INSTITUTIONAL ETHICS COMMITTEE (IEC)

INDIRA GANDHI INSTITUTE OF MEDICAL SCIENCES SHEIKHPURA, PATNA – 800014.

STANDARD OPERATING PROCEDURE (SOP)

Approved by IEC at its 11th Meeting on 12th December 2013

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Standard Operating Procedure (SOP) for Institutional Ethics Committee for Human Research at Indira Gandhi Institute of Medical Sciences, Sheikhpura, Patna -800 014.

1. Objective

The objective of Standard Operating Procedure (SOP) is to ensure quality and consistency in ethical review of biomedical research proposals in accordance with Ethical Guidelines for Biomedical Research on Human Subjects of ICMR and the Drugs and Cosmetics Act and Rules, Government of India.

2. Functions of Institutional Ethics Committee (IEC)

2.1 IEC should provide independent, competent and timely review of the ethics of proposed studies within the ethical norms laid down by the latest revisions of the Ethical Guidelines for Biomedical Research on Human Subjects of the Indian Council for Medical Research (ICMR) and other relevant guidelines before the commencement of a study and should regularly monitor the ongoing studies. In addition it will ensure that all research it approves will also conform to applicable central, state and local laws and regulations. All research to be conducted in the Institute must be submitted to the IEC for review in the prescribed format.

2.2 IEC will review and approve all research proposals involving human participants with a view to safeguard the dignity, rights, safety and well being of research participants irrespective of the source of funding. The goals of research, however important, should never be permitted to override the health and well being of the research subjects.

2.3 The IEC will ensure that all the cardinal principles of research ethics viz, autonomy, beneficence, non– maleficence and justice are taken care of in planning, conduct and reporting of a proposed study.

2.4 It will look into the aspects of informed consent process, risk benefit ratio, distribution of burden/benefit and provisions for appropriate compensations wherever required.

2.5 It will review the proposals before start of the study as well as monitor the research throughout the study until and after completion of the study through periodic reports, final report and site visits etc.

2.6 The committee will also ensure compliance with all regulatory requirements, applicable guidelines and laws.

3. Composition of IE

3.1 IECs shall be multidisciplinary and multisectorial in composition.

3.2 The number of members in the committee shall be kept small (7-11 members) as a large committee makes it difficult in reaching consensus and in having the presence of all the members. The external members shall be in majority to ensure the independence of the committee.

3.3 The Chairperson of the committee shall be from outside the Institution. The Member Secretary, drawn from IGIMS itself, shall conduct the business of the Committee. Other members will be a mix of medical and non-medical scientific and non-scientific persons including general public to reflect the different viewpoints.

3.4 The composition may be as follows:-

1. Chairperson
2. Basic medical scientists
3. Clinicians
4. Legal expert
5. Social scientist/representative of non-governmental voluntary agency
6. Educated person from the community
7. Member-Secretary

3.5 IEC shall have majority of its members from other institutions. They could be drawn from any public or private institute from anywhere in the country. There shall be adequate representation of age, gender, community etc. in the Committee to safeguard the interests and welfare of all sections of the society. The Committee cannot consist entirely of men or entirely of women.

4. Constitution of IEC

4.1 The Director, IGIMS, Patna shall constitute the IEC, in consultation with the Academic Board in the following pattern:-

1. Chairperson
2. Member Secretary from Institute
3. Dean
4. 5-7 members from different specialties as specified above, some of them should be from the Faculty of the Institute.

4.2 The committee will be normally reconstituted every 3 years

5. Membership Duration and Responsibilities

5.1. The duration of the membership will be 3 years

5.2. There will be no bar on the members serving for more than one term but it is desirable to have around one third fresh members.

5.3. A member can be replaced in the event of long-term non-availability (three consecutive meetings). Authority to replace the member shall be with the Director.

5.4. A member can tender his/her resignation from the committee, with approval from the Director.

5.5. Membership of the IEC is a position of responsibility and members are expected to function in a serious and professional manner appropriate to their role in the advancement of science and protection of research participants.

5.6. Members should maintain confidentiality of all discussions during the meeting and sign a confidentiality form at the start of their term. Each member of the committee will submit a declaration to maintain the confidentiality of the documents submitted to them during their membership period and with each extension.

5.7. Conflict of interest if any shall be declared by members of the IEC at the beginning of every meeting.

5.8. Members should submit an updated CV on joining the IEC and with each extension.

5.9. Members of the IEC who are from outside the institution shall be paid an honorarium for participation at each EC meeting.

