Institutional Ethics Committee
Shaheed Hasan Khan Mewati Govt. Medical College
Nalhar, Nuh (Haryana)-122107

SOP version 2.1 dated 20/June/2020 Page 1 of 50

Complete Name of the Ethics Committee	:	Institutional Ethics Committee **Shaheed Hasan Khan Mewati Govt. Medical College Nalhar, Nuh (Haryana)-122107**
Complete address of the Ethics Committee	:	Office of Ethics Committee,Director office **Shaheed Hasan Khan Mewati Govt. Medical College Nalhar, Nuh (Haryana)-122107**, India
Frequency of Ethics Committee Meeting	:	Once in three months; Expedited meeting is possible on as and when needed basis; Ethics Committee meeting can be held earlier if required or postponed if there is no new/amended protocol and if there is no specific agenda for the meeting.
Lead time required by the Ethics Committee before which they discuss documents submitted to them	:	21 days
Complete contactdetails of Ethics Committee member whose details will appear on the informed consent form	:	Dr. Sheetal Gole, Office of Ethics Committee, Director office, **Shaheed Hasan Khan Mewati Govt. Medical College Nalhar, Nuh (Haryana)-122107**, India +91-8467053963, 9728141421 directorshkmgmc@gmail.com
SOP effective date	:	20th June/2020

Author Name:	Sign and Date:
Dr Sheetal Gole (Member Secretary)	
Dr. Sonia Hasija (Joint Member Secretary)	
Dr Naresh Kumar (Member)	
Approval Name: Dr. Ravi Gupta(Chairperson)	Sign and Date: 15.6.20

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1. Purpose

The purpose of this standard Operating Procedure (SOP) is to outline the

a) Composition, roles and responsibilities of Members of the Ethics Committee
b) Application process for review of submitted clinical trials by Ethics Committee
c) Review guideline for Ethics Committee members
d) Decision-making by the Ethics Committee and notification to the applicant
e) Ongoing review of the conduct, progress, efficacy and safety of a clinical trial
f) Special consideration for vulnerable population

This SOP provides clear, unambiguous instructions so that the related activities of the committee are conducted in accordance with Indian laws and relevant, National and International Guidelines**.**

2. Scope

Each trial, under the GCP principle, should be conducted in compliance with the protocol that has received prior Ethics Committee approval/favorable opinion. This SOP covers all clinical trials from Phase I to Phase IV. This includes the investigator initiated research as well as organization or pharmaceutical company sponsored trials that are submitted to the Institutional Ethics Committee.

3. Objective

The objective of this SOP is to contribute to effective functioning of the Institutional Ethics Committee so that a quality and consistent ethical review mechanism is put in place for all proposals received dealt by the committee received.

The Institutional Ethics Committee is setups to ensure that the clinical research studies that are carried out at Shaheed Hasan Khan Mewati, Govt. Medical College Nalhar, Nuh:

- Is sound in scientific design, have statistical validity and are conducted according to the parameters of ICH-GCP as well as local regulatory requirements.
- Do not compromise the safety, rights and well-being of the patients participating in the research study.
- Are conducted under the supervision of medical persons with the required experience / expertise
- Include safety, patients who either themselves or, through their legally acceptable representative have given informed consent for participation in the research study.

4. Role

The Institutional Ethics Committee will review and approve all types of research proposals involving human participants with a view to safeguard the dignity, right, safety and well-being of all actual and potential research participants. The goals of research, however important, would never be permitted to override the health and well-being of the research subjects.

The Institutional Ethics Committee will take care that all the cardinal principles of research viz. Autonomy, Beneficence, Non-malafide and justice are taken care of in planning, conduct and reporting of the proposed research. For this purpose, the Institutional Ethics Committee will consider the aspects of informed consent process, risk benefit ratio and other applicable details in Protocol and study procedures. The Institutional Ethics Committee will review the proposals before start of the study as well as monitor the research throughout the study until and after completion of the study.

The Institutional Ethics Committee will also examine compliance with applicable regulatory requirements, guidelines, and laws.

5. Composition

1. The Ethics Committee shall have a minimum of seven members and maximum 15 from medical, non-medical, scientific and non-scientific areas with at least-
   (1) One lay person;
   (2) One woman member;
   (3) One legal expert;
   (4) One independent member from any other related field such as social scientist or representative of non-governmental voluntary agency or philosopher or ethicist or theologian.
2. The Ethics Committee referred to in sub-rule (1) preferably consist at least fifty percent of its members who are not affiliated with the institute or organization in which such committee is constituted.
3. One member of the Ethics Committee who is not affiliated with the institute or organization shall be the chairperson, and shall be appointed by such institute or organization.
4. One member who is affiliated with the institute or organization shall be appointed as Member Secretary of the Ethics Committee by such institute or organization.
5. The committee shall include at least one member whose primary area of interest or specialization is non-scientific and at least one member who is independent of the institution.
6. The members of the Ethics Committee shall follow the provisions of these rules, Good Clinical Practices Guidelines and other regulatory requirements to safeguard the rights, safety and well-being of trial subjects.
7. Every member of the Ethics Committee shall be required to undergo such training and development programmes as may be specified by the Central Licensing Authority from time to time.

5.1 New Appointment

The members including the member secretary will be nominated & appointed by the Institutional Head in office and would be a mix of medical, non-medical scientific and non-scientific persons including lay public to reflect differed. The term of office of each member is three years (renewable for two terms). Any change to membership of the Ethics Committee must be approved by Chairman& Institutional Head in office.

5.2 Removal procedure

A member may be relieved of his/her membership in case of conduct unbecoming for a member of the Ethics Committee or inability to participate in the meetings on any grounds.

The members may be replaced at the discretion of the committee members when a majority vote is obtained(2/3rd of majority of members). A member may be disqualified from IEC membership if the member fails to attend more than three regular consecutive IEC meetings without prior intimation.

5.3 Quorum

(1) No clinical trial or bioavailability or bioequivalence protocol and related documents shall be reviewed by an Ethics Committee unless at least five or its members as detailed below are present, namely:-

a. Medical Scientist (preferably a pharmacologist);
b. Clinician;
c. Legal Expert;
d. Social Scientist or representative of non-governmental voluntary agency or philosopher or ethicist or theologian or a similar person;

e. Lay person;

(2) The Ethics Committee may constitute one or more sub-committees of its members to assist in the functions assigned by it.

(3) The Ethics Committee may associate such experts who are not its members, in its deliberations but such experts shall not have voting rights, if any.

(4) Any change in the membership or the constitution of the registered Ethical Committee shall be intimated in writing to the Central Licensing Authority within thirty working days.

Institutional Ethics Committee membership list would be as per ***Annexure 1***

The requisite quorum of 5 members is required to be present at each review meeting.

Decisions will be made only in meetings where quorum is complete. All nominated members including the member secretary have the right to vote.

Ethics Committee Members Conveyance Allowance would be given to the members attending the meeting. The member secretary shall be aware of the amount decided by the Institutional Head.

It is preferable that at least one of the Institutional Ethics Committee members who are not affiliated to the Institute be present during each review meeting as per Schedule-Y.

All members should maintain in absolute confidentiality of all discussions during the meeting. They have no rights to participate if they are principal investigator/investigator in the proposed study.

6. Agenda Preparation, Meeting Procedures, Recording of Minutes and communication by IEC

Preparation of the agenda, minutes and other record keeping, will be the responsibility of the Ethics Committee Member Secretary.

Minutes of the IEC meetings, all the proceedings and deliberation will be documented.

Member having a conflict of interest will indicate to the Chairman prior to the review of application. Any committee member with a conflicting interest in a proposal will abstain from deliberations and in the decision making process on that proposal, except to provide information as requested by the committee. Such abstentions will be recorded in the minutes.

The meeting shall generally proceed in the order organized in the agenda. However, the Chairperson may allow adjustments in the order of issues to be discussed depending on the situation.

It is the responsibility of the Member Secretary to ensure proper recording and dissemination of the minutes after the meeting is over.

The Member Secretary will compose the summary of each meeting discussion and decision in a concise and easy-to-read style in the minutes within 7 working days of the meeting day.

The Member Secretary will make sure to cover all contents in each particular category to include the following:

- Name of person preparing the minutes
- Location where the meeting was held (city, state)
- Meeting number, date/duration of the meeting (time of commencement and end)
- Names of the IEC members and guests attending the meeting
- Name of the individual serving as Chairperson of the meeting
- Determination of a duly constituted quorum by the Chairperson to proceed with the meeting

The Member Secretary will ask the members whether any points need to be discussed regarding minutes of the previous meeting. If no points are raised, the minutes will be considered as confirmed.

The Chairperson will review and finally approve the minutes.

The Member Secretary will place the original version of the minutes in the minutes file.

A decision of the IEC will be communicated to the applicant in writing, within 14 days of the meeting at which the decision was taken.

An investigator is expected to submit reply to the letter of recommended modifications / queries sent by the IEC, within 90 days of date of receipt of the letter. If the investigator fails to reply within this period, the file will be considered closed by the IEC and ethics clearance approval letter will not be issued by IEC. The investigator will have to re-apply for the Ethics Committee approval.

The communication of the decision will include:

- Name and address of IEC.
- The date and place of decision
- The name and designation of the applicant.
- Title of the research proposal reviewed.
- The clear identification of proposal no., version no., date, amendment no., date.
- A clear statement of decision reached.
- Any advice by the IEC to the applicant.
- In case of conditional decision, any requirement by IEC, including suggestions for revision, and the procedure for having the application re reviewed.
- In case of rejection of the proposal, reason(s) for the rejection will be clearly stated. Signature of the member secretary with date

Communication to Institutional official and to Regulatory agencies will be performed by Member Secretary whenever requirement arise as per but not limited to SOP of IEC.

7. Confidentiality and Conflict of Interest Agreement Form

The appropriate Confidentiality and Conflict of Interest Agreement Form will be provided to the Institutional Ethics Committee membersand Independent Consultants

Every member at beginning of the tenure and before he/she commences to review research projects submitted to Institutional Ethics Committee and before he/she starts to function as Institutional Ethics Committee members and before he/she starts attending Institutional Ethics Committee meeting will read the Confidentiality and Conflict of Interest Agreement Form - ***Annexure 2 & 3*** carefully and thoroughly.

Institutional Ethics Committee member; Independent Consultant will fill up the details such as name, designation and will be provided it to Member Secretary of Institutional Ethics Committee.

The newly appointed Institutional Ethics Committee member, before the beginning of their tenure, and Independent Consultants will sign and date the document before a member Secretary. They will give the signed form back to the member Secretary.

The member Secretary keeps the original copies of the signed Agreements at the Ethics Committee for Research on Human Subjects office in the file.

The member Secretary will store the file in a secure cabinet with limited key holders.

8. Training of the Institutional Ethics Committee Members in Research Ethics

- An individual selected as a new member of the Institutional Ethics Committee will be required to attend one meeting as an 'Observer' before being inducted as a member of the Institutional Ethics Committee
- Member-secretary or Institutional Ethics Committee member will provide an introductory training to the new member.
- The Institutional Ethics Committee Member Secretary, members, Chairperson will be encouraged to receive continued training by participating in a workshop, conference and/ or retraining program related to research ethics, as a delegate, faculty, facilitator, etc. at least once every year.
- The Chairperson and Member Secretary will organize workshops or training programs for the committee members. The Institutional Ethics Committee will conduct workshops on ethics in clinical research and good clinical research practices from time to time to impart training to the Institutional Ethics Committee Members to the Institutional faculty members.
- The Chairperson and the Member Secretary will inform all members about any updates on ethical and regulatory guidelines regularly during meetings.
- The Institutional Ethics Committee may sponsor or reimburse the expenses of Institutional Ethics Committee member or prospective members for attending conference, continuing education session workshop and/ or training program etc.

