STANDARD OPERATING PROCEDURE
[SOP]
REVISION v VI
[Effective - February 2018]

INSTITUTIONAL ETHICS COMMMITTEE
HM PATEL CENTRE
FOR
MEDICAL CARE AND EDUCATION
KARAMSAD, GUJARAT 388325

[Reg. No. ECR/ 331/ Inst/ GJ/ 2013/RR-16]

INDEX

ANNEXURES

Annexure No.	Content
I	IEC Member's List
II	Confidentiality and COI agreement for members
II.1	Declaration of conflict of interest for IEC members or investigators
III	Rights and responsibilities of research participants in clinical trial [s] [English]
III.1	Rights and responsibilities of research participants in clinical trial [s] [Gujarati]
V	Application format for industry or government initiated full committee review project
V.1	Participant information sheet [English]
V.2	Participant information sheet [Gujarati]
V.3	Informed consent form [English]
V.4	Informed consent form [Gujarati]
VII	Project submission checklist [s] for investigators
VIII	Format of response to query letter by investigator
IX	Format of approval letter by Institutional Ethics Committee
X	Site monitoring report [Regulated trial]
X.1	AV Consenting Monitoring Report
XI	WHO tool for causality assessment
XII	Naranjo ADR Probability Scale
XIII	Format of IEC report to CDSCO in case of SAE
XIV	Compensation formula, SAE, Death
XV	Compensation formula, SAE, Injury other than death
XVI	Checklist, Informed Consent Document
XVII	Checklist, Review of CTA

XVIII	Checklist, Review of CT Proposal
XIX	Checklist, Review of SAE
XX	Appendix XI – Schedule Y
XXI	Appendix XII – Schedule Y
XXII	Research Participant Interview Guide [English]
XXIII	Research Participant Interview Guide [Gujarati]

STANDARD OPERATING PROCEDURE [SOP]

AUTHORITY FOR FORMATION OF ETHICS COMMITTEE

Table of contents

1. Purpose

To define the authority who will establish and govern the Institutional Ethics Committee, HM Patel Centre for Medical Care and Education, Karamsad.

2. Scope

It covers the procedure for establishment of an independent and competent Institutional Ethics Committee and its functioning as per applicable rules and regulations.

3. The authority under which the Ethics Committee is established and administratively governed

The Chief Executive Officer (CEO), Charutar Arogya Mandal, will be the appointing authority under which Institutional Ethics Committee [IEC], HM Patel Centre for Medical Care and Education is constituted [HMPCMCE]. Currently, IEC, HMPCMCE is registered with ***Central Drugs Standard Control Organization [CDSCO] with registration no. ECR/ 331/ Inst/ GJ/ 2013/ RR-16, valid till 22nd May 2019*** and ***Office of Human Research Protections [OHRP], US Department of Health and Human Services [HHS] – Registration of an Institutional Review Board [IRB] with registration no. IORG0006830, valid till 31st March 2020***.

4. Policy to ensure the independence of the Ethics Committee in its functioning and decision making

The formation letter from CEO, Charutar Arogya Mandal will clearly specify the independence and competence of the formed Ethics Committee. Composition will be as such that conflict of interest [s] are adequately addressed so that it exhibits an independent decision.

5. Functioning as per applicable rules and regulations

The formation letter from CEO, Charutar Arogya Mandal will clearly specify the terms of reference

for functioning of the independent Institutional Ethics Committee, which will be done taking care of existing regulations.

The terms of reference would include:

- Statement on Independence of the committee
- Core value of the committee
- Scope of the committee
- Appointment of Chairperson, Member Secretary and other members; including subject experts, when required
- Communication with regulatory authorities
- Preparation of Standard Operating Procedure for effective functioning of the committee

[Annexure 1]

STANDARD OPERATING PROCEDURE [SOP]

Standard operating Procedures (SOP) for SOPs

Table of contents

1. Purpose

The purpose of this Standard Operating Procedure (SOP) is to define the process for writing, reviewing, distributing and amending SOPs of the Institutional Ethics Committees (IEC). The SOPs provide clear, unambiguous instructions so that the related activities of the committee are conducted in accordance with existing Indian regulations and relevant, national and international ethical guidelines.

2. Scope

This SOP covers the procedures of writing, reviewing, distributing and amending the SOPs of the IEC by member of IEC, HMPCMCE.

3. Procedures for the development, review and revision of SOPs

3.1 Development

It shall be the responsibility of the Chairperson of the IEC to appoint an SOP team to formulate a new SOP or to revise existing SOP. The SOP team shall do this by following the standard procedures and formats while drafting or editing any SOP of the IEC.

Office of the IEC will co-ordinate activities of writing, reviewing, distributing and amending SOPs. It shall:

- ensure that all the IEC members and involved administrative staff have access to the SOPs
- ensure that all the IEC members and involved staff are working according to current version of SOPs
- maintain an up-to-date distribution list for each SOP distributed to the IEC members
- maintain a file of all current SOPs and the list of SOPs

- maintain a file of all past SOPs of the IEC

SOP team will then:

- assess the request(s) for SOP/s revision in consultation with the IEC Office, Member Secretary and Chairperson
- propose new / modified SOP/ s as needed
- draft the SOP/s in consultation with the IEC members and involved administrative staff
- review the draft SOP
- submit the draft for approval to Chairperson
- get it released by Appointing Authority

Chairperson of the IEC will appoint two or more members of IEC as SOP Team and approve the SOPs with sign and date. Similarly, IEC members and involved administrative staff will sign and date the approved SOP when they receive it and maintain a file of all SOPs received

Detailed instructions for development

Identifying the need for new or amendment of current SOP

- Any member of the IEC or its office that would feel the requirement of a revision or notices an inconsistency/ discrepancy / has any suggestions on how to improve the existing SOPs or requests to design an entirely new SOP can put forth his request by writing to the IEC Chairperson either as an email/ letter/ verbal request in a meeting or otherwise.
- The Chairperson will inform all the IEC members about this request at a regular full-board IEC meeting/ through email/ letter [if there is no full board meeting scheduled in near future].
- If the IEC members agree to the request, an appropriate SOP team will be appointed by the Chairperson and designated the task to proceed with the revision process/ formulation process of the SOP.
- If the IEC members do not agree, no further action will be taken.
- The Chairperson will inform the member of the IEC who made the request for modification of the SOP regarding the Committee's decision as well as to the IEC Office.

Appointing an SOP Team

- The Chairperson will constitute an SOP Team consisting of the Member Secretary and two or more members of the IEC who have a thorough understanding of the ethical review process and

are trained in preparation of SOPs.

- The SOP writing team will carry out the subsequent steps as described below.

3.2 Review, approval and distribution

Writing and reviewing a new/ revised SOP

- When the need for a new/ revised SOP/ an amendment has been identified and agreed upon, a draft will be written by one or more designated members of the SOP team, appointed by the Chairperson.
- Each SOP will be given a number and a title that is self-explanatory and easily understood. A unique number will be assigned to each SOP item by the IEC Office. The first SOP of the current version would be SOP VI-1 i.e. it is SOP version No. 06, Document Number 1.
- Each SOP may have annexures which are forms to be filled in by various stakeholders [IEC or Principal Investigator (PI)]. Each annexure will be given a unique digital number with SOP name.
- Each SOP will be prepared according to the standard template [as above].
- Each page of the SOP will bear the footer which will have page number, the effective date i.e. the date of release of the SOP by the Appointing Authority and the SOP number. Header will bear the title of SOP and Name of IEC [*The logo of the Institution/ Hospital may be put in the header if required].*
- The draft SOP written by one or more members of the SOP team will be reviewed by the remaining members of the SOP team [sent either in hard copy or on email].
- After incorporating the suggestions put forth by the SOP team members, a copy of the revised draft SOP will be sent to the Member Secretary, who will circulate it to all the IEC members.
- A new version will then be brought forth subject to the nature of change; if there is a minor administrative addition/ deletion or change, an amendment will be added instead of coming out with a new version. But if the Committee is of opinion that a new version needs to be brought out considering the importance of changes, instead of an amendment, a new version shall be brought forth.

Preparing and submitting final draft

- The suggestions that are agreed upon by the all IEC members will be incorporated in the revised draft SOP and it will be finalized in a formal full committee meeting, wherever possible.

The SOP team would stand automatically dissolved once the IEC takes final decision regarding the SOP.

Approving the new / revised SOP

- The final version will be presented to the Chairperson for review and approval
- The authors, reviewers and the Chairperson will sign and date the SOP on the first page of the SOP document. This date of approval will be declared as the effective date from which the SOP will be implemented. The face page may also contain signature of Appointing Authority *(as per the institutional policy) as releasing authority [both for amendments as well as new version].*

Implementing, distribution and filing of SOPs

- The approved SOP will be implemented from the effective date.
- The Member Secretary will discuss the approved SOP with the administrative staff and instruct them to implement it accordingly.
- One complete original set of current SOP will be filed in the SOP Master file, by the IEC Coordinator in the IEC office.
- The approved SOP will be notified to the Registering Authority and also uploaded on institute's website [www.charutarhealth.org/sop] as well as on online portal [www.iecmanager.org/institution/15] for everybody's access.
- Only one copy of the earlier version will be filed in the file entitled 'Past SOPs of the IEC' by the IEC Coordinator in the IEC office.

3.3 Revision interval

- The IEC members and the Office will review the SOPs at least once in every 2 years.

STANDARD OPERATING PROCEDURE [SOP]

ETHICS COMMITTEE COMPOSITION

Table of contents

1. Purpose

The purpose of this Standard Operating Procedure (SOP) is to describe the terms of reference (TOR), which provide the framework for constitution, selection, roles and responsibilities of the Institutional Ethics Committee (IEC) members, subject experts and procedures for maintaining confidentiality of all activities and documents. It would also include policy for continuous training of the IEC Members.

2. Scope

The SOP applies to the constitution of Institutional Ethics Committee for its independent and competent functioning.

3. Multidisciplinary and multi-sectorial composition, adequate for its functioning

The IEC will be established by the **Head of the Institution (HOI) – Chief Executive Officer, Charutar Arogya Mandal**. The Chairperson will suggest names of potential members but the final decision will remain with the Head of the Institute.

- Its hierarchical position in the organization and authority under which it is established will be clearly indicated. The IEC will be multidisciplinary and multi-sectoral in composition.
- The IEC will be composed of at least 7 members upto a maximum of 15 (as per current CDSCO

requirements).

- The members will include a combination of medical and non-medical, scientific and non-scientific persons including lay persons to represent the different points of view for participant's benefit.
    - Shall be from differing backgrounds to promote complete and adequate review of research.
    - Shall have the required qualifications as prescribed by applicable regulations and guidelines from time to time.
    - Shall have the expertise, time and commitment to perform all functions.
    - Shall not have any past record of scientific or ethical misconduct.
- The IEC will have representation that is varied in terms of gender, age and social background to safeguard the interests and welfare of all sections of the community / society.
- The committee will include at least one member whose primary area of expertise is in a non-scientific area, a clinician and at least two members who are independent of the institution/ research site.

4. Invitation to subject experts and representatives of vulnerable subjects

- The IEC will invite member(s) of specific patient groups or other special interest groups for an IEC Meeting (based on the requirement of research area, e.g. HIV patient groups in research related to HIV/ AIDS, Donor groups for stem cell research etc.) for eliciting their views. Such individuals will have to sign confidentiality agreement and declare in writing, conflicts of interest, if any prior to attending the meeting. They will attend the meeting in the capacity of 'Guest/ Observer' and will not have the right to vote.
- It will also invite subject experts for an IEC Meeting [when required based on the type of research protocol and non-availability of such subject expert in the committee membership e.g. Paediatrician for researches involving children, Surgeon for researches involving a new interventional surgical device, Critical Care Specialist for trial involving participants in ICUs etc.] for eliciting their expert opinions on the specific research protocol. Such individuals will have to sign confidentiality agreement and declare in writing, conflicts of interest, if any prior to attending the meeting. They will attend the meeting in the capacity of 'Guest/ Observer' and will not have the right to vote.

