STANDARD OPERATING PROCEDURE FOR THE

INSTITUTIONAL REVIEW COMMITTEE (IRC)

OF

LUMBINI MEDICAL COLLEGE AND TEACHING HOSPITAL (LMCTH)

1. Introduction

   One of the objective of the institute (LMCTH) is to promote scientific study and quality research. The institute will form an institutional review committee (IRC) to review all health research proposals to be conducted in the institute for the scientific quality and ethical propriety and to take the necessary steps to approve or disapprove such research proposals.

   In order to carry out this task, LMCTH developed the Institutional Ethical Guidelines for Health Research in the Institute based on National Ethical Guidelines for Health research in Nepal, issued by Nepal Health Research Council (NHRC) and constituted an Institutional review committee (IRC) in accordance with the provisions made in the Guidelines.

   In order to facilitate the work of IRC, a Standard Operating Procedure (SOP) has been developed. This SOP will guide the IRB to carry out its responsibilities in a consistent and smooth manner.

   The purpose of this SOP is to safeguard the dignity, rights, safety and well-being of research participants and promote scientific and ethical health research in Nepal.

2. Functions and Duties of the IRC
   a. To review research proposals according to the LMCTH Ethical Guidelines for Health Research with a view to approve, amend or reject the proposal
   b. To supervise or monitor the implementation of health research projects approved by IRC
   c. To conduct training programs for members and reviewers of IRC on the ethical review process
   d. To resolve ethical issues arising out of reviewing, approving , supervising and disseminating the research findings
   e. To promote research in the process of review, implementation, supervision of research and dissemination of research findings.

3. Membership of ERC
   a. Executive Board (EB) of LMC will appoint the members and chairman of the IRC; one of the members or IRC will act as the member-secretary of the IRC.

b. Member-secretary of IRC will prepare a list of potential candidates for the IRC membership and submit these names to the Chairman of LMC who in consultation with EB of LMC will make the appointments. Members will be drawn from multiple departments, both basic and clinical, and members unaffiliated with LMC will be included in the IRC. Potential candidates should be drawn from among the senior faculty members possessing at least postgraduate qualification in a related scientific discipline, having received training in ethics and the ethical review process.
c. Member-secretary of IRC, while preparing the list of potential candidate will give due consideration to the possible conflicts of interest of the different candidates. Each potential candidate will be asked to indicate possible conflicts of interests that might arise in the course of their IRC work. The Secretary records this data and informs the Chairman.
d. While making the appointment, at least 33% of the members of the existing IRC will be retained in order to ensure continuity of experience.

4. Term of appointment to the IRC
    a. The IRC member will be appointed for the duration of a three year term.
    b. Policy for renewal: in order to maintain continuity of experience at least 33% of the members will be retained in a new IRC.
    c. Disqualification procedure: A member who was found upon an investigation conducted by IRC acting contrary to the interests of LMC, breaching the conditions of appointment will be disqualified from continuing in the IRC. This qualification would be made by the EB of LMC. Legal prosecution will also lead to disqualification.
    d. Resignation: a member who does not want to continue in on the IRC can submit his or her resignation to IRC of LMC, which will be forwarded to the Chairman. On acceptance of the resignation, membership on the IRC will cease.
    e. Replacement procedure: the process followed for appointment of members will be followed to replace the IRC members.

5. Conditions of appointment to the IRC
    a. Member accepting to serve on the IRC should agree that his or her name, professional qualification, experience and affiliations would be publicized through the reports of LMC, IRC.
    b. Member accepting to serve in the IRC should agree that the remunerations paid to him or her in course of IRC work will be recorded and will be made available to the public on request.
    c. Member accepting to serve in the IRC will have to sign a confidentiality agreement regarding meeting deliberations, applications, information on research participants and related matters.

d. All administrative staff working for IRC will also have to sign a confidentiality agreement regarding meeting deliberations, applications information on research participants and related matters.

6. Office of the IRC
    a. LMC will assign space within the premises of LMC for the exclusive use by Chairman or members of the IRC and administrative staff.
    b. IRC of LMC will have its own phone, fax, photocopy cupboard and administrative staff.

7. Meetings
    a. Secretary of the IRC will prepare the agenda for the meeting in consultation with the Chairman of the IRC. The Secretary will also keep minutes of the meeting and notify decisions to the researcher. The Secretary will be assisted in his or her tasks by an administrative secretary.
    b. IRC will prepare a regular annual report which will be published after its approval by EB of LMC.

