acceptable LAR in the absence of intended LAR. Participants' decision-making capacity might be so low (they might be under traumatized conditions) that they are unable to figure out the difference between benefits in the forms of reliefs offered Vs autonomy, justice and non-maleficence as participants of the research. Researchers must explain this while taking informed consent and provide additional protections (counseling, psychological help, medical advice, etc.) to research participants because of their vulnerability. For children with untraceable or deceased relatives, the consent must be obtained from an individual from the same community, who could represent the parents and is not a part of the study team. If investigators may need to waive the consent or get the consent from the participants at a later stage when community comes out of panic stage or the situation allows, he/she must have to provide its justification and obtain prior approval from ERB for obtaining gate keeper consent and individual consent at a later stage. Roles of investigators, volunteer workers and caregivers should be clarified, and potential CoI must be declared, if any.

Investigators should consider fair selection of participants. There should not be over-sampling, especially from vulnerable segments of the population. Participant selection criteria with proper justification must be provided in the proposal. The inflow of visitors/members of media during emergencies may at times lead to a breach of privacy and confidentiality. So, researchers must put extra efforts to protect participants' personal data or identifiers. Investigators and sponsors must attempt to provide beneficial interventions, which may be part of the study initiative even after completing the research project and till the local social support system is restored to deliver routine services.

### **7.16 Stem Cell Research for Health**

Research on stem cell provides novel treatment for some incurable diseases. With appropriate approvals from ERB, stem cell research is permissible in areas of embryonic, adult and cord blood as clinical trial except in the area of reproductive cloning. Clinical trial should follow all the requirements as mentioned in ICH/GCP and Clinical Trial section in the guideline. It should be conducted with clinical grade cells processed by GCLP, GMP, and GCP. Investigator should keep himself/herself updated in accordance with the changes in

guidelines regarding use of these cells.

### **7.17 Use of Animals in Research for Health**

Animals are being used for health research and these animals feel and experience same emotions as humans do. Therefore, inflicting redundant suffering or harm on animals by abusing and mistreating them during their involvement in health research should be avoided. The use of animals for research in medicine is in gradual decline and efforts are being made to replace animal experiment by other laboratory experiments. However, wherever there is absolute need, use of animals in health research could be approved by NHRC/ERB provided that the researcher complies with ‘Ethical Guidelines for the Use of Animals in Health Research in Nepal- 2005’.

#### ***The fundamental principles in animal experimentation for health research:***

1. No animals should be used in human health research until written ethical approval is obtained.
2. Ensure that the number, type, species, etc., of animals selected for the health research are appropriate and justified.
3. When designing the research protocol, the number of animals used should reflect the minimum necessary to yield valid answers to the research hypothesis.
4. Ensure that the animals used for the health research are not purchased from the illegal sources.
5. Ensure that the researchers involved in the use of animals in health research are qualified, responsible and respectful of animals’ worth and rights.
6. Ensure that the use of animals in health research is justified.
7. The species chosen for study should be best suited to answer the question(s) posed, taking into account their biological characteristics, including behavior, genetic constitution and, nutritional, microbiological and general health status.
8. Necessary steps should be taken to ensure that the animals used in health research are well sheltered (with the provision of food, water, etc.) and protected (from abuse, cruelty, exposure to contamination, etc.);
9. Proper care should be taken to minimize animals’ discomfort, distress, and pain;
10. Before using animals for the research purpose, a detailed proposal illustrating about the research plan, design and the procedures should be submitted to concerned authority. Researcher should also give clarification as to why the use of animal in the research is indispensable.
11. Upon the completion of research involving animals (that cannot be rehabilitated or returned back to their natural habitat), researcher is obliged to euthanize animals. Decision to not euthanize animals should be backed by valid scientific reasons. In case researcher decides not to kill animal, it is researcher’s responsibility to take care of the experimental animals.
12. Use of wild/endangered/threatened animals is generally restricted. However, for a research of an essential value, use of such restricted animals must abide by the law and policies for wildlife conservation. Wild animals for experimentation shall be

acquired as National Parks and Wildlife Conservation Act 2029 BS (1977 AD) (3) and the Wildlife Farming, Breeding and Research Policy 2059 BS (2002 AD), Convention on International Trade in Endangered Species of Wild Flora & Fauna, Animal Health and Livestock Service Act 2055 BS (1999 AD) (4) and rules 2057 BS (2001 AD) (5).