5. Terms of reference defining membership, appointment, reconstitution and resignation

- The Composition of the Committee will be as follows:
    - Chairperson [mandatorily from outside the institution as per regulatory requirements as well

as for maintenance of its independence]

- Deputy Chairperson [to officiate in absence of Chairperson/ when Chairperson himself/ herself is an investigator or has any other declared conflict of interest]
- Member Secretary [from within the institution]
- Deputy Member Secretary [optional]
- Legal expert
- Social scientist/ representative of non-governmental voluntary agency
- Lay person from the community
- 1 – 7 members from different departments/ specialties/ disciplines etc.
  - Basic medical scientists
  - Clinicians
  - Ethics Expert/ Ethicist/ Theologian [as invited member as and when need arises]
  - Subject Expert and representatives of different potential participant groups [as invited member as and when need arises]

Criteria for selection of IEC Members:

Sr. No.	Member [s]	Qualification
1	Chairperson/ Deputy Chairperson	• Non-affiliated; • Can be from scientific/ nonscientific discipline; Masters/ MD/ Retired • A well-respected person from any background with prior experience of having served/ serving in an EC
2*	Basic Medical Scientist	• Affiliated/ non-affiliated • Non-medical or medical person with qualifications in basic medical sciences; PG qualification; adequate experience in his/ her respective field; • In case of EC reviewing clinical trials with drugs, the basic medical scientist should preferably be a pharmacologist
3*	Clinician	• Affiliated/ non-affiliated • Person whose training, background and occupation would incline them to view scientific activities with a behavioral or biomedical research discipline [PG Qualified like MD Medicine, Pediatrics/ MS Surgery, Orthopedics; not limited to]
4*	Layperson	• Affiliated/ non-affiliated • Person having no specific qualification with respect to biomedical research, medicine or health care • Primary role will be to share insights about the communities

		from which participants are likely to be taken • Literate person from the public or community • May be a representative of the community from which the participants are to be drawn • Is aware of the local language, cultural and moral values of the community • Desirable: involved in social and community welfare activities
5*	Social Scientist	• Affiliated/ non-affiliated • Someone expert in the study of human society and its personal relationship like anthropologist/ scientist/ penologist; • Should be an individual with social/ behavioural science/ philosophy/ religious qualification and training and/or expertise and be sensitive to local cultural and moral values • Can be from an NGO involved in health-related activities
6	Ethicist/ Ethics Expert	• Affiliated/ non-affiliated • Person with background in law/ philosophy/ bioethics
7	Theologian	• Affiliated/ non-affiliated • Person involved in preaching of various religious activities
8*	Legal expert	• Affiliated/ non-affiliated • Person with degree in law as per Bar Council of India; Preferably with training in medical law
9	Member Secretary	• Affiliated • Any senior faculty working in the institution; • Should have knowledge and experience in clinical research and ethics, be motivated and have good communication skills
10**	Subject Expert	• Affiliated/ non-affiliated • Person whose training, background and occupation would incline them to view scientific activities with a behavioral or biomedical research discipline respectively [Pediatrician in a research proposal involving children; anesthetist in a research proposal involving use of anesthetic drugs etc.]

*Mandatory;

**Invited member for a specific proposal without voting rights

Tenure of Membership

- The tenure of IEC will be for a continuous period of 3 years from the date of appointment.
- After 3 years, it may further be extended for not more than 3 years [50% reconstitution to be done every 3 years]
- No member can hold the office for more than 6 consecutive years

Appointment of New Members

The IEC members will be appointed by the Head of Institute. They will be appointed under the following circumstances:

- When a new committee is being formed/ reconstituted
- When regular member completes his/ her tenure
- If a regular member resigns before the tenure is completed
- If a regular member ceases to be a member for any reason including death or disqualification
- To fulfil the membership requirements as stated in this SOP

New members will be identified by the Chairperson according to the membership requirements and provided the potential member fulfils the conditions of appointment after discussion with the appointing authority. The names of new members to be appointed will be suggested by the IEC members and the Chairperson to the Head of Institute [HOI]. The final decision regarding appointment of members will be taken by the HOI.

Conditions to be fulfilled by a member after appointment

- Members to be appointed on the IEC will need to fulfil the following conditions:
    - Submit a current detailed CV with signature, date and photograph
    - Preferably, if available training certificates in Ethics and/ or GCP [if not available at time of induction as member in the IEC, the member must submit these within 6months of appointment].
- Members must be willing to:
    - publicize his/her full name, profession and affiliation
    - sign the Confidentiality Agreement and Conflict of Interest Form and maintain confidentiality regarding meetings, deliberations, research proposals, information on research participants and all related matters of IEC. ***[Annexure 2]***

Resignation and Disqualification of Members

- Resignation:
    - An IEC member may resign from membership by submitting a letter of resignation to the Chairperson. The member may or may not assign reasons for resignation. The resignation will become effective from the day it is accepted by the Chairperson. The same will then be forwarded to the Head of Institute for a suitable replacement.

- Disqualification for conduct unsuitable of an IEC member:
    - A member may be disqualified from continuance should IEC determine by a three-fourth majority specifically called for the purpose that the member's conduct has been inappropriate of an IEC member.
    - The process will be initiated if IEC Chairperson or Member-secretary receives a communication in writing (provided by IEC member or a member of the public) alleging misconduct by a member.
    - The Chairperson will satisfy himself/ herself that a prima facie case exists before initiating action. If, in the opinion of the Chairperson, the matter is of grave significance where integrity of IEC could be questioned, the Chairperson may suspend the membership of the concerned IEC member till final decision is taken by IEC. During the period of suspension, the concerned individual will not have any rights, privileges or responsibilities of an IEC member and will not perform any duties of IEC member.
    - The Chairperson will call for a meeting of the IEC specifically to discuss this issue or the matter will be taken up for discussion in forthcoming meeting. The meeting convened will follow the usual rules of quorum. The allegation will be discussed at the IEC meeting and the member alleged of misconduct will be provided adequate opportunity to defend himself / herself.
    - The member would stand disqualified, if members present approve of disqualification by voting (voting by 2/3rd of majority of members present in the meeting and voting).
    - The Chairperson will convey the disqualification to the concerned member through a written communication as well as to the Head of the Institute.
- Disqualification for not attending IEC meetings:
    - A member may be disqualified from IEC membership if the member fails to attend more than 3 regular consecutive IEC meetings without valid reason and prior intimation. The process conducted will be as follows:
        - The Member Secretary will inform Chairperson, in writing, if a member has not attended more than three consecutive regular meetings of the IEC without valid reason and prior intimation to the IEC.
        - The Chairperson will initiate the process of review of membership of such a member by including the matter in the Agenda of the next regular IEC meeting.
        - A written communication will be sent to the concerned IEC member informing

him/ her that the issue of disqualification would be discussed at the meeting inviting the member to be present at the meeting to put up his/ her case. Alternately, the concerned IEC member will be allowed to state his/ her arguments regarding unauthorized absence in writing by a letter addressed to the Chairperson.

- The matter will be discussed and reviewed at the IEC meeting. The concerned member will be provided adequate opportunity to represent his/ her case. A written communication, if received from the concerned member will be read and reviewed at the meeting.
- The Chairperson or Member-Secretary will inform the IEC members about the cessation/ continuation of membership by a confidential written communication to other members of IEC or at the next meeting of IEC.

- For research involving human participants, eligibility criteria undertaken as Principal Investigator will be as follows:
  1. Medical Faculty [includes medical and dental branches]
     - Short Current CV
     - Medical Registration Certificate
     - Copy of GCP Training Certificate
     - At least 2 years' experience in Research as Co-investigator
  2. Non-Medical Faculty
     - Short Current CV
     - Medical Registration Certificate from respective council [if applicable]
     - Copy of GCP Training Certificate [preferable]
     - At least 2 years' experience in Research as Co-investigator
- Eligibility of different investigators will be decided by the Committee depending upon the type of research proposal submitted. With regards to research experience, a PI may be asked to submit evidence of 2 research projects undertaken in past to qualify for PI.

Types of projects reviewed by IEC

- The IEC will review scientific and ethical aspects of all types of research studies involving human participants that are sponsored by pharmaceutical companies, sponsored by Government of India / NGOs, studies in collaborations with international organizations/universities [namely Regulated

Clinical Trials], including Clinical Trial Registry.

Quorum Requirements

- The full committee meeting will be held as scheduled provided there is quorum.
- For the IEC meeting, a quorum will consist of at least 5 members for regulatory clinical trials with the following representation: one basic medical scientist (preferably one pharmacologist), one clinician, one legal expert, one social scientist/representatives of non-governmental voluntary agency, one Lay person from the community, apart from Member Secretary and Chairperson as mandated by Schedule Y.
- Without satisfying this condition, any decision taken by the committee will remain null and void.
- In absence of the Chairperson, Co-Chairperson will chair the meeting.
- In absence of legal expert/ lay person/ social scientist, IEC HMPCME may request the member with same position from IEC-2, HMPCMCE to officiate.

6. Roles and responsibilities of members

Each IEC Member at the time of appointment will be provided with a copy of SOP, defining his/ her roles and responsibilities. These will be as follows:

1. **Chairperson**:
    - Appointment of members
    - Formation of committee for review/ new version of IEC SOPs
    - Conduct of meeting & be accountable for independent and efficient functioning of the committee
    - Ensure active participation by all the members [particularly non-affiliated, non-medical/ non-technical in all discussions and deliberations
    - Appoint another member as Chairperson, in his/ her absence
    - Approval of minutes of meeting
    - Sign all documents on behalf of IEC
    - Ensure that any conflict of interest is well taken care of
    - Seek COI declaration from members and ensure quorum and fair decision making
    - Handle complaints against researchers, EC members, conflict of interest issues and requests for use of EC data, etc.

2. **Deputy Chairperson**:
    - Manages role of Chairperson in his absence, as and deputed by Chairperson

3. **Member Secretary**:
    - Manage administrative work of IEC
    - Call for proposals; assess need for full committee/ expedite review

- Review and check submitted proposals for completeness
- Propose and circulate the agenda for meetings
- Ensure adequate number of clinical trials in a single meeting
- Review and reporting of Serious Adverse Event [s] [SAE]
- Review protocol deviations
- Communication with various stake holders [researchers, regulatory body etc.]
- Archiving of all IEC documents
- Monitor conduct of trials and their progress
- Prepare for audits
- Prepare meetings and agenda for subcommittees
- Preparing minutes of meeting
- Review of Standard Operating Procedures [SOP]
- Preparation of annual reports
- Updating of new rules and regulations
- Arrange for capacity building among IEC members
- Arrange for subject experts, when required

4. **Lay Person**:

- Ethical 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
- Review of compensation processes
- Review of post-trial benefits
- Review of non-trial related injuries
- Issues with vulnerability
- Monitoring of ongoing research projects

5. **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.
- Review of compensation processes
- Analysis of risks and benefits, review of post-trial benefits
- Review of non-trial related injuries
- Issues with vulnerability
- Monitoring of ongoing research projects

6. **Lawyer**:

- 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, such as, stem cell committee for stem cell research, HMSC for international collaboration, compliance with guidelines etc.
- Interpret and inform EC members about new regulations, if any
- Review of compensation processes
- Compliance with current National Laws
- Analysis of risks and benefits
- Review of post-trial benefits
- Issues with vulnerability
- Monitoring of ongoing research projects

7. **Basic Scientist**:

- 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 pharmacodynamics [Investigator brochure]
- Analysis of risks and benefits
- Review of post-trial benefits
- Review of non-trial related injuries
- Issues with vulnerability
- Monitoring of ongoing research projects

8. **Clinician**:

- 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
- Review of informed consent process
- Analysis of risks and benefits
- Review of post-trial benefits
- Review of non-trial related injuries
- Issues with vulnerability
- Monitoring of ongoing research projects

Office Assistant/ Co-ordinator

- Maintaining an effective and efficient tracking procedure for each proposal received
- Preparation, maintenance and distribution of study files
- Allocation of project reviews to specific members to facilitate efficient dispensation of the projects
- Organizing IEC meetings
- Preparation and maintenance of meeting agenda and minutes

- Receive and check for the completeness of the documents for review by the EC
- Co-ordinate with the investigators
- Maintaining the IEC's documentation and archival
- Communicating with the IEC members and investigator applicants
- Arrangement of training for personnel and IEC members
- Organizing the preparation, review, revision and distribution of SOPs
- Work in unison with the EC members and the investigators to reduce the turn-around time of the study proposals sent to the EC for review
- Providing updates on relevant and contemporary issues related to ethics in health research, as well as relevant contemporary literature to the Committee members

7. Training of Ethics Committee members in applicable rules and regulations and Ethics Committee SOPs

- An individual selected as a new member of the IEC will be required to attend one meeting as an 'Observer' before being inducted as a member of the IEC [without voting rights].
- Member Secretary or an IEC member will provide introductory training in Research Ethics, GCP and SOPs to the new member, followed by an evaluation.
- A newly inducted member should submit certificate of training in 6 months by attending required training at workshops etc.
- All members including Chairperson and Member Secretary will be encouraged to receive continued training by participating in a workshop, conference and/ or re-training program related to research ethics, as a delegate, faculty, facilitator, etc.
- The IEC itself will conduct workshops on ethics in clinical research, GCP, SOPs preparation or changing regulations or guidelines at least once a year to impart training and update the IEC Members and Institutional faculty members.
- These workshops shall also fulfil the need to fill gaps in current IEC members' knowledge as determined from regular self-assessments or issues raised during review of research protocols at full committee meeting or whenever new guidelines or regulations come into force.
- The IEC may nominate *and / or sponsor the expenses of (as applicable)* an IEC member or prospective members for attending conference, continuing education session workshop and/ or training program etc. outside the institution too.

8. Conflict of interest and confidentiality of members

It is the responsibility of each IEC member, reviewing research project or attending IEC meetings, to read, understand, accept and sign the agreement contained in the Confidentiality and Conflict of

Interest Form.

- The Office Coordinator will provide Confidentiality and Conflict of Interest Form, get it signed at the time of acceptance of membership and will be filed with the IEC office.
- He/ she will obtain the signature of the IEC Chairperson on the Confidentiality form and provide IEC member a photocopy of the Confidentiality and Conflict of Interest Form for their records (duly signed and dated by them and IEC Chairperson) and acknowledge the receipt of agreement with their signature.
- The IEC Coordinator will keep the original copies of the signed Agreements in the IEC office in a separate file and if possible, photocopies of the agreement in the individual member's files.

