INSTITUTIONAL ETHICS COMMITTEE
H. M. PATEL CENTRE FOR MEDICAL CARE & EDUCATION
KARAMSAD, GUJARAT -388325

[Reg. No. ECR/ 331/ Inst/ GJ/ 2013]

STANDARD OPERATING PROCEDURE [SOP]

Revision – III, October 2015

I. OBJECTIVE

The objective of this SOP is to contribute to the effective functioning of the Institutional Ethics Committee [henceforth referred as "IEC"] of H. M. Patel Centre for Medical Care and Education, Karamsad [HMPCMCE, henceforth referred as "Centre"] so that a quality and consistent ethical review mechanism for health and biomedical research is put in place for all proposals dealt by the Committee as prescribed by the Ethical Guidelines for Biomedical Research on Human Participants, ICMR [2006] and Schedule Y [Drugs and Cosmetic Rules, 1945 as amended in 2013].

II. ROLE OF IEC

IEC shall review and approve all types of research proposals involving human participants with a view to safeguard the dignity, rights, safety and well being of all actual and potential research participants. The goals of research, however important, shall never be permitted to override the health and well being of the research participants. The IEC shall 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 shall look into the aspects of:

i. Informed consent process
ii. Risk benefit ratio
iii. Distribution of burden
iv. Benefit and provisions for appropriate compensations, wherever required

It shall:

i. Review the proposals before start of the study
ii. Examine compliance with all regulatory requirements, applicable guidelines and laws
iii. Monitor the research throughout the study until and after completion of the study through appropriate well documented procedures like annual reports, final reports, site visits etc.

The mandate of the IEC shall be to review the research proposals of:

1. Research proposals involving human participants to be conducted on site at the Institutions of HMPCMCE by its staff members/ postgraduate students/ undergraduate students
2. Researchers of HMPCMCE involved either as Principal or Co-investigator at sites other than HMPCMCE
3. Research proposals having staff members/ students of HMPCMCE as Co-investigator [proposed from outside the institution] but conducted within the institutions of HMPCMCE

III. AUTHORITY UNDER WHICH IEC IS CONSTITUTED

The Chief Executive Officer (CEO), Charutar Arogya Mandal who also heads the H M Patel Center for Medical Care & Education and its institutions.

IV. COMPOSITION OF IEC

IEC shall be multidisciplinary and multi-sectorial in composition. Independence and competence shall be its two hallmarks. The number of persons in the ethical committee shall not be of less than 7 members, maximum being 15. A minimum of five persons shall be required to compose a quorum [this would include a clinician, basic scientist, legal expert, lay person and social worker].

As per ICMR Guidelines, the Chairperson of the Committee shall be from outside the institution to maintain the independence of the Committee. The Member Secretary shall conduct the business of the Committee. Other members shall be a mix of medical/ non-medical scientific and non-scientific persons including lay person to reflect the different viewpoints.

A subcommittee may be delegated to function independently by ensuring consistent ethical framework for competent review and evaluation of ethical aspects of research proposals related to post graduate dissertation and undergraduate research projects received. Similarly, another subcommittee may be delegated to function independently by ensuring consistent ethical framework for competent review, evaluation and reporting of ethical aspects as per regulatory requirements arising out of adverse events [AE] or serious adverse events [SAE], as and when they occur. Similarly, expedited reviews may be delegated to panel of committee members as and when submitted.

The composition of the IEC shall be as follows:-

IEC, HMPCMCE shall be constituted in the following pattern:

i. Chairperson
ii. Deputy Chairperson, if need be
iii. Member Secretary
iv. 5-15 members from different departments/ specialties/ disciplines etc.