6. Quorum Requirements

6.1 A minimum of 5 members including at least three outside members is required for quorum. All decisions should be taken in meetings and not by circulation of project proposals. For drug trials the quorum must necessarily include a basic medical scientist (preferably pharmacologist), one clinician, one legal expert, one social scientist/ representative of non-governmental organization, an educated person from the community.

7. Offices/Conduct of the Meeting

7.1 The Chairperson will conduct all meetings of the IEC. If for reasons beyond control, the Chairperson is not available, an alternate Chairperson will be elected by the members present from among themselves.

7.2 The Member Secretary will be responsible for organizing the meetings, maintaining the records and communicating with all concerned. He/she will prepare the minutes of the meetings and get them approved by the Chairperson before communicating to the PI.

8. Independent Consultants

8.1 IEC may call upon subject experts as consultants for review of selected research protocols. These experts may be specialists in ethical or legal aspects, specific diseases or methodologies, or represent specific communities, patient groups or special interest groups e.g. cancer patients, HIV/AIDS positive persons or ethnic minorities. They will not take part in the decision making process

9. Research on Vulnerable Participants

9.1 Vulnerable research participants are individuals whose consent to participate in a research project such as a clinical trial may be driven by the expectation of benefits associated with participation, or out of pressure or fear of senior members of a hierarchy, or those whose consent may not be valid due to a variety of reasons. Vulnerable participants include those who are economically disadvantaged, those with mental disorders that impair their capacity to consent, children, pregnant and nursing women, the institutionalised, those in a dependant and relatively un-empowered relationship such as students, employees, military and prisoners, and patients with life threatening diseases.

9.2 Research using vulnerable participants is not prohibited by international ethical codes or regulations but their inclusion needs to be justified and special precautions need to be implemented for their protection.

9.3 Research using children and adolescents:-

The purpose of including children in research is to gain knowledge relevant to the health needs of children. The ICMR guidelines state:-

9.3.1 "Before undertaking trial in children the investigator must ensure that:-

(i) Children will not be involved in research that could be carried out equally well with adults.

(ii) 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.

(iii) A parent or legal guardian of each child has given proxy consent.

(iv) 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 seven years up to the age of 18 years.

(v) Research should be conducted in settings in which the child and parent can obtain adequate medical and psychological support.

(vi) 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.

(vii) 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.

(viii)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.

(ix) 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."

9.4. Research in the economically disadvantaged

Persons who are economically or socially disadvantaged should not be used to benefit those who are better off than them. The economically disadvantaged have limited access to health care, may enrol in research to receive treatment, or enrol for compensation, are often educationally disadvantaged too with limitations in understanding and the potential for undue influence or manipulation. It is, therefore, important that the informed consent process uses simple language and enlists the help of family and significant others to explain the potential for risks, the uncertainty of personal health benefits, if appropriate, and clearly delineates those aspects of the study that are purely for research and those that are part of standard care. Undue financial inducements should be avoided. Particularly for illiterate and vulnerable participants in research, the informed consent process should be witnessed by an impartial witness, who is not part of the research team.

9.5. Research using students and employees

9.5.1. Research involving trainees of any description or employees including faculty often confers no therapeutic advantage for the participant. However, students and employees have the same rights as any other potential recruit to participate or refuse to participate in a research project, irrespective of the degree of risk, provided certain conditions are met:

- The research must not bestow upon participating employees or students any competitive academic or occupational advantage or benefit over other staff and students who do not participate, and the researchers must not impose any academic or occupational penalty on those students or staff who do not participate.
- Students and employees must not be systematically treated differently from non-employee or non-student participants as part of the project.

9.5.2 Due to the potential for perceived or real coercion to participate, students and employees who desire to participate in the research (especially those under the direct supervision of the principal investigator or listed research collaborators) should ideally have a witness of their

choice present during the informed consent process to ensure that participation was voluntary. A suitable representative may be invited to be present during the ethics review of the proposal

9.6. Research involving people with life threatening diseases or who are medically vulnerable

9.6.1. Prospective participants in a study which has a therapeutic component who are by reason of mental or behavioural disorders not capable of giving adequately informed consent, persons with serious, potentially disabling, or life-threatening diseases, and persons rendered incapable of informed consent by an acute condition [emergency], are also vulnerable to exploitation, as are people who by virtue of progressive cognitive impairment may become vulnerable during the process of research (e.g., long term studies of those with cognitive decline who develop dementia).

