STANDARD OPERATING PROCEDURES FOR RESEARCH ETHICS BOARD, RIMS IMPHAL (SOP REB RIMS VERSION 3.0)

Amended on 17th April 2024

REGIONAL INSTITUTE OF MEDICAL SCIENCES, IMPHAL

STANDARD OPERATING PROCEDURES
FOR
RESEARCH ETHICS BOARD RIMS, IMPHAL

REGIONAL INSTITUTE OF MEDICAL SCIENCES
IMPHAL-795004, MANIPUR, INDIA

	Name	Designation	Signature	Date
Prepared by	Dr Akoijam Joy Singh	Member Secretary, REB RIMS Imphal		10th February 2024
Reviewed by	Prof. L. Bishwanath Sharma	Chairman, REB RIMS Imphal		15th February 2024
Approved by	Prof. G Sunil Kumar Sharma	Director, RIMS Imphal		17th April 2024

Date of Implementation: **17th April 2024**
Version Number: **SOP REB RIMS Version 3**
Valid till: **16th April 2027**

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Standard Operating Procedures (SOP) of the RIMS Research Ethics Board for Biomedical and Health Research Involving Human Participants

1. Introduction

In accordance with the Declaration of Helsinki and subsequent international ethical guidelines, including ICMR for biomedical research, it is necessary for all research proposals involving human subjects to be cleared by an appropriately constituted Research Board or Ethics Committee to safeguard the welfare and rights of participants. Ethics Committees are entrusted not only with the initial review of the proposed research protocols prior to initiation of the projects but also have a continuing responsibility to regularly monitor compliance with all ethical requirements till the completion of the study.

This Standard Operating Procedure (SOP) document outlines the policies, procedures, and guidelines for the ethical review and oversight of research involving human participants by the Research Ethics Board (REB) of the Regional Institute of Medical Sciences, Imphal. The REB is responsible for ensuring that all research activities carried out under the auspices of the Regional Institute of Medical Sciences, Imphal, comply with the highest ethical standards and applicable regulations, guidelines, and laws.

The primary objective of the REB is to protect the rights, safety, and well-being of human participants involved in research projects conducted by the Regional Institute of Medical Sciences, Imphal, or external researchers seeking approval from the committee. The REB is committed to facilitating ethical and scientifically sound research while upholding the principles of respect for persons, beneficence, and justice, as outlined in the Indian Council of Medical Research (ICMR) National Ethical Guidelines for Biomedical and Health Research Involving Human Participants (2017), Drugs and Cosmetics Act 1940 and Drugs and Cosmetics Rules 1945 (including the amendments), and New Drugs and Clinical Trials Act and Trial (2019).

The SOP document is designed to ensure consistency, transparency, and accountability in the REB operations and decision-making processes. It is aligned with the ICMR National Ethical Guidelines, as well as other relevant national and international regulations, guidelines, and best practices.

2. Objective

The objective of this SOP is to contribute to the effective functioning of the Research Ethics Board (REB) of RIMS so that a quality, consistent and unambiguous ethical review mechanism for health and biomedical research is put in place for all proposals dealt with by the REB RIMS based on the existing Indian regulations and relevant international guidelines.

3. Roles and responsibilities of the REB RIMS

3A. Terms of reference of REB

The **terms of reference of REB RIMS are** aligned with the Indian Council of Medical Research (ICMR) National Ethical Guidelines for Biomedical and Health Research Involving Human Participants (2017). They are,

1. **Review and approval of research proposals:** REB RIMS shall be responsible for reviewing and approving research proposals involving human participants, ensuring that the proposed research adheres to ethical principles, such as respect for persons, beneficence, and justice.
2. **Protection of participants' rights and welfare**: REB RIMS shall ensure that the rights, safety, and well-being of research participants are adequately protected. This includes evaluating the potential risks and benefits of the research, ensuring informed consent processes are in place, and monitoring ongoing research for any potential ethical issues.
3. **Oversight and monitoring**: REB RIMS shall provide ongoing oversight and monitoring of approved research projects. This includes reviewing progress reports, monitoring adverse events, and addressing any ethical concerns that may arise during the course of the research.
4. **Conflict of interest management**: REB RIMS shall identify and manage potential conflicts of interest that may arise among researchers, sponsors, or committee members to ensure the integrity and objectivity of the research review process.
5. **Compliance with regulations and guidelines**: REB RIMS shall ensure that research complies with relevant national and international regulations, guidelines, and ethical standards, such as the ICMR National Ethical Guidelines, New Drugs and Clinical Trial Act and Rules (2019), Good Clinical Practice (GCP) guidelines, and other relevant laws and regulations.
6. **Capacity building and education**: REB RIMS shall promote ethical awareness and provide training and education to researchers, staff, and committee members on ethical principles, guidelines, and best practices in research involving human participants.
7. **Record-keeping and documentation:** REB RIMS shall maintain detailed records and documentation of their review processes, decisions, and ongoing monitoring activities to ensure transparency and accountability.

3B. Roles & Responsibilities based on the above terms of references

1. The REB RIMS will review and approve all types of research proposals involving human participants with a view to safeguarding the dignity, rights, safety and well-being of all actual and potential research participants regardless of the source of funding. The goals of research, however important, should never be permitted to override the health and well-being of the research participant.
2. The REB RIMS will ensure that all the cardinal principles of research ethics, viz. Autonomy, Beneficence, Non - malfeasance and Justice are taken care of in planning, conducting and reporting the proposed research.
3. It will review the proposals before the start of the study as well as monitor the research throughout the study until and after completion of the study through appropriate well-documented procedures (for example, interim reports, final reports and site visits, etc.).

4. **The REB RIMS shall take up the dual responsibilities of reviewing both the scientific content and ethical aspects of the proposal.**
5. The REB RIMS will also examine compliance with all regulatory requirements, applicable guidelines and laws of the country and/or other countries/organizations wherever applicable/feasible.
6. The REB RIMS will ensure that universal ethical values and international scientific standards are expressed in terms of local community values and customs.
7. The REB RIMS will assist in the development and education of a research community responsive to local healthcare requirements.

8. **Undergraduate and Postgraduate Research Ethics Committee**

   A separate Research Ethics Sub-committee shall be formed from time to time to review research proposals from the students (both undergraduate and postgraduate, including PhD work). Members of the sub-committee shall be from amongst the four technical (medical science) members of the REB RIMS (two basic medical scientists and two clinicians). The Member Secretary of REB RIMS shall chair the sub-committee.

4. Types of the projects to be reviewed by REB RIMS

Aligning the National Ethical Guidelines for Biomedical and Health Research Involving Human Participants (2017) of the Indian Council of Medical Research (ICMR), the following types of projects will be reviewed.

a. Clinical trials: These include studies involving investigational new drugs, devices, or interventions on human participants.

b. Epidemiological studies: Research involving the study of the distribution and determinants of health-related events, states, or processes in specified populations.

c. Genetic studies: Research involving the study of human genes, gene products, or genetic disorders.

d. Stem cell research: Studies involving the use of stem cells, including embryonic stem cells, induced pluripotent stem cells, and adult stem cells.

e. Research on reproductive health: Studies related to fertility, contraception, abortion, and other aspects of reproductive health.

f. Research on vulnerable populations: Studies involving participants who may be vulnerable due to their age (children, elderly), socioeconomic status, or other factors that may affect their ability to make voluntary informed consent.

g. Public health research: Research aimed at improving the health of populations or communities, including studies on disease prevention, health promotion, and health services.

h. Behavioural and social science research: Studies involving human participants in the fields of psychology, sociology, anthropology, and other behavioural and social sciences.

i. Qualitative research: Research involving the collection and analysis of non-numerical data, such as interviews, focus groups, or observational studies.

j. Research on biological materials: Studies involving the collection, storage, and use of human biological materials, such as blood, tissues, or other bodily fluids.

k. Research on medical records or data: Studies involving the use of medical records, health registries, or other sources of personal health data.

5. Review of proposals from outside the institute

REB, RIMS Imphal may review research proposals from outside the institute, provided the following conditions are met.

a. The REB RIMS have the necessary geographical access to the site(s) where the research is proposed to be conducted. This is important for the committee to be able to monitor and oversee the research activities effectively.
b. The REB RIMS have the competence and expertise to review the specific type of research proposal from outside.
c. There should be a formal agreement or Memorandum of Understanding (MoU) between the REB RIMS and the institution or organization submitting the proposal from outside. This agreement should clearly define the roles, responsibilities, and expectations of both parties.
d. The REB RIMS shall ensure that the proposed research complies with all relevant local ethical and regulatory requirements, including obtaining necessary approvals from relevant authorities, if applicable.
e. The REB RIMS shall have adequate funding to effectively review and monitor the proposed research from outside the institute.
f. The REB RIMS shall maintain detailed documentation and records of the review process, including minutes of meetings, decisions, and any relevant communications with the external organization or researchers.

It is important to note that the decision to review proposals from outside the institute is at the discretion of the REB RIMS, and it may choose to accept or decline such proposals based on their capacity, expertise, and other relevant considerations.

6. Review of academic proposals from Diplomat of National Board (DNB) students or investigator-initiated studies

REB RIMS will typically follow the same review process and ethical considerations when dealing with academic proposals from Diplomat of National Board (DNB) students or investigator-initiated studies. Therefore, proposals from DNB students or investigator-initiated studies must comply with relevant institutional policies, guidelines, and standard operating procedures related to research involving human participants. However, REB may take some specific considerations or guidelines:

7. SOP for research on vulnerable population

To ensure the rights, safety, and well-being of vulnerable participants, the following guidelines shall be followed.

a. REB RIMS shall have a clear process for identifying and categorizing vulnerable populations, such as children, pregnant women, individuals with cognitive impairments, prisoners, economically or educationally disadvantaged groups, or other populations that may be vulnerable to coercion or undue influence.

b. REB RIMS shall conduct a comprehensive risk assessment to evaluate the potential risks and benefits of the proposed research for vulnerable participants. This assessment should consider physical, psychological, social, economic, and legal risks, as well as the potential for stigmatization or discrimination.

c. Proposals involving vulnerable populations shall undergo an enhanced review process, which may include additional expertise or representation on the REB, such as members with specific knowledge or experience related to the vulnerable population being studied.

d. REB RIMS shall carefully review the informed consent process and documentation to ensure that it is appropriate for the vulnerable population and addresses their specific needs and vulnerabilities. This may involve the use of assent procedures for children, the involvement of legally authorized representatives, or the use of culturally appropriate language and formats.

e. Strict measures shall be in place to protect the privacy and confidentiality of vulnerable participants, including data management and storage procedures, access controls, and protocols for reporting and handling breaches.

f. REB RIMS may require researchers to engage with relevant communities, stakeholders, or advocacy groups representing the vulnerable population to ensure that the research is culturally appropriate, respectful, and addresses community concerns or priorities.

g. REB RIMS shall establish procedures for ongoing monitoring and oversight of research involving vulnerable populations, which may include regular progress reports, site visits, or the appointment of independent monitors or data safety monitoring boards.

h. REB RIMS shall ensure that researchers and study staff receive appropriate training and education on working with vulnerable populations, including ethical considerations, cultural competence, and strategies for minimizing risks and protecting participants' rights and welfare.

i. REB RIMS should ensure that research involving vulnerable populations complies with relevant national and international regulations, guidelines, and ethical standards, such as the ICMR National Ethical Guidelines for Biomedical and Health Research Involving Human Participants (2017) and other applicable laws or policies.

j. REB RIMS shall maintain detailed documentation and records of the review process, decisions, and ongoing monitoring activities for research involving vulnerable populations, ensuring transparency and accountability.