- Every member will individually submit Conflict of Interest Declaration prior to review of a research project involving himself/ herself and will not be part of discussion and decision making process of the full committee. ***[Annexure 2.1]***

STANDARD OPERATING PROCEDURE [SOP]

REVIEW OF CLINICAL TRIAL PROTOCOL

Table of contents

1. Purpose

The purpose of this Standard Operating Procedure (SOP) is to describe what and how the Institutional Ethics Committee (IEC) members will review a new research study protocol, at a formal meeting with use of basic principles of research ethics, autonomy, no harm, beneficence and justice keeping in mind. It will also help committee for critical monitoring post approval including SAEs and grievances of different stakeholders.

2. Scope

This SOP applies to the initial review and assessment of all research study protocols submitted for review and approval from the IEC. All research studies presented for full committee or expedited review are covered in this SOP. Scope will be extended to principles of monitoring and grievance handling.

3. Review of clinical trial protocol

IEC will review and take decision regarding approval of REGULATED research proposals/ trials involving human participants that conform to safeguard the dignity, rights, safety and well-being of all actual and potential research participants. **The goals of research, however important, will never be permitted to override the health and well-being of the research participants.** IEC will take care that all the cardinal principles of ethics viz. autonomy, beneficence, non - maleficence and justice are taken care of in planning, conducting and reporting of the proposed research.

For this purpose, it will look into the aspects of Informed consent process, risk benefit ratio, distribution of burden and provisions for appropriate compensations, wherever required. It will review the proposals before start of the study; once approved, will examine its compliance with all regulatory requirements, applicable guidelines and laws as updated with time and monitor the research throughout the study until and after completion of the study.

The mandate of the IEC will be to review those research proposals that

1. involve participants taken from HMPCMCE institutions
2. are undertaken at HMPCMCE institutions
3. carried out by faculty of HMPCMCE institutions

IEC shall ensure that all research involving human participants is conducted in accordance with the basic and general ethical principles. The researcher and the team shall be responsible for protecting the dignity, rights, safety and well-being of the participants enrolled in the study. They should have the appropriate qualifications and competence in research methodology and should be aware of and comply with the scientific, medical, ethical, legal and social requirements of the research proposal.

Each review will be based on Statement of General Principles as per ICMR Ethical Guidelines for Biomedical Research on Human Participants, 2017. If the case may be that these Guidelines are updated, then the same will be the basis of review, for the period new guidelines are in vogue.

Any research using the human beings as participants will follow the principles given below –

1. **Principles of essentiality**, whereby the research entailing the use of human participants is considered to be absolutely essential after a due consideration of all alternatives in the light of the existing knowledge in the proposed area of research and after the proposed research has been duly vetted and considered by an appropriate and responsible body of persons who are external to the particular research and who, after careful consideration, come to the conclusion that the said research is necessary for the advancement of knowledge and for the benefit of all members of the human species and for the ecological and environmental wellbeing of the planet.

2. **Principles of voluntariness**, informed consent and community agreement whereby research participants are fully apprised of the research and the impact and risk of such research on the research participant and others; and whereby the research participants retain the right to abstain from further participation in the research irrespective of any legal or other obligation that may have been entered into by such human participants or someone on their behalf, subject to only minimal restitutive obligations of any advance consideration received and outstanding. Where any such research entails treating any community or group of persons as a research participant, these principles of voluntariness and informed consent will apply, mutatis mutandis, to the community as a whole and to each individual member who is the participant of the research or experiment. Where the human participant is incapable of giving consent and it is considered essential that research or experimentation be conducted on such Statement of General Principles in Biomedical Research Involving Human Participants a person incompetent to give consent, the principle of voluntariness and informed consent will continue to apply and such consent and voluntariness will be obtained and exercised on behalf of such research participants by someone who is empowered and under a duty to act on their behalf. The principles of informed consent and voluntariness are cardinal principles to be observed throughout the research and experiment, including its aftermath and applied use so that research participants are continually kept informed of any and all developments in so far as they affect them and others. However, without in any way undermining the cardinal importance of obtaining informed consent from any human participant involved in any research, the nature and form of the consent and the evidentiary requirements to prove that such consent was taken, will depend upon the degree and seriousness of the invasiveness into the concerned human participant's person and privacy, health and life generally, and, the overall purpose and the importance of the research. Ethics committee will decide on the form of consent to be taken or its waiver based on the degree of risk that may be involved.
3. **Principles of non-exploitation**, whereby as a general rule, research participants are remunerated for their involvement in the research or experiment; and, irrespective of the social and economic condition or status, or literacy or educational levels attained by the research participants kept fully apprised of all the dangers arising in and out of the research so that they can appreciate all the physical and psychological risks as well as moral implications of the research whether to themselves or others, including those yet to be born. Such human participants should be selected so that the burdens and benefits of the research are distributed without arbitrariness, discrimination or caprice. Each research will include an in-built mechanism for compensation for

the human participants either through insurance cover or any other appropriate means to cover all foreseeable and unforeseeable risks by providing for remedial action and comprehensive aftercare, including treatment during and after the research or experiment, in respect of any effect that the conduct of research or experimentation may have on the human participant and to ensure that immediate recompense and rehabilitative measures are taken in respect of all affected, if and when necessary.

4. **Principles of privacy and confidentiality**, whereby the identity and records of the human participants of the research or experiment are as far as possible kept confidential; and that no details about identity of said human participants, which would result in the disclosure of their identity, are disclosed without valid scientific and legal reasons which may be essential for the purposes of therapeutics or other interventions, without the specific consent in writing of the human participant concerned, or someone authorized on their behalf; and after ensuring that the said human participant does not suffer from any form of hardship, discrimination or stigmatization as a consequence of having participated in the research or experiment.
5. **Principles of precaution and risk minimization**, whereby due care and caution is taken at all stages of the research and experiment (from its inception as a research idea, its subsequent research design, the conduct of the research or experiment and its applicative use) to ensure that the research participant and those affected by it including community are put to the minimum risk, suffer from no known irreversible adverse effects, and generally, benefit from and by the research or experiment; and that requisite steps are taken to ensure that both professional and ethical reviews of the research are undertaken at appropriate stages so that further and specific guidelines are laid down, and necessary directions given, in respect of the conduct of the research or experiment.
6. **Principles of professional competence**, whereby the research is conducted at all times by competent and qualified persons who act with total integrity and impartiality and who have been made aware of, and are mindful of, preferably through training, the ethical considerations to be borne in mind in respect of such research or experiment.
7. **Principles of accountability and transparency**, whereby the research or experiment will be conducted in a fair, honest, impartial and transparent manner after full disclosure is made by those associated with the research or experiment of each aspect of their interest in the research, and any conflict of interest that may exist; and whereby, subject to the principles of privacy and confidentiality and the rights of the researcher, full and complete records of the research inclusive of data and notes are retained for such reasonable period as may be prescribed or considered

necessary for the purposes of post-research monitoring, evaluation of the research, conducting further research (whether by the initial researcher or otherwise) and in order to make such records available for scrutiny by the appropriate legal and administrative authority, if necessary.

8. **Principles of the maximization of the public interest and of distributive justice**, whereby the research or experiment and its subsequent applicative use are conducted and used to benefit all human kind and not just those who are socially better off but also the least advantaged; and in particular, the research participants themselves and or the community from which they are drawn.
9. **Principles of institutional arrangements**, whereby there will be a duty on all persons connected with the research to ensure that all the procedures required to be complied with and all institutional arrangements required to be made in respect of the research and its subsequent use or application are duly made in a bonafide and transparent manner; and to take all appropriate steps to ensure that research reports, materials and data connected with the research are duly preserved and archived.
10. **Principles of public domain**, whereby the research and any further research, experimentation or evaluation in response to, and emanating from such research is brought into the public domain so that its results are generally made known through scientific and other publications subject to such rights as are available to the researcher and those associated with the research under the law in force at that time.
11. **Principles of totality of responsibility**, whereby the professional and moral responsibility, for the due observance of all the principles, guidelines or prescriptions laid down generally or in respect of the research or experiment in question, devolves on all those directly or indirectly connected with the research or experiment including the researchers, those responsible for funding or contributing to the funding of the research, the institution or institutions where the research is conducted and the various persons, groups or undertakings who sponsor, use or derive benefit from the research, market the product (if any) or prescribe its use so that, inter alia, the effect of the research or experiment is duly monitored and constantly subject to review and remedial action at all stages of the research and experiment and its future use.
12. **Principles of compliance**, whereby, there is a general and positive duty on all persons, conducting, associated or connected with any research entailing the use of a human participant to ensure that both the letter and the spirit of these guidelines, as well as any other norms, directions and guidelines which have been specifically laid down or prescribed and which are

applicable for that area of research or experimentation, are scrupulously observed and duly complied with.]

During the review process, the IEC will consider the following elements of a given research proposal:

a. Scientific design and conduct of the study
b. Examination of predictable risks/harms & potential benefits with communication to the study participants
c. Recruitment strategies
d. Procedure for independent selection of subjects in methodology including inclusion/ exclusion, withdrawal, removal criteria and other issues like advertisement details etc.
e. Protection of subject rights and responsibilities
f. Issues related to protocol deviation and violation
g. Management of research related injuries, serious adverse events
h. Payment for participation & Compensation provisions
i. Justification for placebo in control arm, if any
j. Availability of products after the study, if applicable
k. Informed Consent Process [includes participant information sheet, informed consent form in local languages, along with AV recording protocols [where necessary]; Requirement of assent if indicated.
l. Protection of privacy and confidentiality
m. Involvement of the community, wherever required
n. Plans for data analysis and reporting
o. Adherence to all regulatory requirements and applicable guidelines changing from time to time [including CDSCO, GOI, ICMR etc.]
p. Competence of investigators, research and supporting staff
q. Facilities and infrastructure of study sites
r. Criteria for withdrawal of patients, suspending or terminating the study
s. Mechanism declared for trial participant to contact IEC, if need arises
t. Justification for waiver of informed consent
u. Protection of vulnerable population [as stated later]
v. Community need & Social values: Outcome of the planned results should be relevant to the health problem of the society.
w. Disclosure of conflict of interest

[Law of the land will be given absolute preference to any prevailing national or international guidelines

while reviewing any research proposal]

Protection of vulnerable population

1. Vulnerability

- The Council for International Organizations of Medical Sciences (CIOMS) new guidelines [2016] no longer label entire classes of individuals as vulnerable. CIOMS more clearly emphasizes that unless a good scientific reason justifies their exclusion, children and persons who are incapable of giving informed consent must be included in research investigations, provided that appropriate safeguards are in place. Ethics Committees should evaluate the specific context-dependent characteristics that may place study participants at increased risk of being harmed or wronged.
- Just as the definition of vulnerability is context dependent, so is the delineation of special protections. Ethics Committees are expected to devise special protections for groups considered to be vulnerable, including allowing for no more than minimal risks for research procedures that offer no potential individual benefits for participants, or requiring that the research be carried out only when it targets conditions that affect these groups. Ethics committees are expected now to enable the participation of vulnerable individuals by protecting their rights and interests through special safeguards and protections.
- Vulnerable persons are those who are relatively (or absolutely) incapable of protecting their own interests. More formally, they may have insufficient power, intelligence, education, resources, strength, or other needed attributes to protect their own interests.
- Individuals whose willingness to volunteer in a research study may be unduly influenced by the expectation, whether justified or not, of benefits associated with participation, or of a retaliatory response from senior members of a hierarchy in case of refusal to participate may also be considered vulnerable (WHO).

2. Responsibility

- EC members will identify study proposals including vulnerable participants (population) and ensure that these are considered for full board review.
- EC will ensure that measures for safeguarding rights and interests of vulnerable participants are taken care of in the study proposal. They will ensure that the vulnerable population is not exploited and guide the investigators to design protocols and describe the process of informed consent in such a manner that this will be done.

- EC will see whether the inclusion of vulnerable populations in the study is justifiable or the population is just being exploited to generate clinical data. In such cases, the risk benefit analysis needs to be done critically.
- Effort may be made to ensure that individuals or communities invited for research be selected in such a way that the burdens and benefits of the research are equally distributed:
  - Research on genetics should not lead to racial inequalities.
  - Persons who are economically or socially disadvantaged should not be used to benefit those who are better off than them.
  - Rights and welfare of mentally challenged and differently able persons who are incapable of giving informed consent or those with behavioral disorders must be protected. Appropriate proxy consent from the legally acceptable representative should be taken after the person is well informed about the study, need for participation, risks and benefits involved and the privacy and confidentiality procedures. The entire consent process should be properly documented.
  - Adequate justification is required for the involvement of participants such as prisoners, students, subordinates, employees, service personnel etc. who have reduced autonomy as research participants, since the consent provided may be under duress or various other compelling reasons.
  - Persons, who are terminally ill, have incurable disease and mental illness.
- Before undertaking research/trial in children the investigator must ensure that:
  - Children are not involved in research that could be carried out equally well with adults.
  - The purpose of the research is to obtain knowledge relevant to health needs of children. For clinical evaluation of a new drug the study in children should always be carried out after the phase III clinical trials in adults. It can be studied earlier only if the drug has a therapeutic value in a primary disease of the children.
  - A parent or legally acceptable representative of each child has given proxy consent.
  - The assent of the child should be obtained to the extent of the child's capabilities such as in the case of mature minors from the age of 7 years up to the age of 18 years.
  - Research should be conducted in settings in which the child and parent can obtain adequate medical and psychological support.
  - Interventions intended to provide direct diagnostic, therapeutic or preventive benefit for the individual child participant must be justified in relation to anticipated risks involved in the study and anticipated benefits to society.