9. Roles and Responsibilities of IEC Members

There will be one Chairperson and one Member Secretary in the IEC. The Chairperson will head the committee. The Member Secretary will be the guardian of all documents and funds in the possession of the committee. Other IEC members will be regular committee members with equal ranking. The roles and responsibilities of Chairperson, Member Secretary and IEC Members are as follows:

Chairperson:

- The Chairperson will be responsible for conducting committee meetings, leading all discussions and deliberations pertinent to the review of research proposals.
- The Chairperson will sign documents and communications related to IEC functioning.
- Conduct EC meetings and be accountable for independent and efficient functioning of the committee
- Ensure active participation of all members (particularly non-affiliated, non-medical/ non- technical) in all discussions and deliberations.
- Seek COI declaration from members and ensure quorum and fair decision making.
- Handle complaints against researchers, IEC members, conflict of interest issues and requests for use of IEC data, etc.

Member Secretary

- Receive research proposals
- Organize an effective and efficient tracking procedure for each proposal received
- Schedule and organize IEC meetings
- Prepare and maintain meeting agenda and minutes
- Maintain IEC documentation and to archive them
- Sign documents and communications related to IEC functioning
- Communicate with the IEC members and applicants/ investigators
- Notify the Principal Investigator regarding IEC decisions related to the submitted research proposal
- Arrange for training of personnel and IEC members
- Organize the preparations, review, revision and distribution of SOPs and guidelines
- Provide necessary administrative support for IEC related activities to the Chairperson
- Provide updates on relevant and contemporary issues to ethics in health research as well as relevant contemporary literature to the committee members
- Receive ethics committee review processing fees and issue official receipts for the same
- Delegate various responsibilities to appropriate and authorized individuals
- Ensure adherence of IEC functioning as per SOPs
- Prepare for audits and inspections

Functions of all IEC members

- Attend IEC Meetings and participate in discussions and deliberations so that appropriate decisions can be arrived at
- Review, discuss and consider research Proposals submitted for evaluation
- Monitor Serious Adverse Event reports and recommend appropriate action(s) whenever required to do so.
- Review the progress reports and monitor ongoing studies as appropriate
- Do onsite visits wherever needed
- Evaluate final reports and outcomes
- Maintain confidentiality of the documents and deliberations of IEC meetings
- Declare any conflict of interest in writing to the Chairperson, if any, at each meeting
- Participate in continuing education activities in biomedical ethics and biomedical research
- Carry out the work delegated by Chairperson and Member-secretary
- Assist Chairperson and Member-secretary in carrying out IEC work as per SOPs
- Be up to date on relevant laws and regulations

Apart from above, few specific responsibilities are required by each member as per their roles in IEC.

Basic Medical Scientist(s):

- Scientific and ethical review with special emphasis on the intervention, benefit-risk analysis, research design, methodology and statistics, continuing review process, SAE, protocol deviation, progress and completion report
- For clinical trials, pharmacologist to review the drug safety and Pharmaco dynamics

Clinician(s):

- Scientific review of protocols including review of the intervention, benefit-risk analysis, research design, methodology, sample size, site of study and statistics
- Ongoing review of the protocol (SAE, protocol deviation or violation, progress and completion report)
- Review medical care, facility and appropriateness of the principal investigator, provision for medical car, management and compensation.
- Thorough review of protocol, investigators brochure (if applicable) and all other protocol details and submitted documents.

Legal Expert:

- Ethical review of the proposal, ICD along with translations, MoU, Clinical Trial Agreement (CTA), regulatory approval, insurance document, other site approvals, researcher's undertaking, protocol specific other permissions as appropriate.
- Interpret and inform EC members about new regulations if any

Social Scientist:

- Ethical review of the proposal, ICD along with the translations
- Assess impact on community involvement, socio–cultural context, religious or philosophical context, if any
- Serve as a patient/participant/ societal /community representative and bring in ethical and societal concerns
- Ensure relevance of research to the society

Lay Person:

- Review of the proposal, ICD along with translation(s)
- Evaluate benefits and risks from the participant's perspective and opine whether benefits justify the risks
- Serve as a patient/participant/ community representative and bring in ethical and societal concerns.
- Assess on societal aspects if any
- Assess routine day to day aspects and its impact on study participation

10. Correspondence Record

Correspondence between the Institutional Ethics Committee and the Principal Investigator / study team and other relevant records (response letter, minutes of meetings, membership list composition etc.) will be retained for minimum period of 5 years after completion of the trial.

The Institutional Ethics Committee will review all research projects and also the on-going research projects at intervals appropriate to the degree of risk to the study subjects.

The committee will maintain a list of projects submitted, approved / disapproved and the outcome of each project including subject in formation, relevant correspondence and all study related documents.

11. Procedure and List of Documents required for review

11.1 List of Documents

The applicant of the proposal generally the principal investigator is required to submit his/her application letter and 2hardcopies of the project and submit the project at the Ethics Committee websiteswww.iecmanager.org, at least 3 weeks before a scheduled meeting:

- A letter of intent or proposal by the Investigator (Annexure- 4 A & B)
- Research protocol.
- Protocol Amendment, if any.
- Investigator's Brochure.
- Case Report Form
- Informed consent form, [English]
- Informed consent form, [English to Hindi translation].
- Patient/ volunteer information Leaflet [English]
- Patient/ volunteer information Leaflet [English to Hindi translation].
- Any written information to be provided to subjects including patient emergency card, study related questionnaire
- Subject recruitment procedures (e.g. Advertisements) Safety Reports
- DCGI Approval Letter (DCGI Submission letter would be accepted in lieu of DCGI Approval letter. However, DCGI Approval letter should be notified to Ethics Committee once available. Even though after receipt of Ethics Committee approval, trial would not be initiated until DCGI Approval letter is notified to Ethics Committee)
- Insurance Policy
- Import license, where applicable
- Investigator's undertaking
- The investigator's current curriculum vitae
- Clinical Trial Agreement
- Document Receipt Form For Initial Review (Annexure-5)
- The Institutional Ethics Committee is to be notified of any payments proposed to be made to study patients towards reimbursement of incidental expenses.
- Fee for ethical clearance of extramural projects (Industry driven projects) by IEC is Rs. 50000/-. (Annexure-6)
- Rs. 10000/- will be applicable for ethical clearance of amendments of the extramural projects (Industry driven projects).
- Fee of Rs. 10000/- will be charged for ethical clearance of projects funded or approved by Government agencies outside the Institute/professional bodies/agencies other than industry.
- Institutional Ethics Committee will carefully review all elements of the proposed research study. And fill initial review Form (Annexure-7). Checklist guide for IEC review is included as (Annexure-8)

Key elements for review include following:

A. Scientific Design and Conduct of the Study

- The appropriateness of the study design in relation to the objectives of the study, the statistical methodology (including sample size calculation), and the potential for reaching sound conclusions with the smallest number of research participants;
- The justification of predictable risks and inconveniences weighed against the anticipated benefits for the research participants and the concerned communities;
- The justification for the use of control arms;
- Criteria for prematurely withdrawing research participants;
- criteria for suspending or terminating the research as a whole;
- The adequacy of the site, including the supporting staff, available facilities, and emergency procedures;
- The manner in which the results of the research will be reported and published.

B. Protection of Research Participant Confidentiality

- A description of the persons who will have access to personal data of the research participants, including medical records and biological samples;
- the measures taken to ensure the confidentiality and security of personal information concerning research participants.

C. Community Considerations

- The impact and relevance of the research on the local community and on the concerned communities from which the research participants are drawn;
- The steps taken to consult with the concerned communities during the course of designing the research;
- The influence of the community on the consent of individuals;
- Proposed community consultation during the course of the research;
- The extent to which the research contributes to capacity building, such as the enhancement of local healthcare, research, and the ability to respond to public health needs;
- A description of the availability and affordability of any successful study product to the concerned communities following the research;
- The manner in which the results of the research will be made available to the research participants and the concerned communities.

D. Recruitment of Research Participants

IEC will carefully review and ensure:

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

In addition to its review for scientific merit and protection of subjects from unnecessary research risks, the EC will evaluate all protocols for subject recruitment especially with respect to women with childbearing potential, minority groups and children. Exclusion of

minorities, women or children will be recommended or approved when inclusion is inappropriate with respect to the health of the subjects or the purpose of the research.
IEC will also evaluate recruitment methodologies that are involved to recruit patients into the studies. IEC will discuss this in detail with Principal Investigator of the study. The methods by which patients can be recruited are out patient or inpatient department and consultation, referral from doctors within and outside Institution, through camps, database review etc.

All recruitment and retention materials that are patient facing such as study related stationary, schedule reminders, small tokens of appreciation, study specific small instruments to be given to patients should be reviewed and approved and/or notified, as appropriate to IEC prior to their implementation.

E. Clinical Trial Agreement and Insurance

Clinical Trial Agreement and Insurance are two very important study related documents that involve careful consideration and review by IEC. IEC should check following:

Insurance:

-Start and stop date of the insurance
-Tenure of insurance and its renewal time to time to cover entire study duration
-Number of research participants covered by insurance
-Adequate insurance cover for the participants
-Coverage for study related injuries and medical management
- Local or global, both insurances are accepted as long as it covers involved parties

Clinical Trial Agreement:

-Draft clinical trial agreement is accepted for the review. However, study can only be initiated once final executed agreement is provided to IEC
- IEC will ensure budgets are appropriate for the study conduct and not very high that appear disproportionate
-Agreement is fully executed and signed by all parties
-Agreement includes the clauses related to compensation and medical management in the event of research related injuries per relevant regulations
- Travel reimbursement for patients is covered

The Institutional Ethics Committee expects from the principal investigator to be informed about:

- The initiation of the study/randomization of the first patient (in the status report),
- The progress of the study at interval of every One year,
- Any Serious Adverse Events occurring in the course of the study within 24 hours of their occurring.
- In case Member Secretary is not available personally due to weekend or any other condition, it can be notified to Ethics Committee member secretary by email at ethicalcommitteeshkm@gmail.comwhich will be followed by signature of Member secretary or Chairman within 7days.
- Any changes in the protocol and patient information /informed consent documents, prior to their implementation.
- Amendments/revisions to any study-related document as well as patient safety related information

- Study completion and discontinuation with reasons
- Justification for approval to restart studies discontinued earlier

The final report of the study shall be submitted to the Institutional Ethics Committee in all cases, even when the study abandoned for any reason (s).

11.2 Categorization of New Research Study Protocols Received for Initial Review

- New research study proposals received by the 20th of the month will be considered for review in the next monthly meeting of the IEC. *(This date can be as per individual IEC's policy).*
- The Member secretary will ensure that application of the research proposal is complete in terms of required documents.
- The Member secretary will forward the soft copy of the research proposal to the Joint Member Secretary for initial screening within 2 working days of receiving the proposal.
- The Joint Member Secretary will screen the research proposals and categorize the proposals.
- The Member Secretary [in consultation with Chairperson (as applicable)] will categorize the proposals into three types. The types of review processes and the criteria to decide the type of review are explained below (*www.icmr.nc.in*)*Ethical Guidelines for Biomedical Research on Human Participants, Indian Council of Medical Research, October 2006*):

Full Board Review: When new research proposals and other related documents are tabled in a formally convened meeting of the Ethics Committee for detailed discussion and decision, this is called Full Board Review.

a. Research studies involving more than minimal risk to human study participants are required by national and international regulations to be reviewed by the Ethics Committee full board.
b. Research that is considered minimal risk but involves vulnerable population may be referred for Full Board Review.
c. Research proposals that have undergone expedited review and are referred to Full Board as no decision could be reached.

