INSTITUTIONAL ETHICS COMMITTEE

GULBARGA INSTITUTE OF MEDICAL SCIENCES
KALABURAGI.

(Autonomous Medical Institution , Government of Karnataka)

STANDARD OPERATING PROCEDURES

INDEX FOR SOP

1. Authority for constitution of Ethics committee

The Dean and Director, GIMS will appoint the Chairperson and all the committee members based on their competence, experience and integrity by sending an official request letter. Members will confirm their acceptance to the Dean by providing all the required information for membership. The Chairperson will furnish any information or report to the Director, GIMS when required.

2. Appointment of Ethics Committee Members

- Head of the Institute and Chairman are responsible for appointing suitable members for the IEC, GIMS, Kalaburagi.
- Head of the Institute in consultation with chairman will nominate the members of IEC, who have the qualification and experience to review and evaluate the scientific, medical and ethical aspect of proposed study.
- The regular members of the committee will include at least 7 individuals.
- **Current committee is as follows:**
    - Two persons from basic medical science area
    - Two persons from clinical side
    - One social scientist/ representative of non-governmental voluntary agency
    - One philosopher/ethicist/theologian
    - One legal person
    - One lay person from the community
    - Whenever required the expert person on particular subject would be invited.

Members and Independent Consultants are appointed to the IEC under the following conditions:

- Willingness to abide by the requirements laid in the SOP
- Willingness to publicize his/her full name, profession, and affiliation
- All financial accountability, reimbursement for work and expenses, if any, within or related to the IEC should be recorded and made available to the public upon request

- All IEC Members and Independent Consultants must sign Confidentiality / Conflict of Interest Agreements regarding meeting deliberations, applications, information on research participants and related matters

3. Frequency of Ethics Committee meetings:

- The meetings shall be convened 4 times in a year following a standard protocol mentioning the last dates for submission of the project documents.
- The members should gather in IEC meeting room for the scheduled meeting.
- The Annual schedule of regular meetings shall ordinarily be as under:

Sr. No.	Month	Week
1.	September	Second/Third week of the month
2.	December	Second/Third week of the month
3.	March	Second/Third week of the month
4.	June	Second/Third week of the month

- Clinical trial meetings shall be conducted separately.
- As and when required(SOS) meeting may be convened at the discretion of the Chairperson and the Members of the IEC in view of the:
    - Bulk Quantum of research projects
    - Projects requiring expedited review
    - Projects already approved but requiring minor changes
    - In case of Serious adverse events
- IEC meets once in every three months or soon depending on the number of research proposals.
- Investigators are advised to submit proposals well in advance to ensure that their projects would be reviewed in either of the two meetings scheduled in a given month.
- No limit is placed on the number of items on the agenda.
- The IEC meeting will be conducted in reserved room on the scheduled meeting date and time.

- It will be ensured that the room, equipment (projectors, recorder, etc) and facilities are available in good working conditions.
- All original files of studies on the agenda will be kept in the meeting room for ready reference before the meeting.
- E-copy of SOPs, New Drugs and Clinical Trial rules 2019, ICMR guidelines will be kept available for ready reference.
- Secretariat informs the scheduled meeting date and time to the Principal Investigators.
- The meeting will be re-scheduled or canceled if it becomes apparent that meeting requirements (quorum, sufficient expertise) will not be met.
- The members should gather in IEC meeting room on scheduled time.
- The Chairperson before beginning the discussion will: Ensured that the quorum is fulfilled and be maintained throughout the meeting and at the time of decision making.
- At the beginning of each convened IEC meeting, the IEC Chair or designee will ask the members if anyone has a financial or non-financial conflict of interest with regard to any of the research projects that will be reviewed at the meeting.
- The IEC Chair or designee will announce that members with a conflict of interest must excuse themselves from deliberation and voting on that research protocol.
- If an IEC member has conflict of interest involving a project then he/she should declare the same, before the meeting commences and leave the meeting room before the discussion on the same.
- This should be recorded in the minutes. The excused member can answer questions from the IEC, but cannot be present for IEC deliberations and voting.
- The Member Secretary should discuss the minutes of the previous full board/expedited meeting of IEC as well as major issues/policies discussed in minutes of the other IEC and present the agenda for the current meeting.
- The list of protocols that were exempted should be notified.
- The IEC may invite investigators to attend the full board meeting related to their studies, and clarify doubts, if any.
- All proposals that are determined to undergo full board review must be deliberated and decision about the proposal taken at a full board meeting.
- Time allotted for the meeting should be reasonable to allow ample discussion on the each agenda item.