9.6.2. Participants with serious medical diseases are vulnerable to (possibly) misplaced therapeutic optimism. For such participants, attempts should be made to include them only if there is minimal risk if non-therapeutic research; for therapeutic research potential risks should be emphasized, as should realistic estimates of benefits. If the disease cannot otherwise be treated, a "compassionate use" of the experimental intervention is ethically justified.

9.7. Research on pregnant or nursing women

The *ICMR guidelines* state, "Pregnant or nursing women should in no circumstances be the subject of any research unless the research carries no more than minimal risk to the foetus or nursing infant and the object of the research is to obtain new knowledge about the foetus, pregnancy and lactation. As a general rule, pregnant or nursing women should not be subjects of any clinical trial except such trials as are designed to protect or advance the health of pregnant or nursing women or foetuses or nursing infants, and for which women who are not pregnant or nursing would not be suitable participants.

i) 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 foetal 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.

ii) 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.

iii) Research related to pre-natal diagnostic techniques: In pregnant women such research should be limited to detect the foetal abnormalities or genetic disorders as per the Prenatal Diagnostic Techniques (Regulation and Prevention of Misuse) Act, GOI, 1994 and not for sex determination of the foetus".

10. Application Procedure

10.1 All proposals should be submitted in the prescribed application form failing which applications will not be accepted. Application forms can be downloaded from the Institute website.

10.2 All relevant documents detailed under Documentation should be enclosed with application.

10.3 The checklist for submission should also be submitted along with the application; if this indicates incomplete submission, the application will be returned.

10.4 The required number of copies of the proposal along with the application and documents in prescribed format duly signed by the PI and Co-investigators/Collaborators should be forwarded by the Head of the Department.

10.5 A *non-refundable processing fee* will be levied on all external research proposals that are funded by agencies or organizations with a commercial orientation (pharmaceutical companies, contract research organizations, etc) for IEC approval. This fee is not applicable to proposals that are funded by non-commercial sponsors (governmental or non-governmental funding agency) or to Institute intramural projects. The processing fee applicable will be Rs. 50, 000 (Rs. Fifty thousand only) per proposal for proposals sponsored by overseas organizations or agencies and Rs. 20,000 per proposal for Indian organizations or agencies. The fee in form of demand draft in favour of "Director IGIMS " payable at Patna must be submitted along with the application to the IEC.

10.6 The Member Secretary will acknowledge the receipt and indicate any lacunae. Missing information should be supplied within two weeks.

10.7 The date of meeting will be intimated to the Principal Investigator/Coinvestigators who should be available to offer clarifications if necessary. If none of the investigators are present for discussion of the proposal, it will not be taken up for review.

10.8. The decision of IEC will be communicated in writing. If revision is to be made, the revised document in required number of copies should be submitted within a stipulated period of time as specified in the communication.

11. Documentation

All research proposals should be submitted with the following documents:-

11. 1. Title of the project
11. 2. Names of the PI and Co-investigators with designation and signatures.
11. 3. Name of any other Institute/Hospital/Field area where research will be conducted.
11. 4. Approval of the Departmental Research Committee.
11. 5. Protocol of the proposed research: including sample size (with justification), type of study design, inclusion & exclusion criteria, intended intervention, dosages of drugs, route of administration, duration of treatment and details of invasive procedures, as appropriate. A diagrammatic representation of the study participant flow is encouraged for all study designs, where appropriate.
11. 6. Plan to withdraw or withhold standard therapies in the course of research.
11. 7. Plan for statistical analysis of the study.
11. 8. An account of storage and maintenance of all data collected during the trial.

11. 9. Ethical issues in the study and plans to address these issues and steps taken to address these, such as the justification for washout of a standard drug, or the use of a placebo control.

11. 10. Proposal should be submitted with all relevant annexure like proforma, case report forms, questionnaires, follow–up cards, etc. to be used in the study.

11.11. Patient information sheet and informed consent form in English/Hindi and local language(s) should be enclosed. The patient information sheet should provide adequate and complete information in understandable language. It should also assure that any new information that becomes relevant during the trial and is related to their participation will be given to them. The consent form should be as per schedule Y published in Gazette of India (2005).

11. 12. For any drug/device trial, all relevant pre-clinical animal data and clinical trial data from other centers within the country/other countries, if available.

11.13. All significant previous decisions (e.g., those leading to a negative decision or modified protocol) by other regulatory authorities for the proposed study and an indication of the modification(s) to the protocol made on that account. The reasons for negative decisions should be provided.