Expedited Review: When new research proposals and related documents undergo a speedy review process by only two or three designated (by the Chairperson) Ethics Committee members this is called Expedited Review.

a. Expedited review may be sufficient if the research study involves not more than minimal risk as defined in the ICMR guidelines.
b. Research involving data, documents or specimens that have been already collected or will be collected for ongoing medical treatment or diagnosis.
c. Research on interventions in emergency situations.
d. Collection of data for research purposes through non-invasive procedures (not involving general anesthesia or sedation) routinely employed in clinical practice and using medical devices which have been already approved for use. Examples of such procedures include collection of data through application of EEG or ECG electrodes, acoustic testing, tests using the Doppler principle, non-invasive blood pressure and other routine clinical measurements, exercise tolerance etc. However procedures involving the use of x-rays or microwaves are NOT recommended for expedited review.
e. Clinical studies of drugs and medical devices only when research is on already approved drugs except when studying drug interaction or conducting trial on vulnerable population or
f. Research on Disaster management.

A PI may also apply to the IEC for expedited review if the proposed research study satisfies the criteria for expedited review as per ICMR Guidelines.

The following are examples of documents that will undergo expedited review but are NOT in the category of INITIAL review

- Revised proposal with minor modifications previously approved through full review by the IEC.
- Adverse Event (AE) or unexpected Adverse Drug Reaction (ADR) of minor nature is reported.
- Other documents which would be considered for expedited review are as follows but may not restrict to:
- Minor deviations from originally approved research during the period of approval (usually of one year duration)
- Change in the name, address of sponsor
- Change in contact details of principal investigator, and Member-Secretary, IEC
- Request for change in principal investigator, co-investigator, change in any member involved in the research
- Minor amendments in the protocol, case record form
- Minor corrections in budget
- Other administrative changes in the investigator brochure, informed consent document

Exemption from review: When research fulfils the following criteria, the IEC may grant an exemption from review:

a. Research does not involve live human participants, is on data in the public domain orison anoymised data derived from participants and the research has less than minimal risk to participants, an exemption from IEC review may be considered.
b. Examples that may be eligible for exemption from review include:
    - 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
c. PI may also apply to IEC for exemption from review if he or she finds that the proposed research study satisfies the criteria for exemption.

Glossary(***www.icmr.nic.inEthicalGuidelinesforBiomedicalResearchonHuman Participants,IndianCouncilofMedicalResearch,October2006***)

- **Minimal Risk:** It means that the probability and magnitude of harm or discomfort anticipated in the research are not greater in and of themselves than those ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests. However, in some cases like surgery, chemotherapy or radiation therapy, great risk would be inherent in the treatment itself, but this may be within the range of minimal risk for their search participant undergoing these interventions in ceit would be undertaken as part of current everyday life. Example for minimal risk :retrospective review of patient case records to determine the incidence of disease/recurrence of disease]

- **Less than minimal risk:** Research, in which there is no known physical, emotional, psychological, or economical risk to the study participants. This research qualifies as exempt if it does not involve special populations (i.e., minors, prisoners, pregnant women, etc.)

Exemption from Ethics Review of Research Study Protocols

- The Member secretary will receive the Exemption from review Application Form *(Annexure-9)*
- Protocol and other documents submitted by the investigators.
- The Member secretary will check that the package and will review it.
- The Member Secretary will screen the research study proposal and determine whether the study qualifies for exemption from review based on the criteria laid down in the Indian Council of Medical Research (ICMR) Ethical Guidelines. The proposals that involve less than minimal risk fall under this category.
- In some circumstances, research that appears to meet low risk criteria may need to be reviewed by the IEC. This might be because of requirements of the publisher of the research or the organization which is providing funding resources, data, and access to participants etc.

Exemption Process

- If the protocol and related documents satisfy the above stated criteria, the Member Secretary in consultation with the Chairperson will review the brief summary of the project and the Exemption Form.
- The Member Secretary records the decision on the Exemption Form
- The Member secretary communicates the decision to the investigator.
- The Member Secretary / Chairperson may keep the application for review and decision regarding exemption at the next full board meeting.
- The decision regarding request for Exemption from review, signed by the IEC Member secretary, will be forwarded to the Principal Investigator within 14 working days after the decision regarding the exemption is taken.
- The Member Secretary will inform the IEC members of the decision at the next regular meeting and minute it.

11.3 Meeting Schedule:

The Institutional Ethics Committee will meet once in three months. Advance notice, 07 days before each meeting will be sent out to the members, along with the agenda. Expedited meeting is possible on as and when needed basis; Ethics Committee meeting can be held earlier if required or postponed if there is no new/amended protocol and if there is no specific agenda for the meeting at the discretion of Member Secretary or Chairman.

11.4 Decision Making:

The Member secretary, designated by the Chairperson, will record the Minutes of the meeting and circulate the same to the members within two weeks of the meeting.

The Investigator/Co-investigator is called to the meeting to present the study or answer specific queries. However, he / she will not participate in the decision making / voting process of that study even if he / she is a regular member of the ethics committee.

A Study Team member including the Principal Investigator will be deemed an interested party with regard to the review.

The Study Team Member's non participation in the decision making / voting process will be recorded in the response letter from the Ethics Committee. Only those Ethics

Committee members who are independent of the investigator and the sponsor of the trial should vote/provide opinion on a trial-related matter.
The Institutional Ethics Committee may call upon subject experts as independent consultants who may provide special review of selected research protocols, if need be. These experts 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 person or ethnic minorities. They are required to give their specialized views but do not take part in the decision making process which will be made by the members of the Institutional Ethics Committee
The decision of the committee will take by a majority vote after the quorum requirements are fulfilled to recommend / reject / suggest modifications for a repeat review or advise appropriate steps.
If subject experts are invited to offer their views, they will not take part in the voting process.

The Institutional Ethics Committee will give its opinion on the Decision Form (Annexure-10)
In case Institutional Ethics Committee revokes its approval accorded to a trial protocol, it must record the reasons for doing so and at once communicate such a decision to the Investigator.
In all cases, the study will be unambiguously identified by protocol title and number.
All documents reviewed will be listed in the response letter, which will also state the list of members present and date of the meeting at which the study was reviewed.
The member-secretary will convey the decision of the committee to the Principal Investigator in writing. The response letter will include the signature and date by the Institutional Ethics Committee Member Secretary.

The decision letter must contain following information:

- Date and time of Ethics Committee meeting.
- Place of the meeting
- Names and designation of the Chairperson and members who attend the meeting.
- Title of the Research proposal
- Name of the Chief investigator
- List of documents (with date and version number wherever possible) reviewed by the Institutional Ethics Committee
- A clear Statement of the Decision Reached. Any advice (non-binding) by the Institutional Ethics Committee
- In the case of Negative decision, reasons for not approving the proposal must be mentioned
- In the case of "approval" decision, the responsibilities of the chief investigator must be communicated
- Approval Letter is issued to the PI if the decision is approved(Annexure-11 A & B)

Should an amendment to a study related document be administrative in nature and not involving study design or safety criteria, it may be provisionally approved in writing, by the Chairperson/Member-Secretary of the Institutional Ethics Committee without calling a full meeting.
The Chairperson/member-secretary will inform other members of the Institutional Ethics Committee of amendment and his / her decision during the subsequent regular meeting of the committee. The decision will be ratified and comminuted.

11.5 Expedited Review of Research Study Protocols

- Institutional Ethics Committee (IEC) members will perform an expedited review on a new research study protocol using the Assessment Form *(Annexure-12)*
- After determining that the Protocol / Project qualifies for an expedited review, the Member Secretary (in consultation with Chairperson) will nominate two or more IEC members to review the amended protocol.
- The Member secretary will fill in the required details in the nomination form to the IEC Members requesting initial review *(Annexure-13)*and in the study assessment form.
- The Member secretary will send a packet *(hard or soft copy)* to the designated IEC members.
  - Nomination letter to IEC Members requesting Initial Review,
  - Study assessment form
  - Project Submission Application Form
  - Protocol and related documents
- Designated IEC members will receive the protocol package with the Project Application Form, in a CD or pen drive or as hard copy (if desired so).
- The IEC member will verify all the contents.
- The IEC member will notify the IEC Member secretary if any documents are missing
- IEC members will review the protocol within the stipulated timeline.
- The comments of the IEC members will be recorded.
- The IEC Member secretary will collect the Assessment Forms with the comments from each designated reviewer and file in the original study file
- The Member Secretary will discuss the comments of the members with the Chairperson and a decision about the protocol will be taken.
- If there are queries these will be sent to the PI within one working day after receipt by the Member secretary in consultation with Member Secretary.
- The reply from the PI will be discussed by the Member Secretary with the Chairperson or the designated IEC members and a decision be reached.
- The final decision will be recorded on the Study Assessment Form for Expedited Review
- The decision will be informed to the IEC members at the full board meeting.
- If deemed necessary by reviewer(s), Member Secretary/ Chairperson, the project shall be discussed at the forthcoming full board meeting before final decision. The final decision by the Chairperson is recorded on the Study Assessment Form for Expedited Review
- The Member secretary will send the Study approval letter to the PI (Annexure-14)
- If project is disapproved or requires resubmission after certain modifications, this will be informed to the Principal Investigator in writing.
- The reasons for disapproval of a project will be specified in the letter sent to PI.
- The expedited review process should be completed within 14 working days.

12. Review of Amended Protocols and Protocol-related Documents

- It is the responsibility of the IEC Member Secretary to ensure the completeness of the documents submitted to the IEC.
- A re-submitted protocol and related documents may be reviewed by either the Chairperson and two or more IEC members designated by the Chairperson/ Member

- secretary (in expedited review meeting), or all the IEC members as per IEC decision determined by the IEC at the time of the initial review of the project during the full board IEC meeting. This information would be recorded in the minutes of the meetings.
  The amended protocol/ protocol related document will require Full Board review if any of the following criteria are met:
  The Protocol amendment changes the risk-benefit assessment such as
- a change in study design,
- additional treatments or the deletion of treatments
- changes in inclusion/exclusion criteria.
- change in method of dosage formulation, such as, oral changed to intravenous
- a significant change in the number of research participants (if the decrease/increase in the number of research participants alters the fundamental characteristics of the study, it is significant)

➢ For regulatory studies, a protocol amendment with above changes would require DCGI approval

- In the case of an amended study protocol and related documents, The Member Secretary/Chairperson will decide whether the proposed protocol amendment(s) needs to undergo a full board review or expedited review. If the amendment(s) is / are of administrative nature the Member Secretary/Chairperson can recommend an expedited review, while if the amendment/s relate to participant safety or data capture, it should be recommended for full board review. Additionally, primary reviewers who had reviewed the initial submission may be asked to review the resubmitted protocol.\

<u>Detailed instructions</u>

- The Member secretary will verify if the PI has replied to IEC queries within 180 days of receipt of the letter of comments by the IEC.
- The Member secretary will check the resubmitted protocol & related documents (hard and soft copy) for the following items
  - ➢ Reply to the IEC letter of comments
  - ➢ Revised version of protocol and/ or the informed consent document and /or any other related documents such as, case report forms, diary sheets, etc. are submitted with the changes made to the documents either underlined or highlighted.
- The Member secretary will refer to the IEC Decision Form on the given protocol and distribute the documents containing the reply to the query letter, revised protocol and related documents along with Assessment Form for resubmitted protocol to
  - ➢ The Member Secretary for summarizing and including it on the agenda for full board discussion in the forthcoming meeting if the decision on the protocol was 'to be discussed at full board'
  - ➢ The designated IEC members if the decision on the protocol was 'to be reviewed by two or more IEC members'.
  - ➢ The Chairperson/Member Secretary if the decision on the protocol was 'Approved with recommendations subject to review by Chairperson/Member Secretary only' as per IEC Decision Form.