8. Composition of REB RIMS

The REB RIMS should be multidisciplinary and multi-sectorial in composition. Independence and competence are the two hallmarks of an REB. The number of persons in the Research Ethics Board should preferably be 8-15 members, out of which at least 50% of the members, including the chairperson, should be non-affiliated to RIMS, Imphal. The composition shall be as close as follows:-

A. Chairperson
B. One - to three persons from the basic medical science area
C. One – three clinicians
D. One legal expert or retired judge
E. One social scientist/ representative of a non-governmental voluntary agency
F. One philosopher/ ethicist/ theologian
G. One layperson from the community
H. Member Secretary

The REB RIMS approving drug trials shall have in the quorum at least one representative from the following groups:

A. One basic medical scientist (preferably one pharmacologist).
B. One clinician
C. One legal expert or retired judge
D. One social scientist/ representative of a non-governmental organization/philosopher/ ethicist/ theologian or a similar person
E. One layperson from the community

9. Power and Functions of the REB RIMS members

a. Chairperson

i. The Chairperson will chair all meetings of the REB RIMS. The Chairperson is empowered to convene emergency meetings of the full REB, RIMS or a sub-group/committee as per requirement. The Chairperson will be responsible for conducting committee meetings and leading all discussions and deliberations pertinent to the review of the research proposals.

ii. The Chairperson will preside over all administrative and financial matters pertinent to the committee's functions. The Chairperson will sign documents and communications related to REB functioning.

iii. The Chairperson will represent the REB RIMS at various meetings and fore. In case of anticipated absence, the chairperson will nominate preferably the Member Secretary or an REB member to represent the REB, RIMS.

iv. In case of anticipated absence of the Chairperson at a planned REB meeting, the Chairperson will nominate a committee member from outside the Institute as acting Chairperson, or if, for reasons beyond control, the Chairperson is not available, an acting Chairperson will be elected from amongst the external members by the members present. The acting chairperson will have all the powers of the chairperson for that meeting.

v. The chairperson will inform all members of the REB RIMS of any request/ suggestions from the REB members or its secretariat staff in a regular full board REB meeting for discussion and subsequent actions thereafter.

vi. The chairperson will appoint an SOP team to improve the existing SOP or formulate a new SOP, if necessary.

b. Member Secretary

i. The Member Secretary will conduct the business of the REB RIMS in consultation with the Chairperson. He or She, assisted by the Secretariat staff, will maintain records and communicate with all concerned including the Director, RIMS.

ii. The Member Secretary is in charge of the Secretariat of the REB, RIMS.

iii. The Member Secretary will prepare and maintain the meeting agenda and minutes and REB documentation. He/She will sign documents and communications related to REB functioning.

iv. The Member Secretary will receive research proposals submitted to the Secretariat. He/She shall prepare and distribute study files and organize an effective and efficient tracking procedure for each proposal.

v. The Member Secretary will report to the Chairperson on all matters related to the REB RIMS, including monitoring of the research proposals reviewed by the REB, RIMS.

vi. The Member Secretary will communicate with the Principal Investigator regarding REB decisions related to the submitted research proposal.

vii. The Member Secretary will arrange to provide updates on relevant and contemporary issues of health research to the committee members, and training of REB members, if needed.

viii. The Member Secretary will receive Research Board review processing fees and issue official receipts for the same, prepare for audits, inspections, annual reports and financial statements of the REB, RIMS.

c. Members

i. Members should be aware of local, social and cultural norms, as this is the most important social control mechanism.

ii. It is the responsibility of each REB member to review research proposals, attend REB meetings and participate in discussions and deliberations so that appropriate decisions can be arrived at. Members should read, understand, accept and sign the agreement contained in the confidentiality Form (**Annexure IV**).

iii. Any REB member can put forth suggestions/requests to the Chairperson/ Member Secretary by mail/letter/verbal request (during the meeting).

iv. REB members should participate in continuing education activities in biomedical ethics and biomedical research and provide information and documents related to training obtained to the REB secretariat. Members should remain updated on relevant laws and regulations relating to ethics.

v. REB members will assist the Chairperson and Member Secretary in carrying out REB activities as per the SOP.

d. REB secretariat staff

i. The staff shall assist the Chairperson/ Member secretary and help in the distribution of SOPs to REB members and in keeping the records of the investigators.

ii. The staff will make available the Forms for Submission of Research Proposal and will maintain files for SOPs (both current and past), all proposals submitted to the REB, RIMS and minutes of the REB meetings.

iii. The Secretariat staff will screen all Research proposals submitted online for the prerequisite requirements, and forward it to the Member Secretary.

iv. All the staff of the Secretariat will sign a confidentiality agreement, which should be filed with the REB. (**Annexure V**)

10. Terms of Reference

a. The Director, Regional Institute of Medical Sciences (RIMS), Imphal, constitutes the REB RIMS. It would be preferable to appoint persons trained in bioethics or persons conversant with ethical guidelines and laws of the country.

b. The Director, RIMS, Imphal, will appoint the Chairperson of the REB, RIMS, who will be from outside the Institute to maintain the independence of the committee. The chairperson should preferably have at least a minimum of 1-3 years of experience serving on the Research Ethics Board of an institute.

c. The Director, RIMS, Imphal, will also appoint the Member-Secretary, who will be a medical faculty member of the Institution with domain speciality experience, preferably with knowledge of clinical research and ethics, with a personal interest in ethics and a capacity of good communication skills.

d. Members should be a mix of medical/ non-medical, persons from basic sciences and applied sciences and other laypersons to represent the different points of view.

e. The REB members will be appointed by the Director, RIMS, Imphal. Members will be selected in their personal capacities based on their qualifications, experience in the domain field, interest, ethical and/or scientific knowledge and expertise, as well as on their commitment and willingness to volunteer the necessary time and effort for the REB. They should not have any known record of professional misconduct.

f. **New members will be appointed** under the following circumstances:

   i. When a regular member completes his/ her tenure.
   ii. If a regular member resigns before the tenure is completed.
   iii. If a regular member ceases to be a member for any reason, including death or disqualification (long-term non-availability, absence in 3 consecutive meetings).
   iv. To fulfil the membership requirements as stated in this SOP

g. The new members will be identified by the Chairperson according to the membership requirement i.e. as per the composition specified in this SOP, provided the potential member fulfils the conditions of appointment after discussion by the REB.

h. The names of new members to be appointed may be suggested by the REB members and the Chairperson to the Director, RIMS, for the final decision regarding the appointment.

i. The duration of appointment in the REB, RIMS is initially for a period of 2 years. At the end of 2 years, the committee will be reconstituted, and up to 50% of the members may be replaced by a procedure that includes nominations by the Chairperson of the REB, RIMS and Head of the Institute.

j. The REB RIMS can have as its members, individuals from other institutions/ organizations or communities with adequate representation of age and gender to safeguard the interests and welfare of all sections of the community/society.

k. The REB, RIMS may invite member(s) of specific patient groups or subject experts for REB meetings, if required, based on the requirement of the research area (e.g. HIV AIDS, genetic disorders, stem cell research, etc.) for eliciting their views. Such individuals will have to sign a confidentiality agreement and declare in writing conflicts of interest, if any, prior to attending the meeting. They will attend the meeting in the capacity of 'Guest/ Observer' and will not have the right to vote.

l. The REB, RIMS members should be encouraged to keep abreast of all national and international developments in ethics through orientation courses or regular training. The Chairperson and Member Secretary will take care of such activities in consultation with the Director, RIMS, Imphal.

m. A member can tender her/his resignation to the chairperson of the REB, RIMS, with reasons in writing, and the committee will take the decision. If a member wishes to resign from the membership, he/ she has to address his /her letter to the Chairman REB, RIMS, Imphal, and if reasonable, it will be forwarded to the Director, RIMS, for final decision. The resignation will become effective from the day it is accepted by the Director.

n. **Disqualification of a member**

i. A member may be disqualified by the Chairperson if his/ her conduct is inappropriate for an REB member. The process will be initiated if the REB chairperson or member-secretary receives a communication in writing for alleged misconduct from anybody. The chairperson will call for a meeting of the REB specifically to discuss this issue or the matter will be taken up for discussion. The meeting convened will follow the usual rules of quorum. The allegation(s) will be discussed at the REB meeting and the member alleged of misconduct will be provided adequate opportunity to defend himself/herself. He / She will be disqualified; if REB members present in the meeting approve of disqualification by voting (At least 2/3rd of the votes should be in favor of disqualification. The alleged person will not have the voting right.) The chairperson will convey the disqualification to the concerned member through a written communication.

ii. If, in the opinion of the Chairperson, the allegation is of grave significance where the integrity of REB could be questioned, the Chairperson may suspend the membership of the concerned REB member till a final decision is taken by REB. During the period of suspension, the concerned member will not have any right, privilege or responsibility of an REB member and will not perform any duty of an REB member.

o. All members should maintain absolute confidentiality of all discussions during the meeting.

p. Conflict of interest should be declared by members of the REB RIMS

q. Normally, the REB RIMS will meet in the months of February, May, August and November every year on the fourth Friday of the month. However, meetings may also be called with the consent of the Chairperson for discussion of urgent matters.

r. A minimum of seven members is required to form the quorum of the meeting. Out of the seven members, at least two members, including the Chairperson, should be from outside the institute.

s. Honorarium will be paid for attending the review meeting for the members of the REB RIMS including invited experts, which will be subjected to changes from time to time.

t. The SOP of the REB RIMS shall be updated periodically based on the changing requirements.

11. Financial matters:

REB, RIMS, Imphal will have a savings bank account in a nationalised bank, which will be operated by the following members. At least two out of the three operators, of which a Member Secretary is compulsory, have to sign in any transaction with the permission of the Director, RIMS, Imphal.

1. Member Secretary, REB, RIMS, Imphal
2. CAO/ FA, RIMS, Imphal
3. One of the members of REB, RIMS, Imphal (to be identified by the Chairperson / Honorary. Member Secretary)

An audited statement of account has to be presented at the end of every financial year.

12. Application Procedures

a. All proposals should be submitted in the prescribed application form duly signed by the investigator(s) / collaborators and forwarded by the Departmental Research Committee (DRC) with comments to the REB, the details of which is given in **Annexure II**.

b. Fifteen (12) hard copies and one soft copy on a CD (3 hard copies and one soft copy on a CD in the case of the students/scholars) should be submitted along with the application form. The application should also be submitted online at www.rims.edu.in by the Principal Investigator.

c. All relevant documents are enclosed with the application form and the same is uploaded to the website.

d. The date of the meeting will be intimated to the researcher to be present, if necessary, to offer clarifications. **The processing fee should be remitted along with the application wherever applicable.**

e. The REB RIMS secretariat shall screen all proposals for their completeness and, depending on the risk involved, categorize them into three types, namely, exemption from review, expedited review and full review.

f. Generally, research proposals should be submitted at least one month before the scheduled meetings.

g. For senior faculties who apply as a P.I., his/her service period must cover at least 80% of the project period.