- The child's refusal to participate in research must always be respected unless there is no medically acceptable alternative to the therapy provided/ tested, provided the consent has been obtained from parents/ guardian.
- Interventions that are intended to provide therapeutic benefit are likely to be at least as advantageous to the individual child participant as any available alternative interventions.
- The risk presented by interventions not intended to benefit the individual child participant is low when compared to the importance of the knowledge that is to be gained.

➢ As a general rule, pregnant or nursing women should not be participants of any clinical trial except such trials as are designed to protect or advance the health of pregnant or nursing women or fetuses or nursing infants, and for which women who are not pregnant or nursing would not be suitable participants.

- The justification of participation of these women in clinical trials would be that they should not be deprived arbitrarily of the opportunity to benefit from investigations, drugs, vaccines or other agents that promise therapeutic or preventive benefits. Example of such trials are:
  - To test the efficacy and safety of a drug for reducing perinatal transmission of HIV infection from mother to child
  - Trials for detecting fetal abnormalities and for conditions associated with or aggravated by pregnancy etc.
- Women should not be encouraged to discontinue nursing for the sake of participation in research and in case she decides to do so, harm of cessation of breast-feeding to the nursing child should be properly assessed except in those studies where breast feeding is harmful to the infant. Compensation in terms of supplying supplementary food such as milk formula should be considered in such instances.
- Only consent of the women should be mandatory and no proxy consent/ refusal allowed.
- Research related to termination of pregnancy:
  - Pregnant women who desire to undergo Medical Termination of Pregnancy (MTP) could be made participants for such research as per The Medical Termination of Pregnancy Act, GOI, 1971.
- Research related to pre-natal diagnostic techniques:
  - In pregnant women such research should be limited to detect the fetal abnormalities or genetic disorders as per the Pre Conception and Prenatal

Diagnostic Techniques (Regulation and Prevention of Misuse) Act, GOI, 1994 and not for sex determination of the fetus.

4. Rights and responsibilities of participant

The committee shall ensure that all potential clinical trial participants are aware of their rights and responsibilities. For the same, a board in both English as well as Local Language shall be displayed at clinical trial sites where consenting process is done. In order to ensure that rights and responsibilities are protected, IEC shall review Informed Consent Document to see that participant is well informed. Apart from this, IEC shall regularly monitor ongoing trial to oversee protection of rights and responsibilities of the participant.

RIGHTS OF PARTICIPANTS IN A RESEARCH

A] What should you know about trial regulation?

1. Every research/ trial is undertaken only after due approval from competent government authorities and a local Institutional Ethics Committee made up of scientists, doctors, advocates and community members.
    a. These committees ensure that trial participants are exposed to the minimum possible risks and that the risks associated with the trial are reasonable in relation to the expected benefits.
    b. All participants need to be informed about the Institutional Ethics Committee details and are free to approach it for any grievance related to research/ clinical trial
2. To further ensure the safety of participants, a Data Safety Monitoring Board (DSMB) is commonly used.
    a. The DSMB is an impartial group that monitors the progress of clinical trials.
    b. They are not involved in the conduct of the trial but ensure patient safety by analyzing the safety and effectiveness of the experimental treatment periodically during ongoing trial.
    c. They can terminate a trial if expected risk-benefit ratio is not being achieved.

B] What should you know about trial before consenting to participate in research?

1. Rights of Participants of research/ clinical trials are protected under law when participating in clinical trials.

2. The informed consent process is one of the key aspects of protecting research participants and decision to volunteer for a study is individual and free from undue influences. Before consenting to participate in clinical trial, potential participants are expected to
    a. Understand all the possible benefits and risks involved
    b. Understand duration and overall conduct of the study including follow up plan
    c. Understand what will be expected of you as a participant
    d. Understand what will happen if trial is over or in case of a drop out or if discontinued by the investigator
3. The participant has the right to know everything that is going to happen in a study.
    a. He can ask any question and express all concerns about participation in the study
4. The potential participant has the right to refuse to take part in research without affecting his right to get due medical treatment [without prejudice or loss of future treatment].
    a. Participant is also free to withdraw from the study at any time without giving any reason and without having any effect on future treatment
5. During the research/ trial, the privacy of participants and the confidentiality of their data are maintained.
6. If new benefits, risks or side effects are discovered during a study, you will be informed about the same by investigator

RESPONSIBILITIES OF PARTICIPANTS IN A RESEARCH

- To adhere to taking the trial medication according to the prescribed dosages and schedule
- To undergo periodic investigations/ follow up as prescribed in trial protocol on schedule
- To immediately report any observation/untoward event (possible side effect) during the trial

5. Voluntariness and prior intimation with regards to participant's involvement and withdrawal from the trial

IEC shall ensure that no participant is forced to enter into a clinical trial. The informed consent document shall clearly indicate voluntariness for the trial and any refusal shall not have any effect on the ongoing medical treatment. EC shall also review the recruitment procedure, vulnerability and reimbursements decided, which shall also be part of the regular monitoring process. IEC will ensure that each participant is aware of the following:

- Only, to withdraw him/herself from the study at any point of time without affecting his / her ongoing medical treatment as part of standard of care.

- He / she is educated about the predefined conditions or risk analysis when investigators may remove participants from the study. He / she is given chance for re-consenting whenever risk benefit analysis changes due to change in protocol or reports of AE/SAEs or interim review results have achieved the desired outcome or there is increased risk.

[Annexure 5.2, 5.3, 16]

6. Information and comprehension of participants regarding (initial and ongoing) the associated risks and benefits of the trial

Benefits to the individual, community or society refer to any sort of favourable outcome of the research, whether direct or indirect. The social and scientific value of research should justify the risk, which is the probability of causing discomfort or harm anticipated as physical, psychological, social, economic or legal. The researcher, sponsor and EC shall attempt to maximize benefits and minimize risks to participants so that risks are balanced to lead to potential benefits at individual, societal and/or community levels.

To ensure the same, EC shall assess the inherent benefits and risks, ensure a favourable balance of benefits and risks, evaluate plans for minimizing the risk and discomfort and decide on the merit of the research before approving it. As a part of continuing review at appropriate interval and focused review based on notifications of SAEs at the study site or other study sites when notified, EC will also assess any altered risks in the study. For the same, a predetermined checklist shall be used by the members while reviewing research protocol especially informed consent document.

[Annexure 5.2, 5.3, 16]

7. Protection of confidentiality and privacy of participants

Privacy is the right of an individual to control or influence the information that can be collected and stored and by whom and to whom that information may be disclosed or shared. Confidentiality is the obligation of the researcher/research team/organization to the participant to safeguard the entrusted information. It includes the obligation to protect information from unauthorized access, use, disclosure, modification, loss or theft. The researcher should safeguard the confidentiality of research related data of participants and the community.

Potential limitations to ensure strict confidentiality must be explained to the participant. Researchers must inform prospective participants that although every effort will be made to protect privacy and ensure confidentiality, it may not be possible to do so under certain circumstances. Any publication arising out of research should uphold the privacy of the individuals by ensuring that

photographs or other information that may reveal the individual's identity are not published. A specific re-consent would be required for publication, if this was not previously obtained.

EC team will be taking special note on this aspect while going on site visit and interim review. Some information may be sensitive and should be protected to avoid stigmatization and/or discrimination (for example, HIV status; sexual orientation such as lesbian, gay, bisexual, and transgender (LGBT); genetic information; or any other sensitive information). While conducting research with stored biological samples or medical records/data, coding or anonymization of personal information is important and access to both samples and records should be limited.

Data of individual participants/community may be disclosed in certain circumstances with the permission of the EC such as specific orders of a court of law, threat to a person's or community's life, public health risk that would supersede personal rights to privacy, serious adverse events (SAEs) that are required to be communicated to an appropriate regulatory authority etc.

[Annexure 5.2, 5.3, 16]

8. Monitoring to ensure equitable selection of subjects, with special attention to vulnerable and high risk subjects

Efforts must be made to ensure that individuals or communities invited for research are selected in such a way that the benefits and burdens of research are equitably distributed. Vulnerable individuals/groups should not be included in research to solely benefit others who are better-off than themselves. Research should not lead to social, racial or ethnic inequalities. Plans for direct or indirect benefit sharing in all types of research with participants, donors of biological materials or data should be included in the study, especially if there is a potential for commercialization. This shall be decided a priori in consultation with the stakeholders and reviewed by the EC. Any advertisement or leaflet inviting the participants, if there, will be reviewed by the EC.

While regular site visit monitoring by EC and time to time review of ongoing projects recruitment log will be checked to confirm the equitable distribution of participants.

[Annexure 10, 10.1, 22, 23]

9. Compensation for participation in the trial

Payment for participation: Participants shall be reimbursed for expenses incurred relating to their participation in research, such as travel related expenses. Participants shall also be paid for inconvenience incurred, time spent and other incidental expenses in either cash or kind or both as deemed necessary (for example, loss of wages and food supplies). Participants will not be made to pay for any expenses incurred beyond routine clinical care and which are research related including

investigations, patient work up, any interventions or associated treatment. This is applicable to all participants, including those in comparator/control groups. If there are provisions, participants may also receive additional medical services at no cost.

When the LAR is giving consent on behalf of a participant, payment shall not become an undue inducement and will be reviewed carefully by the EC. Reimbursement will be offered for travel and other incidental expenses incurred due to participation of the child/ward in the research. ECs will review and approve the payments (in cash or kind or both) and free services and the processes involved, and also determine that this does not amount to undue inducement. Once approved, EC will look for documents verifying that participants actually got the reimbursement [s].

Compensation for research-related harm: Research participants who suffer direct physical, psychological, social, legal or economic harm as a result of their participation are entitled, after due assessment, to financial or other assistance to compensate them equitably for any temporary or permanent impairment or disability. In case of death, participant's dependents are entitled to financial compensation. IEC shall ensure that the research proposal has an in-built provision for mitigating research related harm.

[Annexure 14, 15]

10. Addressing Serious adverse events as per applicable rules and regulations

- The researcher shall be responsible for reporting all SAEs to the EC within 24 hours of knowledge. Reporting of SAE may be done through email on non-working days. A report on how the SAE was related to the research must also be submitted within 14 days. IEC will also be responsible for reviewing the relatedness of the SAE to the research, using either WHO Causality Assessment Criteria or Naranjo Scale as reported by the researcher, and determining the quantum and type of assistance to be provided to the participants. For clinical trials under the purview of CDSCO, the timeline and procedures as notified from time to time may be followed.
- While deliberating on the quantum of compensation to be awarded to participants who have suffered research-related injury, the EC shall consider aspects including the type of research (interventional, observational, etc.), extent of injury (temporary/permanent, short/long term), loss of wages, etc. All AEs will be recorded and reported to the EC according to a pre-planned timetable, depending on the level of risk and as recommended by the EC.

[[Annexure 19]

11. Compensation for injury as per the rules and regulations with monitoring for noncompliance

The compensation amount in case of trial related injury [if deemed necessary] will be determined based on the guidelines provided by CDSCO as available at:

a. Formula to determine the quantum of compensation in case of clinical trial related serious adverse events [SAE] of deaths occurring during clinical trials: http://www.cdsco.nic.in/writereaddata/formula2013SAE.pdf
b. Formula to determine the quantum of compensation in case of clinical trial related injury [other than death]: http://www.cdsco.nic.in/writereaddata/ORDER%20and%20Formula%20to%20Determine%20the%20quantum%20of%20compensation%20in%20the%20cases%20of%20Clinical%20Trial%20related%20serious%20Adverse%20Events(SAEs)%20of%20Injury%20other%20than%20Death.pdf

The IEC report to CDSCO with regards to evaluation of any trial related/ unrelated serious adverse event shall specifically include that final decision of the Expert Committee, CDSCO be intimated to IEC also. In addition, the Principal Investigator, through Sponsor shall ensure that a copy of acknowledgment of compensation been paid to participant or LAR also be submitted to IEC for record purposes.

12. Addressing complaints and concerns of subjects

- The IEC requires, as a condition of approval of each project, that the investigator immediately report to it any concerns or complaints received with regards to the ongoing approved research project.
- The IEC shall also review complaints and concerns from trial participants.
- The Member Secretary will be the nominated person to receive such concerns and complaints from investigator as well as participants in research or members of the public about the conduct of projects approved by the IEC. He will be responsible for obtaining, in writing, the grounds of the concern or complaint that will be notified to the Chairperson, as soon as possible.
- Upon receipt of such complaint, Member Secretary will acknowledge to the complainant outlining the mechanism for investigating the concern or complaint.
- The Chairperson will examine the concern or complaint and determine whether the concern or complaint warrants a further investigation or not. Where there is to be no further investigation deemed necessary, the Chairperson will inform the complainant, through Member Secretary in writing about the same. All the members will be intimated of such episodes in the next Full

Committee/ Board Meeting and included in the Minutes of the Meeting too.