11.14. Any regulatory clearances required. This is necessary for new drug/device not approved for marketing in India or use of approved drug in new indication, justification for sending of biological samples outside India and use of radioactive pharmaceuticals in clinical studies. Clearance from appropriate Committees under other agencies/ authority like Drug Controller General of India (DCGI); clearance from the Department of Biotechnology (DBT) for recombinant DNA experiments; and from the Bhabha Atomic Energy Commission (BARC) for experiments involving ionizing radiation.

11.15. For clinical trials in humans, undertaking to prospectively register the trial in the Clinical Trials Register- India (www.ctri.in) and/or other clinical trial registries as required by Indian regulatory authorities.

11.16. Source of funding and Budget along with the supporting documents.

11.17. Proposed compensation and reimbursement of incidental expenses and management of research related and unrelated injury/ illness during and after research period.

11.18. Indemnity issues including insurance for the compensation to the participants and copy of insurance documents from an Indian insurance agency.

11.19. An undertaking to immediately report Serious Adverse Events (SAE) to IEC.

11.20. An undertaking to inform the IEC in writing of any deviations to the approved protocol.

11.21. An undertaking to follow the latest version of the ICMR guidelines and the Declaration of Helsinki with amendments, if any.

11.22. Statement of conflicts of interest, if any.

11.23. Plans for publication of results–positive or negative–while maintaining the privacy and confidentiality of the study participants.

11.24. Any other information relevant to the study.

11.25. Agreement to submit annual progress report and final report within 6 months of the end of study.

11.26. The PI should provide the details of other ongoing research projects (Title of the project, Date of starting and duration, source and amount of funding).

12. Review Procedure

12. 1. Meetings of IEC shall be held on scheduled intervals as prescribed (once in 3 months, for which the dates will be decided at the end of previous meeting). Additional meetings will be held as and when necessary.

12.2 The proposals will be sent to members at least 2 weeks in advance.

12.3 Decisions will be taken by consensus after discussions, and voting will be done if necessary.

12.4 PI should be available during the meeting and may be invited to offer clarifications.

12.5 Independent consultants/Experts may be invited to offer their opinion on specific research proposals. The invited expert will have to follow the SOP of the IEC and have to confirm in writing that they understand the terms of reference and will sign a confidentiality agreement.

12.6 The decisions of the meeting shall be recorded in the minutes book and shall be confirmed during the next meeting with signature of Chairperson at each page.

13. Element of Review

13.1 Scientific design and conduct of the study

13.1.1 The rationale and need for the study in view of existing literature

13.1.2 The appropriateness of the study design in relation to the objectives of the study, the statistical methodology (including sample size calculation)

13.1.3 The explanation of risks and benefits, the justification for the use of control arms including use of placebo, criteria for withdrawal or study termination.

13.1.4 Procedure for selection of subjects including inclusion/exclusion, withdrawal criteria and advertisement details.

13.1.5 The adequacy of provisions made for monitoring and auditing the conduct of the research, including the constitution of a data safety monitoring board (DSMB).

13.1.6 The adequacy of the investigative team, site, available facilities, and procedures. Competence of investigators, research and supporting staff.

13.1.7 Protocol and proforma of the study including the consent form.

13.1.8 Facilities and infrastructure.

13.1.9 The manner in which the results of the research will be reported and published. Plans for data analysis and reporting.

13.1.10 Approval of Departmental Research committee and regulatory agencies.

13.2 Care and Protection of Research Participants

13.2.1 The suitability of the investigators' qualifications and experience for the proposed study.

13.2.2 Any plans to withdraw or withhold standard therapies for the purpose of the research, and the justification for such action.

13.2.3 The medical care to be provided to research participants during and after the course of the research.

13.2.3 The adequacy of medical supervision and psycho-social support for the research participants.

13.2.4 Steps to be taken if research participants voluntarily withdraw during the course of the research.

13.2.5 The criteria for extended access to, the emergency use of, and/or the compassionate use of study products.

13.2.6 The arrangements, if appropriate, for informing the research participant's general practitioner or consultant, including procedures for seeking the participant's consent to do so.

13.2.7 A description of any plans to make the study product available to the research participants following the research.

13.2.8 A description of any financial costs to research participants; the rewards and compensations for research participants (including money, services, and/or gifts);

13.2.9 The provisions for compensation/treatment in the case of the injury/disability/death of a research participant attributable to participation in the research;

13.2.10 The insurance and indemnity arrangements;

13.3 Protection of Research Participant Confidentiality

13.3.1 A description of the persons who will have access to personal data of the research participants, including medical records and biological samples.

13.3.2 The measures taken to ensure the confidentiality and security of personal information concerning research participants.

13.4 Informed Consent Process

13.4.1 A full description of the process for obtaining informed consent, including the identification of those responsible for obtaining consent.