13. Review Process

Depending on the nature of the research project and the degree of risk involved to participants, the project may be assessed under one of the three different types of assessment process. e.g. full assessment, expedited assessment, exempt review.

Students' research projects, including thesis protocols, may be assessed for clearance by a sub-committee of three members of REB, RIMS, and Imphal.

13.1.Element of the review

a. Essentiality of the study
b. Scientific design and conduct of the study
c. Examination of predictable risks/harms
d. Examination of potential benefits
e. Procedure for selection of participants, including inclusion/ exclusion of participants and other issues like advertisement details
f. Management of research-related injuries, adverse events
g. Compensation provisions
h. Justification for placebo in the control arm, if any
i. Availability of products after the study, if applicable
j. Patient information sheet and informed consent form in the local language or dialect or the language in which it is going to be administered (as per existing guidelines).
k. Protection of privacy and confidentiality.
l. Involvement of the community, wherever necessary.
m. Plans for data analysis and reporting
n. Adherence to all regulatory requirements and applicable guidelines
o. Competence of investigators, research and supporting staff
p. Facilities and infrastructure of study sites
q. Criteria for withdrawal of participants, suspending or terminating the study
r. Account for storage and maintenance of all data collected during the trial/research
s. Plans for publication of results – positive or negative while maintaining the privacy and confidentiality of the study participants
t. Details of foreign collaborators and documents for review by the Health Ministry's Screening Committee (HMSC) or appropriate Committees/ agencies/authorities like the Drug Controller General of India (DCGI) for international collaborative studies
u. Memorandum of Understanding (MoU) for the exchange of biological material in national/international collaborative study

13.2. Exemption from review

a. Research conducted in established or commonly accepted educational settings involving normal educational practices such as (i) research on regular and special educational instruction strategies or (ii) research on the effectiveness of or the comparison among instruction techniques, curricula, or classroom management methods, etc.

b. Research involving the use of educational tests (cognitive, diagnostic, aptitude, achievement), survey procedures, interview procedures or observation of public behaviour unless:

i. information obtained is recorded in such a manner that human subjects can be identified, directly or through identifiers linked to the subjects;

ii. any disclosure of the human subjects' responses outside the research could reasonably place the subjects at risk of criminal or civil liability or be damaging to the subjects' financial standing, employability, or reputation.

c. Research involving the collection or study of existing data, documents, records, pathological specimens, or diagnostic specimens, if these sources are publicly available or if the information is recorded by the investigator in such a manner that subjects cannot be identified, directly or through identifiers linked to the subjects.

d. While normally, the research in the above three categories will be considered for exemption, it may not be considered for exemption if it involves children and other vulnerable groups as participants.

Annexure VI provides the Review Exemption Application Form

13.3. Expedited review

a. The proposals presenting no more than minimal risk to research participants may be subjected to expedited review.

i. The Chairperson and/or REB member(s) designated by the Chair or a Sub-committee of the REB constituted by it will undertake the expedited review.

ii. If the PI believes that her/his proposal qualifies for the expedited review, she/he should make a request for the same while submitting the application for review to the REB.

iii. The person(s) undertaking expedited review may take any action that the full committee may take except disapproval of the research proposal. Thus, in the expedited review, the reviewer(s) may approve or request modification(s) in the proposal/protocol and/or consent form and other study materials or defer action pending additional information, but if disapproval is the decision, then the proposal must be referred to the full REB for review at its next convened meeting.

iv. A list of all research proposals approved using expedited review procedures is provided to the REB at its next convened meeting. When a research proposal is reviewed pursuant to the expedited review process, REB records of the review must include documentation of the determination of minimal risk and the permissible category of research justifying the expedited review.

v. Genetic studies should not be considered for expedited review.

Annexure VII provides the categories of research that will be considered for the expedited review as per ICMR guidelines, and **Annexure VIII & IX** provide Study Assessment Form for Expedited Review and Approval letter format in case of Expedited Review

13.4. Full review

i. All research proposals/ protocols which do not qualify for exempted or expedited review.
ii. Proposals that involve vulnerable populations and special groups shall be subjected to full review by all the members.

13.5. Review meeting

a. The mandate of the REB RIMS will be to review all research proposals involving human subjects to be conducted at the Institute or outside the Institute involving personnel of RIMS, irrespective of the funding agency. If outside laboratories are involved while carrying out such works, they should be recognized by the Institute.
b. The review shall be done by all reviewers (members of REB RIMS).
c. The REB RIMS should not keep a decision pending normally for more than 3 months after its first discussion.
d. All the proposals received in time shall be reviewed in the ensuing REB RIMS meeting. The meeting can be extended to another day(s) to complete the review process.
e. Researcher will be invited to offer clarifications if need be. Independent consultants/experts will be invited to offer their opinions on specific research proposals if needed, but they will not take part in the final decision-making.
f. Decision will be taken by consensus after discussion.
g. All decisions will be taken in meetings and not by circulation of project proposals.
h. All proposals submitted at least one month before the scheduled meetings should be put up for review.
i. An interim review can be resorted to by a Sub-committee, to be constituted by the Chairperson, instead of waiting for the scheduled time of the meeting like a re-examination of a proposal already examined by the REB or any other matter which should be brought to the attention of the REB. However, decisions taken should be brought to the notice of the main committee.
j. Modified proposals may be reviewed by an expedited review through identified members, and it will be discussed in the next meeting of the REB.
k. In the case of urgency/emergency, after reviewing the nature of urgency/emergency, the Chairperson is empowered to call a meeting of the REB, RIMS or form an interim review committee to review the proposal. In case of decisions taken by the interim review committee, it shall be brought up in the next REB, RIMS meeting for discussion and ratification.
l. If required, subject experts could be invited to offer their views. These experts/consultants may be specialists in ethical or legal aspects, specific diseases or methodologies, or represent specific communities, patient groups or special interest groups (e.g. cancer patients, HIV/AIDS positive persons or ethnic minorities).

13.6. Inviting experts:

a. The Member Secretary will take the responsibility for getting the expert opinion in the REB review process if he/she thinks so. This shall be communicated to the Chairperson and all the REB members.
b. The Member Secretary, in consultation with the Chairperson (or at a full board meeting, as deemed necessary), will identify and select the consultant to be invited based on the area of expertise, independence and availability. The Member Secretary, on behalf of the REB, will invite the expert in writing to assist in the review of the research study and provide his/ her independent opinion in writing. This will be done after seeking concurrence and confirming the availability of the expert through telephonic/electronic communication.
c. The Member Secretary will request the expert to declare a conflict of interest, if any, in writing and sign confidentiality and conflict of interest agreements. The Secretariat will forward copies of the Confidentiality Agreement and Conflict of Interest Agreement to the expert(s) for careful reading, understanding and signing.
d. The Member Secretary will provide explanations/ clarifications (telephonically or in writing) to the expert(s) if any doubts or questions are raised.
e. The expert(s) will attend the REB meeting to provide additional information or clarifications if invited by the Member Secretary/ Chairperson. However, the expert(s) will not participate in the decision-making process of the research study.
f. The services of the expert(s) get automatically terminated once the final decision regarding the study is taken by the REB. The REB will document the termination of the services of the expert by providing a letter of gratitude.

13.7.Guest/observer to visit REB, RIMS or attend REB, RIMS meeting

a. On receiving a written/email request from a guest/ an observer intending to visit REB, RIMS or attend its meeting, the Member Secretary, in consultation with the Chairperson, will decide the matter.
b. He/She will be permitted to do so after submitting the written permission signed either by the Chairperson or Member Secretary of the REB RIMS, to the REB secretariat.
c. The date and time of the visit to the REB or REB meeting will be informed to the guest/observer in writing/email.
d. The Secretariat will ensure that the Confidentiality Form is duly signed and dated by the guest or observer for the REB / REB meeting and will file it in REB records. The request letter/email will also be filed in REB records by the secretariat.

13.8.Decision-making

a. Members will discuss the various issues before arriving at a consensus decision.
b. Member should withdraw from the meeting during the decision procedure concerning an application where a conflict of interest arises, and this should be indicated to the Chairperson prior to the review of the application and recorded in the minutes.
c. Decisions will be made only in meetings where a quorum is complete.
d. Only members can make the decision. The experts/ consultants will only offer their opinions and shall not take part in decision-making.

e. Decision may be 'to approve', 'to reject' or 'to revise the proposals'. Specific suggestions for modifications and reasons for rejection should be given.
f. In cases of conditional decisions, clear suggestions for revision and the procedure for having the application re-reviewed should be specified.
g. In case of an appeal against the decision of the REB, RIMS, an application should be submitted to the Chairperson by the Principal Investigator within two weeks of communication of that decision.

13.9.Communicating the decision

1. The decision will be communicated by the Member Secretary in writing.
2. Suggestions for modifications, if any, should be communicated to the Principal Investigator.
3. Reasons for rejection should be informed to the researchers.
4. If a revision is to be made, fifteen copies of the revised document, along with a soft copy on a CD, should be submitted within a stipulated period of time as specified in the communication. The same should be submitted online.
5. The schedule/plan of ongoing review by the REB should be communicated to the Principal Investigator.

14. Processing Fee (Revised after the REB-related meeting held on 17th April 2024)

a. Rs. 20000/- for projects sponsored by the Pharmaceutical Companies.
b. Rs. 10,000/- for all externally funded extramural projects not related to 14. a and funding is more than Rs. 1.5 lakhs. However, Rs. 5000 only will be charged for extramural projects where funding upto Rs. 1.5 lakhs.
c. Rs. 10,000/- as a resubmission processing fee for starting an already approved project that was not initiated within the sanctioned project period.
d. No processing fee for all internally funded intramural projects.
e. No processing fee for all self-financed projects with a maximum of one each in a financial year.
f. Rs. 10,000/- for projects, including PhD project works submitted by non-RIMS applicants who will be working under the supervision of a RIMS Faculty member as Supervisor/ Guide/Co-Guide
g. Rs. 2,000/- for REB clearance of the fieldwork in RIMS by the students from other Universities/colleges under the supervision of a faculty member in RIMS Imphal
h. Processing fee is exempted for the following RIMS projects
    i. Projects by MBBS/BDS/B.Sc Nursing students (upto internship) of RIMS
    ii. Thesis of RIMS MD/MS/DM/MCh/MSc Nursing/MDS/MPhil/Diploma students/other course works related to a course
    iii. PhD thesis of RIMS
    iv. Other Student projects that are done on academic interest without financial involvement
    v. Revised submission
i. Processing fee must be paid online only to the Account of REB RIMS Imphal in Baroda Bank, RIMS Campus.
j. Validity of ethical clearance by the REB RIMS Imphal is for the period of the study to a maximum of 2 years starting from the date of the approval by the REB RIMS Imphal.

k. REB approval will be renewed after the completion of 2 years and yearly thereafter on payment of the processing fee based on the amount of funding.
l. For non-starter projects within the first 2 years of the ethical clearance, their ethical clearance will be withdrawn automatically.
m. Projects that could not be completed or started within the stipulated time need a fresh renewal of the ethical clearance. The processing fee will remain the same depending on the amount of funding.
n. No new project, except for the exempted ones will be processed without prior submission of the processing fee.