(Annexure I)

A. Full committee shall constitute:

- Chairperson
- Deputy Chairperson [to Chair, in absence of Chairperson or when Chairperson is an investigator of the proposal being reviewed]
- Member Secretary
- 1-2 basic medical scientists
- 1-2 clinicians from various departments
- One legal expert
- One social scientist/ representative of non-governmental voluntary agency
- One philosopher/ ethicist/ theologian
- One lay person from the community
- Subject Expert [as invited member as and when need arises]

B. Subcommittee [s] shall constitute:

Some of the members of full committee & co-opted members from different disciplines depending upon the need; SAE Subcommittee shall mandatorily include a clinician, basic scientist, legal expert, lay person and social worker.

Membership to IEC

The IEC, HMPCMCE shall have as its member's individuals from other institutions or communities if required. There shall be an adequate representation of age, gender, community, field etc. in the committee to safeguard the interests and welfare of all sections of the community/ society. Members shall be required to be aware of local, social and cultural norms, as this is the most important social control mechanism. If required, subject experts may be invited to offer their

views [for example an anesthetist, may be included for trials related to anesthetic drugs or procedures]. Similarly, based on the requirement of research area, for example HIV, genetic disorders etc. specific patient groups may also be represented in the Committee.

Reconstitution of IEC & Terms of Appointment of members

1. The IEC appointing authority [as in point no. 3] shall appoint the members in consultation with existing members of IEC.
2. Members shall be appointed based on their competencies and integrity and could be drawn from any public or private institute from anywhere in the country. The members shall provide a copy of their Curriculum vitae to the committee.
3. The letter of appointment shall include the date of appointment, length of tenure, an assurance from appointing authority that indemnity will be provided in respect of liabilities that may arise in the course of bona fide conduct of their duties as an IEC member.
4. Members shall be required to sign a confidentiality undertaking upon appointment, stating that all matters of which he/she becomes aware during the course of his/her work on the IEC shall be kept confidential and that any conflicts of interest, which exist or may arise during his/her tenure on the IEC, shall be declared.
5. Upon appointment, members shall be provided with the following documentation:
   - IEC Standard Operating Procedures (SOP)
   - Up to date list of members' names and contact information
   - Any previous reports on the IEC's activities
   - Any other relevant information
6. The duration of appointment shall usually be for a period of 3 years. At the end of 3 years, as the case may be, the committee may be reconstituted, and one third of the members shall be replaced by a committee constituted by the Head of the institution, IEC Chairperson and the Member Secretary.
7. A member can be replaced in the event of death or be discontinued in certain circumstances [like for any action not commensurate with the responsibilities laid down in the guidelines deemed unfit for a member]
8. A member can tender resignation [with one month's notice period or till suitable replacement is arranged] from the committee with proper reasons to do so; the resignation shall be sent to the appointing authority, routed through the Chairperson/ Deputy

Chairperson [as per the circumstances]

9. In case of vacancy arising due to death/ resignation/ termination of a member, necessary steps shall be taken to fill the vacancy of the former member as soon as possible.
10. Each new member shall have orientation on joining with introduction to other IEC members prior to the IEC meeting and informal meeting with Chairman, who will explain his/her responsibilities as an IEC member, the IEC processes and procedure.
11. All members shall be expected to maintain absolute confidentiality of all discussions during the meeting.
12. New members are expected to attend training sessions as soon as practicable after their appointment.
13. The costs associated with attendance at training and education sessions shall be met by Center.
14. Members may seek a leave of absence from the IEC for extended periods. Accordingly steps shall be taken to fill the vacancy during leave of absence of the particular member.
15. Membership will lapse, if a member fails to attend three consecutive meetings of the IEC, without prior written intimation unless exceptional circumstances exist. The Chairman shall notify the member of such lapse of membership in writing.
16. Membership shall also lapse if a member fails to attend in full at least two thirds of all scheduled IEC meetings in each year, barring exceptional circumstances.