- Where the Chairperson determines that the concern or complaint warrants a further investigation, he/ she will notify the Head of the Institution of the same. He shall then form a Review Committee to investigate and determine the consequences. This committee would include EC Chairperson, Member Secretary, one EC member designated by Chairperson and one Subject Expert [where required].
- The Member Secretary will then issue a letter of notification to the PI of the concern or complaint about the project received by the IEC outlining the mechanism for investigating the concern or complaint. Where the complaint concerns the conduct of the any other person, Committee will also notify that person too.
- Clarification or answer from the Principal Investigator will be sought on the raised issue. If warranted, surprise research site visit may also be arranged by the members of EC.
- The Review Committee will immediately go for an investigation into the concern or complaint. The investigation will not take longer than 2 weeks from the time of notification for the concern or complaint to be addressed, unless exceptional circumstances exist.
- The Review Committee will give the complainant and the PI an opportunity to make submissions. Where the complaint concerns the conduct of any other person, the Review Committee will also provide that person with an opportunity to make submissions.
- The Review Committee may seek any other information it requires and may access any documents relating to the project, interview other people, and seek internal and external expert advice, as it sees fit.

Consequences

- The Review Committee will meet in person and if it is satisfied that the concern or complaint is justified, it will determine the consequences by considering the following matters:
    a. Severity of the matter
    b. Sensitivity of any information concerned including the amount and type of information and the level of identifiability
    c. Whether any breach of the approved protocol, which may be established, was inadvertent, negligent or unintentional
- The possible consequences will include the following:
    a. Noting on the file of the occurrence of the matter;
    b. Increased monitoring of the project;
    c. Counseling on security practices;

d. Amendments to the approved protocol;

e. Reporting the individuals responsible for any breach of ethics to the Head of the Institute, with a complaint of misconduct in the execution of the project;

f. Revoking of approval for the project

- The Chairman, Review Committee will notify the HOI the consequences in writing along with options for an appeal. The Chairman, Review Committee will also notify the Ethics Committee regarding the complaint received, investigation undertaken and the outcome of the investigation in next full committee meeting, which shall be minuted too.
- The IEC will then re-review the ethical approval of any project in the light of the outcome of the investigation of any breach of ethics or justifiable complaint and will notify the responsible PI & HOI if ethical approval for the project is to be revoked.
- The Chairman, Review Committee will also send a written report of the outcome of the investigation and the consequences to the complainant [whosoever] in writing.
- In cases of protocol deviation/ violation reported by the PI, they will be reviewed in the next Full Committee Meeting, unless any such deviation/ violation has a risk on participant wellbeing/ safety.
- In case of a risk on participant wellbeing/ safety, the Member Secretary will convene an Expedite Review Meeting to deal with the reported matter. Procedure for conduct of meeting, review, minutes as well as communication with the PI will remain the same as above.

STANDARD OPERATING PROCEDURE [SOP]

PROCESS OF REVIEW

Table of contents

1. Purpose

The purpose of this standard operating procedure (SOP) is to describe the initial review of research proposals prior to their initiation and regular monitoring of the approved research project to ensure ethical compliance during the conduct of research. By this the committee also ensures to safeguard the dignity, rights, safety and well-being of all research participants.

2. Scope

This SOP applies to all studies submitted to IEC for establishment of an appropriate and sustainable system for quality ethical review and monitoring.

3. Review by formal meeting

All proposals that are submitted for full committee review will be deliberated and the decision about the proposal will be taken at a full committee meeting. A meeting will be considered valid only

if the quorum is fulfilled. This will be maintained throughout the meeting and at the time of decision making. If a member has declared a conflict of interest for any research proposal, then it will be taken in writing by the Chairperson before beginning of the meeting and shall be recorded in the minutes of the meeting. The member who has declared conflict of interest will be asked to withdraw from the EC meeting (leave the room) while the research proposal is being discussed upon, if he/ she is not an investigatory. If the IEC Member is an investigator, he/ she shall be present for review process only. At the time of discussion amongst members and final decision, the concerned member shall leave the meeting. This will be minuted and the quorum rechecked. A list of absentee members as well as members leaving or entering in-between the meeting will be recorded. Proposals will be taken up item-wise, as given in the agenda. Number of proposals reviewed in a meeting will justify that there is ample time devoted for review of each proposal. If there are more number of proposals for consideration per meeting, meetings will be more frequently arranged to review them. Time allotted for the meeting will be reasonable to allow ample discussion on each agenda item. The minutes of the previous meeting and list of protocols that underwent expedited review will be ratified. The contents of the patient/participation information sheet including the local language translations back translations of the informed consent document in English, wherever required; provision for audio-visual recording of consent process, if applicable, as per relevant regulations; and if consent waiver or verbal/oral consent request has been asked for, this will be specifically reviewed.

Apart from research proposals taken for Full Committee/ Board Meeting, investigator [s] can submit their research projects any time to the IEC, in the same way as mentioned above, with justification as to why their research project should be considered for an expedited review.

Project [s] will be considered eligible for Expedite Review where they involve:

a. Minor amendments and extensions of approved protocols
b. Urgent amendments to approved protocols for safety reasons
c. Urgent proposal of national interest
d. Research on interventions in emergency situations i.e. epidemic
e. Research on Disaster management

Few examples that may be eligible for Expedited Review:

- Revised proposal with minor modifications previously approved through full review by the IEC
- 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 etc.

- Minor corrections in budget
- Other administrative changes in the investigator brochure, informed consent document etc.

Expedited Review [s] of research projects may be undertaken between scheduled meetings at the discretion of the Member Secretary, depending upon the need. The Member Secretary will be free to seek advice from other IEC members or suitably qualified experts, as appropriate [usually 2-3 members/ experts], before reaching a decision. Any research that is deemed to have potential risk/ raises ethical issue after such expedite review may be slotted for review in the next full committee meeting and the decision of the same will be communicated to the investigator, in hard as well as soft copy. Methodology for conduct of the meeting, review procedure, noting of minutes and communication with the PI will remain same as stated above. The decision and minutes of this review will be noted down for ratification at the next IEC meeting.

Any research with the potential for physical or psychological harm to the trial participant will generally be not considered for expedited review. This includes, and is not limited to, regulated clinical trials, research involving invasive physical procedures and research exploring sensitive personal or cultural issues. Where any research involves a departure from the ethical principles of integrity, respect for persons, beneficence and justice, the protocol will be considered in the Full Committee/ Board Meeting and not dealt with Expedited Review.

[Annexure 5, 5.1]

4. Initial review of proposed clinical trial

EC members will undergo initial and continuing training in Human Research Protection, IEC SOPs and related regulatory requirements. All trainings will be documented. The EC will perform its function through competent initial and continuing review of all scientific, ethical, medical and social aspects of research proposals received by it in an objective, timely and independent manner by attending meetings, participation in discussion and deliberations. Only the full committee will do initial and continuing review of such proposals. IEC may have empowered representatives from the specific populations during deliberations. Meetings of IEC shall be held on scheduled intervals as prescribed (once in 2 months, for which the dates will be finalized at the end of previous meeting). Additional meetings will be held as and when necessary especially for reported Serious Adverse Events and Expedite Reviews. Last date for receipt of new research proposals shall ordinarily be 3 weeks prior to scheduled meeting but never less than 2 weeks. IEC Manager is the software being

used by IEC for electronic submission. Apart from it, a hard copy [master file] of the whole proposal need to be submitted to IEC Office too. On receipt of hard copy as well as electronic version, IEC Co-ordinator shall forward the project [s] to Member Secretary. After MS review for completion of submitted documents, he/ she shall forward the project to all the members. About 2 weeks' time shall be ordinarily be given for each member to review the project. In case where a subject expert is needed, it shall be identified from already available pool of experts [within/ outside the institution] and the documents of the project shall even be forwarded to him. Primary reviewers may be identified for reviewing specific components of a given research proposal.

After initial review of the project, all members shall enter their comments/ suggestions in the online software that automatically reach the Member Secretary. Upon receiving suggestions from all the members, MS then prepares a consolidated suggestion sheet for forwarding it to the Principal Investigator.

PI will be available during the meeting and will be invited to offer clarifications. Decisions will be taken by consensus after discussions, and voting will be done if necessary. If a decision is reached by voting, specific comments of minority votes shall specifically be included in the minutes of meeting. The decisions of the meeting shall be recorded as minutes of meeting. It then shall be circulated on email to all members for suggestions or corrections, to be replied within a stipulated time frame. On receiving replies from all members, MS shall then finalize the minutes of meeting and put to Chairperson for signature. These minutes of meeting shall be archieved as a separate file and confirmed during the next meeting.

[Annexure 17, 18]

5. Review of informed consent document, assent form (as applicable) and translations

The informed consent process will be reviewed keeping in mind the following:

- The process used for obtaining informed consent, including the identification of those responsible for obtaining consent and the procedures adopted for vulnerable populations
- The adequacy, completeness and understandability of the information to be given to the research participants, and when appropriate, their LARs;
- Contents of the patient/participation information sheet including the local language translations;
- Back translations of the informed consent document in English, wherever required;
- Provision for audio-visual recording of consent process, if applicable, as per relevant regulations;

- If consent waiver or verbal/oral consent request has been asked for, this will be reviewed by assessing whether the protocol meets the criteria.

[Annexure 16]

6. Review of the informed consent processes

In a reviewed research project, verbal/oral consent/waiver of consent/re-consent may be obtained under certain conditions after due consideration and approval by the EC. It is the responsibility of the IEC to review and approve a request for verbal/written consent waiver. The Member Secretary will record this decision in the minutes. If the proposal has undergone expedited review, the waiver of consent will be granted only after full board review. The final decision whether to grant the waiver will be taken at a full board meeting unless the project is considered under expedited review. Criteria shall be as per existing ethical guidelines and regulatory requirements confirmed with entries as per predetermined checklists. The decision regarding approval / disapproval of waiver will be informed to the Principal Investigator in writing. If the waiver is not granted, the IEC will provide reasons for the same. In certain circumstances audio/audio-visual recording of the informed consent process will be required, for example in certain clinical trials as notified by CDSCO. These shall be approved as per the existing regulatory requirements for the same.

[Annexure 16]

7. Evaluation of recruitment strategies

Recruitment strategies will be evaluated to ensure equitable inclusion of participants without any skew towards particular patient population with regard to socio-economic class, gender or literacy. Particular emphasis will be placed on following aspects of recruitment strategies:

a. The characteristics of the population from which the research participants will be drawn (including gender, age, literacy, culture, economic status, and ethnicity)
b. The means by which initial contact and recruitment is to be conducted
c. The means by which full information is to be conveyed to potential research participants or their representatives
d. Inclusion criteria for research participants
e. Exclusion criteria for research participants
f. Students or staff recruitment in research
g. Healthy volunteers
h. Information contained in the advertisement and mode of its communication.
i. Final copy of printed advertisements

j. Final audio or video taped advertisements

k. Compensation being provide for travel as well as daily wages on case to case basis

[Annexure 10, 22, 23]

8. Evaluation of proposals involving special group and vulnerable population

Ethics Committee will evaluate the specific context-dependent characteristics that may place study participants at increased risk of being harmed or wronged (CIOMS). Ethics Committee will ensure special protections for groups considered to be vulnerable, including allowing for no more than minimal risks for research procedures that offer no potential individual benefits for participants, or requiring that the research be carried out only when it targets conditions that affect these groups. Ethics committee will enable the participation of vulnerable individuals by protecting their rights and interests through special safeguards and protections. The Member Secretary with Secretariat will maintain up-to-date tools, like checklists, for reviewing research concerning vulnerable groups based on new and evolving applicable regulations and guidelines. IEC Chairperson / Member Secretary will be responsible for ensuring that IEC members are well-versed in new and evolving regulations and guidelines pertaining to vulnerable populations, through regular training programmes. The Member Secretary/ Chairperson will be responsible for selecting primary reviewers with appropriate expertise to conduct the reviews of such research and for securing consulting expertise as and when required for selected reviews. IEC member will be responsible for conducting review of research planned for vulnerable populations, including an assessment of potential for coercion.

In such research projects, subject experts from identified pool within the institution or as the case may by specific population groups will be invited for the meeting. Subject expert will be selected from the ones who meet criteria as for specific EC member mentioned in EC composition. They will be asked to submit confidentiality and conflict of interest document prior to meeting and shall not have voting rights.

[Annexure 18]

9. Evaluation of budget with regards to indemnity, compensation, roles and responsibilities

IEC will review the proposed plan for tackling any medical injuries or emergencies. Source and means for compensation for study related injury will be ascertained. Plans for payment for participation, reimbursement of incurred costs, such as travel or lost wages, incidental expenses and other inconveniences will be reviewed. After the approval from IEC, the Sponsor/CRO will submit the Clinical Trial Agreement [CTA]/ Memorandum of Understanding and Indemnity Agreement document on Rs. 100 stamp paper separately (two copies) to the Institute which will be signed by sponsor and the CEO of the institution with the counter signature of PI. All CTAs shall be evaluated with

predetermined checklist to confirm required inclusions/ exclusions. The drug trial will be started by the PI after the agreement is signed by both the parties as well as DCGI and required regulatory approvals are available for the concerned trial.

IEC will approve travel costs to tune of Rs. 500/- [from within Anand District] and Rs. 1000/- [from outside Anand District] where actual travel bills are not available. In cases where actual bills are available, the same amount would need to be reimbursed to a maximum of a specific amount as agreed with Sponsor and mentioned in CTA.