15. Sitting allowance.

Sitting allowance of Rs.2000/- for the Chairman and Rs.1,500/- for the Hony. Member Secretary, Rs.1,000/- for the rest of the members and Rs. 500/- for office assistant (s) will be entitled for the day of the scheduled meeting of the REB, RIMS and REB, RIMS Undergraduate and Postgraduate Ethics Committee.

16. Monitoring

Once REB RIMS gives a certificate of approval, it is the duty of the REB RIMS to monitor the approved studies. The Full Board or Chairperson and Member Secretary will take the responsibility to decide to conduct on-site monitoring. It is further the responsibility of the designated REB member(s) to perform on-site monitoring of selected study site(s).

1. **Periodic review**: The ongoing research may be reviewed at regular intervals of six months if the study period is more than 6 months.
2. **Continuing review**: The REB has the responsibility to continue reviewing approved projects for continuation, new information, adverse event monitoring, follow-up and later after completion if need be.

3. **Monitoring / Follow-up procedures**

A. **Selection of study sites:-**

1. Routine monitoring for a site may be decided at the time of approval of the project by the Full Board.
2. "For-cause monitoring" will be performed at sites for reasons identified by any member of the REB, after approval by the Chairperson.
3. The reasons for identifying a particular site for "for-cause monitoring" could include any one or more of the following:
    a. High number of protocol violations
    b. Large number of studies carried out at the study site or by the investigator
    c. Large number of Serious Adverse Events (SAE) reports,
    d. High recruitment rate
    e. Large number of Protocol deviations
    f. Complaints received from participants or any other person
    g. Frequent failure to submit the required documents
    h. Any other cause as decided by REB

B. Before the visit

i. The Chairperson will identify and select one or more REB members to conduct monitoring of a site.
ii. The selected members will be given an appointment letter and the agenda of monitoring will be decided by the identified members in consultation with the Member Secretary and Chairperson
iii. The Secretariat will decide the date of the monitoring in consultation with the members and the PI.
iv. The final date will be communicated to the PI and designated members.
v. The members will review the relevant project documents and make appropriate notes.
vi. The Secretariat will provide the monitoring Members with relevant reference material/documents related to the project
vii. These members will carry with them Site Monitoring Visit Report Forms (Annexure X) collected from the Secretariat.

C. During the visit

1. The members of the monitoring team will check the log of delegation of responsibilities of the study team, and check if the site is using REB-approved protocol, informed consent documents, case record forms, diaries, advertisements, etc.
2. Observe the informed consent process, if possible
3. Review randomly selected participants' files to ensure that participants are signing the correct informed consent
4. Check investigational product accountability is adequately controlled and documented throughout the product flow at the study site (arrival, dispensing, use, return from the subject and return/destruction after the study), check for storage times, conditions and expiry dates to be acceptable and sufficient supplies available, wherever applicable,
5. Verify that the investigator follows the approved protocol and all approved amendment(s), if any,
6. Ensure that the investigator and the investigator's trial staff are adequately informed about the trial
7. Verify that the investigator and the investigator's trial staff are performing the specified study functions, in accordance with the approved protocol and any other written agreement between the sponsor and the investigator/ institution, and have not delegated these functions to unauthorized individuals
8. Verify that the investigator is enrolling only eligible subject
9. Determine whether all serious adverse effects (SAEs) are appropriately reported within the time as per the applicable regulatory requirement(s). Case record forms would be checked to review the safety data i.e. Adverse Events (AEs) and SAEs for the volume or severity of adverse events,
10. Review the project files of the study to ensure that documentation is filed appropriately,

11. Review the source documents for their completeness and collect views of the study participants, if possible
12. The member of the monitoring team will fill out the Site Monitoring Visit Report Form and sign and date it.

D. After the visit

i. The member of the monitoring team will submit the completed Site Monitoring Visit Report Form and submit it to the REB secretariat within 7 working days of conducting a site monitoring visit or at the time of full board meeting (whichever is earlier).

ii. The report should describe the findings of the monitoring visit.

iii. The Member-Secretary will present the monitoring report at the next full board REB meeting and the concerned member will provide additional details/ clarifications to members, as required.

iv. The REB will discuss the findings of the monitoring process and take appropriate specific action by voting or a combination of actions, some of which are listed below:

a. Continuation of the project with or without changes

b. Restrictions on enrolment

c. Recommendations for additional training

d. Recruiting additional members in the study team

e. Revising/ providing qualifications/ experience criteria for members of the study team, termination of the study

f. Suspension of the study, etc.

v. If the member has findings that impact on safety of the participant, he/she will inform the Member Secretary on the same day. The Member Secretary will discuss with the Chairperson, and any one of the actions described above will be taken.

vi. The final decision taken at the full board REB meeting by the Chairperson will be recorded in the Site Monitoring Visit Report Form.

vii. The Secretariat will convey the decision to the Principal Investigator in writing within 14 working days of the meeting.

viii. The Secretariat will place a copy of the report in the protocol file.

17. Reporting of Adverse Events (AE)/Serious Field Incidents (SFI)

a. All research proposals need to define the anticipated adverse events and the criteria for assessing their seriousness

b. Adverse events must be reported to the REB RIMS within one week of their occurrence. The REB RIMS will decide the course of action.

c. In the multi-site/centric research, serious adverse events from the site(s) of the study must be reported to the Data Safety Monitoring Board (DSMB)/ REB RIMS within 24 hours. In SAE-like death, the study should be stopped till further directive comes from the REB RIMS. Normally, the decision to continue the study shall be taken by REB RIMS within 48 hr of the receipt of the SAE report.

d. In all other cases, all serious adverse events/field incidents must be reported to the REB RIMS/DSMB within 24 hours of their occurrence.

e. While reporting adverse events/SFI to the REB /DSMB, the PI must provide her/his views on whether:

   i. the event(s) is/are related to the study,

   ii. it/they warrant any change in the protocol and/or informed consent form,

   iii. it/they warrant any change in the care or management of the participants

f. All reports of the adverse events, opinions of the DSMB/Monitor and the action taken will be placed before the REB RIMS at its next meeting

g. Compensation:- The participants will be entitled to financial compensation as per existing Rules (**Annexure XI**)

18. Record keeping and Archiving

All documentation and communication are to be dated, filed and preserved. Confidentiality is to be maintained during access and retrieval procedures. The following records should be maintained:

a. The Constitution and composition of the REB RIMS

b. Signed and dated copies of the latest curriculum vitae of all REB members;

c. Standing operating procedures of the REB RIMS;

d. Relevant National and International guidelines;

e. Copies of protocols submitted for review, progress reports, and SAEs;

f. All correspondence with REB RIMS members and investigators and other regulatory bodies regarding application decisions and follow-up;

g. Agenda of all REB RIMS meetings;

h. Minutes of all REB RIMS meetings with the signature of the Chairperson;

i. Copies of decisions communicated to the applicants;

j. Record of all notifications issued for premature termination of a study with a summary of the reasons;

k. Final report of the study including microfilms, CDs and Video recordings.

l. All records must be safely maintained for a period of 5 years after the completion/termination/publication of the study, whichever occurred later.

m. The Member-Secretary must hand over full custody of such records to her/his successor, and the handing over must be documented.

19. Education on Ethics

a. The REB RIMS members should be encouraged to keep abreast of all national and international developments in ethics through orientation courses on related topics by the REB members or regular training organized by bodies.
b. All relevant new guidelines should be brought to the attention of the members.
c. Members should be encouraged to attend national and international training programs in research ethics to maintain quality in ethical review and be aware of the latest developments in this area.
d. Any change in the regulatory requirements should be brought to their attention and they should be aware of local, social and cultural norms, as this is the most important social control mechanism.
e. The REB RIMS will also conduct CME on research ethics for the Institute or other organizations whenever feasible.

20. Special Considerations

There are certain specific concerns pertaining to specialised areas of research which require additional safeguards/protection and specific considerations for the REB to take note of. Examples of such instances are research involving children, pregnant and lactating women, vulnerable subjects and those with diminished autonomy, besides issues pertaining to commercialization of research and international collaboration.

Again, while reviewing the proposals, the following situations may be carefully assessed against the existing facilities at the research site for risk/benefit analysis:

A. Collection of blood samples by finger prick, heel prick, ear prick, or venipuncture:

i. From healthy adults and non-pregnant women who weigh normal for their age, not more than 500 ml blood is drawn in an 8-week period, and the frequency of collection is not more than 2 times per week;

ii. From other adults and children, the age, weight, health of the participants, the collection procedure, the amount of blood to be collected, and the frequency with which it will be collected should be considered. The volume of blood collected will not be more than 50 ml or 3 ml per kg, or whichever is less in a period of 8 weeks and not more than 2 times per week;

iii. From neonates, depending on the haemodynamic, body weight of the baby and other purposes, not more than 10% of blood is drawn within 48 – 72 hours. If more than

this amount is to be drawn, it becomes a risky condition requiring infusion/blood transfusion;

iv. Prospective collection of biological specimens for research purposes by non-invasive means. For instance:

1. Skin appendages like hair and nail clippings in a non-disfiguring manner;
2. Dental procedures - deciduous teeth at the time of exfoliation or if routine patient care indicates a need for extraction of permanent teeth; supra and sub-gingival dental plaque and calculus, provided the collection procedure is not more invasive than routine prophylactic scaling of the teeth;
3. Excreta and external secretions (including sweat);
4. Non-cannulated saliva collected either in an un-stimulated fashion or stimulated by chewing gum or by applying a dilute citric solution to the tongue;
5. Placenta removed at delivery;
6. Amniotic fluid obtained at the time of rupture of the membrane prior to or during labour;
7. Mucosal and skin cells collected by buccal scraping or swab, skin swab, or mouth washings;
8. Sputum collected after saline mist nebulization and bronchial lavages.

B. Collection of data through non-invasive procedures routinely employed in clinical practice. Where medical devices are employed, they must be cleared/approved for marketing, for instance –

i. Physical sensors that are applied either to the surface of the body or at a distance and do not involve input of significant amounts of energy into the participant or an invasion of the participant's privacy;

ii. Weighing or testing sensory acuity;

iii. Magnetic resonance imaging;

iv. Electrocardiography, echocardiography, electroencephalography, thermography, detection of naturally occurring radioactivity, electroretinography, ultrasound, diagnostic infrared imaging, Doppler blood flow.

v. Moderate exercise, muscular strength testing, body composition assessment, and flexibility testing where appropriate given the age, weight, and health of the individual.

C. Research involving clinical materials (data, documents, records, or specimens) that will be collected solely for non-research (clinical) purposes.

D. Collection of data from voice, video, digital, or image recordings made for research purposes.

E. Research on individual or group characteristics or behaviour not limited to research on perception, cognition, motivation, identity, language, communication, cultural beliefs or practices, and social behaviour or research employing survey, interview, oral history, focus group, program evaluation, human factors evaluation, or quality assurance methodology.