V. PROCEDURE FOR SUBMISSION OF NEW APPLICATION

1. Beginning each year, IEC shall prepare a meeting calendar and try to strictly adhere to it [barring unforeseen circumstances]. Based on the calendar, The Member Secretary shall announce the date of forthcoming IEC meeting along with closing date of submission of proposals.
2. Upon such announcement, the potential investigators shall submit applications for ethical review and approval prior to conduct of research to the IEC Secretariat, on or before the announced closing date of submission.
3. Routinely, the closing dates for applications shall be no earlier than 10 – 14 days prior to each IEC meeting. Care shall be taken that investigators get the announcement at least 10 days prior to closing date of submission.
4. Applications must be submitted in the appropriate format ***(Annexure II, III)*** as

determined by the IEC, and shall include all documentation as required by the IEC as per check list ***(Annexure IV)***.

5. The procedures for application to the IEC and the application format shall be made readily available to all applicants.
6. No fee shall be charged for applications submitted by the investigators of the institution [HMPCMCE] for review EXCEPT for Clinical trials.
    a. IEC fees for Clinical trials:
        - Rs. 40,000/- for initial review of each protocol
        - Rs. 4,000/- per year till site closure
7. Research projects initiated and submitted by investigators outside the institution [HMPCMCE] but to be conducted within the centre shall be accepted only after written permission granted by Institutional Research Group.
8. Research projects initiated and submitted by investigators outside the institution [HMPCMCE] and also to be conducted outside the institution shall not be accepted for review.
9. Research proposal review fees shall need to be deposited in favour of "Charutar Arogya Mandal" having PAN No: AAATC 1264G.

VI. CONDUCT OF MEETING

1. The IEC shall meet on a regular basis, preferably each month but not later than 2 months from previous meeting. Closing date for submission along with date of forthcoming meeting shall be made publicly available.
2. Agenda along with the time at which investigators/ co-investigators are required to be present shall be intimated at least 2 days prior to the scheduled meeting.
3. No proposal shall be considered for approval unless the review meeting is attended by respective investigator/ co-investigator.
4. Committee members are required to attend IEC meetings in person. Members shall be informed of the meeting room details in the meeting agenda.
5. Members who are unable to attend a meeting can contribute prior to the meeting through written submissions to the Member Secretary. Accordingly the minutes shall be recorded in respect to submission of such written comments.
6. Meetings shall be scheduled for an allocated time. If the issues have not been completed

within the allocated time, then the IEC may either continue the meeting until all agenda items have been considered or schedule an additional meeting. If an additional meeting is called for, then the meeting shall try to be held within 14 working days.

7. Review of postgraduate dissertations/ thesis shall be conducted by Subcommittee [if constituted] as per the yearly calendar.
8. The IEC meetings shall be conducted in a way to ensure confidentiality and open discussion between members and the researcher [s].
9. A quorum has to be mandatorily present in order for the IEC to reach a final decision on any agenda item. A quorum is achieved when at least 5 members are physically present as per Schedule Y of Drugs and Cosmetics Act, 1940 amended in 2005. According to it, one member of each of the following categories must be there to fulfill a quorum:
    - Basic Medical scientist (preferably pharmacologist)
    - Clinician
    - Legal expert
    - Social scientist/ethics expert
    - Lay person
10. The Chairperson/ Deputy Chairperson shall have authority to cancel a scheduled meeting, if a quorum cannot be achieved. Should this occur the IEC shall try to convene next meeting within 14 working days of the cancelled meeting to ensure that all agenda items are reviewed in time.
11. Any member of the IEC having any conflict of interest - financial or otherwise, in a project or other related matter (s) considered by the IEC has to mandatorily declare such interest prior to review in the meeting.
12. The IEC shall determine whether a conflict of interest does exist or not, and if it exists, shall require the member to withdraw from the meeting until the IEC's consideration of the relevant matter has been completed. The concerned member [s] shall not be permitted to adjudicate on the research.
13. All such declarations of conflict of interest and the absence of the member concerned shall be noted in minutes of the meeting.
14. Compliance arising out of suggestions given to investigators during a review meeting shall be reviewed by panel of committee members before grant of approval. All such approvals shall be ratified in subsequent full committee meeting.