Review of revised protocol by IEC member/ Member Secretary/Chairperson:

- The IEC member/ Member Secretary/ Chairperson will refer to the query letter/ comments as guidance for the review and consider whether the recommendations of the IEC have been followed or adequately responded to.
- The IEC member/ Member Secretary/ Chairperson will make further comments where appropriate, in the Assessment Form for resubmitted protocol (*Annexure -15)*.
- The Member secretary will retrieve the Assessment Form for resubmitted protocol from the members/Member Secretary/Chairperson.
- In case the decision is to discuss the revised protocol at the full board meeting, the Member Secretary will present a brief oral summary of the study design and the comments of the IEC members/Chairperson in the IEC Full Board meeting.
- The Chairperson shall entertain discussion on the protocol revision from all the IEC members.
- The final decision regarding the research project shall be reached by voting (2/3rd majority of the members present and voting) and shall include one of the following:
    a) Approved
    b) Modifications to items noted at the convened meeting and follow-up by the Chairperson/ Member Secretary /IEC members after receipt of the requested modifications:
    c) Disapproved giving reasons ford is approval
- In case the revised protocol is already approved through expedited review, the decision is informed to the members at the full board meeting.

Receipt of protocol for amendments

- The documents for amendments (hard and soft copy) forwarded by the PI will be received by the Member secretary and verified.
- The Member secretary will confirm the request for review of amended Protocol/Protocol related documents from the Principal Investigator on previously approved Protocol/Protocol related documents as per the form (*Annexure -16)*.
- The administrative staff will confirm that the amended version of the protocol and related documents are attached with the application and that the changes or modifications in the protocol are underlined or highlighted in the amended version.

Notify Member Secretary

- The Member secretary will inform the Member Secretary of receipt of the protocol amendment
- Determine whether full review or review by designated members.
- After review of the materials, the Chairperson / Member Secretary will determine whether the protocol requires a full board review or expedited review. The Chairperson/Member Secretary will indicate this decision on the Protocol Amendment Assessment Form.
- The amended protocol/ protocol related document will require Full Board review if any of the following criteria are met:
- The Protocol amendment changes the risk-benefit assessment such as
- a change in study design,
- additional treatments or the deletion of treatments
- changes in inclusion/exclusion criteria.

- change in method of dosage formulation, such as, oral changed to intravenous
- a significant change in the number of research participants (if the decrease/increase in the number of research participants alters the fundamental characteristics of the study, it is significant)
- For regulatory studies, a protocol amendment with above changes would require DCGI approval
- For expedited review, members name will be nominated by the Chairperson/ Member Secretary.

Distribution to IEC members

- The following documents will be distributed to the designated IEC members as per the decision regarding review
- The amendment's revision documents to clearly identify each change.
- Protocol Amendment Assessment Form.
- Whenever the decision is Full Board review, the Member secretary shall summarize the points for discussion regarding the amended protocol/protocol related documents and shall place the protocol amendment request on the agenda for discussion at the next convened meeting.

Protocol Amendment Review Process

-
- The IEC member will review the amended documents and write his/her comments in the Protocol Amendment Assessment Form.
- The reviewer may request the member secretary to keep the documents for full board discussion after review.
- The IEC members performing the review must sign and return this to the Member secretary after there views.

IEC Decision on Amended Protocols

-
- In case the project is kept for full board review, the Member Secretary / designated member will present a brief oral summary of the study design and read the comments on the amended protocol/ protocol related documents in themeeting.
- The decision by the designated reviewers maybe
    a. Approved
    b. Disapproved
    c. Suggested Recommendation
    d. Next full board discussion
- The final decision regarding the research project shall be reached by voting (2/3rd majority of the members present and voting) and shall include one of the following:
    a. Approve the protocol amendment
    b. Require a modification to the proposed amendment or informed consent documents, stating the reason and action required to sustain the study with a follow-up full IEC review/ IEC review.
- Not approve the amendment request, stating the reason – but allow the study to continue as previously approved.

- Suspend the study, until further information is obtained

Recording of the decision

- This IEC decision will be recorded by the Member secretary in the IEC Decision Form.

Communication of the Decision to the Principal Investigator

- If the IEC approves the protocol/ informed consent documents (ICDs) amendment, the Member secretary staff will send a signed and dated Amendment Approval Letter i.e. (Annexure-17) to the Principal Investigator (PI) within 14 working days of the meeting. The decision regarding disapproval (stating reasons) or request for modifications (stating specific changes needed) shall be communicated in writing to the investigator within 14 working days of the meeting.
- The letter of comments sent to the investigator shall state that the reply to the letter is expected within 180 days of date of receipt of the letter and in the absence of any response, the project will be declared closed for the IEC office records.
- The Member Secretary shall inform other members about the decision taken on the amended document/s at the next full board meeting.

13 Review of informed Consent Document (subject information sheet and informed consent form) and informed consent process

Patient information sheet and informed consent form in English/Hindi and local language(s) should be enclosed. The patient information sheet should provide adequate and complete information in understandable language. It should also assure that any new information that becomes relevant during the trial and is related to their participation will be given to them. Requirement of Audio-Visual informed consent/Audio informed consent/ only written informed consent will be discussed during each initial study review as per the applicable regulations published in Gazette of India.

Following points will be considered while reviewing informed consent:

- Understandable language
- Statement that study involves research
- Sponsor of study
- Purpose and procedures
- Risks & discomforts
- Benefits
- Compensation for participation
- Compensation for study related injury
- Alternatives to participation
- Confidentiality of records
- Statement that consent is voluntary
- Right to withdraw

Waiver of Written / Verbal Informed Consent

It is the responsibility of the IEC to review and approve a request for verbal/written consent waiver.
The Member Secretary will record the decision in the minutes and in the Application Form.
The Chairperson will sign and date letter conveying the decision.
If the proposal has undergone expedited review, the waiver of consent has to be granted only after full board review.

Detailed instructions

- The Application Form (*Annexure-18)* is designed to standardize the process of applying for consent waiver.
- When a request for waiver of consent is received from the Principal Investigator (PI) to the IEC in the given format, the following steps are taken:
- The IEC Member secretary will check if the concerned documents are filled completely and the required list of documents is enclosed.
- The IEC members will review the request taking into consideration the types of studies for which waiver of consent may be granted
- The IEC will ensure that there are adequate mechanisms described in the protocol for protection of the identity of the research participants and maintaining confidentiality of the study data. (*This is necessary as the participant cannot be assured directly about confidentiality of health data through a formal informed consent process, when consent waiver is granted*).

  The final decision whether to grant the waiver is take meeting unless n at a full board the projects is considered under expedited review.

  The decision regarding approval / disapproval of waiver is informed to the Principal Investigator in writing. If the waiver is not granted, the IEC will provide reasons for the same.

  Type of research projects which may qualify for consent waiver:

  A request to waive written informed consent must be accompanied by a detailed explanation. The investigator is also required to provide assurance regarding protection of identity of research participants and maintenance of confidentiality about the data of the research participants. The following criteria (ICMR 2006 guidelines) must be met for a research project so that it can qualify for granting a waiver of both written and verbal consent.

- The proposed research presents no more than minimal risk to participants. e.g. a retrospective review of patient case records to determine the incidence of disease / recurrence of disease. [Minimal risk would be defined as that which may be anticipated as harm or discomfort not greater than that encountered in routine daily life activities of general population or during the performance of routine physical or psychological examinations or tests. However, in some cases like surgery, chemotherapy or radiation therapy, great risk would be inherent in the treatment itself, but this may be within the range of minimal risk for the research participant undergoing these interventions since it would be undertaken as part of current everyday life].

- When it is impractical to conduct research since confidentiality of personally identifiable information has to be maintained throughout research as maybe required by the sensitivity of the research objective. e.g. *conducting interviews with citizens about their religious beliefs/peoplewithHIVandAIDS/conductingphoneinterviewswithhomosexuals.*
  The only record linking the participant and the research would be the consent document and when there is a possible legal, social or economic risk to the participant entailed in signing the consent form as they might be identified as such by signing the consent form, the requirement for obtaining consent can be waived of by the IEC.
  [In case of ***telephonic interviews***, waiver of written informed consent may be requested but verbal consent is mandatory].
- The following documents need to be submitted for the IEC review for verbal consent
- A script for verbal consent - a verbal consent script provides all of the elements of consent in a more informal style. In addition, each subject should be provided with an information sheet that describes the study and gives contact names and numbers.
- The interview schedule (questions to be asked) will confirm that the interview is a simple 5 minute call and that no questions are asked that compromise a person's confidentiality or position.
- Normally, investigators will be asked to keep a log of those who were approached about the study, and offered verbal consent. A simple chart indicating the participants as participant 1, participant 2, etc. and a column indicating that verbal consent was given along with the date.
- Research on publicly available information, documents, records, work performances, reviews, quality assurance studies, archival materials or third party interviews, service programs for benefit of public having a bearing on public health programs, and consumer acceptance studies.
- Research on anoymised biological samples from deceased individuals, left over samples after clinical investigation, cell lines or cell free derivatives like viral isolates, DNA or RNA from recognized institutions or qualified investigators, samples or data from repositories or registries etc.
- In emergency situations when no surrogate consents can be taken. When consent of person/ patient/ responsible relative or custodian/ team of designated doctors for such an event is not possible, the IEC can allow waiver of consent for recruiting participant in a research study. However, information about the intervention should be given to the patients whenever he/she gains consciousness or to relative/legal guardian when available later.

14. Continuing Review of Study Protocols

It is the responsibility of the IEC Member Secretary to remind the PIs regarding continued review of protocols at the correct interval as per format (Annexure-19 A). All the approved protocols will be reviewed annually. It is the responsibility of the Member Secretary to ensure a decision regarding whether the project needs to be reviewed more frequently is taken during the IEC meeting in which the project is finally approved. This must be recorded in the minutes if there is any change from annual review. A fresh decision to increase review may be taken if required based on the SAE reports, monitoring reports, or safety concerns. This is responsibility of the Member Secretary.

The IEC is responsible for reviewing the progress made in the protocol (number of patients recruited, dropped out, reasons for drop-out), the occurrence of unexpected events or problems, and compliance of the investigator regarding IEC communication.

Determining the date of continuing review

- The date of the continuing review will always be at least once in the year.
- The IEC may recommend more reviews during the approval process depending on the level of risk. This will be documented in the minutes.
- The Member Secretary will inspect the minutes of meeting to set a timetable for continuing review.
- The Member Secretary will identify and record the due dates for each project

Content of Status Report

The Member Secretary will receive a letter submitted by the PI for continuing review of each approved protocol (Annexure- 19B). Only one set of Status Report (continuing review report) shall be submitted by the PI to the IEC which should contains following points:

- No. of participants screened
- No. of recruited participants
- No. of ongoing participants
- No. of completed participants
- No of participants withdrawn from study
- Has any information appeared in the literature, or evolved from this or similar research that might affect the IEC/IEC's evaluation of the risk/benefit analysis of participants involved in this protocol?
- Details of SAE
- Details of PDs/PVs

Review process

The Continuing review submission may undergo expedited review or full board review as deemed appropriate by the IEC Chairperson/ Member Secretary.

The IEC Chairperson/ Member Secretary/ Member/s will use the Status Report (continuing review report) to guide the review and deliberation process.