13. Experimental animals should be housed safely in adequate spaces with appropriate temperature, ventilation, and stress-free housing. They should not be exposed to extreme environments. Transfer delivery boxes should be strong and well secured to avoid escape.
14. The researcher should be adequately qualified, have knowledge on the behavioral characteristics of the animal subjects so as to be aware of normal, species-specific behaviors and unusual behaviors that could forewarn the researcher of potential health problems.
15. Animals used in health research should be housed in a separate location away from public housing. In addition, animals involved in research should not be exposed to dust, smoke, noise, rodents, insects, and birds. In order to avoid infection and stress, animal facility must be equipped with systems that can control infection, temperature, humidity, ventilation, lighting and sound, to suit the needs of each species.
16. Animal facility should be developed and maintained following nationally approved standards, particularly in terms of maintaining biosafety and biosecurity.
17. Since experimental animals are at high risk of being exposed to pathogens and/or hazardous agents, it is important for the researcher to adopt safety measures in line with biosafety and biosecurity guidelines to reduce the risk of spread of animals related diseases/infections.
18. Procedures subjecting animals to pain, stress, misery or death should be used only when an acceptable alternative procedure is unavailable.
19. Ensure that the animals involved in research are taken good care of, have a well-managed house and is not subject to cruelty. safe
20. Animal housing should be managed in such a way that it reflects effective involvement/supervision/accountability of a qualified and trained veterinarian.
21. Animals should be fed palatable, non-contaminated and nutritionally adequate food daily or according to their requirements unless the protocol in which they are being used requires otherwise.
22. Cages for animals should be made of suitable material and of size. Cages should also have adequate space to avoid any injury to animals. Since bedding can affect animals' well-being as well as the research outcomes, researcher should provide clean and comfortable bedding for the animals involved in research. For comfortable bedding, researcher (in consultation with the veterinarian) should select bedding materials suitable for animals.
23. All transportation of animals should be planned to minimize transit time and the risk of zoonosis, protect against environmental extremes, avoid overcrowding, provide food and water when indicated and, protect against physical trauma. Each shipment of animals should be inspected for compliance. A health certificate for the animal should be obtained at the point of transportation origin and destination. Newly received

animals should be given a period for physiologic, psychological, and nutritional stabilization before their use.

24. Same experimental animals should not be used in more than one study either in the same or different projects, without the approval of the ERB.
25. Animals cannot be subjected to successive surgical procedures unless these are required by the nature of the research, the nature of the surgery, or for the well-being of the animal. Multiple surgeries on the same animal must receive special approval of the ERB, NHRC.
26. Releasing captivated animals back to their natural habitat can pose substantial risks both to the captivated animals and other animals in the wild. Animals, that are not suitable for rehabilitation, must be euthanized upon the completion of research. However, selection and use of euthanasia method on animals should ensure less suffering and immediate death. Death should be confirmed by the personnel who can recognize and certify the cessation of vital signs in the species. A registered veterinarian should closely monitor the method of euthanasia.
27. It is important for the investigators to maintain records for the animals in research. These records should include type of species, birth profile, sex, identifier, behavior profile, etc. Animals' records should also be kept simple and comprehensive. All animals used in health research must regularly be monitored and have updated records.
28. The NHRC may form a committee responsible for monitoring the ethical use of animals in research, testing, and, production of biological materials in line with the Ethical Guidelines for the Care and Use of Animals in Health Research in Nepal-2005.

## **Section 8. Establishment of the Institutional Review Committees**

### **8.1 Establishment and Functions of Institutional Review Committees (IRC)**

The ERB, NHRC cannot possibly review and monitor all research conducted in the country. So, NHRC has been supporting the establishment of the IRCs at different health facilities and academic institutions. An IRC is a committee established within an institution for ethical review of proposals with less than minimal and minimal risk submitted by students, faculties, staff, etc. The purpose of IRC is to function as an ethics committee as its actions primarily contribute towards ensuring protection of rights, safety and well-being of human participant in the research.