VII. ELEMENTS OF REVIEW

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

a. Scientific design and conduct of the study
b. Examination of predictable risks/harms
c. Examination of potential benefits
d. Procedure for selection of subjects in methodology including inclusion/ exclusion, withdrawal criteria and other issues like advertisement details etc.
e. Management of research related injuries, serious adverse events
f. Compensation provisions
g. Justification for placebo in control arm, if any
h. Availability of products after the study, if applicable
i. Patient information sheet and informed consent form in local languages, along with AV recording protocols [where necessary]
j. Protection of privacy and confidentiality
k. Involvement of the community, wherever required
l. Plans for data analysis and reporting
m. Adherence to all regulatory requirements and applicable guidelines changing from time to time [including CDSCO, GOI, ICMR etc.]
n. Competence of investigators, research and supporting staff
o. Facilities and infrastructure of study sites
p. Criteria for withdrawal of patients, suspending or terminating the study
q. Justification for waiver of informed consent
r. Law of the land shall be given absolute preference to any prevailing national or international guidelines

[Each review shall be based on Statement of General Principles as per ICMR Ethical Guidelines for Biomedical Research on Human Participant, 2006.

Any research using the human beings as participants shall 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 shall 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 shall continue to apply and such consent and voluntariness shall 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, shall 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 shall 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*
shall 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 shall 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.]*

VIII. PREPARATION OF MINUTES

1. The Member Secretary shall prepare and maintain minutes of all meetings of the IEC. The format of the minutes will include the following items:
    - Confirmation of quorum
    - Attendance of members
    - Notifying approval of minutes of previous meeting
    - Conflicts of interest, if any
    - Review and suggestions of new proposals
    - Review and suggestions to amendments for approved proposals
    - Monitoring reports, if any
    - Any other issue [e.g. expedited reviews, subcommittee minutes etc.]
2. The minutes shall also include the recording of decisions taken by the IEC as well as a summary of relevant discussion. This shall include reference to views expressed by absent members also. In relation to the review of new applications or amendments, the minutes shall record a summary of the main ethical issues considered, including any requests for additional information, clarification or modification of the project.
3. While recording a decision made by the IEC after voting, any significant minority views (i.e. 2 or more members) if any, shall also be noted in the minutes.
4. To encourage free and open discussion and to emphasis the collegiate character of the IEC, particular views shall not attribute to particular individuals in the minutes, except in circumstances where a member seeks to have his/her opinions or objections recorded.
5. 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 shall be included in the minutes too.

6. The minutes shall be circulated to all, following the respective meeting, corrected [if any corrections suggested by members] and approved by either the Chairperson and/or the Deputy Chairperson.
7. The minutes shall be formally ratified at the next IEC meeting. The original copy of each meeting's minutes shall be retained in a confidential 'Minutes of meeting' file.

IX. COMMUNICATION OF DECISIONS OF THE IEC

1. The IEC shall 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.
2. If the IEC determines that further information, clarification or modification is required for the consideration of a project, the correspondence to the PI shall clearly articulate the reasons for this determination, and clearly set out the information that is required.
3. For non regulated trials, if the requested information is not received from the applicant within 1 month of issue of suggestion letter, the project may be dismissed and the applicant shall be required to resubmit the project at a later date
4. For regulated trials, 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.
5. In case of non-regulated projects as well as regulated trials, the IEC notifies the applicant 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 shall be issued in Schedule Y Format, Appendix VIII [2] ***(Annexure XI)***
6. 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.
7. The status of the projects shall be regularly updated in the IEC's data of received and reviewed applications.
8. Communication from IEC to Investigator regarding decision on the proposal shall ordinarily be done within 15 working days after review of the application.