13.4.2.The adequacy, completeness, and understandability of written and oral information to be given to the research participants, and, when appropriate, their legally acceptable representative(s)

13.4.3 Patient information sheet and informed consent form in English/Hindi and local language.

13.4.4 Clear justification for the intention to include in the research individuals who cannot consent, and a full account of the arrangements for obtaining consent or authorization for the participation of such individuals.

13.4.5 Assurances that research participants will receive information that becomes available during the course of the research relevant to their participation including their rights, safety, and well-being.

13.4.6 The provisions made for receiving and responding to queries and complaints from research participants or their representatives during the course of a research project.

13.5 Informed consent in emergency protocols

13.5.1 This section describes responsibilities related to informed consent when research participants are enrolled in emergent circumstances, as when human participants are in a life-threatening situation, available treatments are unproven or unsatisfactory, and the collection of valid scientific evidence, which may include evidence obtained through randomized placebo-controlled investigations, is necessary to determine the safety and effectiveness of particular interventions.

13.5.2 Obtaining informed consent is not feasible because(i) the participants will not be able to give their informed consent as a result of their medical condition, (ii) the intervention involved in the research must be administered before consent from the participants' legally authorized representatives is feasible, and (iii) there is no reasonable way to identify prospectively the individuals likely to become eligible for participation in the research.

13.5.3 Participation in the research holds out the prospect of direct benefit to the participants because (i) participants are facing a life-threatening situation that necessitates intervention, (ii) appropriate animal and other preclinical studies have been conducted, and the information derived from those studies and related evidence support the potential for the intervention to provide a direct benefit to the individual participants; and(iii) risks associated with the research are reasonable in relation to what is known about the medical condition of the potential class of participants, the risks and benefits of standard therapy, if any, and what is known about the risks and benefits of the proposed intervention or activity.

13.5.4 The research could not practicably be carried out without the waiver.

13.5.5 The proposed research protocol defines the length of the potential therapeutic window based on scientific evidence, and the investigator has committed to attempting to contact a legally authorized representative for each participant within that window of time and, if feasible, to asking the legally authorized representative contacted for consent within that window rather than proceeding without consent. The investigator will summarize efforts made to contact representatives and make this information available to the IEC at the time of continuing review.

13.5.6 The IEC has reviewed and approved informed consent procedures and an informed consent document. These procedures and the informed consent document are to be used with participants or their legally authorized representatives in situations where use of such procedures and documents is feasible. The IEC has reviewed and approved procedures and information to be used when providing an opportunity for a family member to object to a participant's participation in the research.

13.5.7 In addition, the IEC is responsible for ensuring that procedures are in place to inform, at the earliest feasible opportunity, each participant, or if the participant remains incapacitated, a legally authorized representative of the participant, or if such a representative is not reasonably available, a family member, of the participant's inclusion in the research, the details of the research and other information contained in the informed consent document. The IEC shall also ensure that there is a procedure to inform the participant, or if the participant remains incapacitated, a legally authorized representative of the participant, or if such a representative is not reasonably available, a family member, that he or she may discontinue the participant's participation at any time without penalty or loss of benefits to which the participant is otherwise entitled. If a legally authorized representative or family member is told about the research and the participant's condition improves, the participant is also to be informed as soon as feasible. If a participant is entered into research with waived consent and the participant dies

before a legally authorized representative or family member can be contacted, information about the research is to be provided to the subject's legally authorized representative or family member, if feasible.

13.6 Recruitment of Research Participants

13.6.1 The characteristics of the population from which the research participants will be drawn (including gender, age, literacy, culture, economic status, and ethnicity).

13.6.2 The means by which initial contact and recruitment is to be conducted.

13.6.3. The means by which full information is to be conveyed to potential research participants or their representatives.

13.6.4. The inclusion and exclusion criteria for research participants.

13.7. Community Considerations

13.7.1 The impact and relevance of the research on the local community and on the concerned communities from which the research participants are drawn.

13.7.2. The steps taken to consult with the concerned communities during the course of designing the research.

13.7.3 The influence of the community on the consent of individuals.

13.7.4. Proposed community consultation during the course of the research.

13.7.5. The extent to which the research contributes to capacity building, such as the enhancement of local healthcare, research, and the ability to respond to public health needs.

13.7.6. A description of the availability and affordability of any successful study product to the concerned communities following the research.

13.7.7. The manner in which the results of the research will be made available to the research participants and the concerned communities.