IRC gets its official recognition from NHRC. Hence, it is important for IRC to take accreditation from NHRC immediately after its formation. IRC's job is to ensure that research proposals are ethical, and within the framework of Guidelines for IRCs for Health Research in Nepal. Given the nature of its work, IRC should be multidisciplinary and independent, autonomous to maintain ethical and scientific standards. Institutions that IRC represents should have research department/section, appropriate physical infrastructures, administrative and financial provisions/arrangements for IRC to function independently. Besides working independently, IRC should function transparently based on the SOP without any interference from anywhere. The SOP should be developed for IRC's effective functioning. Any institution which undertakes at least 10 health related researches in a year is eligible to establish an IRC. The members should be given an initial orientation and periodic refresher training on basic principles of research ethics and the proposal review and approval process adopted by the IRC.

While selecting the members of IRC, the institute may follow similar procedure as for ERB, which includes 7-15 members with a balance in gender and discipline (clinical, bio-medical, legal, social sector, etc), affiliated and non-affiliated. An individual shall serve up to two Ethics Committee at a time. The administrative chief and Executive Committee members of the same institution should not be the member of IRC, to minimize potential CoI. IRC should display the organogram of the institution and its working procedure. IRC should inform ERB of any changes in IRC composition and SOP, and submit annual progress reports to NHRC.

#### **8.1.1 Renewal of Institutional Review Committees**

IRC should be renewed in every 3 years. IRC should apply to NHRC at least one month before the expiry of the approval timeline along with the required documents and processing fee as per the NHRC rules. If not renewed in time, registration will be terminated after 6 months of renewal deadline.

#### **8.1.2 Withdrawal of Institutional Review Committees**

Non-compliance with the ‘Guidelines for Institutional Review Committees for Health Research in Nepal, 2016’, unjustified approval of research projects against national and international laws/guidelines of research ethics, non-renewal and inability to conduct at least 10 research studies in a year may result in the withdrawal of IRC.

## **8.2 Networking and Regulation of Institutional Review Committees**

Nepal Health Research Council (NHRC) has established IRC Accreditation Sub-committee, with a mandate to monitor and evaluate IRC’s activities. NHRC organizes IRC/ERB network meeting at least once a year to review IRC’s performance and keep abreast of changes in national/international guidelines and SOPs (related to IRC). Performance of IRCs will be evaluated annually based on the annual reports, while physical site visit of the IRCs will be done frequently. In order to strengthen the capacity of IRC, ERB should organize trainings/workshops on ethical principles, risk categorization, GCP guidelines, proposal review, monitoring the implementation of the research and reporting procedure to ERB.

Research proposals reviewed and approved by the ERB, do not require further review, approval and ethical review processing fee by any IRCs. However, for multi-centric studies, researchers should obtain the acceptance letter from the institution or IRCs and submit it to the ERB. ERB also organizes joint review and monitoring visit.

The guidelines are as follows:

### **Do’s**

- Proposal having less than minimal and minimal risk that are self-funded by the students, faculty and staff of the institute and/or published publically and proposals with a national funding of upto two lakhs.
- Single centered study/thesis submitted by the students from any university of Nepal (i.e. bachelor and master's)
- Single centered study submitted by another institute faculty having less than minimal and minimal risk can be reviewed, if there is an academic collaboration.

### **Don’ts**

- Research proposals in high risk category (trial using drugs, vaccination, invasive procedure involving human)
- Externally sponsored/funded multicentric studies at national and international level (the term "externally indicates sponsored from outside and within the country")

*Note: Please refer to Institutional Review Committee Guidelines for Health Research in Nepal-2016 for further details on IRC.*