X. EXEMPT REVIEW AND EXPEDITED REVIEW PROCESS

Researcher [s] has [ve] to submit application, along with proposal, justifying as to why their

research proposal should be considered for exempt or expedite review.

1. A project shall be considered for exempt from ethical review where they:

a. Involve the use of existing collections of data or records that contain only non-identifiable data about human beings
b. Research is on data available in the public domain
c. Research is on anonymized data derived from participants
d. Research has less than minimal risk to participants

Examples that may be eligible for exemption from review include:

- Audits of educational practices
- Research on microbes cultured in the laboratory without identifiers

Upon submission of such a proposal, the IEC shall review and decide whether a project is eligible for exempt from ethical review. The Member Secretary shall provide written communication to the Principal Investigator as to whether a project is exempt from ethical review by the IEC or not. If not, it shall need to be submitted for either expedited review or full committee review.

2. The Member Secretary shall undertake expedited review of:

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
f. Case reports, submitted before publication/ presentation

Examples that may be eligible for expedited review:

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

Other documents that may be considered for expedited review are as follows but may not restrict to:

- Change in the name, address of sponsor
- Change in contact details of Principal Investigator, and Member- Secretary, IEC
- Request for change in principal investigator, co-investigator, change in any member involved in the research
- Minor corrections in budget
- Other administrative changes in the investigator brochure, informed consent document

3. Expedited review of research projects shall be undertaken between scheduled meetings at the discretion of the Member Secretary. The Member Secretary seeks 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 review may be slotted for review in the next full committee meeting and the decision of the same shall be communicated to the researcher.
4. The decision and minutes of this review shall be noted down for ratification at the next IEC meeting.
5. Any research with the potential for physical or psychological harm shall generally be not considered for expedited review. This includes regulated clinical trials, research involving invasive physical procedures and research exploring sensitive personal or cultural issues.
6. Where any research involves a departure from the ethical principles of integrity, respect for persons, beneficence and justice, the protocol shall be considered in the full IEC Committee Meeting and not dealt with expedited review.

XI. PROCEDURE FOR AMENDMENTS

1. Proposed changes to approved projects shall require to be reported by the PI to the IEC for review.
2. Requests shall outline the nature of the proposed changes, reasons for the request, and an assessment of any ethical implications arising from the request on the conduct of the research. All amended documents must have the changes highlighted and contain revised version numbers and dates.
3. Expedited review of requests for minor amendments, and urgent amendments to approved protocols for safety reasons are undertaken by the Member Secretary between scheduled meetings at the discretion of the Chairperson, which shall be ratified at the next IEC meeting.
4. All other requests for amendments shall be reviewed by the IEC at its next scheduled meeting, provided the request has been received by the Member Secretary by the agenda closing date.
5. The IEC reports in writing to the PI, advising whether the proposed amendment and/or request for extension has been given ethical approval within 7 working days of the meeting at which the request was considered (this may be the Full Committee meeting or Subcommittee Meeting/ the Expedited Review).

6. Notification of the approval of amendments and extensions shall be conveyed in writing in the standard format.
7. 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 shall clearly articulate the reasons for this determination, and shall clearly set out the information that is required.
8. All received and approved requests for amendments and extensions shall be recorded, and the status of the project updated in the IEC's data of received and reviewed applications.
9. In case where deviation from or changes to the protocol need 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].

XII. CONCERNS AND COMPLAINTS ABOUT THE CONDUCT OF A PROJECT

Reporting

1. The IEC requires, as a condition of approval of each project, that the researchers immediately report to the IEC any concerns or complaints received.
2. The Member Secretary, IEC is the person nominated to receive concerns and complaints from participants in research or members of the public about the conduct of projects approved by the IEC.
3. The Member Secretary, IEC is responsible for obtaining, in writing, the grounds of the concern or complaint. He/ She shall then notify the Chairperson of the IEC of the report as soon as possible.
4. The Member Secretary also acknowledges to the complainant outlining the mechanism for investigating the concern or complaint.