8. Quorum requirements for IRC
    a. IRC will have 11 members.
    b. At least 6 members must be present to compose a quorum. Presence of members of only one gender will not constitute a quorum.
    c. At least one member present should have expertise in areas other than the subject under discussion. Preferably a member from outside of the health science background must be present.

9. Independent Consultant(s) to the IRC
    a. IRC will prepare a list of independent consultants who can be called upon by IRC to provide expert opinion on proposed research proposals. These consultants will be subject specialists, methodologists, Environmentalists, legal specialists, ethicists, sociologists, psychologists, anthropologists or representative of specific communities, patient groups and special interest groups.
    b. Independent consultants who agree to help the IRC will have to sign a confidentiality agreement regarding their assignment, meeting deliberations, applications, information on research participants and related matters.
    c. Independent consultants will be paid remuneration as per LMC regulations.

10. On-Going Education of the IRC Members
    a. All new IRC members will be provided with orientation training.
    b. IRC will conduct regular training programs for IRC members at least two times in a year. Such training programs will provide opportunities for hands on experience

of reviewing the research proposals as well as problems faced while reviewing, implementing or disseminating of research.

c. IRC will forward requests from IRC members for participation in national, regional or international training programs' on ethics in health research. EB of LMC will try to accommodate such requests as far as possible.

11. Submitting the Application
    a. Individuals desirous of conducting health research in LMC are required to submit their health research proposal to IRC of LMC.
    b. Application Submission
        i. The Principal Investigator (PI) and/or the one responsible for the health research will submit the health research proposal for review.
    c. Application Requirements Include
        i. Application: Application should be addressing to the Member-secretary of IRC
        ii. Format for Application: Application should be submitted in the format provided by LMC. The prescribed format can be accessed from the website (www.lmc.edu.np) of LMC or a hard copy can be obtained from LMC office.
        iii. Language of Applications: All Applications should be submitted in English
        iv. Application should include one hard copy and an electronic copy of the proposal.
        v. Only those applications fulfilling the requirements will be accepted for review. Deficits in the application shall be informed to the applicants within two weeks of submission. Incomplete applications will have to be resubmitted.
        vi. A receipt of the accepted application will be provided to the researcher
        vii. Application Fee: Applications should be submitted along with processing fee as per LMC rule/decision made by the Executive Board of LMC.
        viii. Additional documents or changes: IRC can request the applicant for supplementary documents/or changes to the proposal during the review which will be communicated to the applicant and the application will be considered in the subsequent meeting after those changes are made by the researcher.
        ix. Amendments: If any amendments are made in the proposal already submitted and approved, the researcher must submit in writing the changes made with reasoning. The proposal will be reviewed again in the IRC, taking the amendments into consideration during the re-approval process.
        x. Informed consent: Application should include the Informed Consent Form as a separate copy which is to be used while undertaking the research. In

addition, this can include a translation copy, in a local language if that is applicable.

12. Documentation Requirements for the Application
    a. All the documents that are required by the IRC for a process of review and approval should be submitted along with the application. If any additional documents are required during the review process, the researcher will be notified by IRC.
        i. The application form should be submitted with the signature and date of submission using the LMC format.
        ii. Application must include the most current version of the curriculum vitae of the Principal Investigator and co-investigators with special mention of academic qualification and research experiences.
        iii. Application must include the protocol of the proposed research project in the provided format together with the supporting documents. (A copy of research tools, questionnaires etc.)
        iv. A copy of informed consent form should be included in the application. This should include a detail description of the process of giving the information to the research participant and its content, process of obtaining the consent, the person responsible for obtaining the informed consent and documentation of the signature of the researcher/research participant and /witness if applicable.
        v. Any compensation to be given to the research participant should be clearly mentioned. (e.g. any transportation costs, food, free health care or insurance coverage etc. that is to be borne by the researcher)
        vi. In case of clinical trials, description about the study design, the trial phase, and a detail description of the safety of the product or procedures must be mentioned. It should include the pharmacological, pharmaceutical, and toxicological data available and also include the investigators brochure.
        vii. A signed statement by the researcher stating that he or she will abide by the ethical principles of research.
        viii. Information about any previous submission of this application to IRC or any other Institutional Review Committee and the result of such submission in the past will have to be provided along with the application.
        ix. A declaration of the conflict of interest, if applicable, should be mentioned in the application.