The IEC Chairperson/ Member Secretary/ Member/s could reach one of the following decisions after review:

- Noted - The IEC approves the continuation of the project without any modifications.
- Modifications recommended: The study protocols that have been suggested modifications by the IEC may not proceed until the conditions set by the IEC in the decision have been met. The amendments and the required documents should be amended and submitted to the IEC within one month for re-review.
- The project cannot be continued: The reasons for discontinuation of the project should be mentioned in the letter notifying the decision to the Principal Investigator.

The IEC Chairperson will sign and date the IEC decision on minute of meeting after a decision has been reached.

The decision on continuing review taken by the Chairperson/ Member Secretary/ Member/s will be informed to all IEC members at the next full board meeting.

The Status Report (continuing review report) may be discussed at full board if deemed necessary by Chairperson/Member Secretary.

The IEC Member Secretary will maintain and keep the IEC minutes of the meeting relevant to the continuing review as part of the official record of the review process in the project file.

Communicating IEC Decision to the PI

The Member Secretary will notify the PI of the decision within 14 days of the meeting at which the report was discussed or of the date of review by the Chairperson/ Member Secretary/ IEC Member/s.

Non-submission of continuing review report by principal investigator before due date

If a PI fails to submit the continuing review report within one month of the due date (i.e. 11thmonths from the date of approval, or earlier on the dates as specified), the Member Secretary will send a telephonic and /or email reminder at least 15 days prior to due date of review. If there is no response, the IEC Member Secretary will put up the matter for discussion at the forthcoming full board meeting for appropriate action which may consist of but not limited to sending:

I. A reminder letter again
II. A letter asking explanation for non-submission
III. A letter asking the PI to put recruitment of new participants on hold till report is submitted
IV. Any other action as deemed appropriate by IEC

15. Review of Protocol Deviations/violations

Detection of Protocol deviation/ violation

Protocol deviation/ violation Protocol deviation/ violation may be detected in one the following ways (but not limited to those listed below):

I. Protocol deviation/ violation may be reported by Investigator/ study site/ sponsor/ Contract-Research Organization to the IEC in the prescribed format (Annexure-20).
II. The IEC members performing monitoring of the project at trial site may detect protocol deviation/violation if the project is not being conducted as per protocol/ national/ international regulations.
III. The Member Secretary may detect protocol deviation/ violation from failure to comply with statutory requirements/ failure to respond to requests from IEC within reasonable time limit/failure to respond to communication made by IEC.
IV. The IEC members may detect protocol deviation/ violation when scrutinizing annual/ periodic reports/ SAE reports/ any other communication received from the Investigator/ trial site/ sponsor/study monitor/ contract research organization.
V. The IEC Member Secretary and/ or IEC members may become aware of a protocol deviation/violation while reviewing study-related documents including reports filed in by the Principal Investigator (PI).
VI. Communication/ complaint/ information received from a research participant who has been enrolled or any individual who has been approached for enrolment.
VII. Any report/ communication brought to the notice of Member, Secretary/ Jt. Secretary/ Chairperson of IEC by an independent person.
VIII. Communication received from the Head of the Institution informing IEC about an alleged protocol violation/ protocol deviation.

Receipt of protocol deviation / violation report by the Member Secretary

Protocol deviation/ violation may be detected in one the following ways (but not limited to those listed below):

I. Protocol deviation/ violation may be reported by Investigator/ study site/ sponsor/ Contract-Research Organization to the IEC.
II. The IEC members performing monitoring of the project at trial site may detect protocol deviation/violation if the project is not being conducted as per protocol/ national/ international regulations.
III. The Member Secretary may detect protocol deviation/ violation from failure to comply with statutory requirements/ failure to respond to requests from IEC within reasonable time limit/ failure to respond to communication made by IEC.
IV. The IEC members may detect protocol deviation/ violation when scrutinizing annual/ periodic reports/ SAE reports/ any other communication received from the Investigator/ trial site/ sponsor/ study monitor/ contract research organization.
V. The IEC Member Secretary and/ or IEC members may become aware of a protocol deviation/ violation while reviewing study-related documents including reports filed in by the Principal Investigator (PI)
VI. Communication/ complaint/ information received from a research participant who has been enrolled or any individual who has been approached for enrolment.
VII. Any report/ communication brought to the notice of Member, Secretary/ Jt. Secretary/ Chairperson of IEC by an independent person.
VIII. Communication received from the Head of the Institution informing IEC about an alleged protocol violation/ protocol deviation.

Receipt of protocol deviation / violation report by the Member Secretary

I. The PI will report the protocol deviation/violation
II. In case protocol deviation/violation is detected by any other person and reported to the IEC (there is no format for this), the Member Secretary will write to the PI to submit a protocol deviation/violation

Actions to be taken

1. The action of the IEC will be based on:
- The nature and seriousness of the deviation / violation.
- Frequency of deviation/ violation in the study in the past.
- Frequency of deviation/ violation in previous studies conducted by the same PI/ Co-PI or in the same department.

2. Member Secretary will decide on the impact of the protocol deviation / violation and act accordingly. Depending upon the seriousness, the IEC shall do the following (not limited to these actions):
- Ask PI for written clarification as soon as the deviation is received o
- If the impact is serious, this report will be shared with the Chairperson and two or more IEC members designated by the Chairperson.

- If the impact of the protocol deviation is serious enough, the Member Secretary will schedule a full-board meeting specifically to discuss the issue within 7 working days of the initial scrutiny
- The Member Secretary will put up the information and communication at the next full board meeting for discussion.

3. The Member Secretary in consultation with IEC members will review the information available and deliberate on it.
4. The Chairperson will take a final decision depending on the seriousness of the violation. The decision will be taken to ensure that the safety and rights of the research participants are safeguarded. The decision will be taken by voting. A majority vote for approval, disapproval or request for modifications of a study suspension or termination of an ongoing study is defined as 2/3rd of the voting members present at the meeting.
5. The decision taken by IEC could include one or more of the following:

- Determine that no further action is required, or take other actions as appropriate.
- Inform the PI that the IEC has noted the violation / deviation, and instruct the PI to ensure that deviations/ violations do not occur in future and to follow IEC recommendations.
- Enlist measures that the PI would undertake to ensure that such deviations / violations do not occur in future.
- Observe the research or consent process (depending on the nature and frequency of the deviation).
- Suggest modifications to the protocol.
- Alter the interval for submission of the continuing review/ annual project status.
- Ask for additional training of the investigator and study team of Reprimand the PI.
- Seek additional information from the PI.
- Conduct audit of trial by the IEC.
- Suspend the study till additional information is made available and scrutinized. o Suspend the study till recommendations made by the IEC are implemented by the PI and found to be satisfactory by the IEC.
- Suspend the study for a fixed duration of time.
- Suspension or termination of the study.
- Revoke approval of the current study. Inform DCGI/ other relevant regulatory authorities.
- Keep other research proposals from the PI/ Co-PI under abeyance. Review and/ or inspect other studies undertaken by PI/Co-PI.

This final decision will be recorded on minutes of the meeting by the Member Secretary.

<u>Procedure for notifying the PI and other concerned authorities</u>

The Member Secretary will draft a notification letter.

- The signed letter by Member Secretary will be sent to the PI and Institutional Officials (if required on case to case basis).
- The IEC Member Secretary will send a copy of the notification to the relevant national authorities (if required on case to case basis) and institutes (if required on case to case basis in case of multi-centric trials).

Records and follow up to be kept by IEC Member Secretary

- The Member Secretary will keep a copy of the notification letter in the respective project file.

16. Review of Serious Adverse Event (SAE) Reports

Receipt of SAE report

The IEC Member Secretary will receive the following documents within the specified time frame if an SAE is experienced by any research participant:

i. Initial SAE report to be submitted by the Principal Investigator (PI) within 24 hours of occurrence in the prescribed format (Annexure-21A).
ii. Due analysis should be submitted by the PI within 14 days from the occurrence of the SAE in the prescribed format (Annexure-21 B & C).
iii. Due analysis will also be submitted by the sponsor within 14 days in the prescribed format (Annexure-21 B & C).
iv. The follow up reports of all on-site SAE till the event is resolved.

The IEC Member Secretary will verify that the report is complete in all respects and that it has been received at the IEC office within the specified timelines.

The IEC Member Secretary will sign and write the date on which the report is received.

Review and Decision on SAE Reports and Communication to PI and Regulatory Authority by IEC

Member Secretary of the SAE will review the SAE report and present to the full board/SAE subcommittee for review and opinion. An emergency IEC meeting (full board or SAE subcommittee) will be scheduled within 7 days for the same.

At the meeting of IEC, the SAE reports will be reviewed with a special focus on relatedness to the clinical trial, medical management and financial compensation to be given to the research participants.

The applicable formulae and guidelines from the regulatory authority will be used during this discussion
New Drugs and Clinical Trials Rules, 2019.
[http://cdsco.nic.in/writereaddata/GSR%2053(E)%20dated%2030.01.2013.pdf
http://www.iscr.org/pdf/Gazaate_notification.PDF dated 12th December 2014,
Formula for calculating amount of compensation study related death,
http://www.cdsco.nic.in/writereaddata/formula2013SAE.pdf
and for study related injury other than death
http://www.cdsco.nic.in/writereaddata/uploaded_for_website__1_final2014.pdf]
The decision can be arrived at by consensus. If not agreed by consensus, the issue would be put for voting. (a majority vote for a decision is 2/3rd majority of the members present and voting)

The minutes of the IEC meeting will include the information on SAE at the site along with the opinion on the above points on the onsite SAE.

Participant ID	Letter no./ and date of reporting	Type of Report (I/FU)	Date of onset	whether study drug withheld	SAE Outcome	Causality in the opinion of PI	Recommendation(s) by the IEC

I-initial, FU- Follow-Up

The IEC Member Secretary will draft a formal letter to the concerned PI and inform him/ her about the IEC decision. This letter will be signed and dated by the Member-Secretary or Chairperson (IEC) and will be sent to the PI within a period of 7 days from the date of the IEC meeting.

PI will be requested to reply to the query letter on the SAE report within 7 working days.

The opinion regarding relatedness, medical management and compensation for research related injury will be communicated to the Licensing authority (DCGI) within 30 calendar days of the occurrence of the SAE in case of regulatory clinical trials.

The Member Secretary will file a copy of these letters in the study file.

Reports of SAE Occurring at other Sites

The investigator will need to submit the SAEs occurring at other sites (CIOMS and SUSARS) in the form of hard or soft copies along with the appropriate covering letter (hard copy) mentioning the total number of reports.

The SAEs occurring at other sites will be reviewed by the Secretary of the IEC informed to other members and discussed in the forthcoming scheduled meeting. The agenda and minutes of the meeting will include the information on SAEs at other sites.

Onsite AE

The IEC Member Secretary will receive the following documents pertaining to AE experienced by the research participants for research proposals approved by the IEC:

- Onsite AE reports to be submitted by the PI annually in the continuing review report.
- In view of the risk assessment of a given research proposal the IEC can request adverse events to be reported earlier, if deemed necessary at specified timelines in the project approval letter.

The IEC Member Secretary will verify that the report is complete in all respects and signed and dated by the PI and that it has been received at the IEC office within the specified timelines. If the report has been received beyond the specified time, it will be considered as deviation.

Member Secretary of IEC may put the AE reports for discussion at full board if deemed necessary

Queries, if any on the report will be communicated to the PI by the Member Secretary of IEC following full board meeting

Decision of IEC on SAE review

The IEC may take one or more of the following decisions on review of the SAE reports.