Investigation

1. The Chairperson, IEC shall examine the concern or complaint and determine whether the concern or complaint warrants a further investigation. Where there is to be no further investigation, the Chairperson, IEC shall inform the complainant, through Member Secretary.
2. Where the Chairperson determines that the concern or complaint warrants a further investigation, he/ she shall notify the Head of the Institution who shall then convene a

Review Committee to investigate and determine the consequences. Clarification or answer from the Principal Investigator shall be sought on the raised issue.

3. The Member Secretary shall then issue a letter of notification to the PI of any concern or complaint about a 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, the review Committee shall also notify that person.
4. The Review Committee shall immediately go for an investigation into the concern or complaint. The investigation shall not take longer than 2 weeks from the time of notification for the concern or complaint to be addressed, unless exceptional circumstances exist.
5. The Review Committee shall give the complainant and the PI an opportunity to make submissions. Where the complaint concerns the conduct of any other person, the Review Committee shall also provide that person with an opportunity to make submissions.
6. 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

1. If the Review Committee is satisfied that the concern or complaint is justified, it shall determine the consequences by considering the following matters:
   - Severity of the matter
   - Sensitivity of any information concerned including the amount and type of information and the level of identifiability
   - Whether any breach of the approved protocol, which may be established, was inadvertent, negligent or unintentional
2. The possible consequences shall include the following:
   - Noting on the file of the occurrence of the matter;
   - Increased monitoring of the project;
   - Counseling on security practices;
   - Amendments to the approved protocol;
   - Revoking of approval for the project
   - Reporting the individuals responsible for any breach to the Head of the Institute, with a complaint of misconduct in the execution of the project
3. The Chairman, Review Committee shall notify the institution, the PI and any other person

for whom there is an individual consequence to the outcome of the investigation and the consequences in writing.

4. The Chairman, Review Committee shall also notify the IEC and any other Institutional IECs concerned with the project to the outcome of the investigation and the consequences in writing.
5. The IEC has to review the ethical approval of any project in the light of the outcome of the investigation of any breach or complaint and will notify the responsible institution and the PI, if ethical approval for the project is withdrawn.
6. The Chair of the Incident Review Committee shall also send a written report of the outcome of the investigation and the consequences to the complainant.

XIII. REPORTING AND HANDLING 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 shall 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:

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: -

a. Principal Investigator shall, within 24 hours, report [by telephone, email as well as 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.

b. 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

c. The same [serious adverse events and the response to those events] shall be included in the periodic and final reports for the project also.

Handling: -

In case of serious adverse event occurring to the clinical trial subject, the IEC shall forward its report in Appendix XI on the serious adverse event [SAE], after due analysis, along with its opinion on the financial compensation, if any, to be paid by the Sponsor or his representative, whosoever had obtained permission from the Licensing Authority as referred to in clause [b] of rule 21 for conducting the clinical trial, to the Licensing Authority within 30 calendar days of the occurrence of the serious adverse event.

The compensation amount shall be determined based on the guidelines provided by CDSCO as available at:

1. 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 XV]***

2. 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 XVI]***

XIV. PROTOCOL FOR HANDLING VULNERABLE PARTICIPANTS

1. Vulnerability

- The Council for International Organizations of Medical Sciences (CIOMS) defines vulnerability as ***'substantial incapacity to protect one's own interests owing to such impediments as lack of capability to give informed consent, lack of alternative means of obtaining medical care or other expensive necessities, or being a junior or subordinate member of a hierarchical group'***.

2. Vulnerable (research) participants

- 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).

3. Responsibility

- EC members shall identify study proposals including vulnerable participants (population) and ensure that these are considered for full board review.
- EC shall ensure that measures for safeguarding rights and interests of vulnerable participants are taken care of in the study proposal. They shall 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 shall 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 abled 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 will not be 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.
  - 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.