[Annexure 17, 18]

10. Review of amendments to the originally approved protocol, consent forms and investigators brochure

a. Post decision communication

After review of any research protocol, IEC will give one of the following decisions:

- Letter of suggestions – for revision with minor modifications/amendments
- Approval with or without mandatory regulatory instructions [as the case may be]
    - Approval will be given after examination by the Member Secretary or expedited review, as the case may be;
- Revision with major modifications for resubmission
    - This will be placed before the full committee for reconsideration for approval; or not approved (or termination/revoking of permission if applicable)
- Disapproval/ revoking of permission
    - Clearly defined reasons will be given for not approving/ terminating/ revoking of permission.

b. Amendments submitted

Amendments will be incorporated in the proposal(s) to align to the research needs arising from the emergency including issues related to re-consent from participants. IEC will ensure that the clinical trials should be conducted in accordance with the ethical principles described in these guidelines, Indian GCP as well as applicable regulations for medical and medicated devices, that is, GSR 78 (E) dated 31.1.2017 or as per amendments/modifications issued from time-to-time.

- Any proposed changes to approved projects will require to be reported by the PI to the IEC for review. All amended documents [submitted in hard as well as online] will have the changes highlighted and contain revised version numbers and dates [where applicable]. Additionally, summary of changes outlining the nature of the proposed changes, reasons for the changes, and an assessment of any ethical implications arising from the request on the conduct of the research

will also need to be submitted.

- Expedited Review of requests for minor amendments and urgent amendments to approved protocols for safety reasons may be undertaken by the Member Secretary between scheduled meetings at the discretion of the Chairperson [as above], which will be ratified at the next IEC meeting. MS shall ensure that such requests do not hamper patient safety and fall within the ambit of IEC mandate for expedited reviews.
- All other requests for amendments will be reviewed by the IEC at its next scheduled Full Committee/ Board meeting, provided the request has been received by the Member Secretary by the agenda closing date. The procedure of review of amendment shall remain the same as to be followed for reviewing a new research project.
- The decision of the IEC will be communicated in writing to the PI, advising whether the proposed amendment and/or request for extension has been given ethical approval within 15 working days of the meeting at which the request was considered [this may be the Full Committee meeting or Expedited Review Meeting].
- Notification of the approval of amendments and extensions will be conveyed in writing in the standard format as per Schedule Y [as stated above].
- If the IEC determines that further information, clarification or modification is required for the consideration of the request for amendment or extension, the correspondence to the investigator will clearly articulate the reasons for this determination, and will clearly set out the information that is required.
- All received and approved requests for amendments and extensions will be recorded, and the status of the project updated in the IEC's data of received and reviewed applications.
- In cases of re-consenting or use of newly updated consent forms, IEC shall ask for submission of a copy of re-consented document or a copy of newly update consent form.

[Annexure 18]

11. Periodic review of trial

IEC will review the ongoing research at six-month interval (or more often, if deemed necessary depending on the level of risk). It will make sure that the progress report, safety report [s] and the final reports will be submitted at the regular intervals.

- Progress reports:
  - In those cases, where the IEC has requested the submission of progress reports, these will be submitted to the IEC, generally within six weeks of the anniversary of the IEC approval.

- The progress report consists of a simple declaration notifying the IEC of any ethical problems or adverse events which may have occurred during this period.

- SUSAR & CIOMS Reports:
  - IEC expects to be regularly updated with SUSAR and CIOMS reports of ongoing trials indicating adverse events or newly identified risk factors at other sites or any relevant published data in reference to the investigational drug
- Safety reporting:
  - A Serious Adverse Event (SAE) occurring to a research participant will be reported to the IEC as per existing regulatory requirements.
- Protocol deviations and violations:
  - In case where deviation/ violation from or changes to the protocol [s] occur, they are to be reported by the PI within 15 days of such deviation/ violation.
  - Along with its report, it needs to be clearly stated whether such protocol deviation or violation has/ had any impact on participant safety and what measures have been initiated by PI to ensure that such deviations or violations are prevented in future.
- Final reports:
  - The IEC will receive a final report as soon as the research gets completed.
  - It would include information on whether the study achieved its objectives, the main findings and arrangements for publication or dissemination of the research including any feedback to participants.

[Annexure 10]

STANDARD OPERATING PROCEDURE [SOP]

DECISION MAKING AND POST REVIEW ACTIVITIES

Table of contents

1. Purpose

The purpose of this Standard Operating Procedure (SOP) is to describe how the Institutional Ethics Committee (IEC) members will objectively reach to a decision after full review of a submitted research project and perform post review activities.

2. Scope

This SOP applies to the initial review and assessment of all research study protocols submitted for review and approval from the IEC, amendments, SAE Review, handling of complaints as well as expedite reviews.

3. Decision making process

The Member Secretary will appoint two or more primary reviewers for each study on the basis of expertise in the related field and experience. They should include one clinician and one non-technical person as applicable. More than two may be appointed, if necessary.

Primary reviewers will have to mandatorily review the assigned protocol and put forth their comment [s] first at the review meeting. The protocol will be reviewed by the member [s] as per guidelines to review a study protocol with existing checklists.

An IEC member will consider the following criteria when performing the review of the study protocol and the study related documents:

- Scientific design and conduct of the study
- Investigators brochure about the trial product
- Risks and potential benefits
- Selection of study population and recruitment of research participants
- Inducements, financial benefits, financial costs, provision of compensation
- Data analysis and reporting
- Protection of research participants' privacy and confidentiality
- Community considerations [availability of the investigational product after trial is over]
- Qualifications of Investigators and assess adequacy of study sites
- Disclosure or declaration of potential conflicts of interest
- Compliance to national and international guidelines and existing regulatory requirements

An IEC member will consider the following criteria when performing the review of the Informed Consent Document [including assent]:

- Voluntary, non-coercive recruitment, participation/ withdrawal
- Procedures for obtaining informed consent
- Contents of the patient information sheet - title, objective, study design and procedures
- Contents and language of the informed consent document
- Translation of the informed consent document in the local languages
- Language used – plain and easy to understand by general public
- Contact persons with address and phone numbers for questions about research participant' rights and study or injury
- Privacy and confidentiality of study participants
- Risks and discomforts – physical / mental / social of study participants
- Alternative treatments availability [their efficacy or toxicity]
- Benefits – to participants, community, institution and society
- Compensation for participation (whether it will act as undue inducement)

- Involvement of vulnerable participants
- Provisions for medical/ psychosocial support
- Treatment for study related injuries
- Compensation for study-related injuries: as per applicable local regulations
- Use of biological specimens for research purposes
- Check for provision for signatures with dates of participant, person conducting informed consent discussion, investigator and witness
- Provision for audio visual recording of consent process in case of regulatory drug trials

4. Participant recruitment process

Recruitment strategies will be evaluated to ensure equitable inclusion of participants without any skew towards particular patient population with regard to socio-economic class, gender or literacy. Particular emphasis will be placed on following aspects of recruitment strategies:

a. The characteristics of the population from which the research participants will be drawn (including gender, age, literacy, culture, economic status, and ethnicity)
b. The means by which initial contact and recruitment is to be conducted
c. The means by which full information is to be conveyed to potential research participants or their representatives
d. Inclusion criteria for research participants
e. Exclusion criteria for research participants
f. Students or staff recruitment in research
g. Healthy volunteers
h. Information contained in the advertisement and mode of its communication.
i. Final copy of printed advertisements
j. Final audio or video taped advertisements

5. Conflict of interest declaration including voluntary withdrawal during decision making process

- In cases of declared conflict of interest [of member/ investigator], the IEC will determine whether a conflict of interest does exist or not, and if it exists, will require the member to withdraw from the meeting until the IEC's consideration of the relevant matter has been completed. The concerned member [s] will not be permitted to adjudicate on the research or be part of the decision making process and shall be asked to be out of the meeting hall.

[Annexure 2.1]

- All such declarations of conflict of interest and the absence of the member concerned will be noted in minutes of the meeting.

6. Basis of decisions for the initial and periodic approvals

Based on above, members will fill out the respective checklists and write their comments related to review of the research proposal. The duly filled, signed and dated assessment forms will be submitted during the full committee meeting. The IEC Secretariat will collect the checklists, review forms from each reviewer and file in the original study file.

During the discussion at the meeting:

- The primary reviewer shall brief the members about summary of the study protocol and read out the comments and evaluation provided on the review form [s].
- The comments of an independent subject expert (if applicable) will be put forth by the Member Secretary.
- The other IEC members shall give their comments right after the presentation.
- The investigator/sub-investigator shall always be called in to provide clarifications on the study protocol that he/she has submitted for review to the IEC.
- The IEC members will discuss and clarify the comments and suggestions.
- The Member secretary (assisted by the Secretarial staff) shall record the discussions
- The final decision on the study will be recorded as either Approved/ Disapproved/ Suggested to comply or any other (as per a given instance) in the meeting and shall be made by voting or by majority consensus and will be recorded in the IEC Minutes of the meeting. Voting or consensus shall be recorded by asking the members to raise their hands, if consenting to the decision put forth [approval/ rejection/ compliance].
- 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.
- The following will not be eligible to vote:
    - Member(s) of the committee who is/are listed as investigator(s) on a research proposal
    - An investigator or study team member invited for the meeting.
    - The Subject Expert invited for the meeting to provide opinion
    - Specific patient groups invited for the meeting will not vote or participate in the decision making procedures of the committee.

The Committee will decide whether responses to IEC queries and (if applicable) revised protocol will go only to Member Secretary, to primary reviewers or to Full Board before final approval. The response and changes carried out may be considered for discussion at a future IEC meeting. If the IEC decision is 'Disapproved' or any other, the decision should be made on the basis of specific reasons, which are communicated by the IEC to the principal investigator in the letter of notification.

7. Approval of deliberations and decisions during the meetings and maintenance of minutes of meeting.

- The Secretariat will obtain the signature of all the members and of the Chairperson of the IEC on the IEC Meeting Attendance List during each meeting. If the study is approved, the Committee will recommend additional monitoring for a study if it is so determined at the meeting depending on factors like risk is high in the protocol, the PI has a history of repeated protocol violations, PI has many protocols and any other reason so deemed.
- The Secretariat will list participating members in the meeting and summarize the guidance, advice and decision reached by the IEC members. With the study protocol, the relevant checklists and review forms from all members will be filed in the study file by the Co-ordinator.
- It will be the duty of Member Secretary to prepare and maintain minutes of all meetings of the IEC. The format will include: Attendance of members, brief agenda, notification of approval of minutes of previous meeting, Suggestions for new proposals/ amendments, conflicts of interest, if any, monitoring reports, if any and any other issues [e.g. any expedited review undertaken/ concerns or complain received etc.], if required.
- The minutes will also include the recording of decisions taken by the IEC as well as a summary of relevant discussion. This will include reference to views expressed by absent members also, if necessary. In relation to the review of new applications or amendments, the minutes will record a summary of the main ethical issues considered [if any apart from expected elements of review], including any requests for additional information, clarification or modification of the project etc.
- While recording a decision made by the IEC after voting [in a particular case], any significant minority views (i.e. 2 or more members) if any, will also be noted in the minutes. To encourage free and open discussion and to emphasis the collegiate character of the IEC, particular views will not attribute to particular individuals in the minutes, except in circumstances where a member seeks to have his/her opinions or objections recorded.
- Declarations of conflicts of interest by any member of the IEC and the absence of the member concerned during the IEC consideration of the relevant application will be included in the minutes

too.

- The minutes will be circulated to all, following the respective meeting on email and any suggestions/ corrections sought. Corrections/ suggestions [if any by members] will be incorporated and approved by Chairperson/ Deputy Chairperson. The same will be officially read out in subsequent meeting for approval by all the members; which again will be recorded in the minutes of that particular meeting.
- The original copy of each meeting's minutes will be retained in a confidential 'Minutes of meeting' file at the IEC Office.

8. Protocol deviations and non-compliances shall be evaluated and appropriate actions shall be taken as per rules & regulations

- In case where deviation/ violation from or changes to the protocol [s] occur, they are to be reported by the PI within 15 days of such deviation/ violation.

  A protocol deviation occurs when the activities during a study diverge from the IRB - approved protocol; a variance from protocol

  Examples of protocol deviations:

  - Vital signs obtained prior to informed consent
  - Weighing participant with shoes on
  - Urine dipstick is completed, but not sent for formal U/A
  - Targeted physical exam documented instead of complete PE
  - Conjugated bilirubin, part of the protocol, is left off the lab request form, but total bilirubin was drawn and is normal

  A protocol violation occurs when there is divergence from the IRB - approved protocol (a deviation) that also: – reduces the quality or completeness of the data impacts a subject's safety, rights or welfare – affects the scientific integrity

  Examples of Protocol Violations

  - Inadequate informed consent
  - Enrolment of subjects not meeting the inclusion /exclusion criteria
  - Initiation of study procedure prior to completion of informed consent
  - Unreported SAE's
  - Improper breaking of the blinding of the study
  - Use of prohibited medication
  - Incorrect or missing tests

- Mishandled samples
- Multiple visits missed or outside permissible windows
- Inadequate record – keeping
- Intentional deviation from the protocol, GCP or regulations by study personnel in a non - emergency setting
- Repeated noncompliance by the subject
- Repeated deviations of the same nature
- Falsification

- On the other hand, if any deviation is needed to be implemented without prior written approval of Ethics Committee [as in to eliminate immediate hazards to the trial subject (s) or when change (s) involve (s) only logistic or administrative aspects of the trial], they should be notified to the Ethics Committee within 30 days of such deviation/ change in protocol [time limits subject to change as per the latest regulations].
- All such deviations/ violations reported will clearly indicate the effect of such deviation has any adverse effect on participant safety or not?