13. Ethical Review Process

    The IRC will review all the submitted health research proposals in a timely manner and in accordance with the set review process.

a. Meeting of the IRC

The meetings of the IRC will be held on a regularly scheduled dates that will be announced in advance. The Member-secretary of IRC with the permission of the Chairman of the IRC will call the meeting. The followings are considered as applicable for an IRC meeting:

i. The meeting of IRC will be planned in accordance with the workloads and number of proposals received for review. Normally, IRC will meet once a month.
ii. IRC members will be informed about the meeting at least 72 hours prior to the scheduled date.
iii. If felt necessary by the IRC, the applicant researcher or sponsor of the research can be invited to present the proposal or elaborate on specific issues of the proposal. Similarly, if necessary, experts can also be invited to the meeting for expert opinion about the research.
iv. Minutes will be kept of all decisions and procedures of the meeting
v. All the members and invitees present in the meeting should sign the minutes to indicate their presence.

b. Elements of the Review Process
    i. Technical Review by the Reviewers: Once the application is submitted and screened for completeness of documents, technical review of the proposal is done by the internal reviewers for the scientific and technical contents. The application received after internal review is then subjected for review by the external reviewers.
    ii. Ethical Review: Those applications which qualify are then submitted to the Secretary of the Ethical Review Board and then discussed in full board IRC meeting for ethical review.
        1. Scientific Design of Research Proposal and Conduct of Research
        2. The appropriateness of the study design in relation to the objectives of the study
        3. Statistical methods: sampling method, sample size and analysis of data
        4. Justification of predictable risks and inconveniences against the anticipated benefits for the research participants and community by the proposed study
        5. Justification of the use of control arm (if relevant for the study)
        6. Criteria for prematurely withdrawing research participants
        7. Criteria for suspending or terminating the research
        8. Provisions for data safety monitoring board (DSMB)
        9. Plan for dissemination or publication of research results

10. Infrastructure and other facilities in the institutions conducting the research
11. Suitability of researcher's qualification and experiences for The proposed research
12. Description of the population from which the research participants will be drawn
13. Inclusion criteria for the research participants
14. Exclusion criteria for the research participants
15. Protection of research participants
16. Measures to ensure the confidentiality of the research participants
17. Description about who has access to data and biological samples
18. The compensation provided to the participants in case of adverse drug reaction and or adverse events
19. Description of the process of reporting any adverse drug reaction and/or adverse event
20. Description about the provision of availability of the research product for the participants after completion of the research project.

iii. Informed consent process
    1. A full description of the process for obtaining informed consent including the description about who is responsible for obtaining the informed consent
    2. Process of communication with the research Participants about the objectives, methods, risks and benefit of the research
    3. Description about obtaining consent from the vulnerable research participant (e.g. children, elderly, disabled, prison population, people in uniform services, etc.)
    4. Description about the provision for the participants to queries and complaints during the course of research.

iv. Community considerations
    1. The relevance of the research for the community from where research participants are drawn
    2. The process taken for the consultation and communication with the community
    3. Description about how the research results will be available for the community

v. Expedited Review

In the following situations the IRC will allow the Member Secretary to expedite the review of the proposal.

1. If the research is non interventional, based on secondary data, leading to thesis.
2. If the research is carried out under the circumstances of outbreak, disaster and other emergency conditions.
3. If the proposal is found technically and scientifically sound after reviewing by internal reviewer of LMC.
4. The Secretary should inform to LMC Chairman and in the IRC meeting about the proposals expedited.

14. Decision Making

The IRC will consider the following while making decision about the research proposal

a. The IRC will make the decision only if the meeting has met required quorum as noted in 8b
b. Normally the decision will be taken by consensus, (if consensus is not possible then a vote will be taken)
c. The IRC member should withdraw from the decision process when conflict of interests arises; the member should declare the conflict of interest.
d. The IRC may approve the proposal conditionally with specific suggestions to the researcher.
e. The negative decision on a proposal should be supported by clearly stated reasons.