14. Expedited Review

Research activities that present no more than minimal risk to human participants, and involve only procedures listed in one or more of the categories listed below may be reviewed by the Sub-Committee of the IEC through the expedited review procedure. The recommendations of the Sub-committee will be approved by the Chairperson IEC and placed in the next meeting of the IEC for perusal.

14.1 Categories of research considered for expedited review

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

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

14.1.3 Research activities that involve only procedures listed in one or more of the following categories

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

- Research involving clinical materials (data, documents, records, or specimens) that will be collected solely for non-research (clinical) purposes.
- Collection of data from voice, video, digital, or image recordings made for research purposes.
- Research on individual or group characteristics or behaviour not limited to research on perception, cognition, motivation, identity, language, communication, cultural beliefs or practices, and social behaviour or research employing survey, interview, oral history, focus group, program evaluation, human factors evaluation, or quality assurance methodologies.

14.1.4 Proposals requesting expedited review should provide sufficient detail to enable a decision to be made in this regard. In the case of minor protocol amendments of approved research studies, the application should clearly specify the amendments that need expedited review.

14.1.5 All projects, whether internally or externally funded, are expected to submit a **report to the IEC annually for monitoring**. In approved and ongoing studies, the report will undergo expedited review by the Sub-Committee of the IEC. Currently used informed consent forms must be submitted for ongoing review, along with an update on the study and any relevant new information that may affect the conduct of the study.

14.1.6 A brief summary and all review decisions will be placed before the IEC members in the next meeting.

14.1.7 The expedited review procedure may not be used where identification of the participants and/or their responses would reasonably place them at risk of criminal or civil liability or be damaging to the participants' financial standing, employability, insurability, reputation, or be stigmatizing, unless reasonable and appropriate protections will be implemented so that risks related to invasion of privacy and breach of confidentiality are no greater than minimal.

14.1.8 The expedited review procedure may not be used for fresh applications with prospective data collection or interventions involving human participants.

14.1.9 The expedited review process does not apply to studies on vulnerable populations.

14.1.10 The Expedited review cannot be given to overseas investigators.

14.1.11 The standard requirements for informed consent (or its waiver, alteration, or exception) apply regardless of the type of review, expedited or convened, utilized by the IEC.

15. Decisions Making

15.1. A member shall withdraw from the meeting during the decision procedure concerning an application where a conflict of interest arises. This shall be indicated to the chairperson prior to the review of the application and recorded in the minutes.

15. 2. Only members will make the decision. The decisions shall be taken in the absence of investigators, representatives of sponsors, consultants.

15.3. Decision may be to approve, reject or revise the proposals. Specific suggestions for modifications and reasons for rejection should be given.

15.4. Revised proposals may be subjected to an expedited review.

15.5. All approved proposals will be subject to the following standard conditions. Additional conditions may be added by the IEC.

15.6 PI should submit annual report of the ongoing project on format prescribed by the Institute, to the IEC.

15.7 The final report of the completed study should be submitted by PI.

15.8 The PI should highlight the changes in the protocols/brochures/informed consent form etc. being amended from the previous documents while submitting amended documents to IEC.

16. Communicating the Decision

16.1. Decision will be communicated to PI by the Member Secretary in writing, preferably within two weeks time after the meeting in which the project was reviewed

16.2. The decision of the IEC communicated to the PI shall contain , but is not limited to the following elements:

a) The exact title of the research project which was reviewed.

b) The clear identification of the protocol of the proposed research or amendment, date and version number (if applicable).

c) The names and specific identification number version numbers/dates of the documents reviewed, including the potential research participant information sheet/material and informed consent form and local translations.

d) If applicable, the following will also be mentioned- Investigator's Brochure, proposed methods for patient accrual including advertisement (s) etc. proposed to be used for the purpose, principal investigator's current CV, insurance policy / compensation for participation and for serious adverse events occurring during the study participation, Investigator's Agreement with the Sponsor, and Investigator's Undertaking.

e) The names and designations of all members present during the presentation and discussion of the proposal.

f) In case of a conditional decision, any requirements by the IEC, including suggestions for revision and the procedure for having the application re-reviewed.

g) In the case of a positive decision, a statement of the responsibilities of the applicant, for example, confirmation of the acceptance of any requirements imposed by the IEC, submission of progress report(s), the need to notify the IEC in cases of protocol amendments (other than amendments involving only logistical or administrative aspects of the study); the need to notify the IEC in the case of amendments to the recruitment material, the potential research participant information, or the informed consent form, the need to report serious and unexpected adverse events related to the conduct of the study, the need to report unforeseen circumstances, the termination of the study, or significant decisions by other IECs or the Drug Controller General if India, the information the IEC expects to receive in order to perform ongoing review, the final summary or final report, and the need to store documents for at least 10 years after the end of the study.