Type of Actions Taken by IEC on Review of SAE Report:

Following detailed review of the SAE reports and related documents, the IEC can suggest one of the following actions:

- Note the information about the SAE in records for future reference.
- Request further follow up information and/ or additional details.
- Ask for periodic follow-up of the research participant till SAE is resolved
- Depending on complexities of issue, IEC may decide to seek opinion of outside expert consultant who is requested to respond within 14 working days.
- Provide recommendations regarding/ raise queries related to compensation for study related injury and death
- Suggest changes/ amendments in protocol, Patient Information Sheet/ Informed Consent Document/ Investigators' Brochure/ any other study related documents.
- Suspend the study till additional information is available.
- Suspend the study till review is completed (safety monitoring of ongoing patients to be continued).
- Suspend the study till amendments requested for by the IEC are carried out.
- Suspend enrollment of new participants.
- Suspend certain activities under the protocol.
- Direct the PI to inform participants already enrolled in the study about the AEs and if required obtain their consent again (re-consent) regarding continuation in the research trial.
- Direct the PI to inform participants already enrolled in the study about the AE and request them to undertake additional visits, additional
- procedures, additional investigations, etc. as prescribed in the amendment
- Terminate the study.
- Any other appropriate action.

The decision shall be recorded in the minutes of the full board IEC meeting

If the recommendation from the IEC includes suspension of the study or suspension of any one or more of the study-related procedures or activities, amendments in the protocol or other study-related documents (excluding Investigators' brochure), re-consenting of research participants, the decision will be conveyed to the PI through telephone, fax or email within 24 hours. Such a communication will be documented by the IEC Member-Secretary in the study file. A formal letter to the PI informing about the IEC recommendations in such situations will be sent within 5 working days of the IEC meeting having taken place.

17. Review of Study Completion Reports

The Member Secretary will receive 1 copy (soft and hard) of Study Completion Report filled as per the format (Annexure-22) from the PI. The study completion report is expected from the investigator within 1 month of completion of the study at the site.

- It is the responsibility of the IEC Member Secretary to review the report for completeness.
- The Joint Member Secretary shall verify the submitted Study Completion Report along with Study Completion Report Form and forward it to the Member Secretary within 7 working days of receipt.
- The Member Secretary will review the Study Completion Report, confirm that it is complete and present it at the next full board meeting.
- If there is a need felt (e.g. a deviation/ violation is noted), the Member Secretary will handle it as per SOP
- The Member Secretary shall include the Study Completion Report Form in the agenda for IEC members for discussion at the full board meeting.
- Following the discussion, the Chairperson may take one of the following decision:
  a)noted /approved
  b)request for additional information /clarification

- The Member Secretary will note the decision in the meeting minutes
- The Member Secretary will draft a letter to the PI conveying decision on the study completion report.
- The study shall be considered as closed if the decision by IEC is "Noted" or "Approved".
- The Member Secretary will accept and file the Report and get the Study Completion Report Form signed by the Chairperson.
- The final report will be placed in the master file and kept in the archival area.
- The Administrative Officer will archive the entire study for a period of 5 years from the date of completion of the project if the decision is noted and closed.

18. Policy for Studies on Vulnerable Population

The purpose of this section is to detail the requirements for Institutional Ethics Committee approval of research involving vulnerable populations. Vulnerable populations must be given special consideration.

Examples of Vulnerable Populations:-

I. **Handicapped persons:** Persons with mental or physical handicaps are considered to be a vulnerable population.
II. **Elderly persons:**
III. **Research on persons below 18 years of Age**
IV. **Subordinate Individuals:** Subordinate relationships can be unduly influenced by their superior. The following are examples of such relationships:
V. Employer/employee
VI. Military officer/soldier
VII. **Persons with mental health conditions**
VIII. **Traumatic or emergency situations:** Individuals who are in the midst of a traumatic or emergency situation or otherwise under emotional duress can be potentially vulnerable.
IX. **Low Socioeconomic Status:** Low socioeconomic status can create a vulnerability of subjects resulting from unique socioeconomic factors. For example, an offer of financial
X. compensation for participation in research may be interpreted as exploitive when directed toward impoverished subjects.

XI. **Incurable disease:** The following are examples of such disease:
-Cancer Patient with no cure therapy is available
-HIV etc.

XII. **Research on pregnant women, fetuses and neonates**

Special Considerations and Procedure to review studies on Vulnerable

The inclusion of certain groups of participants who may be vulnerable to undue influence or coercion may require additional protections. When the Ethics Committee reviews research involving vulnerable populations, the Ethics Committee applies any additional Indian regulations as applicable. The Ethics Committee evaluates whether additional safeguards have been included in the study to protect the rights and welfare of participants who may be vulnerable to undue influence. The IEC requires at least one or more individuals who are knowledgeable about or have experience in working with these participants are part of the review process.

The IEC reviews research involving vulnerable populations according to applicable requirements and guidelines and makes determinations. If the research includes a vulnerable population that does not have additional protections, the Ethics Committee Reviewer will evaluate the research proposal to ensure that precautions are taken to protect the participants and must address all the point in the checklist for different vulnerable population (Annexure- 23 A to E).

The Institutional Ethics Committee must consider risks to participants when reviewing proposed research. There are risks to vulnerable populations that would not normally need consideration, such as the following:

A. To what risks, unique to their status, will participants be exposed?

B. What protections will be made to mitigate risks?

C . Are subjects capable of providing consent?

a. If the Institutional Ethics Committee determines that a legal representative is appropriate, such as when the subject is an adult with a cognitive disability, the IEC will work together with its legal advisor to determine who is most appropriate according to Indian Regulations and state law to provide legally effective consent on behalf of the subject.

C. **Research involving children**

a. Where possible, parent/guardian consent should be accompanied by assent from the child showing them to be a willing participant in the research project. It is recommended that the assent of the child be sought when deemed appropriate by the study team

b. Participant Information Sheets and Consent/Assent forms must be presented in a form and language that is understandable by a child of 10 years of age (that is, to a fifth grade level) Also based on the requirement of the research area such as HIV, Genetic disorder etc. specific population group may also be represented in ethics committee.

19. Process for Calling Experts for IEC Meeting

It is the responsibility of the Chairperson/ Member Secretary/ IEC member/s to nominate the name of one or more Independent experts. The Chairperson is responsible for

endorsing the choice of expert nominated by IEC Member Secretary/ IEC member/s. The administrative procedures regarding selection, confidentiality agreement and maintenance of roster of experts will be carried out by administrative staff under guidance from Member Secretary.

Recommendation of names of Experts and making a roster of Experts for the IEC

- Chairperson/ Member Secretary/ IEC members will nominate the names of experts from different specialties of Medicine as & when required.
- Member Secretary will issue an appointment letter to the expert after confirming their willingness through telephonic/ electronic communication.
- After receiving written approval from experts, a list of experts will be maintained in the IEC records. The details of each expert (name, designation, specialty, affiliation, contact details and updated curriculum vitae) will be maintained in the IEC records.

Consulting an Expert during IEC review process

- An IEC member/ Member Secretary/ Chairperson may suggest that the opinion be sought from one or more expert(s) and may suggest the name of a particular expert (s) from the list of experts maintained by the IEC or from outside the list. The experts shall be suggested from outside the list only if during the review process of any given research study it is felt that the study involves procedures or information that is not within the area of collective expertise of the IEC members or all the experts of the specialty are not available for the meeting.
- The Member Secretary in consultation with Chairperson (or at full board meeting; as deemed necessary) will decide to identify and select the experts outside the roster to be invited based on area of expertise, independence and availability.
- Member Secretary on behalf of the IEC will invite expert(s) in writing to assist in the review of the research study and provide his/ her independent opinion in writing. This may be done after seeking concurrence and confirming availability of the expert through telephonic/ electronic communication.

Communication with experts

- The Member Secretary may request a copy of the updated curriculum vitae of the expert (those outside roster) for IEC records and future reference.
- The Member Secretary will request expert to declare conflict of interest, if any, in writing and sign confidentiality and conflict of interest agreements.
- The Member Secretary will provide explanations/ clarifications (telephonically or in writing) to the expert(s) if any doubts or questions are raised. Any further explanations can be provided by the Chairperson/ IEC members / Investigator.

Review of research study proposal

- The Study Protocol and other study related documents will be provided to expert for review
- The expert will provide his assessment in writing to IEC which will become permanent part of the IEC documents.
- The assessment feedback will be reviewed by Member Secretary in the IEC meeting when the concerned study is being discussed.

- If deemed necessary, the Chairperson or Member-secretary may seek additional information or clarifications from the expert in writing. Additional Information provided by the expert will be considered as a part of the Assessment feedback.
- If deemed necessary, the Chairperson or Member-secretary may invite the expert to attend an IEC meeting for providing additional information or clarifications that may be sought by IEC members or Chairperson. However, the expert will not participate in the decision-making process on the research study.

- If deemed necessary, expert may be reimbursed for expenses on travel, time spent, documents referred to in library/ internet or any other incidental expenses, etc.

Tenure of Services of Expert

- The list of experts maintained at the IER office will be updated every time a new expert is appointed
- An expert shall serve for maximum duration of 4 years
- For expert appointed for a particular study, the services of expert get automatically terminated once the final decision regarding the study is taken by the IEC. The IEC will document the termination of the services of expert by providing a letter thanking the expert for the services rendered.

Responsibilities of Expert

- If expert agrees to review a research proposal, he/she will comply with IEC requirements of signing confidentiality and conflict of interest agreements.
- Expert will review the research study and complete the Assessment feedback (duly signed and dated) within a stipulated period or by a stipulated date.
- Expert will attend an IEC meeting for providing additional information or clarifications, if invited by Member Secretary/ Chairperson. However, the expert will not participate in the decision-making process on the research study.
- Expert will remain available for telephonic and email communication till the review process of the given research proposal is complete.

20. Policy for Expedited review

All revised proposals, epidemiological and/or Academic proposal unless specifically required to go to the main committee, will be examined in a meeting of identified members convened by the Chairman to expedite decision-making. Expedited review may also be ordered by the Chairman and/or Member Secretary in cases of nationally relevant proposals requiring urgent review.

21. Dealing with Participants' Requests and/or Complaints to Institutional Ethics Committee

- A request, complaint or query, from a research participant will be accepted by the Member Secretary (Annexure-24).
- The Member Secretary will additionally ascertain details of the request/ complaint by examining any relevant documents and by interviewing the participant if necessary. If required, the Member Secretary will call for additional relevant information and documents from the Principal Investigator (PI).

- The Member Secretary will inform the Chairperson about the request, query or complaint received from the research participant.
- In case of a request for additional information or clarification, the Member Secretary in consultation with the Chairperson will provide the information himself / herself or will designate one or more IEC member(s) to provide such information
- In case of a complaint received from a research participant:
- ➢ The Member Secretary, in consultation with the Chairperson will initiate a process to address any injustice that may have occurred. Depending on the seriousness of the matter, the Chairperson will direct the Member Secretary to:
- ➢ Appoint a subcommittee of two or more IEC members for enquiry in order to resolve the matter.
- ➢ Call an emergency meeting of two or more IEC members for discussion or
- ➢ Consider the matter for discussion at the next full board meeting
- ➢ The Chairperson/ Member Secretary/ designated IEC members will assess the situation and mediate a dialogue between the research participant and PI in an attempt to resolve the matter.
- ➢ The IEC will insist on factual details to determine gap, if any, between truth and individual perception.
- The final decision will be taken by the Member Secretary in consultation with the Chairperson based on the recommendation of any one of the above and it will be informed to the research participant and the PI by the Member Secretary.
- The IEC members will be informed about the action taken and the outcomes in the forthcoming IEC meeting (in case of requests/ complaints not discussed in full board meeting) and minutes.
- The Member Secretary will place all documents in the relevant study file.