ANNEXURE I

Regional Institute of Medical Sciences
Imphal, Manipur
RESEARCH ETHICS BOARD
APPLICATION FOR ETHICS REVIEW

Section I: ADMINISTRATIVE

Application No. _____

Date of Receipt: ____(DD)/____(MM)/_____(YYYY)

(A) INVESTIGATORS: *(Attach brief CV of each investigator – not more than 2 pages each)*

Principal Investigator:	
Name: ENTER NAME Address: ENTER ADDRESS	Degree: Click here to enter text.
Co-Principal Investigator(s)	
(1) Name: ENTER NAME Address: ENTER ADDRESS	Degree: Click here to enter text.
(2) Name: ENTER NAME Address: ENTER ADDRESS	Degree: Click here to enter text.
(3) Name: ENTER NAME Address: ENTER ADDRESS	Degree: Click here to enter text.
(4) Name: ENTER NAME Address: ENTER ADDRESS	Degree: Click here to enter text.
(5) Name: ENTER NAME Address: ENTER ADDRESS	Degree: Click here to enter text.
Enter here if more	

(B) TITLE AND DURATION OF PROPOSED STUDY:

Study Title:enter title here
Month and year of likely commencement of the study:mm/yyyy
Duration of the study:enter here.

(C) FUNDING:

Type of funding:
☐ Contract/Grant ☐ Subcontract ☐Gift/donation of drugs/devices ☐ Student Project ☐Other (specify)

Source of funding: *(If multiple sources, give information on primary source)*
☐ **Government:** *specify:*☐*Central*☐*State*☐ *Local* ☐ **Private Foundation:** *specify:* ☐*Indian*☐*Foreign* ☐ **Industry:** *specify:*☐*Private*☐*Public*☐ *Other* ☐ **Other** ☐ **No funding required**
If multiple sources of funding, give information on secondary source(s):
Click here to enter text.
Status of funding:
☐Funding awarded/available; ☐Funding partially awarded/available;☐ Fund application pending ☐No funding application made;☐ No funding required
Name, address and tel/fax/email of (primary) sponsor with the name of contact person
Click here to enter text.
Budget Details (show fund allocation to various heads)
Click here to enter text.
Are the study subjects protected by insurance coverage? ☐ **Yes** ☐**No** If yes, specify the amount and conditions of coverage Click here to enter text.

(D) DRUG, DEVICES AND BIOLOGICS:

Does your study involve testing of drug(s), device(s) and/or biologics? ☐**Yes** ☐**No**
If yes,Click here to enter text.
Are they already approved by the regulatory authorities and available in the market or are they new ones? ☐ **Already approved** ☐ **New one**
Who has prepared and/or is manufacturing the drug(s), device(s) and biologics under investigation?

Click here to enter text.
Who holds the patent or IND/IDE of the drug(s), Device(s) and biologics under investigation? Click here to enter text.
What are the reasonable possibilities of the availability after the study of the investigational drug(s), device(s) and biologics for the study participants/subjects if it is found to be effective? Click here to enter text.

(D) PERMISSIONS: *(Attach copy of relevant permission letters)*

Does your study require permission from regulatory authorities? ☐ **Yes** ☐ **No**
If yes, specify the following:
(i) From Drug Controller: ☐ Yes ☐ No. Whether permission obtained: ☐ Yes ☐ No
(ii) From the ICMR: ☐ Yes ☐ No. Whether permission obtained: ☐ Yes ☐ No
(iii) From other Government department(s): ☐ Yes ☐ No If yes, specify departments: (a) Dept. Click here to enter text. Whether permission obtained: ☐ Yes ☐ No (b) Dept. Click here to enter text. Whether permission obtained: ☐ Yes ☐ No
Does your study require you to send human biological material outside India? ☐ **Yes** ☐ **No**
If yes, have you:
(i) Obtained permission of the Director, RIMS? ☐ **Yes** ☐ **No**
(ii) Has RIMS and the foreign party signed agreement/MoU for that? ☐ **Yes** ☐ **No** *(if yes, attach a copy of the agreement/MoU)*

(E) STATEMENT ON CONFLICT OF INTERESTS, IF ANY:

Describe briefly, if any, the financial and other interests of any of the investigators and/or close relative(s), with the sponsor(s) and outcome of the study. Click here to enter text.

Section II: STUDY DESIGN, SUBJECT/PARTICIPANT SELECTION AND DATA COLLECTION PROCEDURES

Note: As far as possible, complete items A to F given below using non-technical, lay language. Give full form or definition of all *abbreviations and acronyms*. The word limit prescribed is recommendatory, but as far as possible, the total length of items A to E should not exceed five pages or 1500 words.

(A) STUDY BACKGROUND:

Give summary of literature review and rationale for the proposed study: 300 words
Click here to enter text.

(B) STUDY PURPOSE:

Give specific hypothesis, aim/goal and objectives: 200 words
Click here to enter text.

(C) DESIGN (check all applicable)

☐ **Phase – I Trial,** ☐ **Phase – II Trial,** ☐**Phase – III Trial,** ☐**Phase –IV Trial;** ☐**Randomised,** ☐ **Blinded,** ☐ **Case-Control,** ☐ **Social Sciences,** ☐ **Case Studies,** ☐**Cross-sectional,** ☐ **Cohort,** ☐ **Multi-Centre. If Multi-Ce**ntre, coordinating centreenter here ☐ **Qualitative,** ☐**Any other (specify)**Click here to enter text.
Any general description of design (100 words)
Click here to enter text.

(D) SUBJECT/PARTICIPANT SELECTION

(a) TYPE: Explain who will be the subjects/participants and rationale for selecting them (specific explanation if participants will include Minor, Pregnant woman, Neonate, Person incompetent to give informed consent, Prisoner, Normal/Healthy volunteer, Student, Staff of the institute). (100 words)

Click here to enter text.
(b) NUMBER: Explain about subject/participant selection (please respond to each item)**: (i) total number, (ii) rational for having that number or sample size, (iii) sampling method, if any, (iv) what proportion of them will be women, (v) from where they will be recruited and (vi) whether screening of larger number will be required.** (200 words)
Click here to enter text.
(c) ELIGIBILITY: Explain Inclusion and Exclusion criteria, with specific explanation if the gender, class, caste, ethnicity, race, will be used as Inclusion and/or Exclusion criteria (50 words)
Click here to enter text.
(d) RECRUITMENT: Explain who will do the recruitment of the subjects/participants and how. (50 words)
Click here to enter text.

(E) DATA COLLECTION PROCEDURES:

Explain, in sequence, the conduct of study and all data collection procedures. Please include information on (a) medical/surgical procedures, tests, (b) treatment, (c) interviews, discussions, observations, (d) follow up, (e) specific locations where they will be performed and (f) by whom. Specify if procedure involves banking of biological samples, HIV testing, genetic testing. (200 words)
Click here to enter text.

(F) DATA ANALYSIS:

Plan of data analysis – including by whom and how. Please mention whether data will be analysed to understand gender, caste, class, ethnicity, race differentials. (150 words)
Click here to enter text.

Section III: RISKS, BENEFITS, PRIVACY AND CONFIDENTIALITY

(A) RISKS:

(a) RISKS, DISCOMFORT AND SIDE EFFECTS: Describe all possible risks and discomfort for subject/participant due to use of intervention and/or interaction procedures/data collection methods proposed. Describe expected degree and frequency of such risk, discomfort, side effect of drug etc.
Click here to enter text.
(b) MINIMISATION: Describe steps you have taken or propose to take to minimise such risk, discomfort or for early recognition of side effects and their management.
Click here to enter text.
(c) DATA AND SAFETY MONIORING:
i) Describe how you define adverse events in your study, how and to whom you propose to report them, and what rules you will use for stopping the study due to adverse events. Describe Data and Safety Monitoring Plan of your project. Click here to enter text. **ii) Does the project require appointment of an Internal *Data Safety Monitoring Baard* (DSMB)? If Yes, suggest 5 or 6 names and addresses of the proposed DSMB members for the REB approval.** Click here to enter text.
(d) PRIVACY AND CONFIDENTIALITY: Describe (i) how you propose to provide privacy to subjects/participants while conducting study, (ii) what level of confidentiality you propose to promise, (iii) what are the likely consequences to the subject/participant in the event of violation of confidentiality.
Click here to enter text.
(e) IDENTIFIERS: Describe (i) the types of identifiable information on subject/participant you intend to collect, (ii) how do you propose to mask/remove identifiers, (iii) how do you propose to ensure safe keeping and storage of identifiable data.

Click here to enter text.
(f) BENEFITS: Describe benefits to the subject/participant in participating in the study. Also describe the benefits, if any, to the society.
Click here to enter text.
(g) RISK/BENEFIT: Analyse the extent to which the benefits of the study out-weigh the risk to the subjects/participants.
Click here to enter text.

Section IV: INFORMED CONSENT PROCESS

(a) TYPE: (Check all applicable)
☐ Signed witnessed consent; ☐Signed non-witnessed consent; ☐Witnessed Thumb Impression ☐ Non-witnessed thumb impression; ☐Verbal consent; ☐No consent will be obtained ☐ Consent from Surrogate will be obtained (If so, specify from whom)Click here to enter text.
(b) PROCESS: Describe (i) How, Where, When and By Whom the Informed Consent will be obtained. (ii) how much time the subject/participant will be given to consider participation and decide, (iii) describe additional plans/needs for informed consent in case the study involves special population such as minors, pregnant mothers, neonates, prisoners, etc. (iv) Describe how you will assess that information is correctly understood by the participant.
Click here to enter text.
(c) CONTENT OF PARTICIPANT INFORMATION SHEET: Please attach Informed Consent form in English and translated local language(s). The IC form must contain the following information: (1) a statement that consent is for a study/research/experiment, (2) an explanation of the purpose of research and nature of procedure, (3) all foreseeable risks/discomforts to participants due to research, (4) any benefits to be expected, (5) alternative procedures or courses of treatment in case subject does not want to participate, (6) the extent of confidentiality protection provided, (7) explanation on provision of compensation for injury caused to participant during the study, (8) whom to contact to know more about the study and participants' rights, (9) a statement that participation is voluntary, (10) A statement that participant can withdraw consent and from the study at any time without any facing

any penalty.
(d) INFORMED CONSENT SHEET (ICS): This is the statement signed by the patient or local guardian in case of minor or disabled. It should have the following components **1). Pt have read or being read about the patient information sheet (PIS).** **2). Pt had understood It .** **3). Agreed to join voluntarily** **4). Can be withdrawn from the study at any point of time without giving any version and without any penalty / risk.** **5.) signed in presence of a witness**
e) Assent : In case of minor ,assent form should be submitted in addition to consent form by parent/ legal guardian in presence of a witness
f) COST AND PAYMENT: Describe the cost for participating in the study to the subject/participant. Describe plan to reimburse or compensate participant – if yes, the amount of payment proposed.
Click here to enter text.