## Bibliography

- Burke, R.E. and L.H. Friedman (2011). *Essentials of management and leadership in public health*, Jones & Bartlett Publishers.
- CIOMS (2002). *International ethical guidelines for biomedical research involving human subjects*. Council for International Organizations of Medical Sciences, Geneva.
- ICMR (2017). *National Ethical Guidelines for Biomedical and Health Research involving Human Participants*, New Delhi, India
- NHRC (2005). *National Guidelines on Clinical Trials with the Use of Pharmaceutical Products*. Ramshah Path, Kathmandu, Nepal
- NHRC (2005). *Ethical Guidelines for the Care and Use of Animals in Health Research in Nepal*. Ramshah Path, Kathmandu, Nepal
- NHRC(2011). *National Ethical Guidelines for Health Research in Nepal and Standard Operating Procedure*, Ramshah Path, Kathmandu, Nepal
- NHRC(2015). *Health Research Ethics Training Manual*, Nepal Health Research Council, Ramshah Path, Kathmandu, Nepal
- NHRC (2016). *Guidelines for Institutional Review Committees (IRCs) for Health Research in Nepal*. Nepal Health Research Council, Ramshah Path, Kathmandu, Nepal
- NHRC (2047). *Nepal Health Research council Act*, Ramshah Path, Kathmandu, Nepal
- Philippine Health Research Ethics Board (2017). *National Ethical Guidelines for Health and Health Related Research*. Bicutan, Taguig City 1631, Philippines.
- Thomas, S.B. and S.C. Quinn (2000). *Public health then and now: the Tuskegee Syphilis Study, 1932 to 1972*. *Worlds of difference*, p. 297-298.
- Thomas, S.B. and S.C. Quinn (1991). *The Tuskegee Syphilis Study, 1932 to 1972: implications for HIV education and AIDS risk education programs in the black community*. *American journal of public health*, 81(11):p.1498-1505.

## **Glossary**

**Accountability:** The obligation of an individual or organization to account for its activities, accept responsibility for them and disclose the results in a transparent manner.

**Adverse Event:** Any untoward medical occurrence in a patient or participant involved in a study which does not necessarily have a causal relationship with the intervention. The adverse event can therefore be any unfavorable or unintended sign or experience, regardless of whether or not it is related to the product under investigation.

**Assent:** To agree or approve after thoughtful consideration of an idea or suggestion in order to participate in research by children (above 7 years and under 18 years), who is old enough to understand the implications of any proposed research but not legally eligible to give consent. The assent has to be corroborated with informed consent of parent/LAR.

**Audit:** A systematic and independent examination of research activities and documents in order to determine whether the review and approval activities were conducted, and, data recorded and accurately reported as per applicable guidelines and regulatory requirements.

**Autonomy:** The ability and capacity of a rational individual to make an independently informed decision to volunteer as a research participant.

**Beneficence:** To try to do good or an action which weighs the risks against benefits to prevent, reduce or remove harm for the welfare of the research participant(s) in any type of research.

**Bio-availability:** It is the measurement of the proportion of the total administered dose of a therapeutically active drug that reaches the systemic circulation and is therefore available at the site of action.

**Bio-bank:** It is a systematic collection of bio-specimens in standard laboratory/health institution for research and related activities in future.

**Bio-equivalence:** It is a term used in pharmacokinetics when there are two or more medicinal products (proprietary preparations of a drug), containing the same active substance that needs to be compared in vivo for biological equivalence.

**Capacity:** Capacity of vulnerable population may be reduced because of their personal disability, lack of understanding or ability to communicate, lack of power, social injustice, environmental burdens and/or situation that prevents the vulnerable population to work in best of their interests.

**Case Report Form:** It is a printed, optical or electronic document designed to record all the required information in the protocol on each study participant, to be reported to the sponsor.



**Clinical Trial Registry:** An official platform for registering a clinical trial.

**Cognitive Impairment:** When a person has trouble remembering, learning new things, concentrating, and/or making decisions that affect their everyday life.

**Compensation:** Provision of financial payment to the research participants or their legal beneficiaries when temporary or permanent injury or death occurs due to participation in health research.

**Confidentiality:** It is the duty of the investigator(s) or research agency to not disclose any personal or confidential information of the research participant to protect their rights, safety, dignity and well-being. Hence, maintaining confidentiality incorporates the requirement to safeguard information from unauthorized access, use, disclosure, alteration, damage or stealing.