22. Patient Charter – Rights and Responsibilities of Research Participants

Rights of Research Participant

- Subject should be given enough time to decide whether or not to be in the research study;
- Research Participant Is allowed make that decision without any pressure from the people who are conducting the research
- Understands his/her right to refuse to be in the study at all, or to stop participating at any time after beginning the study
- Research Participant should be told the purpose of the study, what will happen during the research, and what the participant will be asked to do if he/she is in the study in a level of language that is easily understood
- Research Participant should be told about known and reasonably foreseeable risks of being in the study, including the chances of experiencing those risks and the possible severity of the risks
- Research Participant should be told about the possible benefits of being in the study.
- Research Participant should be told whether there are any costs associated with being in the study and whether the participant will be compensated for participating in the study
- Research Participant should be told who will have access to information collected during or after the study, to what extent confidentiality can be assured, and how his/her confidentiality will be protected
- Research Participant should be told who to contact with questions about the research, who to tell about a research-related injury, and who to ask about his/her rights as a research participant

- If the study involves treatment or therapy:
  - Research Participant should be told about other non-research treatment choices; and
  - Research Participant should be told where treatment is available should a research-related injury occur, and who will pay for research-related treatment.

Responsibilities of Research Participant

- Completely read the consent form and ask the Principal Investigator (PI) questions, if any. Participant should understand what will happen to him/her during the study before he/she agrees to participate.
- Know the dates when study participation starts and ends.
- Carefully weigh the possible benefits (if any) and risks of being in the study.
- Talk to the Principal Investigator (PI; the person in charge of the study) if he/she wants to stop being part of the research study.
- Contact the PI and/or the EC with complaints or concerns about participation in the study.
- Report to the PI immediately any and all problems he/she may be having with the study drug/procedure/device.
- Fulfill the responsibilities of participation as described on the consent forms unless he/she is stopping his/her participation in the study.
- Inform the PI or the person responsible study when reimbursement have been received that was promised for participating in the study.
- Ask for the results of the study
- Keep a copy of the consent form for records

Subject's participation and withdrawal

- Participants always have the right to withdraw from their participation in research at any time and for any reason without penalty or loss of benefits to which they would otherwise be entitled.

Patient Feedback:

- Patient feedback can be collected on adhoc basis to evaluate the subject's understanding for clinical Research. Annexure 25 covers the form for research feedback from patient.

23. Corrective and Preventive Actions (CAPA) Process

Any issues that are identified by IEC during initial and ongoing review of studies should be brought to the attention of Investigator and site team and appropriate response should be sought. For issues that considered repetitive, serious and directly affects study conduct, IEC should request Investigator to perform route cause analysis and implement CAPA and submit a detailed report to IEC.

The Drugs Controller General India (DCGI) in its gazette notification GSR 72E, dated 08th February 2013, 122DD states, 'The Ethics Committee shall allow inspectors of officials authorized by the Central Drugs Standard Control Organization to enter its premises to inspect any record, data or any document related to clinical trial and provide adequate replies to any query raised by such inspectors or officials, as the case may be, in relation to the conduct of the trial.'

Correction of deficiencies observed at audit/ inspection

- Member Secretary/ designated IEC member/ Member Secretary will review comments and recommendations of the auditor/inspector.
- On receipt of Audit/ Inspection Report the Chairperson should implement corrective and preventive measures and set the timeline for implementation of corrections as stated by the auditor/inspector
- Action plan should be communicated by the Member Secretary/ designated IEC member to the auditor/inspector after seeking approval of the Chairperson.
- A review date for an internal follow-up audit will be decided by the Chairperson (if applicable).

24. Application Procedure

24.1 Pre Meeting Procedure

Inquiry to Ethics Office/ Investigator regarding submission procedures.

Ethics Office to forward to Investigator the EC SOP

Submission must be received by Ethics Office at least 3 weeks prior to next review meeting.

All details of

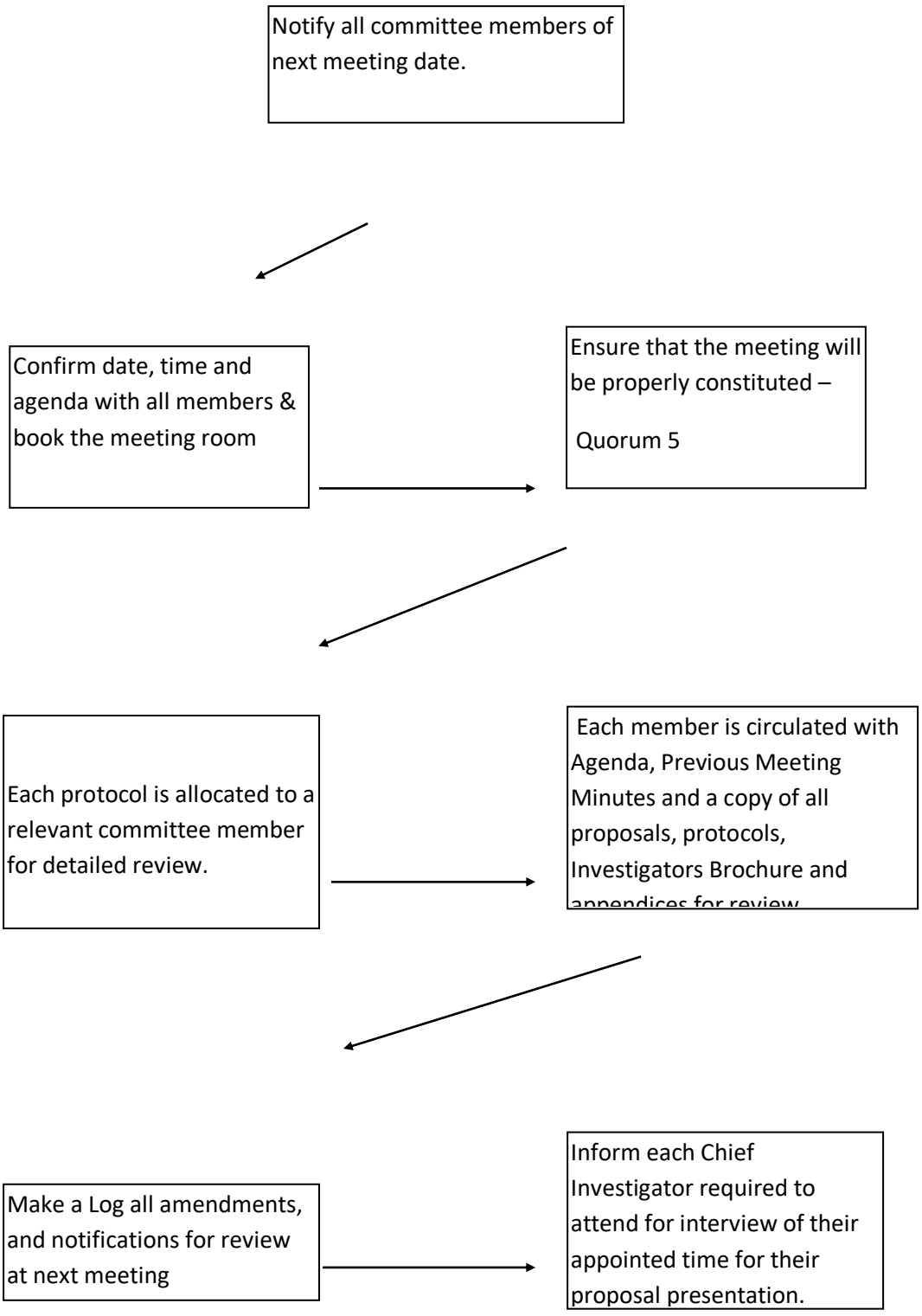
1. Letter of Intent
2. Patient consent forms in English and Hindi*
3. Patient Information sheet
4. Questionnaires
5. Protocol
6. Investigator

All documents must be bound Processed by Ethics Office.

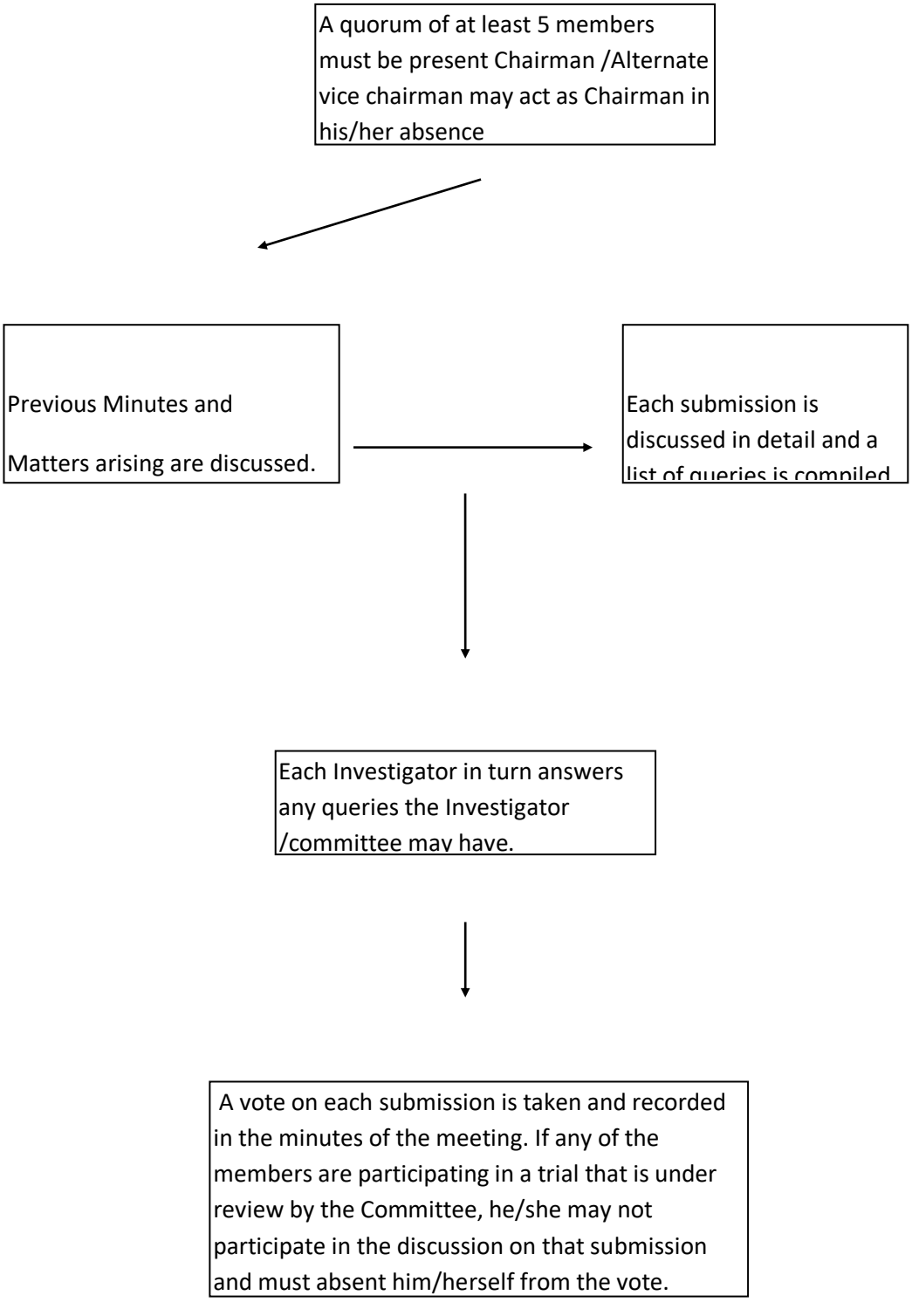
When all the above requirements are processed,

1. Record receipt of the Proposal in the Log book
2. Include on Agenda for next Ethics Committee Meeting.

a. Pre-Meeting Procedure



24.2 Committee Meeting Procedure



24.3 Post Meeting Procedure

Recorded Minutes are maintained.