- The meeting proceeds in the sequential order of the agenda; however the Chairperson may change the order, if the situation so demands.

4. Roles and Responsibilities of IEC members and Qualification Requirements Of Ethics Committee Members

- **Role of Chairperson**
  - He/ She will be responsible for conducting all committee meetings and he/ she will lead all discussions and deliberations pertinent to all research proposals.
  - Ensure active participation of all members in all discussions and deliberations.
  - Ratify minutes of the previous meetings
  - Seek COI declaration from members and ensure quorum and fair decision making.
  - Handle complaints against researchers, EC members, conflict of interest issues and requests for use of EC data, etc.

b) Role of Member secretary

- The Member Secretary is responsible for organizing the meetings, maintaining the records and communicating with all concerned.
- He/ she will prepare the minutes of the meeting and get it approved by the chairman.
- Ensure completeness of documentation at the time of receipt and timely inclusion in agenda for EC review.
- Assess the need to invite independent consultant, patient or community representatives.
- Ensure SOPs are updated as and when required and adherence of EC functioning to the SOPs.
- Ensure training of EC secretariat and EC members
- Prepare for and respond to audits and inspections
- Assess the need for expedited review/ exemption from review or full review.
- Assess the need to obtain prior scientific review, invite independent consultant, patient or community representatives.
- Ensure quorum during the meeting and record discussions and decisions

c) Role of Basic Medical Scientist

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

d) Role of Clinician

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

e) Role of Legal Experts

- Role of Legal expert is as a primary reviewer of the contract to review the insurance, compensation, trial agreements.
- Review MoU, Clinical trial agreement, regulatory approval, insurance document, other site approvals, researcher's undertaking, protocol specific other permissions, compliance with guidelines etc.
- The clear articulation of law by legal person improves the ethical analysis of study.
- Law can help physicians and others in decision-making and legalized approaches are similarly said to foster deliberation and careful weighing of evidence as well as playing a fundamental role in tempering subjective discretion and minimizing arbitrariness.
- Interpret and inform EC members about new regulations, if any.

f) Role of social scientist/NGO representative/philosopher/ethicist/theologian or similar person

- Ethical review of the proposal, ICD along with the translations.
- Role of theologian is to understand if there are any religious implications to any of the trial activities.

- A graduate with specialization in social ethics, intercultural ethics, and the ethics of gender and vulnerable population
- Serve as resource person to religious beliefs and faith concerning the spiritual and value dimensions and values of illness and health even if patients or their families have no apparent religious affiliation.
- Bring expertise in spiritual, theological, ethical, and moral values to the multidisciplinary team in the clinical setting.
- Serve as a patient/participant/ societal /community representative and bring in ethical and societal concerns.

g) Role of Lay persons:

- Person having no specific qualification with respect to biomedical research, medicine or health care.
- Lay person's primary role is to share their insights about the communities from which participants are likely to be drawn. The role of a lay person is to emphasize on aspects like the comprehensibility of the informed consent and other study documents to be used for participants, the study schedule and related activities and caregiver's involvement.
- The term 'lay' is used to cover people with a diversity of backgrounds outside of the specific science being reviewed or conducted. This could include individuals with expertise in ethics, animal welfare, social sciences as well as members of the local community.
- Represent the interests of the community/participant at large.
- Evaluate benefits and risks from the participant's perspective and opine whether benefits justify the risks.

Qualification Requirements Of Ethics Committee Members

1. Chairperson

He/ She should be Non-affiliated.

Qualifications -A well-respected person from any background with prior experience of having served/ serving in an EC.

2. Member Secretary

Can be Affiliated .

Qualifications -

- Should be a staff member of the institution
- Should have knowledge and experience in clinical research and ethics, be motivated and have good communication skills
- Should be able to devote adequate time to this activity which should be protected by the institution.