The IEC requires, as a condition of approval of each project, that the researchers immediately report any deviation or violation of protocol with regards to the ongoing approved research project. In cases of protocol deviation/ violation reported by the PI, they will be reviewed in the next Full Committee/ Board Meeting, unless any such deviation/ violation has a risk on participant wellbeing/ safety. In case of a risk on participant wellbeing/ safety, the Member Secretary will convene an Expedite Review Meeting to deal with the reported matter. Procedure for conduct of meeting, review, minutes as well as communication with the PI will remain the same as above. Depending upon the deviation or violation risking patient safety or PI misconduct, appropriate action shall be undertaken as per existing regulatory guidelines and actions as listed earlier in process of review.

9. Analysis and reporting of Serious Adverse Events

A Serious Adverse Event (SAE) or Serious Adverse Drug Reaction (SADR) refers to an adverse event (AE) or adverse drug reaction (ADR) that is associated with death, inpatient hospitalization (in case the study was being conducted on out-patients), prolongation of hospitalization (in case the study was being conducted on in-patients), persistent or significant disability or incapacity, a congenital anomaly or birth defect, or is otherwise life threatening.

Any injury or death of the subject occurring in any approved research project [including clinical

trial] due to following reasons will be considered as clinical trial related injury or death and the subject or his/ her nominee (s), as the case may be, are entitled for financial compensation for such injury or death *[7 criteria as mentioned under Rule 122 DAB and Appendix XII of Schedule Y to the Drugs and Cosmetics Rules]*:

a. adverse effect of the investigational product [s]
b. violation of the approved protocol, scientific misconduct or negligence by Sponsor or his representative or the investigator
c. failure of investigational product to provide intended therapeutic effect
d. use of placebo in a placebo-controlled trial
e. adverse effects due to concomitant medication excluding standard care, necessitated as part of approved protocol
f. for injury to a child in-utero because of the participation of the parent in clinical trial
g. any clinical trial procedures involved in the study

Reporting of a SAE:

1. Principal Investigator will, within 24 hours, report [by telephone/ email/ in hard copy to the Chairperson, IEC] all Serious Adverse Events in clinical trials to the IEC in accordance with the reporting conditions required by Schedule Y, Drugs and Cosmetic Rules, 1945 [Subparagraph (3) relating to the 'Responsibilities of the Investigator (s)] as per Appendix XI of the said rules.
2. In case there is a holiday/ weekend on the day of electronic reporting, PI will report the same in hard copy on next 1st working day.
3. The Sponsor and Investigator are expected to forward the reports on all the serious adverse event [s], after analysis to the Ethics Committee and Head of the Institution [CAM], along with a copy of the report to the Licensing Authority within 14 calendar days after occurrence of the serious adverse event [s] of death
4. The same [serious adverse events and the response to those events] will be included in the periodic and final reports for the project also.

IEC Analysis, Causality Assessment & Justification and Opinion:

1. In case of serious adverse event occurring to the clinical trial subject, the IEC will convene either a Full Committee/ Board Meeting or SAE Sub-Committee [if it exists] meeting within 30 days of date of reporting by PI.

2. As stated earlier, to complete a quorum, minimum of 5 [five] members [as per Schedule Y] will be required for the meeting to review the SAE.
3. The reported SAE will be reviewed in presence of PI or Co-Investigator [Co-I]. [If none of the investigator [s] attends the meeting, the Committee will review the matter based on available documents. If deemed necessary, the Committee may approach the participant or his/ her legally acceptable representative, before arriving at any decision. In such an event, the decision of the Committee will be binding to the PI and Sponsor].
4. Necessary document [s] will be reviewed and investigator may even be asked to submit a copy of relevant documents too.
5. The Committee will ensure during the review that trial participant has been provided with adequate medical care as per applicable rules and regulations. For the same, it may even direct the Sponsor to bear the costs of the medical treatment of reported SAE till it is proved that current medical condition has no relation the trial in question [as per current CDSCO Regulations].
6. Causality assessment & justification will be done using WHO/ Naranjo Causality Assessment Tool.

[Annexures 11, 12]

7. As usual, minutes of meeting will be prepared by Member Secretary [with all required elements as stated above and additional SAE reporting requirements] and got approved by the SAE Sub-Committee Members.
8. Once minutes approved, IEC Report will be prepared and forwarded to CDSCO with its recommendations so as to reach it by mail/ post within 30 days of reporting of the SAE.

[Annexure 13]

   a. The report will include copy of Appendix XI, Duly Analysis Report by Investigator, Sponsor's Report, WHO/ Naranjo Causality Assessment Tool [with signatures of attending members] and Minutes of Full Committee/ Board or SAE Sub-Committee Meeting wherein the SAE was reviewed.
   b. The report will also include a request to Expert Committee [for review of SAE at CDSCO] to forward a copy of its decision for record purposes.
   c. In case the Expert Committee decides to award compensation to the study participant/ legally acceptable representative, the committee will request to be provided an acknowledgement of disbursement of compensation for confirmation and record purposes.

8. The compensation amount [if deemed necessary] will be determined based on the guidelines provided by CDSCO as available at:

a. Formula to determine the quantum of compensation in case of clinical trial related serious adverse events [SAE] of deaths occurring during clinical trials; http://www.cdsco.nic.in/writereaddata/formula2013SAE.pdf ***[Annexure 14]***

b. Formula to determine the quantum of compensation in case of clinical trial related injury [other than death]; http://www.cdsco.nic.in/writereaddata/ORDER%20and%20Formula%20to%20Determine%20the%20quantum%20of%20compensation%20in%20the%20cases%20of%20Clinical%20Trial%20related%20serious%20Adverse%20Events(SAEs)%20of%20Injury%20other%20than%20Death.pdf ***[Annexure 15]***

10. Notification of all decisions/opinions to the stake holders especially investigator [s]

- Following online review by members of IEC, a query letter prior to the scheduled meeting may be sent online through eEC Software, where needed.
- After the review meeting, The IEC will report in writing to the Principal Investigator (PI) the decision of the committee after the minutes are approved by all members and signed by the Chairperson/ Deputy Chairperson. A copy of the same will also be sent through eEC Software too.
- If the IEC determines that further information, clarification or modification is required for the consideration of a project, the correspondence to the PI will clearly articulate the reasons for this determination, and clearly set out the information that is required.
- If the requested information is not received from the applicant within 3 months of issue of suggestion letter, the project may be dismissed and the applicant will be required to resubmit the project at a later date as fresh application.
- Once a compliance to suggestions of reviewed proposals is received, it will be the discretion of the Member Secretary to get the re-submission reviewed by one/ more members of IEC without convening a Full Committee/ Board Meeting ***[Annexure 8]***
- After receipt of the comments of the IEC members, depending upon them, approval may be granted to the concerned research project.
- In all cases, IEC will notify the PI of the ethical approval of a project only when all outstanding requests for further information, clarification or modification have been satisfactorily resolved. Ethical approval letter will be issued in Schedule Y Format, Appendix VIII [2].

[Annexure 9]

  - Under no circumstance, IEC shall approve a study, pending approval from regulatory

authorities. No conditional approvals are to be given for want of required documents

- The approval letter shall clearly state that PI needs to submit the copy of ICD of 1st participant screened/ recruited into the study to ensure that participants are included only after submitted protocol is approved by IEC.

- If the IEC determines that a project is ethically unacceptable or the approval needs to be revoked, the notification of the IEC's decision will include the grounds for the same while communicating to the PI, in hard copy as well as soft copy.
- The status of the projects will be regularly updated in the IEC's data of received and reviewed applications for record purposes.
- Communication from IEC to Investigator regarding decision on the proposal will ordinarily be done within 15 working days after review of the application in the full committee/ in cases of Exempt from Full Committee/ in cases of Expedite Reviews/ in cases of case report or series.

STANDARD OPERATING PROCEDURE [SOP]

MONITORIING OF RESEARCH PROJECTS

Table of contents

1. Purpose

The purpose of this standard operating procedure (SOP) is to describe the procedures for continuous monitoring of an Institutional Ethics Committees (IEC) approved research project.

2. Scope

This SOP applies to all IEC approved studies for which a routine or for-cause on-site monitoring may be undertaken by the IEC.

3. Monitoring participant's rights, safety and wellbeing

It will be the responsibility of the Full Committee to decide and conduct continuous monitoring of an approved research project. It will be further the responsibility of the designated IEC member(s) to perform on-site monitoring of selected study site(s).

A. Selection of study sites

Routine monitoring for a site may be decided at the time of approval of the project by the full committee. This may be recorded in the IEC decision and in the IEC minutes of the meeting.

B. Before the visit

Irrespective of the cause for conducting monitoring, the following procedure will be followed:

a. The Chairperson will identify and select one or more IEC members (henceforth referred to as monitors) to conduct monitoring of a site.

b. The agenda of monitoring will be decided by the identified monitors in consultation with the

Member Secretary and Chairperson

c. The Member Secretary will decide the date of the monitoring in consultation with the monitors and the PI.
d. The final date will be communicated to the PI (with a request to be available) and monitors.
e. The Member Secretary will provide Monitors with relevant reference material / documents related to the project for review.
f. Monitors will carry with them Site Monitoring Visit Report Forms from IEC Office for documentation of the monitoring findings.

C. During the visit

The Monitor will follow the check list and during the monitoring will:

a. 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.
b. 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),
c. check for storage times, conditions and expiry dates to be acceptable and sufficient supplies available, wherever applicable,
d. verify that the investigator follows the approved protocol and all approved amendment(s), if any,
e. ensure that the investigator and the investigator's trial staff are adequately informed about the trial,
f. 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,
g. verify that the investigator is enrolling only eligible subjects, [1st as well as subsequent ones from recruitment log],
h. 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,
i. review the project files of the study to ensure that documentation is filed appropriately,
j. review the source documents for their completeness,

k. check for unreported protocol deviations or violations,

The Monitor will fill the Site Monitoring Visit Report Form, sign and date it.

[Annexure 10, 22, 23]

4. Ensuring adequacy and continuity of consent process

The monitor will:

a. observe the informed consent process, if possible,

b. review randomly selected participant's files to ensure that participants are signing the correct informed consent

c. may even interview, if participant is available

[Annexure 10.1]

5. Conduct of For-cause assessments following non-compliance and/or complaints for the trials approved by the ethics committee

"For-cause monitoring" will be performed at sites for reasons identified by any member of the IEC, after approval by the Chairperson. The reasons for identifying a particular site for "for-cause monitoring" could include any one or more of the following:

a. High number of protocol deviations/ violations

b. Repeated Serious Adverse Events (SAE) reports in a trial

c. Too many SAEs for a particular investigator over a period

d. High recruitment rate

e. High number of instances requiring active observation

f. Complaints received from participants or any other person

g. Frequent failure to submit the required documents

h. Any other cause as decided by IEC

6. Identifying opportunities for improvement and actions to be initiated

After the on- site visit by the monitor

i. The Monitor will submit the completed Site Monitoring Visit Report Form to the IEC Member Secretary within 7 working days of conducting a site monitoring visit or at the time of full board meeting (whichever is earlier).

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

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

iv. 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:

1. Continuation of the project with or without changes,
2. Restrictions on enrollment
3. Recommendations for additional training
4. Recruiting additional members in the study team
5. Revising/ providing qualifications/ experience criteria for members of the study team, termination of the study, suspension of the study, etc.

v. 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 to decide on the suitable action to be taken.

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

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

viii. The Member Secretary will place the copy of the report in the protocol file.

Measures apart from active monitoring

The Committee can call for and discuss information on any relevant aspect (s) of the project with the investigator (s) at any time. In particular, the Committee may require investigators to provide interim reports on stipulated dates and a final report at completion of the study.

1. The Committee may ask for the following information in the report:
   - Progress to date, outcome/ results and publications/ presentations in the case of completed research
   - Maintenance, security, confidentiality and integrity of records and data
   - Compliance with the approved protocol
   - Compliance with any conditions of approval
   - Changes to the protocol or conduct of the research
   - Changes to the personnel of the PI /other investigators and
   - Serious Adverse events or complaints relating to the project
2. The Committee will require, as a condition of approval of each project, that investigators immediately report anything which might warrant review of ethical approval of the protocol, including:

- proposed changes in the protocol
- any unforeseen events that might affect continued ethical acceptability of the project new information from other published or unpublished studies which may have an impact on the continued ethical acceptability of the trial, or which may indicate the need for amendments to the trial protocol.

3. The Committee will also require, as a condition of approval of each project, that investigators inform the IEC, giving reasons, if the research project is discontinued before the expected date of completion, and that the investigators comply with the approved protocol.
4. The Committee will ensure that adequate information with regards to rights and responsibilities of research participants are displayed at relevant sites too.
5. At the end of each financial year, before preparing its report to the Appointing Authority, the Committee will require all investigator [s], whose projects have been approved in the preceding year, to declare to the Committee, in writing the status of their ongoing research projects.