**Conflict of Interest:** Conflict of interest is a set of conditions in which professional judgment concerning a primary interest like patient's welfare or the validity of research tends to be or appears to be unduly influenced by a secondary interest like non-financial (personal, academic or political) or financial gain.

**Contract Research Organization:** An institution or service organization which is generally recruited by the sponsor for providing research support/services (especially vaccine trial) on a contractual basis nationally or internationally.

**Coercion:** An overt or implicit threat of harm to a participant which is intentional to force compliance.

**Collaborative Research:** An umbrella term for methodologies that actively engage national and international public/private institutions in the research process from the start of the research to its completion.

**Competence:** The broad professional knowledge, attitude and skills required in order to work in a specialized area or profession.

**Deception:** It occurs when investigators provide false or incomplete information to the participants in order to manipulate them into consenting. Deception is sometimes committed to achieve the study objectives and for larger public good. Research employing any type of deception should however undergo full committee review.

**Disaster or Humanitarian Emergency:** It is an event or series of events that represents a critical threat to the health, safety, and/or security or well-being of a community or other large group of people, usually covering a wide land area.

**Exploitation:** The action or fact of treating someone unfairly in order to benefit from their participation.

**Fabrication:** This is the intentional act of making-up data or results and recording or reporting them.

**Falsification:** This is manipulating study supplies, materials, equipment or procedures or altering or skipping/suppressing data or results without scientific or statistical explanation, such that the research is not precisely represented in the study document.

**Impartial Witness:** A person, who is independent of the trial, who cannot be unfairly influenced by people involved in the trial, who attends the informed consent process if the participant or the LAR cannot read, and, who reads the informed consent form and any other written information supplied to the participant.

**Implementation Research:** It is a type of health policy and systems research that draws on many traditions and disciplines of research and practice. It builds on operations research, participatory action research, management science, quality improvement, implementation science, and impact evaluation.

**Informed Consent Document:** Written, signed and dated paper confirming participant's willingness to voluntarily participate in a particular research, after having been informed of all aspects of the research that are relevant for the participant's decision to participate.

**Inducement:** A motive or consideration that leads one to action or to additional or more effective actions without considering the harm that may occur.

**Legally Authorized Representative:** A person who, under applicable law or judicial authority, can give consent on behalf of a prospective participant who, for either legal or medical reasons, is unable to give consent herself/himself to participate in research or to undergo a diagnostic, therapeutic or preventive procedure as per research protocol, duly approved by the ERB.

**Plagiarism:** This is the direct stealing anything (including language, thoughts, ideas, or expressions) from someone's published paper/book etc. and represent these as one's own original work. Sometime duplicating one's own publication also falls under the category of plagiarism, which may be termed as self-plagiarism.

**Pilot Studies:** A pilot study, project or experiment is a small-scale preliminary study conducted in order to evaluate feasibility, time, cost, adverse events and, effect size (statistical variability) in an attempt to predict an appropriate sample size and improve upon the study design prior to the performance of a full-scale research project.

**Principal Investigator:** An individual or the leader of a group of individuals who initiates

and takes full responsibility for the conduct of health research; if there is more than one such individual, they may be called co-principal investigators/co-investigators.

**Privacy:** It is the participant's right to control the information that can be gathered and stored by him/her and to whom that information might be shared.

**Psychosocial harm:** Research, particularly psychology studies, can put participants in situations that may make them feel uncomfortable while learning about their reaction to a situation. The result can be psychological harm that can manifest itself through anxiety (warranted or unwarranted), distress or depression, embarrassment, shame or guilt and/or, the loss of self-confidence.

**Quorum:** Minimum number and/or kind of ERB members required for decision making during a meeting.

**Re-consent:** It is the process of ensuring participant's willingness to remain in the study by re-obtaining and documenting his/her consent.

**Risk:** Probability of harm or discomfort to research participants. Acceptable risk differs depending on the conditions inherent in the conduct of research.

**Standard Operating Procedure:** Detailed written instructions in a certain format describing all activities and actions to be undertaken by an organization to achieve uniformity in performance of a specific function.