h) The schedule/plan of ongoing review by the DSMB.

i) In the case of a negative decision, clearly stated reason(s) for the negative decision.

j) Signature (dated) of the Member Secretary of the IEC

17. Memorandum of Understanding and Indemnity Agreement for Sponsored Drug/Device/Collaborative Trials

17.1. After the approval from IEC, the sponsor/CRO will submit the clinical trial agreement/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 Dean, IGIMS with the counter signature of PI. As per existing policy of the Institute, there will be 25% overhead charges to the total cost of the trial/per patient cost.

17.2 Drug trial shall 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.

18. Follow up and Monitoring

18.1. The IEC may nominate, when necessary, a subcommittee of one or more persons to oversee the day to day conduct of a trial. This subcommittee will usually consist of members of the faculty of IGIMS.

18.2 Reports should be submitted at prescribed intervals for review. This should be no less frequent than an annual report.

18.3 Final report should be submitted at the end of the study (including externally funded studies).

18.4 All SAEs and the interventions undertaken should be intimated to the IEC, in the prescribed format with a copy of the report to the study sponsor, if any.

18.5 Protocol deviations, if any, should be recorded and reported with adequate justifications.

18.6 Any amendment to the protocol should be resubmitted for renewed approval. If these are minor and do not alter the risk-benefit ratio, expedited clearance may be requested.

18.7. Any new information related to the study should be communicated to the IRB and the participants, particularly those that pose additional risks or may warrant premature stopping of the trial.

18.8. Premature termination of study should be notified, with reasons for termination, as well as a summary of the data obtained up to the point of termination.

18.9. Change of investigators / sites should be communicated.

18.10. In case of voluntary withdrawal from studies, the reasons for participant withdrawal need to be recorded and submitted to the IRB along with the monitoring and final reports.

19. Continuing Review

Any research activity involving the use of human participants that has received initial review and approval by the IRB is subject to continuing review and approval. Time intervals for such reviews shall be made at the discretion of the Data Monitoring Committee (if applicable) but shall occur no less than annually.

19.1. **Amendments to protocols**

19.1.1 Amendments to protocols or consent forms must be requested in writing, and reviewed and approved by the IEC prior to making any changes in study procedures.

19.1.2 Requests must describe what modifications are desired, why changes are required, and if the changes pose any additional risks to the participants.

19.1.3 Minor changes (those that do not increase the risk or decrease the potential benefit to participants) may be submitted for expedited review, notified to the IEC at the next convened meeting. Investigators need not be present for this meeting.

19.1.4. Changes considered to be more than minor must be reviewed at a convened meeting of the IEC and the investigator must be available to answer any queries.

19.1.5. All amendments are reported to, discussed and approved by the IEC at a convened meeting.

19.2. Serious Adverse Event Reporting

19.2.1. When a participant who is participating in a research study experiences an unexpected or serious adverse event, the PI must promptly report the incident to the IGIMS IEC Safety Monitor (ISM, a clinical pharmacologist nominated by the Chairperson to review all SAE data for ongoing trials).

19.2.2. In addition, all SAE data from all sites for studies in which IGIMS is a participating site, must be submitted to the ISM in the ADR format, for inclusion in the IGIMS SAE database. This will be used to generate the external SAE report monitored for trends by the ISM and presented at each meeting to the IEC.

19.2.3. If the adverse event or reaction was <u>anticipated</u> in the protocol and the participant was informed about the possibility of the event in the consent form, there is no need to inform the ISM or DMC unless the adverse event was unexpectedly serious, life threatening, or fatal.

19.2.4. If the adverse event or reaction was <u>unanticipated</u>, unexpectedly serious, life-threatening or fatal, the adverse event must be reported to the ISM or DMC within 24 hours of the investigating team becoming aware of the event. If the adverse event occurs after hours or on a week-end, notification should be sent to the Secretary IEC. The Medical Superintendent and concerned consultant in charge of clinical care (if applicable) should also be notified at the earliest, if the affected person was a registered patient of IGIMS.

19.2.5. If the research study is being supported by an industry sponsor, the PI is also responsible for notifying the sponsor. The sponsor must then notify the regulatory authorities within a designated time period.

19.2.6. If the PI holds the Investigational New Drug (IND) or Investigational New Device Exemption (IDE) in his/her name, he/she is required to notify the regulatory authorities of the adverse event or reaction within 24 hours, in addition to notifying the DSMB or DMC, as appropriate.