STANDARD OPERATING PROCEDURE [SOP]

ADMINISTRATIVE SUPPORT

Table of contents

1. Purpose

To provide instructions for establishment and maintenance of IEC Office for its day to day functioning

2. Scope

This SOP applies to IEC Secretariat, investigators and IEC Members

3. Ensuring adequate finance, human resource allocation and secretariat for administrative work and record keeping

- It shall be the duty of the Appointing Authority to provide a separate office and record room for regular functioning of the committee
- An Office Co-ordinator/ Assistant shall be appointed to manage daily work of the IEC. As per existing regulatory requirements, IEC shall have sufficient members to maintain quorum.
- Additional staff may be appointed and duties assigned; as and when deemed necessary by the IEC.
- The eligibility criteria for new staff to be appointed will be laid down depending on the required job profile. The need for appointment of administrative staff, job profile and qualifications, office timing, salary structure and number of leaves may be recommended by IEC members and discussed during regular IEC meeting and will be recorded in minutes
- The administrative staff will report to the Chairperson and/or Member Secretary.
- A separate room within the institution shall be identified for meeting [s] of the committee.

- Office of the IEC shall be well equipped with tables, chairs, computer [with required software], printer, telephone, internet facility, shredders and steel lockable cupboards for its efficient functioning. Any additional requirement too shall be fulfilled depending upon the need.
- Preferably, a separate room shall be provided to facilitate archival and retrieval of documents. Regular pest control measures shall be undertaken in accordance with regulatory requirements with ensured fire safety measures. Steel lockable cupboards shall be used to store the documents.

4. Financial dealings of Ethics Committee activities and functioning

Incomes and Expenditures towards functioning of the committee

1. Standard fee will be charged for review of research proposals submitted by the investigators of the institution [HMPCMCE] for review in case of Industry Sponsored Clinical Trials.
    a. IEC fees for Clinical trials:
        - Rs. 50,000/- for initial review of each protocol
        - Rs. 5,000/- for review of each amendment
            - The revised fee structure will be applicable to new clinical trials submitted on or after 1st August 2017
2. Research projects initiated and submitted by investigators outside the institution [HMPCMCE] but to be conducted within the Centre will be accepted only after written permission granted by Institutional Research Group [on hard copy of the research proposal]
3. Research projects initiated and submitted by investigators outside the institution [HMPCMCE] and also to be conducted outside the institution will not be accepted for review EXCEPT when the participant [s] to be recruited are from HMPCMCE institutions.
4. Research proposal review fees will need to be deposited in favour of **"Charutar Arogya Mandal"** having PAN No: AAATC 1264G, payable at Anand, Gujarat.
5. No member is expected to receive any remuneration, in either cash or kind, from any investigator or industry involved in the research proposal to be reviewed. Conflict [s] of interest, if any, will be declared prior to review as mentioned earlier and if required, depending upon the conflict of interest, will not be part of decision making during review process.
6. Expenses towards conduct of the meeting [s] will be borne by the Centre.
7. A statement of all income and expenditure [including honorarium to internal as well as external members] will be made available to IEC Office for records purposes at the end of each financial year by the Centre.

Honorarium to the Members

Reimbursement of travelling expense and /or reasonable honorarium for attending the IEC meetings will be given to the Chairperson, External Members and Member Secretary as decided by the appointing authority.

5. Procedure for communication between ethics committee, investigator/ relevant site staff, institution and regulatory authority

- Any new project shall be submitted to IEC in Annexure [s] 5, 5.1, 5.2, 5.3, 5.4, 5.5. This includes application, protocol, informed consent documents in English as well as vernacular language. Apart from them, an investigator may submit checklists as per relevant annexures
- All projects need to be uploaded into IEC Software www.iecmanager.org/institution/15 after PI getting duly registered with it.
- Once registered, a PI can upload the necessary documents into the online software. At the same time, one hard copy of all the relevant documents too shall be submitted to IEC as Master file.
- Upon submission, an inward number gets generated. On uploading the inward number into the system, MS can forward it to all the IEC Members for review.
- Online system facilitates the receipt of suggestions from IEC Members after review. These suggestions are then combined and passed on to the PI through email.
- This process shall routinely be completed at least a week before the scheduled meeting.
- After the meeting, PI shall be intimated of IEC decision on both, IEC Software as well as hard copy, after generating outward number.
- The response from PI again has to be through online software as well as one hard copy.
- Apart from PI, all communications to all other stake holders [Appointing authority/ Regulatory Authority etc. shall be made via email/ hard copy.
- Principal Investigator shall be required to update/ communicate IEC for any amendments, adverse events, serious adverse events, 1st recruitment in a new trial, sponsor's site visit report, interim/ yearly updates, compliance to monitoring visits etc. in one hard copy as well as in soft copy.

[Annexure 8, 9, 13]

Preparing an annual activity report of the IEC for submission to the Head of the Institute

The Member Secretary will make a yearly activity report for submission to the Head of the Institute that will include the following elements:

1. Number and dates of the IEC meetings of full committee

2. Number of SAE subcommittee and any other subcommittee (as applicable)
3. Number and type of proposals (Pharma/ Government sponsored/ Registry/ investigator initiated collaborations with foreign universities or international organizations) reviewed in a year, status of each study proposal whether completed / ongoing / terminated
4. Number of approvals for full board review/ expedited review with decisions
5. Brief details about workshops, training programmes and other activities undertaken by the IEC and those attended by IEC members
6. Monitoring reports [if any relevant]
7. Self-assessment report [s]
8. Any other relevant matter/ suggestions

6. Procedure post accreditation and registration

- IEC shall undertake assessment for Accreditation, when necessary.
- All communications with Accreditation Authority shall be done by Member Secretary, in consultation with Chairperson and Head of Institution
- Expenses for Accreditation shall be borne by the institution
- Once accredited, IEC Office shall ensure timely communication with Accreditation Authority for Surveillance Assessment or Re-Accreditation
- Same procedure would apply for Re-registration with CDSCO
- All documents pertaining to Accreditation and Registration shall be archieved at IEC office.

STANDARD OPERATING PROCEDURE [SOP]

RECORD KEEPING AND ARCHIVAL

Table of contents

1. Purpose

To provide instructions for preparation and maintenance of active study files and other related documents presented to the IEC and storing of closed files and retrieval of documents.

2. Scope

This SOP applies to all protocol/study files and their related documents that are maintained in the IEC office and closed files.

3. Review of security, confidentiality and integrity of all proposals and associated documents and maintenance of administrative communication

- All efforts will be made to keep the records under lock and key for maintaining security, integrity and confidentiality using lockable steel cupboards [soft copies to individual members over online software is only visible/ accessible in their dashboard till a decision is not made by Member Secretary; post a decision, no member will have any access to previous research records online].
- Access to the keys of locked steel cupboards will be available only to Co-ordinator and Member Secretary. Fire safety measures will be in place along with regular pest control practices on the lines of Medical Records Department of the institute.
- The Office will maintain register of all projects/ requests submitted along with a register of all its Communications with stake holders [inward as well as outward register]
- Systems department of the institute will be responsible for maintaining the backup of email communications of the IEC email account [s].
    - The register will preferably include:

- Protocol number [as per the inward number generated on submission of application along with date]
- Name [s] of Principal Investigator/ Co-Investigator
- Title of the project
- Ethical approval or recommendations for modifications or rejections with date
- Approval or otherwise of any changes to the project proposed by the researcher
- The terms and conditions if any, with approval of the project
- Whether review/ approval was by Full Committee or Expedited review
- Any action taken by the IEC, while monitoring the conduct of the research
- Communication with external agencies and Appointing Authority
- Any other communication with investigator [s] or stakeholder [s]

- With the use of online software for submission, review, communication and decision of the Committee, the Co-ordinator will function as IEC admin to regulate the use of online software for Committee purposes.
- Apart from online submissions, one hard copy of all the research projects [including amendments, SAE reports etc.] will be maintained by the Committee Office as Master file.
- The physical records [master file] will contain a hard copy of the application, any relevant correspondence between the applicant, other stake holders and the Committee, other material used to inform potential research participants and all approved documents.
- All documents of the IEC, including applications, membership, minutes of meeting and correspondence will be kept confidential and in accordance with Schedule Y and ICMR guidelines.
- Apart from above archival would also include monitoring reports, copy of communication with other stakeholders, self-assessment documents, accreditation related documents and any other relevant communication/ record depicting IEC work.
- To ensure confidentiality, all documents provided to IEC members, which are no longer required, will be disposed of in a secure manner, such as shredding or incineration. A register depicting record of the same will be maintained.

4. Archival of documents and records

- This will be done, preferably in a room available for archival of records, separately from IEC Office
- It will be the responsibility of IEC staff to ensure that all study files are prepared, maintained, and kept securely for a period of 5 years after the closure of the project (under a proper system that

ensures confidentiality and facilitates retrieval at any time) [time period to vary depending upon the existing regulatory requirements from time to time].

5. Record retrieval policies and procedures

- Master files will be made available only after receiving the request in writing.
- This access to the records will be available only to Member Secretary and the Co-ordinator of the Committee during instances like requests from appropriate authority/ internal or external audit or accreditation team/ PI for duplicates etc.
- In case, any investigator needs a copy of any document from the master file, he/she should make a written request. After due approval from Member Secretary [usually within a week of getting the request], Co-ordinator will furnish a copy of the required document.
- A separate register/ file will be maintained in the Office, IEC that will document the access to the records of the Committee along with name of person, time, date and reason for the same [whenever needed].

STANDARD OPERATING PROCEDURE [SOP]

TRAINING & SELF ASSESSMENT

Table of contents

1. Purpose

The purpose of this SOP is to describe requirements and methodology for training and performance assessment of the Institutional Ethics Committee (IEC) members and the IEC Office.

2. Scope

The SOP applies to all the IEC members and the IEC Office.

3. Conduct of training of IEC Member

It will be the responsibility of the IEC Chairperson with the assistance of Member Secretary to ensure that there is adequate initial and continued training of the IEC members and the IEC Office. IEC members should have knowledge of the following:

- Relevant research ethics and regulatory guidelines
- Roles and Responsibilities of IEC members
- Review of protocol and related documents, including concepts of Risk Benefit assessment, Equity in recruitment, Autonomy, Confidentiality and Privacy
- Recent Developments in relevant health science specialities
- SOPs of the IEC

- IEC Office should have knowledge and relevant skills for conducting the following activities:
  - Competency in working on Microsoft word, Excel, IEC office software
  - Maintenance of IEC Database
  - Communication skills- written and verbal
  - Knowledge about the SOPs

Training of new IEC Members

- Every time a new committee is constituted/ re-constituted, the members will undergo initial training on ethics in clinical research and good clinical practices and SOPs. One training every year at the minimum should be acquired by each member as part of continuous development program.
- An individual selected as a new member of the IEC will be required to attend one meeting as an 'Observer' before being inducted as a member of the IEC [no voting rights].
- An IEC member [preferably Member Secretary] will provide an introductory training to the new member. The new IEC member [s] would be encouraged to undergo online EC training program [preferably by ICMR or CDSCO] as well as training for use of IEC-MANAGER software too.
- The IEC Member Secretary, Member [s], 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.
- IEC will conduct workshop [s] on ethics in clinical research and good clinical research practices at least once a year to impart training by the IEC Members to the Institutional faculty members [current/ potential investigators].
- The Appointing Authority will sponsor or reimburse the expenses of an IEC member or prospective members for attending conference, continuing education session workshop and/ or training program (if applicable).

Training of the IEC Office

- The IEC Member Secretary along with other members will train the IEC Office [Co-ordinator] on SOPs.
- There will be initial training and at least one training session per year on SOPs.
- The competency of staff in computers and communication skills will be evaluated and ensured initially at the time of appointment by the Member Secretary and Chairperson.

4. Implementation of corrective and preventive actions (as required)

All in-house trainings will be followed by evaluation of its effectiveness with a test. As indicated by the results, retraining shall be undertaken for members found deficient. Apart from this, the Member Secretary will be responsible for assessment of all IEC members with a self-assessment exercise at least once a year. During such an exercise, if the performance is not found to be satisfactory [<80%], the member will be subjected to training again for the same and again re-evaluated on the same.

Maintenance of training records of the IEC Members and the Administrative Staff

The IEC Office will maintain copies of the certificates of all training workshops and conferences in research ethics attended by the individual IEC members. The copies will be filed in the individual members' files. The records regarding training material [s] will also be maintained in their respective files. For all in-house trainings, all details regarding schedule, resource persons, delegates and training material will be archived [both in hard copies as well as in electronic form].

5. Periodic self-assessments [including corrective and preventive actions]

The Committee will undertake periodic self-assessment, at least 1 every financial year. For the same, Chairperson will form a committee of Member Secretary along with one or two members. If required, member from Quality Improvement Group of institute may also be included for his/ her inputs.

The Committee shall scrutinize the types of research projects reviewed & number of projects approved/ rejected, review monitoring reports from members submitted, analyze minutes of meeting for lacunae, peruse SAE review and participant interview process and whether adequate steps were taken to ensure continuous training of the members in order to evaluate the working of Ethics Committee as a whole unit.

Report of the same will be furnished to the Appointing Authority. Based on the assessment report, corrective measures [if any suggested] will be implemented within 30 days, depending upon their feasibility. In case the recommendations cannot be implemented, a report on the same will be submitted to the Appointing Authority, declaring the reasons for the same and will be asked for assistance, in case of a vital recommendation.