LIST OF ATTACHMENTS:

1. **Full proposal, with protocols/instruments for data collection and budget in detail.**

[The attachments as mentioned in the application form above]

2. Click here to enter text.

3. Click here to enter text.

4. Click here to enter text.

5. Click here to enter text.

6. Click here to enter text.

Principal Investigator's Certification:

- I certify that the information provided in this application is complete and correct.
- I accept ultimate responsibility for the conduct of this study, the ethical performance of the project, and the protection of the rights and welfare of the human subjects who are directly or indirectly involved in this project.
- I will comply with all policies and guidelines of the RIMS REB and affiliated/collaborating institutions where this study will be conducted, as well as with all applicable laws regarding the research.
- I will ensure that personnel performing this study are qualified, appropriately trained and will adhere to the provisions of the RIMS REB approved protocol. I will not modify this RIMS REB certified protocol or any attached materials without first obtaining approval for an amendment to the previously approved protocol.

Date

***Name and Designation**

NOTE: *To be signed by PI or by the guide in case of student project or by the RIMS investigator in case of non-RIMS PI.

Annexure II

Instruction for filling of application form

(General instructions: REB, RIMS normally meets once in the months of February, May, August and November of every year. Application for the proposal should reach the REB secretariat at least one month before the meeting date. Proposal should be written as far as possible using non-technical language and in simple words. Unqualified use of abbreviations and acronyms should be avoided as far as possible. Keep every part of the write up brief and to the point, but should not be missing any important information. While submitting the proposals, make sure that the following points are included)

1. Details of the Investigators – Names, addresses, qualification, corresponding investigator (attach CV not more than 2 pages for each of the investigator)
2. Title of the proposed study
3. Funding type and source, status, name and address of the funding agency
4. Budget details
5. Insurance coverage of the participants and investigators and field staff
6. Details of drugs, devices and biological – already approved one, already in use, new one, investigational one, who holds the patent, manufacturer, permission from the concerned authority (like DCGI, ICMR, Govt. agencies, etc), post study availability, any transfer of biological materials within and outside the country and permission, etc
7. Statement of conflict, if any
8. Study Purpose (250 words)

   Justification

   Hypothesis

   Objectives
9. Background of the study (350 words) Relevant literature review

Justification (Rationale of conducting the study)

10. Study Design (Details)
11. Description of study site(s) and duration

12. Study participants

    Who are the participants? Rationale for selecting them

    Eligibility criteria – Inclusion and Exclusion criteria Number of the participants (sample size)

    How they are selected (sampling)?

Recruitment of participants; who will do it and how?

13. Description of operational definition or criteria, if any
14. Data collection procedure, including the instruments and laboratory procedures, if any
15. Data analysis – Plan, Who will do it, How it will be done
16. List of Risks/Benefits involved in the study. Steps to minimize the risk.
17. How privacy and confidentiality are going to be maintained
18. Data and safety monitoring plan

    Definition of SAEs/AEs/SFIs Reporting – who, whom, when Stopping rules of the study

    Summary of data and safety monitoring plan of the study

19. Informed consent process – type and content, who, where, how and when
20. Certification by the Principal Investigator with name, signature and date

I certify that the information provided in this application is complete and correct.

I accept ultimate responsibility for the conduct of this study, the ethical performance of the project, and the protection of the rights and welfare of the human subjects who are directly or indirectly involved in this project.

I will comply with all policies and guidelines of the REB, RIMS and affiliated/collaborating institutions where this study will be conducted, as well as with all applicable laws regarding the research.

I will ensure that personnel performing this study are qualified, appropriately trained and will adhere to the provisions of the REB, RIMS approved protocol. I will not modify this REB, RIMS-certified protocol or any attached materials without first obtaining approval for an amendment to the previously approved protocol.

21. List of the attachments

Annexure III

CHECK LIST FOR APPLICATION

FOR ETHICAL CLEARANCE OF RESEARCH PROJECT

1. **Prescribed application form of REB, RIMS which can be downloaded from *www.rims.edu.in* being the most important document, please do not leave any item blank (if not applicable write NA).**
2. **Consent form [Patient Inform Consent Sheet (PICS), Patient Information Sheet (PIS) Assent form for Minors- (both in English and Manipuri written in Shree Lippi Script).**
3. **Summary sheet.**
4. **Full protocol with relevant references.**
5. **C.V of investigators (mainly research work, publication etc).**
6. **Application letter should be through Head of Department/ College Information to be filled up for better understanding at a glance and communication**

a.	**First submission / re-submission after correction (please Tick)**
b.	**Title of the study**
c.	**Principal Investigator, designation , contact details**
d.	**Co-Principal Investigator, designation , contact details if the P.I is not from RIMS, Imphal or a Student:**
e.	**Funding: Not Funded/ if Funded:** **Provision of overhead charges –YES / NO** **Status: Applied / Sanctioned / Disbursed /.....**
f.	**Nature of the study :** **Student project / PG thesis / M.Ch or DM thesis / Ph.D. thesis / Faculty project**
g.	**Number of the on-going research project by the Principal Investigator at the time of submission of the present application:**
h.	**For Senior faculties as P.I date of the Superannuation**
i.	**If it is Multicentric study, Ethical Clearance of the Co-ordinating centre. YES / NO. If yes, please submit a copy**

P.T.O

CHECK LIST FOR APPLICATION

FOR ETHICAL CLEARANCE OF RESEARCH PROJECT

Sequence of the documents to be compiled at the time of submission (to be properly bound)

I. Check List

ii. Covering letter through HOD or Head of the College

iii. Prescribed REB application form (duly filled in and signed)

iv. Summary Sheet of the study

v. Full protocol of the study with relevant references

vi. Consent / Assent form (both English and Manipuri)

vii. C.V of the Investigators (one or two pages)

viii. Any other relevant document (s)

Annexure IV

Confidentiality Agreement for REB Members, RIMS

In recognition of the fact, that
I,_____

_____

(Member's name, and his/her affiliation), have been appointed as a member of the REB and have been asked to assess research studies involving research participants in order to ensure that they are conducted in a humane and ethical manner, adhering to the highest standards of care as per the national, and local regulations and institutional policies and guidelines and international and national guidelines;

Whereas, the fundamental duty of an REB member is to independently review both scientific and Ethical aspects of research protocols involving human subjects and make a determination and the best possible objective recommendations, based on the merits of the submissions under review;

Whereas, the REB must meet the highest ethical standards in order to merit the trust and confidence of the communities in the protection of the rights and well-being of research participants;

The undersigned, as a member of the REB, is expected to meet the same high standards of ethical behaviour to carry out its mandate.

This Agreement thus encompasses any information deemed Confidential or Proprietary provided to the Undersigned in conjunction with the duties as a member of the REB. Any written information provided to the undersigned that is of a Confidential, Proprietary, or Privileged nature shall be identified accordingly.

As such, the undersigned agrees to hold all Confidential or Proprietary trade secrets ("information") in trust or confidence and agrees that it shall be used only for contemplated purposes and shall not be used for any other purpose or disclosed to any third party. Written

Confidential information provided for review shall not be copied or retained. All Confidential information (and any copies and notes thereof) shall remain the sole property of the REB. The Undersigned agrees not to disclose or utilize, directly or indirectly, any Confidential or Proprietary information belonging to a third party in fulfilling this agreement. Furthermore, the Undersigned confirms that his/her performance of this agreement is consistent with the Institute's policies and any contractual obligations they may have to third parties.

_____ _____

Undersigned Signature Date

Agreement on Confidentiality for REB Members RIMS

Please sign and date this Agreement, if the Undersigned agrees with the terms and conditions set forth above.

The original (signed and dated Agreement) will be kept in the custody of the REB and a copy will be given to you for your records.

As a member of the REB RIMS, I may be provided with confidential information and documentation (which we will refer to as the Confidential Information; subject to applicable legislation, including the Access to "Confidential Information"). I agree to take reasonable measures to protect the Information Act, not to disclose the Confidential Information to any person; not to use the Confidential Information for any purpose outside the Committee's mandate, and in particular, in a manner which would result in a benefit to myself or any third party; and to destroy all Confidential Information (including any minutes or notes I have made as part of my duties) to the Chairperson upon termination of my functions as a Committee member.

I, _____ (name of the member) have read and accept the aforementioned terms and conditions as explained in this Agreement.

_____ _____

Signature Date

_____ _____

Chairperson's Signature Date

I acknowledge that I have received a copy of this Agreement signed by the REB Chairperson and me.

_____ _____

Signature Date

Annexure V

Confidentiality Agreement Form for Staff of the Secretariat

I,_____

_____

(Staff's name and his /her affiliation), have been appointed as a Secretariat Staff of the REB RIMS.

This Agreement thus encompasses any information deemed Confidential or Proprietary provided to the Undersigned in conjunction with the duties as a Secretariat Staff of the REB. Any written information provided to the undersigned that is of a Confidential, Proprietary, or Privileged nature shall be identified accordingly.
As such, the undersigned agrees to hold all Confidential or Proprietary trade secrets ("information") in trust or confidence and agrees that it shall be used only for contemplated Purposes and shall not be used for any other purpose or disclosed to any third party. Written Confidential information provided for review shall not be copied or retained. All Confidential information (and any copies and notes thereof) shall remain the sole property of the REB. The Undersigned agrees not to disclose or utilize, directly or indirectly, any Confidential or Proprietary information belonging to a third party in fulfilling this agreement. Furthermore, the Undersigned confirms that his/her performance of this agreement is consistent with the institute's policies and any contractual obligations they may have to third parties.

_____ _____

Undersigned Signature Date

Agreement on Confidentiality

Please sign and date this Agreement, if the Undersigned agrees with the terms and conditions set forth above. The original (signed and dated Agreement) will be kept on file in the custody of the REB. *A copy will be given to you for your records.*

In the course of my activities as a Secretariat Staff of the REB, I may be provided with confidential information and documentation (which we will refer to as the Confidential Information; subject to applicable legislation, including the Access to "Confidential Information"). I agree to take reasonable measures to protect the Information Act, not to disclose the Confidential Information to any person; not to use the Confidential Information for any purpose outside the Committee's mandate, and in particular, in a manner which would result in a benefit to myself or any third party; and to destroy all Confidential Information (including any minutes or notes I have made as part of my duties) to the Chairperson upon termination of my functions as a Committee member.

I, _____(name of the member) have read and accept the aforementioned terms and conditions as explained in this Agreement.

_____ _____
Signature Date

_____ _____
Chairperson's Signature Date

I acknowledge that I have received a copy of this Agreement signed by the REB Chairperson and me.

_____ _____

Annexure VI

Review Exemption Application Form

1. Principal Investigator's Name:

   _____

2. Department:

   _____

3. Title of the Project:

   _____

   _____

   _____

4. Names of other co-investigators/participating staff and students:

   _____

   _____

   Brief description of the project: Please give a brief summary (approx. 300 words) of the nature of the proposal, including the aims/objectives/hypotheses of the project, rationale, participants' description, and procedures/methods to be used in the project:-

5. State reasons why exemption from ethics review is requested?

- Audits of educational practices
- Research on microbes cultured in the laboratory
- Research on immortalized cell lines
- Research on cadavers or death certificates provided such research reveals no identifying personal data
- Analysis of data freely available in public domain
- Any other ---------- --
  (This should include justification for exemption e.g. study does not involve human participants. If exemption is being requested on the basis of low risk involved in the study please refer to the backside of this annexure.)