19.2.7. Notifying the ISM or DMC does not relieve the PI from his/her responsibility to notify the sponsor and regulatory authorities.

19.2.8. Within 10 working days, the PI must submit a detailed written report of the adverse event or reaction to the ISM/IEC in the specified format.

19.2.9. industry sponsored research trials of drugs or devices, sponsors are required to inform investigators of adverse events or reactions that occur at other sites. When PIs are informed of the adverse events in sponsor safety memos and other correspondence, the PI must review the adverse event report and then notify the ISM. This should be done as promptly as possible after receipt of the report from the sponsor.

19.2.10. Receipt of adverse events reported must be acknowledged in writing and communicated to IEC members at the next convened meeting. The ISM presents a brief

summary of all external reports received and a presentation of each SAE at IGIMS to the IEC each month. If thought necessary, the IEC may request the PI to be present at that meeting or a subsequent meeting to review the risk-benefit ratio in the light of the new information.

20. Record Keeping and Archiving

20.1.1. Curriculum Vitae (CV) of all members of IEC.

20.1.2. Minutes of all meetings duly signed by the Chairperson. Copy of all correspondence with members, researchers and other regulatory bodies.

20.1.3. Copy of existing relevant national and international guidelines on research ethics and laws along with amendments.

20.1.4. All study related documents (study protocols with enclosed documents, progress reports, and SAEs.) in hard & soft copy should be archived for minimum of ten years after the completion of study. A copy of filled CRF shall remain with the PI for minimum of fifteen years.

20.1.5. Final report of the approved projects.

21. Updating IEC Members

21.1. All IEC members must be conversant with the ICMR guidelines for research involving human participants, Schedule Y of the Drugs and Cosmetics Act, the Declaration of Helsinki and ICH-GCP guidelines.

21.2. IEC members will also be provided with a copy of the Standard Operating Procedure.

21.3. IEC members will be encouraged to attend national and international training programs/conferences/seminars in the field of research ethics to help in improving the quality of research protocols/ethics committee submissions and review.

21.4.A record will be maintained of the training obtained by IEC members and updated annually.

22. Prospective registration of clinical trials

22.1. The ICMR and the WHO require prospective registration of all clinical trials before enrolment of the first participant in a Primary Register of the WHO International Clinical Trials Registry Platform. Further, prior registration is now a condition of publishing clinical trials for many journals. From 1st July 2005 the International Committee of Medical Journal Editors (ICMJE) has declared that their journals will not publish the results of any clinical trials not included on an authorized register.

22.2. The ICMR requires all trials conducted in India to be prospectively registered in the Clinical Trials Registry- India (CTRI; www.ctri.in). Schedule Y requires that all ICMR guidelines be followed for clinical trials. The CTRI is a Primary Register of the WHO International Clinical Trials Registry Platform and trials fully registered here will fulfill the ICMJE criteria of prospective trials registration.

22.3. All interventional clinical trials conducted in India and involving Indian participants need to be registered. An interventional clinical trial is any research study that prospectively assigns people to one or more health-related interventions (e.g., preventive care, drugs, surgical procedures, behavioral treatments, etc.) to evaluate their effects on health-related outcomes. Thus, early and late trials, trials of marketed or non-marketed products, randomized or non-randomized trials -- all should be registered.

22.4. The CTRI currently is accepting completed and initiated trials, but it is a requirement for IGIMS investigators to ensure registration prior to recruitment. As of January 2010, the other major web-site for the database registering clinical trials (www.clinicaltrials.gov) offers the following guidance 'Multi-site trials and multi-sponsor trials are susceptible to duplicate registration, thus care must be taken in how the trials are registered. For multi-sponsor trials it is the lead sponsor who should take responsibility for registration. It is critical that investigators and sponsors work together to ensure that a trial is registered once and only once.' Registration in both these registers is free.

22.5. The "Responsible Registrant" for a trial is either the principal investigator (PI) or the primary sponsor, to be decided by an agreement between the parties. The primary sponsor is ultimately accountable for ensuring that the trial is properly registered. For multi-center and multi-sponsor trials, it is the lead PI or lead sponsor who should take responsibility for registration.

22.6. The CTRI requires, in addition to the entry of the WHO 20-item dataset, contact details of IEC and a copy of the IEC approval (and DCGI approval, if applicable).

22.7. The IEC of IGIMS will only grant provisional approval for clinical trials in humans till the permanent registration number and a copy of the registration document is submitted to the IEC Office. Researchers may not commence recruitment until the final clearance is received.