All Investigators of protocols submitted for review are informed of the committee's decision in writing including any modifications or conditions

Investigators/Companies who submitted Amendments or Serious Adverse events for review will be notified of the committee's decision in writing.

All correspondence must be signed by either the Chairman or Member Secretary

All Ethically Approved Trials Must Include:

Copy of protocol *

Copy of Investigator Brochure *

Copy of Patient Information Sheet

Copy of Patient Consent Form

Copy of Ethics Approval Letter

25. Site Monitoring and Post-Monitoring Activities

It is the responsibility of the Full Board or Chairperson and Member Secretary to decide to conduct on-site monitoring. It is further the responsibility of the designated IEC member(s) to perform on-site monitoring:

- Routine monitoring for the site may be decided at the time of approval of the project by the Full Board.
- This is recorded in the IEC minutes.
- "For-cause monitoring" will be performed at the site for reasons identified by any member of the IEC, after approval by the Chairperson.
- The reasons for identifying for "for-cause monitoring" could include any one or more of the following:

➢ High number of protocol violations,
➢ Large number of studies carried out by the investigator,
➢ Large number of Serious Adverse Events (SAE) reports,
➢ High recruitment rate, or Large number of Protocol deviations,
➢ Complaints received from participants or any other person,
➢ Frequent failure to submit the required documents
➢ Any other cause as decided by IEC.

25.1 Before the visit

- Irrespective of the cause for conducting monitoring the following procedure will be followed
- The Chairperson will identify and select one or more IEC members (henceforth referred to as monitors) to conduct monitoring of the site.
- The selected members will be given an appointment letter in this regard.
- The agenda of monitoring will be decided by the identified monitors in consultation with the Member Secretary and Chairperson
- The Member Secretary will decide the date of the monitoring in consultation with the monitors and the PI.
- The final date will be communicated to the PI (with a request to be available) and monitors.
- The monitor will receive from Member Secretary and review the relevant project documents and make appropriate notes.
- The Member Secretary provided Monitors with relevant reference material / documents related to the project Monitors will carry with them Site Monitoring Visit Report Forms (Anexxure-26 A & B) (if applicable) collected from the Secretariat.

25.2 During the visit

The Monitor will follow the check list and:

- Check the log of delegation of responsibilities of study team,
- Check if the site is using latest IEC approved current versions of the protocol, informed consent documents, case record forms, diaries, advertisements, etc.
- Observe the informed consent process, if possible, review randomly selected participants' files to ensure that participants are signing the correct informed consent,

- 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,
- Verify that the investigator follows the approved protocol and all approved amendment(s), if any,
- Ensure that the investigator and the investigator's trial staff are adequately informed about the trial,
- 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,
- Verify that the investigator is enrolling only eligible subjects,
- Determine whether all 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,
- Review the project files of the study to ensure that documentation is filed appropriately,
- Review the source documents for their completeness,
- Collect views of the study participants, if possible,

25.3 After the visit

- The Monitor will submit the report to the IEC Member Secretary within 7 working days of conducting a site monitoring visit.
- The report should describe the findings of the monitoring visit.
- The Member-Secretary will present the monitoring report at the next full board IEC meeting and the concerned Monitor will provide additional details/ clarifications to members, as required.
- The IEC will discuss the findings of the monitoring process and take appropriate specific action by voting or combination of actions, some of which are listed below:

✓ Continuation of the project with or without changes,
✓ Restrictions on enrollment,
✓ Recommendations for additional training,
✓ Recruiting additional members in the study team,
✓ Revising/ providing qualifications/ experience criteria for members of the study team, termination of the study,
✓ Suspension of the study, etc.

- If the Monitor has findings that impact on safety of the participant the Monitor 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.
- The final decision taken at the full board IEC meeting by the Chairperson in MoM
- The Member Secretary will convey the decision to the Principal Investigator in writing within 14 working days of the meeting.
- The Member Secretary will place the copy of the report in the protocol file.

26. Record Maintenance

- All the documents and communications of IEC will be dated, filed and archived in a secure place.
- Only the member secretary or persons, who are authorized by the Chairman of IEC will have the access to the various documents.
- All the documents related to research proposals will be archived for a minimum period of 5 years in the Institute, following the completion /termination of the study.
- No document (except agenda) will be retained by any IEC member.
- At the end of each meeting, every member must return the CD/DVD containing all the research proposals and documents to IEC Member Secretary. They will archive one copy in IEC office and other copies will be destroyed.

Following documents will be filed and archived with proper label on the top of file for easy identification:

1. Constitution and composition of Ethics Committee
2. CV of the committee member
3. Ethics Committee SOP and their Subsequent changes
4. Copies of documents submitted for review included but not limited to Protocol, IB
5. Agenda of all Ethics Committee meetings
6. MoM with signature of Chairman
7. Copies of decision communicated to the applicants
8. Records of all correspondence with Ethics Committee by applicant including status report, SAE notification, reason for premature termination of the study.

27. Periodic Assessment of IEC Members

For the efficient functioning of ECs, it's very important to ensure all IEC members are assessed on their performance at least once a year. Chairperson should also carry out his/her own self-assessment every year.

<u>The IEC members should be evaluated on following parameters:</u>

- Current tenure
- Terms served
- Training received
- Type of training received
- No of meetings attended
- No of projects reviewed per meeting as primary reviewer
- No of projects reviewed per meeting as secondary reviewer
- Participation in SAE report review process- yes/no
- Participation in site monitoring visits - yes/no
- Number and type of continuing training workshops organized for IEC members (applicable to Member Secretary)
- Number and type of continuing training workshops organized for staff of the IEC Member Secretary
- Any other significant contribution to the field of research ethics
- Remarks by the Chairperson on the assessment

Points for self-assessment for IEC chairperson

- Current tenure-
- Terms served –
- Training received –
- Type of training received –
- No. of meetings held in current year –
- No of meetings attended -
- Whether quorum requirement fulfillment
- Whether considerations related to conflict of interest considered
- Any significant contribution to the field of research ethics
- Any other comments _____

28 Preparing for Ethics Committee Audit/ Inspection

- **Audit:**

I. A systematic and independent examination of trial related activities and documents to determine whether the evaluated trial related activities were conducted, and the data were recorded, analyzed and accurately reported according to the protocol, sponsor's standard operating procedures (SOPs), Good Clinical Practice (GCP), and the applicable regulatory requirement(s).

II. Audit of a Trial- A systematic verification of the study, carried out by persons not directly involved, such as:

(a) Study related activities to determine consistency with the Protocol.

(b) Study data to ensure that there are no contradictions on Source Documents. The audit should also compare data on the Source Documents with the interim or final report. It should also aim to find out if practices were employed in the development of data that would impair their validity.

(c) Compliance with the adopted Standard Operating Procedures (SOPs).

- **Inspection:**

I. An official review/ examination conducted by regulatory authority(ies) of the documents, facilities, records and any other resources that are deemed by the authority(ies) to be related to the study. The inspection may be carried out at the site of the trial, at the sponsor's / or CRO's facilities and Ethics Committee in order to verify adherence to Good Clinical Research Practice.

II. The Drugs Controller General India (DCGI) in its gazette notification GSR 72E, dated 08th February 2013, 122DD states, 'The Ethics Committee shall allow inspectors of officials authorized by the Central Drugs Standard Control Organization to enter its premises to inspect any record, data or any document related to clinical trial and provide adequate replies to any query raised by such inspectors or officials, as the case may be, in relation to the conduct of the trial.'

Receipt of notification of an Audit /Inspection

On receipt of written/ mailed communication regarding audit/ inspection visit, the Member Secretary will inform the Chairperson, IEC members and the Head of Institution, if applicable about the date and purpose of the audit/inspection.

Preparing for the audit

- On receiving information about the audit /inspection, IEC Member Secretary and/ or IEC member/s are given the responsibility by the Chairperson to prepare for the visit with assistance of the Member secretary
- The Member Secretary and / or designated IEC member/s will make arrangements in accordance with the steps mentioned in the checklist(*Annexure 27*)
- The studies with incomplete / missing documents will be dealt with separately and actions taken will be documented.
- Care should be taken to ensure that all documents are kept in the right order for easy and quick access.

On the day/s of Visit

- Chairperson / Member Secretary / designated IEC Member/s should welcome and accompany the auditors/inspectors to the reserved meeting room.
- Designated team members must be present in the meeting room.
- The conversation would start with the auditor/inspector stating the purpose of the visit and the type of information is needed.
- The IEC Chairperson / Member Secretary / IEC Members must answer questions of the auditors/inspectors clearly, politely, truthfully and straight to the point.
- The information and files requested by the auditors/inspectors should be made available by the Member secretary
- The Member Secretary/ designated IEC member/ Member secretary will make note of the comments, recommendation of the auditors/inspectors.

Correction of deficiencies observed at audit/inspection

- Member Secretary/ designated IEC member/ Member secretary will review comments and recommendations of the auditor/inspector. On receipt of Audit/ Inspection Report the Chairperson should implement corrective and preventive measures and set the timeline for implementation of corrections as stated by the auditor/inspector.
- Action plan should be communicated by the Member Secretary/ designated IEC member to the auditor/inspector after seeking approval of the Chairperson.
- A review date for an internal follow-up audit will be decided by the Chairperson (if applicable).
- The Member Secretary/ designated IEC member should report the outcome of the internal follow-up audit to the Chairperson.

Recording the Audit/Inspection Visit

- The Member Secretary/ designated IEC member/ Member secretary must keep record of the audit/inspection visit reports and action plans in a separate audit/inspection file.
- The completed checklist and findings from the internal follow-up audit (if applicable) must also be maintained in the internal audit file.

Audit and Inspection Checklist (Annexure 27)

29. Finances and Administrative Support

Institutional Ethics Committee will be provided financial and administrative support by SHKM GMC Nalhar, Nuh.
The fee received by the IEC for the review of clinical/research studies will solely be used for the functioning of IEC and its associated activities. Any balances that are left after incurring the expenses towards IEC meetings and reimbursement to its members will be utilized for activities such as training of IEC members, organizing workshops and training sessions for IEC members, NABH accreditation process and making payments to necessary bodies towards fee for assessment/compliance. In a nutshell, IEC will work on a no profit basis and will always use its fund for continuous improvement of its functioning and training and development of IEC members in areas of Ethical research.
Expenses such as stationary charges, cupboard and storage cabinets, electricity and telephone bills, infrastructure requirements such as computer, scanner, photocopier, desks and chairs will also be taken care from the fee received by the IEC through SHKM GMC Nalhar, Nuh.
All payments will be received by IEC via wire transfer or cheques. All financial communications and procedures will adhere and comply to Institute's internal routine financial audits, as appropriate.
Member Secretary will be accountable for all administrative matters. Member Secretary will have support from administrative staff as necessary for management of various administrative activities such as filing of EC documents, distribution of EC dossiers, tracking of IEC activities, support in coordination of IEC meetings, adhoc support as needed.
Member Secretary in consultation with Chairperson and other IEC members will evaluate the workload of IEC on an ongoing basis and necessary administrative and other staff will be hired as needed to ensure smooth functioning of IEC.

This Ethics committee is constituted and functions as per ICH-GCP guidelines and Good clinical practice guidelines issued by the Central Drug Standards Control Organization, and Ethical guidelines for Biomedical Research on Human subjects, issued by the Indian council of Medical Research.