Principal Investigator's signature: _____Date _____

Forwarded by the Head of the department:

Name: _____Signature: _____Date_____

Recommendations by the IRB Member Secretary:

[ ] Exemption

[ ] Cannot be exempted, Reasons_____

[ ] Discussion at full board

Signature of the Member Secretary, REB, RIMS: _____

Date _____

Final Decision:

[ ] Exemption

[ ] Cannot be exempted, Reasons_____

[ ] Discussion at full board

Signature of the Chairperson: _____Date _____

Final Decision at Full Board meeting held on

_____

_____

Signature of the Chairperson: _____Date _____

No research can be counted as low risk if it involves:

(i) Invasive physical procedures or potential for physical harm
(ii) Procedures which might cause mental/emotional stress or distress, moral or cultural offence
(iii) Personal or sensitive issues
(iv) Vulnerable groups
(v) Cross cultural research
(vi) Investigation of illegal behaviour(s)
(vii) Invasion of privacy
(viii) Collection of information that might be disadvantageous to the participant
(ix) Use of information already collected that is not in the public arena which might be disadvantageous to the participant
(x) Use of information already collected which was collected under agreement of confidentiality
(xi) Participants who are unable to give informed consent
(xii) Conflict of interest e.g. the researcher is also the lecturer, teacher, treatment-provider, colleague or employer of the research participants, or there is any other power relationship between the researcher and the research participants.
(xiii) Deception
(xiv) Audio or visual recording without consent
(xv) Withholding benefits from "control" groups
(xvi) Inducements
(xvii) Risks to the researcher

Appendix VII

Expedited Review

Categories of research that will be considered for the expedited review by the REB RIMS

1. Minor deviations from originally approved research during the period of approval (usually of one year duration).

2. Revised proposal previously approved through full review by the REB or continuing review of approved proposals where there is no additional risk or activity is limited to data analysis.

3. Research activities that involve only procedures listed in one or more of the following categories:

a. Clinical studies of drugs and medical devices only when -

i. research is on already approved drugs except when studying drug interaction or conducting trial on vulnerable population or

ii. Adverse Event (AE) or unexpected Adverse Drug Reaction (ADR) of minor nature is reported.

4. Research involving clinical materials (data, documents, records, or specimens) that have been collected for non-research (clinical) purposes.

5. When in emergency situations like serious outbreaks or disasters a full review of the research is not possible, prior written permission of REB may be taken before use of the test intervention. Such research can only be approved for pilot study or preliminary work to study the safety and efficacy of the intervention and the same participants should not be included in the clinical trial that may be initiated later based on the findings of the pilot study.

a. Research on interventions in emergency situation

When proven prophylactic, diagnostic, and therapeutic methods do not exist or have been ineffective, physicians may use new intervention as investigational drug (IND) / devices/ vaccine to provide emergency medical care to their patients in life threatening conditions. Research in such instance of medical care could be allowed in patients –

i. When consent of person/ patient/ responsible relative or custodian/ team of designated doctors for such an event is not possible. However, information about the intervention should be given to the relative/ legal guardian when available later;

ii. When the intervention has undergone testing for safety prior to its use in emergency situations and sponsor has obtained prior approval of the concerned regulatory body;

iii. Only if the local REB reviews the protocol since institutional responsibility is of paramount importance in such instances.

iv. If Data Safety Monitoring Board (DSMB) is constituted to review the data;

b. Research on disaster management

A disaster is the sudden occurrence of a calamitous event at any time resulting in substantial material damage, affecting persons, society, community or state(s). It may be periodic, caused by both nature and humans and creates an imbalance between the capacity and resources of the society and the needs of the survivors or the people whose lives are threatened, over a given period of time. It may also be unethical sometimes not to do research in such circumstances. Disasters create vulnerable persons and groups in society, particularly so in disadvantaged communities, and therefore, the following points need to be considered when reviewing such research:

i. Research planned to be conducted after a disaster should be essential culturally sensitive and specific in nature with possible application in future disaster situations.

ii. Participation by the community affected by disaster (before and during) in the research is essential and its representative or advocate must be identified.

iii. Extra care must be taken to protect the privacy and confidentiality of participants and communities.

iv. Protection must be ensured so that only minimal additional risk is impose

v. The research undertaken should provide direct or indirect benefits to the participants, the disaster-affected community or future disaster- affected population and a priori agreement should be reached on this, whenever possible, between the community and the researcher.

vi. All international collaborative research in the disaster-affected area should be done with a local partner on equal partnership basis.

vii. Transfer of biological material, if any, should be as per Government rules taking care of intellectual property rights issues.

Annexure VIII

Study Assessment Form for Expedited Review

Project Title:

_____

_____

_____

Date of receipt at REB office:

Name of the Principal Investigator:

Department:

Contact number:

Total no. of Participants at the site:

No. of Study sites: Sponsor:

Duration of the Study:

Reviewer's name:

Type of the Study: [ ] Intervention [ ] Epidemiology [ ] Observation

[ ] Document based [ ] Genetic

[ ] Social Survey [ ] Others, specify.....

Description of the Study in brief: Mark whatever applied to the study.

[ ] Randomized [ ] Open-labelled

[ ] Double blinded [ ] Placebo controlled [ ] Treatment controlled

[ ] Cross-over [ ] Parallel [ ] Interim Analysis

[ ] Use of Tissue samples [ ] Use of Blood samples [ ] Use of genetic materials

Comments:

_____

_____

Provisional Decision:

[ ] Approved [ ] Resubmission [ ] Disapproved [ ] 1 Full Board

[ ] Approved with modifications

Reason for disapproval

_____

_____

_____

Name of the REB member _____

Signature _____Date_____

Final Decision:

Approved YES [ ] NO [ ]

If disapproved, reasons for disapproval

_____

_____

_____

Further revision or modification required/resubmission [ ]

_____

_____

_____

_____

Any Other [ ]

_____

_____

_____

Signature of the Chairperson, REB, RIMS: _____Date: _____

Annexure IX

Approval letter format in case of Expedited Review

Date:

To

Dr

Department

Ref: Project:-

Dear Dr.

The following documents of the above mentioned project were reviewed and approved through an expedited review process.

1. _____

2._____

3._____

It is understood that the study will be conducted under your direction, in a total of_____research participants, at as per the submitted protocol.

The IRB approves the above mentioned study.

This approval is valid for the entire duration of the study.

It is the policy of IRB that, it be informed about any onsite serious adverse event or any unexpected adverse event report within 24 hours to IRB or by email, if there is holiday. The report of SAE or death after due analysis shall be forwarded by the Investigator to the Chairperson of IRB and the head of the institution where the trial is been conducted within 10 calendar days of SAE or death.

In case of injury or death of participant(s) occurring during the trial, the sponsor (whether a pharmaceutical company or an institution) or his representative, whosoever had obtained permission from the Licensing Authority for conduct of the clinical trial shall make payments for medical management of the subject and also provide financial compensation for the clinical trial related injury or death.

No deviations from, or changes of the protocol and Informed Consent Document should be initiated without prior written approval by the IRB of an appropriate amendment. The IRB expects that the investigator should promptly report to the IRB any deviations from, or changes of, the protocol to eliminate immediate hazards to the research participants and about any new information that may affect adversely the safety of the research participants or the conduct of the trial.

For studies which will continue for more than a year, a continuing review report needs to be submitted (within 1 month of the due date i.e. 11 months from the date of approval) on or before _____.

A copy of the final report should be submitted to IRB for review.

Sincerely,

Member Secretary/ Chairperson

Date of approval of the study:

Annexure X

Site Monitoring Visit Report

Project no. Date of Visit:

Study Title:

Principal Investigator and Department:

Study type: ( ) Investigator initiated ( ) Pharma ( ) Thesis
( ) Government agency ( ) others

Date of REB approval:

Date of Initiation of the study:

Duration of study:

Reason for monitoring :- ( ) Routine
( ) For cause (State reason/s)
( ) Protocol violations/ deviations
( ) SAE reporting
( ) Recruitment rate
( ) Other

Last monitoring done, if any:- Yes ( ) Date of monitoring
No ( )

Project Status: 1. On-going ( )
2. Completed ( )
3. Recruitment Completed ( )
4. Follow-up, extension study ( )
5. Suspended ( )
6. Terminated ( )

In case of the response to the above question is option 5 or 6, kindly provide reason/s: ____

Recruitment status:

- Total no. of patients to be recruited
- Screened
- Screened failures
- Enrolled
- Withdrawn Reason
- Discontinued Reason
- Completed
- Active

•

Are the present study team members as per the list approved by the REB:

- Yes ( ) No ( ) Comment:

Are site facilities appropriate?

- Yes ( ) No ( ) Comment:

Is the recent version of Informed Consent Document (ICD), after REB approval, used?

- Yes ( ) No ( ) Comment:

Whether appropriate vernacular consent has been taken from all patients?

- Yes ( ) No ( ) Comment:

Any other findings noted about the ICDs?

- Yes ( ) No ( ) Comment:

Is recent REB approved version of protocol used?

- Yes ( ) No ( ) Comment:
-

Have the eligibility, inclusion exclusion criteria been adhered to?

- Yes ( ) No ( ) Comment:

Any adverse events found?

- Yes ( ) No ( ) Comment:

Any SAEs found?

- Yes ( ) No ( ) Comment:

Were the SAEs informed to REB within timelines specified by CDSCO?

- Yes ( ) No ( ) Comment:

No. of deaths reported:

( ) Death unrelated to participation in trial
( ) Death possibly related to participation in trial
( ) Death related to participation in trial

Any other non-death study related injury

- Yes ( ) No ( ) NA ( )

Comment:

Compensation paid for study related injury or death

- Yes ( ) No ( ) Comment:

Are there any protocol non-compliance deviations/violations?

- Yes ( ) No ( ) Comment:

Have the protocol non-compliance deviations/violations been informed to REB?

- Yes ( ) No ( ) Comment:

Are all Case Record Forms up to date?

- Yes ( ) No ( ) Comment:

Are storage of data and investigating products locked?

- Yes ( ) No ( ) Comment:

How well are the participants protected?

- Good ( ) Fair ( ) Not good Comment:

Any other remarks

- Yes ( ) No ( ) Give details:

Duration of visit:_____hours Start.....Finish.....

Name of the study team member/s present: Date
Signature _____

Name of REB members and representatives who attended monitoring visit:

Completed by:
Signature:_____ Date:

Final Decision at the REB meeting held on
_____
_____
_____

Signature of Chairperson, REB, RIMS_____**Date**_____

Annexure XI

File No: CT/SAE-ND COMPENSATIONFORMULAE/2014
GOVERNMENT OF INDIA
Ministry of Health & Family Welfare
Directorate General of Health Services
Central Drugs Standard Control Organization
O/o Drugs Controller General (I)
FDA Bhawan, Kotla Road, New Delhi-110 002

Date: 15 DEC 2014

ORDER

Sub: Formulae to determine the quantum of compensation in case of clinical trial related injury (other than death).