**Serious Adverse Event:** It is serious adverse event when the research outcome for the participant is death, life-threatening injury requiring hospitalization, prolongation of hospitalization, significant disability/incapacity, congenital anomaly, or requirement of intervention to prevent permanent impairment or damage.

**Social Harm:** It is a non-medical adverse consequence of study participation, including difficulties in personal relationships and stigma or discrimination from family or community. Social harm can be related to personal relationships, travel, employment, education, health, housing, institutions (government/non- government) and others.

**Sponsor:** An individual, institution, private company and/or government or non-governmental organization (within or outside the country), who initiate the research and are also responsible for its management and funding.

**Transparency:** It implies intentional openness, communication, and accountability operating in such a way that it is easy for others to see the actions being performed.

**Undue Inducement:** Offer of disproportionate benefit in cash or kind that compromises judgment which may lead to acceptance of serious risks that threaten fundamental interests.

**Vulnerability:** It pertains to individuals who are relatively or absolutely incapable of protecting their own interests because of personal disability, environmental burdens or social injustice, lack of power, understanding or ability to communicate and/or, are in a situation that prevents them to act in best of their interests.

## Annex I: Sample Transfer Plan

Biological samples	For what test	Is the required test available in laboratories registered in National Public Health Laboratory in Nepal? Yes / No	Is the required method available in the registered laboratory? Yes / No	If no, is there any plan to make test/method available in the registered laboratory? Yes / No	Is there any plan to transfer biological sample abroad? Yes / No	Remark

## Annex II: Basic requirements and list of documents required for applying online proposal submission

<p><b>Screening:</b></p> <p>Research related to health, national or international researcher and thesis or self-funded study.</p>
<p><b>Administrative information:</b></p> <ul style="list-style-type: none"> <li>• Most current version of the CV of the PI, Co-investigators and other team members with special mention of academic qualification and research experiences in pdf format or Word format;</li> <li>• Photos of PI and Co-Investigator and other team members in jpg format; and</li> <li>• Scanned signature of PI and Co-Investigator and other team members in jpg format.</li> </ul>
<p><b>Financial Details:</b></p> <p>It includes human resource cost, field expenses, transportation cost, laboratory cost, data management cost, report writing and dissemination cost, logistic cost, monitoring and evaluation cost, miscellaneous cost, ethical review cost, and ‘total budget of health research to be spent in Nepal.’</p>
<p><b>Technical Details:</b></p> <p>Title of Research, Research Area, Background, Rationale/justification, Conceptual Framework, General Objective, Specific Objective, Research Hypothesis, Study Variables, Research Method, Research Design, Description of Research Design, Study Site and its Justification, Study Population, Sampling unit, Sample Size, Number of Participants and Justification, Sampling Technique, Criteria for Sample Selection, Data Collection Technique, Data Collection Tools, Pretesting, Validity and Reliability of Tool, Potential Biases, Limitation of the Study, Plan for Supervision and Monitoring, Plan for Data Management and Analysis, Expected Outcome of the Research Results and, Plan for Utilization of Research Findings</p>
<p><b>Ethical Consideration:</b></p> <p>Number of human participants to be involved, frequency, responsibility, vulnerability, risks and benefits, types of informed consent, etc.</p>
<p><b>Documentation:</b></p> <ul style="list-style-type: none"> <li>• Documents: Data collection tools, conceptual framework, consent form, agreement letter, work plan, donor agreement letter (if any), etc.</li> <li>• Data collection tools should be in Nepali and local language (if necessary) including interviews and Focused Group Discussion guideline, observation checklist, and questionnaire sets.</li> <li>• A copy of informed consent/assent form in Nepali and local language (if required) should be included in the application. This should include a detail description of the process of giving the information to the research participants and its content, process of obtaining the consent, the person responsible for obtaining the informed consent and documentation of the signature of the</li> </ul>