15. Communicating a Decision

On behalf of the Ethical Review Board, the Member Secretary will communicate its decision to the applicant in writing within two weeks after the meeting. The communication of the decision will include, but is not limited to the following information:

a. The exact title of the research proposal reviewed
b. The clear identification of the protocol of the proposed Research or amendment, date and version number (if applicable) on which the decision is based.
c. The names and (where possible) specific identification numbers (version numbers/dates) of the documents reviewed, including the potential research participant information sheet/material and informed consent form.
d. The name and title of the applicant.
e. The name of the research site(s)
f. The date and place of the decision
g. A clear statement of the decision reached
h. Any advice by the IRC

i. In the case of a conditional decision, any requirements by the IRC, including suggestions for revision and the procedure for having the application re-reviewed.
j. In the case of a positive decision the following is required:
    i. A statement of the responsibilities of the applicant
    ii. Confirmation of the acceptance of any requirements imposed by the IRC
    iii. Deadlines for the submission of progress report(s)
    iv. The need to notify the IRC in cases of protocol amendments (other than amendments involving only logistical or administrative aspects of the study)
    v. The need to notify the IRC in the case of amendments to the recruitment material, the potential research participant information, or the informed consent form
    vi. The need to report serious and unexpected adverse events related to the conduct of the study
    vii. The need to report unforeseen circumstances, the termination of the study, or significant decisions by other Ethical Committees
    viii. The information the IRC expects to receive in order to perform ongoing review and deadlines for the submission of final report
    ix. The schedule/plan of ongoing monitoring by the IRC
    x. In the case of a negative decision, clearly stated reason(s) for the negative decision
    xi. Signature (dated) of the Secretary (or other Authorized person) of the IRC

16. Follow up of the IRC

IRC will establish a follow-up procedure for following the progress of all studies for which a positive decision has been reached, from the time the decision was taken until the termination of the research.

a. The follow-up review intervals will be determined by the nature and the events of research projects, though each protocol should undergo a follow-up review at least once a year.
b. The following instances or events require the follow-up review of a study.
    i. Any protocol amendment.
    ii. 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
    iii. Any event or new information that may affect the benefit/ risk ratio of the study
c. A decision of a follow-up review will be issued and communicated to the applicant, indicating a modification, suspension, or termination of the IRC's original decision or confirmation that the decision is still valid.

d. In the case of the premature suspension/termination of a study, the applicant should notify the IRC of the reasons for suspension/termination; a summary of results obtained in a study prematurely suspended/terminated should be submitted to the IRC.
e. The applicant will inform the IRC at the time of the completion of a study.
f. The applicant will submit to the IRC a copy of the final summary or final report of a study.
g. The IRC can issue an approval letter for publication as per need.

17. Documentation and Archiving

All documentation and communication of IRC will be dated, filed, and archived according to written procedures. A statement is required defining the access and retrieval procedure (including authorized persons) for the various documents, files, and archives. The documents will be archived for a minimum period of 5 years following the completion of a study.

Documents that should be filed and archived include

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

Appendices

Appendix I

Checklist for the Ethical Review of Proposals

Review of the research proposal for ethical clearance:

Title of the research proposal:

Date of review:

Reviewer:

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

Appendix II

Ethical Questions

ETHICALLY DRIVING QUESTIONS FOR CONSIDERATION BY THE ETHICAL REVIEW BOARD

1. What questions does this research answer?
2. Are those questions relevant to the needs of the country?
3. Has/ve such research (es) been already conducted in Nepal? Elsewhere?
4. Has another IRC reviewed this proposed research? If yes, what was their decision?
5. Is it necessary to involve human subjects for the research?
6. Whom does the research put at risk?
7. What are risks? Identify them.
8. Whom does the research benefit?
9. Do the participants benefit at all from the study?
10. Do the participants have any risk from participating in the study? If so, what are those risks?
11. Do the benefits outweigh any risks?
12. How is informed consent obtained from the participants, and is the type of informed consent appropriate?
13. How can the participants opt out of the research once it is started?
14. Is the research externally sponsored? If yes, what are the responsibilities of the external sponsor?
15. Is there any transfer of technology involved during the research process?
16. How are the sponsors going to strengthen the research capability of the host institution?
17. Is there going to be transfer of biological materials?
18. Is there provision of Data Safety Monitoring Board (DSMB) for clinical trial study?
19. Is the clinical trial registered elsewhere?