As per Rule 122DAB of Drugs and Cosmetics Rules 1945, in case of clinical trial related injury/death, the trial subject is entitled to pay financial compensation. The sponsor or his representative is required to pay the financial compensation as per the order of DCG (I). As per the Rule, the financial compensation will be over and above the expenses incurred on the medical management of the trial subject. The Appendix XII of schedule Y of the Drugs and Cosmetics Rules prescribes the procedure for processing the report of the Serious Adverse Events (SAEs) including death to arrive at the cause of the death/injury to the subject and to decide the quantum of the compensation.

The Independent Expert Committee constituted for examination of SAE of death has already devised a formula being followed for determining the quantum of compensation in case of clinical trial related death.

Another committee was constituted in march 2014 under the Chairmanship of Shri R K Jain, the then Additional Secretary & Director General (CGHS), Ministry of Health & Family Welfare, Government of India to deliberate and work out a formula to be followed to determine the quantum of compensation in case of clinical trial related injury (other than death) in accordance with the provisions of the Drugs and Cosmetics Rules. The draft formula prepared by the committee was made available for comments of public/stakeholders. After having considered the comments received, the formulae have been finalized and approved by the competent authority.

The recommendations/formulae as approved is enclosed for all concerned.

Dr.G.N. Singh
Drugs controller General (India)

To

ISCR IDMA, OPPI, IPA and all Concerned.

CC:

- **PPS to DGHS, Nirman Bhawan, Delhi**
- **PS to AS & DG (CGHS), Ministry of H&FW**
- **PS to JS(R) Ministry of H&FW**

Annexure: Recommendation

COMPENSATION FORMULAE (CLINICAL TRIAL)

FORMULAE TO DETERMINE THE QUANTUM OF COMPENSATION IN THE CASES OF CLINICAL TRIAL RELATED SERIOUS ADVERSE EVENTS OF INJURY OTHER THAN DEATHS OCCURRING DURING CLINICAL TRIALS

Background

As per Rule 122DAB of Drugs and Cosmetics Rules 1945 in case of clinical trial related injury/death, the trial subject is entitled for the financial compensation. The Sponsor or his representative is required to pay the compensation as per the order of DCG (I). As per the rule, the financial compensation will be over and above the expenses incurred on the medical management of the trial subject. The Appendix Xil of schedule Y of the Drugs and Cosmetics Rules prescribes the procedure for processing the reports of Serious Adverse Events (SAES) including death to arrive at the cause of death/injury to the subject and to decide the quantum of compensation.

As per the procedure, in case of Clinical Trial related SAE of death, the DCG(I) will decide the quantum of compensation after considering the recommendation of Independent Expert Committee constituted for the purpose. In case of Clinical Trial related Serious Adverse Events other than death, (here in referred as "Clinical Trial related SAE") the DCGI will decide the quantum of compensation considering the reports of the Investigator, Sponsor and the Ethics Committee. However, there is an option to constitute expert Committee to advise the DCG(1) in the matter.

The Independent Expert Committee constituted for examination of SAE of deaths. has already devised a formula being followed for determining the quantum of compensation in case of clinical trial related death which is as under.

Compensation = (B x F x RJ/99.37)

Where, 8 = Base amount (i.e. 8.lacs) F = Factor depending on the age of the subject as per Annexure XII. (based on Workmen Compensation Act) R= Risk Factor depending on the seriousness and severity of the disease, presence of co-morbidity and duration of disease of the subject at the time of enrolment in the Clinical trial between a scale of 0 5 to 4 as under: 1.0.50 terminally ill patient (expected survival not more than (NMT) 6 months) 2. 1.0 Patient with high risk (expected survival between 6 to 24 months) 3.2.0 Patient with moderate risk. 4. 3:0 Patient with mild risk 6 4.0 Healthy Volunteers or subject of no risk

However, in case of patients whose expected mortality is 90 % or more within 30 days, a fixed amount of Rs. 2 lacs should be given).

The Apex Committee and the Technical Committee in their 7" meeting held on 30.08.2013 and 23.08.2013 respectively, alter detailed discussions agreed to the above formula for determining the quantum of compensation in cases of clinical trial related deaths, The Apex Committee in the said meeting recommended that a separate formula should also be worked out for determining the quantum of compensation in case of clinical trial related injury (other than death).
In view of the above, a committee was constituted under the Chairmanship of Shri R. K. Jain, AS & DG comprising following members to deliberate and work out a formula to be followed to determine the quantum of compensation in case of clinical trial related injury (other than death) in accordance with the provisions of the Drugs and Cosmetics Rules.

1. Dr Y. K. Gupta, Head, Department of Pharmacology. AIIMS, Ansari Nagar, New Delhi - 110 029
2. Dr.Arun Agarwal, Professor of ENT, Maulana Azad Medical College, Bahadur Shah Zafar Marg New. Delhi
3. Dr B T. Kaul, Prof of law. Delhi University, Law Centre -)|, Dhaula Kaun,
4. New Delhi - 110021
5. Dr Mira Shiva, Coordinator. initiative for Health, Equity and Society. A-60, Hauz Khas, New Delhi - 110 016

The Committee in its first meeting held on 04-Apr-2014, discussed various criteria that could be considered for determination of quantum of compensation in case of Clinical Trial related SAE. The Committee opined that for calculation of quantum of compensation in such cases the guiding principle may he linked to the criteria considered for calculation of compensation in cases of death. The Committee also deliberated that the quantum of compensation in case of Clinical Trial related SAE should not exceed the quantum of compensation which would have been due for payment in case of death of the subject since the loss of life is the maximum injury possible, Considering the definition of SAE. the following sequence other than death are possible in a clinical trial subject, in which the subject shall be entitled for compensation in case the SAE is related to clinical trial.

i. A permanent disability
ii. Congenital anomaly or birth defect
iii. Chronic life-threatening disease or
iv. Reversible SAE in case it is resolved.

The Committee considered that unlike clinical trial related SAE of death, the formula for determination of compensation in each of the above A squealed may be different.

Accordingly, the committee in the first meeting. deliberated separately the each of the above four situations and worked out the draft formulae for determination of quantum of compensation in case of clinical trial related injury (other than death).
The draft formula was uploaded on the CDSCO website for seeking the comments/suggestions of stakeholders.

In the second meeting held on 29th September 2014, the committee deliberated separately each of the four situations in light of the comments/suggestions received on the draft formulae and decided for revisions in two situations as under:

a) In case of SAE causing permanent disability to the subject, the quantum of compensation in case of 100% disability should be 90% of the compensation which would have been due for payment to the nominee (s) in case of death of the subject. The quantum for less than 100% disability will be proportional to the actual percentage disability the subject has suffered.

Accordingly, committee arrived at the following formula:

Compensation = (CX D X 90)/ (100 x 100)

Where,

D= Percentage disability the subject has suffered

C= Quantum of Compensation which would have been due for payment to the subject's nominee (s) in case of death of the subject.

b) In case of **SAE** causing life-threatening disease, the quantum of compensation should be linked to the number of days of hospitalization of the subject. The compensation per day of hospitalization should be equal to the wage loss. The wage loss per day should be calculated based upon the minimum *wage* of the unskilled worker (in Delhi)

Since, in case of hospitalization of any patient not only the patient loses his Ther wage there will be direct or indirect losses of various kind including inconvenience, wage loss of attendant etc. The Committee decided that the compensation per day of hospitalization in such case should be double the minimum wage

Accordingly, the committee arrived at the following formula.

Compensation = 2 x W *x N*

Where,
W=Minimum wage per day of the unskilled worker (in Delhi) N= Number of days of hospitalization

In other two situations, the committee did not consider it necessary for any revision.

Recommended formula for determination of quantumn of compensation in case of Clinical Trial related SAE other than death

(i) SAE causing permanent disability to the subject

In case of SAE causing permanent disability to the subject, the Committee deliberated that so far as the quantum of compensation is concerned, 100% permanent disability to a subject may not be considered equivalent to the death of the subject. Therefore, even in case of 100% permanent disability the quantum of compensation should be less than that for the death of the subject. After detailed deliberation the committee arrived at a decision that quantum of compensation in case of 100% disability should be 90% of the compensation which would have been due for payment to the nominee (s) in case of death of the subject. The quantum for less than 100% disability will be proportional to the actual percentage disability the subject has suffered.

Accordingly, the following formula is recommended.

Compensation = (CxDx90) /(100x100)

Where,

D= Percentage disability the subject has suffered.

C= Quantum of Compensation which would have been due for payment to the subject's nominee(s) in case of death of the subject.

(ii) **SAE causing congenital anomaly or birth defect**

The committee opined that the congenital anomaly or birth defect in a baby may occur due to participation of any one or both the parent in clinical trial. Following situations may arise due to congenital anomaly or birth defect.

a) Still birth
b) Early death due to anomaly
c) No death but deformity which can be fully corrected through appropriate Intervention
d) Permanent disability (mental or physical)

The compensation in such cases would be a lump sum amount such that if that amount is kept by way of fixed deposit or alike, it should bring a monthly interest amount which is approximately equivalent to half of minimum wage of the unskilled worker (in Delhi). This aspect was duly considered while fixing Rs. 8 lacs as base amount for determining the amount of compensation in case of SAE resulting into death. Hence, the quantum of compensation in such cases of SAE would be half of the base amount as per formula for determining the compensation for SAE resulting into death.
In case of birth defect leading to (c) &(d) above to any child, the medical management as long as required would be provided by the Sponsor or his representative which will be over and above the financial compensation.

(iii) SAE causing life-threatening disease and
(iv) Reversible SAE in case it is resolved

In case of clinical trial related SAE causing life-threatening disease & reversible SAE in case it is resolved, the quantum of compensation would be linked to the number of days of hospitalization of the subject. The compensation per day of hospitalization would be equal to the wage loss. The wage loss per day would be calculated based upon the minimum wage of the unskilled worker (in Delhi)

Since, in case of hospitalization of any patient not only the patient loses his / her wage, there will be direct or indirect losses of various kind including inconvenience, wage loss of attendant. The compensation per day of hospitalization in such cases would be double the minimum wage.
Accordingly, the following formula is recommended.

$$\textbf{Compensation} = 2 \times W \times N$$

Where,
W-Minimum wage per day of the unskilled worker (in Delhi)
N= Number of days of hospitalization.

Annexure-XII

Factor (F) for calculating the amount of compensation

Age	Factors
1	2
not more than	
16	228.58
17	227.49
18	226.22
19	225.00
20	224.71
21	222.37
22	221.95
23	219.95
24	218.47
25	216.91
26	215.28
27	213.57
28	211.79
29	209.92
30	207.98
31	205.95
32	203.85
33	201.66
34	199.40
35	197.06

36	194.64
37	192.14
38	189.56
39	186.90
40	184.17
41	181.37
42	178.49
43	175.54
44	172.52
45	169.44
46	166.29
47	163.07
48	159.80
49	156.47
50	153.09
51	149.67
52	146.20
53	142.68
54	139.13
55	135.56
56	131.95
57	128.33
58	124.70
59	121.05
60	117.41

61	. . . . .	113.77
62	. . . . .	110.14
63	. . . . .	106.52
64	. . . . .	102.93
65 Or more	. . . . .	99.37