<p>researcher/research participants and/witness if applicable.</p> <ul style="list-style-type: none"> <li>• Consent form should be in Nepali and local language with date and version number.</li> <li>• If the research study is to be conducted in a hospital/organization or institution, a letter of support from the respective hospital/organization or institution should be provided.</li> <li>• Agreement letter with donor, if it is a funded study.</li> <li>• If the PI is a non-Nepali citizen, one additional PI should be a Nepali citizen relevant to the study subject. Nepalese PI should be responsible for all the activities to be done in Nepal. S/he is also responsible for communication and correspondences.</li> <li>• Institutional ethical clearance from his/her own country, if submitted from academic and related institution from outside the country.</li> <li>• If the study requires bio-samples/specimens to be transported outside of Nepal (justification needed), MTA, CVs of the bio-sample/specimens handling person, and, commitment letter from the PI (stating that the proposed tests will be conducted only for this study) must be provided. Only extracted and amplified bio-samples (in most of the cases) will be allowed to transfer. Back up bio-samples should be kept in Nepal (if possible). Or else, PI should provide its justification.</li> </ul>	<ul style="list-style-type: none"> <li>• In case of trial, additional documents are required;</li> <li>• Description about the study design, screening and eligibility assessment including randomization and blinding process (if followed);</li> <li>• The phase of trial, and a detail description of the safety of the product or procedures;</li> <li>• Investigational Medicine Product (IMP) (IMP description, labeling, supply, its storage, etc.);</li> <li>• Investigational brochure;</li> <li>• Safety reporting (definition, causality, procedure for recording and reporting adverse events, etc.);</li> <li>• Independent DSMB;</li> <li>• Pharmacovigilance safety report including the pharmacological, pharmaceutical, and toxicological data available;</li> <li>• Provision of insurance in the event of any participant suffering harm as a result of their involvement in the research;</li> <li>• Results of the previously conducted clinical trial (authentic reports);</li> <li>• Signed final copy of the previously conducted clinical trial documents;</li> <li>• ‘No objection letter’ from the regulatory authorities in Nepal; for example, in the case of drug and vaccine trial, DDA should provide such letter. There may be a need of such letter from National Committee for Immunization Program working under Family Welfare Division of Department of Health Services if vaccine trial will be conducted;</li> <li>• Clinical Trail Registration (CTR) number;</li> </ul>
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<ul style="list-style-type: none"> <li>• Original Protocol (which was submitted to sponsor) ;</li> <li>• Details of Contract Research Organization (CRO) (required if it is a clinical trial proposal);</li> <li>• Other center's ethical approval letter or support letter;</li> <li>• List of abbreviations /acronyms; and</li> <li>• References.</li> </ul>
<p><b>For student applicants:</b></p> <ul style="list-style-type: none"> <li>• Approval Letter from concerned Institute/University, mentioning PI, Co-I, collaboration and funding provision of the study;</li> <li>• Recommendation letter from academic supervisor stating that the student is working under his/her supervision; and</li> <li>• In case of foreign student working for academic thesis in Nepal, the local Nepali supervisor should be the co-investigator.</li> </ul>
<p><b>Ethical review processing fee:</b></p> <p>Ethical review processing fee will be charged as per the NHRC rules and regulations which can be deposited at NHRC office or designated bank account.</p>



### **Annex III:**

#### **List of participants in Residential Workshop on Revision and Updating National Ethical Guideline for Health Research in Nepal [Dhulikhel, Kavre on 30-31 July 2021]**

Prof. Dr. Gehanath Baral, Chairperson, NHRC  
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Prof. Dr. Sabina Shrestha, Member, ERB, NHRC  
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Ms. Namita Ghimire, Research Officer, Ethical Review M&E Section, NHRC  
Prof. Dr. Mohan Raj Sharma (Institute of Medicine, Maharajgunj, Kathmandu)  
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Mr. Sudip Gyanwali, Administrative Officer, NHRC  
Ms. Kamala Luitel, Store Assistant, NHRC  
Mr. Pukka Lal Ghising, Assistant Account Officer, NHRC  
Mr. Subash Ghising, Office Assistant, NHRC, NHRC

#### **List of participants in National Consultation Workshop for National Ethical Guideline Finalization, [NHRC, Kathmandu, 24-26 September 2019]**

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Dr. Bhola Ram Shrestha (Ex-Executive Board Member)  
Dr. Shyam Kumar BK (Ex-Executive Board Member)  
Dr. Ramesh Kharel (Ex-Executive Board Member)