XV. RECORD KEEPING

1. The Member Secretary shall prepare and maintain written records of the IEC's activities, including agenda and minutes of all the meetings.
2. He/ She shall also prepare and maintain a confidential electronic and/or paper record for each application received and reviewed, while recording the following information:
    - Protocol number [as per the inward number generated on submission of application along with date]
    - Names of PI
    - 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 approval was by scheduled Full Committee review or Expedited review or review by Subcommittee
    - Action taken by the IEC, while monitoring the conduct of the research

    The physical records shall contain a hard copy of the application, any relevant correspondence between the applicant, other stake holders and the IEC, other material used to inform potential research participants and all approved documents.
3. All documents of the IEC, including applications, membership, minutes and correspondence shall be kept confidential and in accordance with Schedule Y and ICMR guidelines.
4. To ensure confidentiality, all documents provided to IEC members, which are no longer required, are to be disposed of in a secure manner, such as shredding or incineration.
5. All relevant records pertaining to research projects shall be held for at least a period of 5 years, from the time of closure of research project to allow for future reference and in compliance with regulatory requirements.

XVI. MONITORING OF APPROVED PROJECTS

1. The IEC shall monitor approved projects to ensure compliance with the approved protocol. In doing so it shall call for and discuss information on any relevant aspect (s) of the project with the investigator (s) at any time. In particular, the IEC shall require

applicants to provide interim reports on stipulated dates and a final report at completion of the study. Continuing approval of the research is subject to the PI submitting an interim report by the stipulated date.

2. The IEC shall require the following information in the report:
   - Progress to date, publications or outcome in the case of completed research
   - Maintenance and security 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
3. The IEC may adopt any additional appropriate mechanism (s) for monitoring, as deemed necessary, such as: random inspections of research sites, data and signed consent forms; interview, with the prior consent, of research participants
4. The IEC shall 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.
5. The IEC requires, 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.
6. Where the IEC is satisfied that circumstances have arisen such that a research project is not being or cannot be conducted in accordance with the approved protocol, the IEC may withdraw approval. In such circumstances, the IEC will inform the PI and the Head of the Institute, the research project be discontinued, suspended, or any other necessary steps to be taken.
7. In determining the frequency and type of monitoring required for approved projects, the IEC will give consideration to the degree of risk to participants in the research project.

XVII. REVIEW AND AMENDMENT OF STANDARD OPERATING PROCEDURES

The Standard Operating Procedures [SOP] shall be reviewed based on changed requirements. Following procedure shall be followed for amendments:

- The proposal (s) shall be in writing and circulated to all IEC members for their consideration.
- The views of the members shall be discussed at the next scheduled meeting of the IEC, and a vote taken at that meeting.
- Any member unable to attend such a meeting may register his or her views in writing.
- The amendment will be incorporated after the consensus approval by the full committee.

XVIII. IEC ANNUAL REPORT

1. The IEC shall provide an annual report on its progress for the financial year to the Head of the Institution, including:
   - Membership changes
   - Number of meetings
   - Number of projects reviewed, approved, pending review, pending approval (non compliance by researcher to modifications suggested) and rejected
   - General issues raised

XIX. BIBLIOGRAPHY

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[All accessed on 1st September 2015]

LIST OF ANNEXURES

Annexure No.	Content
I	List of IEC Members
II	Application format for regulated trials including checklist
III	Application format for research proposal, non-regulated including checklist
IV	Check list for review of research proposals
V	Contents of research proposals
VI	Check list for informed consent
VII	ICF template
VIII	Participant information sheet [PIS]
IX	Declaration of not being PI at more than 3 clinical trials
X	Application format for review of case report
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XV	Compensation formula – SAE, Death
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XVII	Format for declaration of conflict of interest of IEC members
XVIII	Confidentiality and Conflict of Interest Declaration of members of IEC