3. Basic Medical Scientist(s)

Can be Affiliated/ non-affiliated.

Qualifications -

- Non-medical or medical person with qualifications in basic medical sciences
- In case of EC reviewing clinical trials with drugs, the basic medical scientist should preferably be a pharmacologist

4. Clinician(s)

Can be Affiliated/ non-affiliated

Qualifications -

- Should be individual/s with recognized medical qualification, expertise and training

5. Legal expert/s

Can be Affiliated/ non-affiliated

Qualifications -

- Should have a basic degree in Law from a recognized university, with experience
- Desirable: Training in medical law.

6. Social scientist/ philosopher/ ethicist/theologian

Can be Affiliated/ non-affiliated

Qualifications -

- Should be an individual with social/ behavioural science/ philosophy/ religious qualification and training and/or expertise and be sensitive to local cultural and moral values. Can be from an NGO involved in health-related activities

7. Lay person(s)

Should be Non-affiliated

Qualifications -

- Literate person from the public or community
- Has not pursued a medical science/ healthrelated career in the last 5 years
- May be a representative of the community from which the participants are to be drawn
- Is aware of the local language, cultural and moral values of the community
- Desirable: involved in social and community welfare

5.Ethics committee administration and Finance

The Secretariat will be responsible for performing and overseeing all the administration of the Institutional Ethics Committee.

The Secretariat is composed of the Member Secretaries of the IECs, and the administrative support staff. The supporting staff consists of staff members of GIMS, Kalaburagi, appointed by the Director, GIMS, Kalaburagi.

The Director, GIMS, Kalaburagi has deputed the responsibility of issuing terms of reference for the IEC staff to the Member Secretary, IEC.

The IEC Administrative Staff: Working Rules

1. The administrative support to the IEC will comprise of IRB administrators, private secretary, administrative assistants, IT support and attendant/s or/helper/s.
2. The IRB administrators along with the support staff will assist the IEC Chairperson and Member Secretary in executing functions of the IEC.
3. Additional staff may be appointed and duties assigned as and when deemed necessary by the IEC.
4. The eligibility criteria for new staff to be appointed will be laid down depending on the required job profile.
5. The need for appointment of administrative staff, job profile and qualifications may be recommended by IEC members during regular IEC meetings and will be recorded in minutes. These will be forwarded to the Director, GIMS, Kalaburagi.
6. The administrative staff will be appointed by conducting formal interviews as per GIMS policy.

Duties of the administrative officer

• Review of new research applications for consistency, completeness, and

compliance with the regulations and institutional guidelines prior to convened IEC review.

• Providing necessary administrative support for IEC related activities to the Member Secretary, IEC.

• Organizing IEC meetings regularly.

• Preparing the agenda and drafting minutes of the meetings.

• Organizing an effective and efficient tracking procedure for each proposal received.

• Preparing, maintaining and distributing study files.

• Supervision of the maintenance, archival, and shredding of the study files.

• Corresponding with the IEC members, external experts and investigators on all IEC related matters.

• Arranging training for study personnel and IEC members

• Receipt of IEC processing fees for pharma-funded projects and the issue of official receipts for the same.

• Supervision of the pre and post arrangements of IEC meetings.

• Answering queries of the investigators.

• Supervision of filing of study related documents.

• Quality check of all study related documents submitted to IEC as well as correspondence from IEC.

• Preparation for accreditation, audits.

• Organizing training for investigators, key study personnel, IEC members, and IEC staff.

• Participating in the development and subsequent implementation of SOPs.

• Participating in, or presenting , research related education sessions

• Initiating research studies in ethics/audits

Duties of the Secretary/Administrative assistant

- Drafting letters, receipt, voucher preparations etc
- Template preparations as instructed by the IRB administrators.
- Liaising with other departments.
- Meeting attendance preparation/ preparation of dispatch folders.
- Hospitality management during IEC meetings.

Duties of the attendant/s /helper/s:

a. Assisting the secretariat in arranging the IEC meetings.

b. Dispatching sets of study documents to IEC members and external experts.

c. Receiving the study related documents from and dispatching the IEC letters to the investigators.

d. Filing study related documents.

e. Archiving and maintaining the study files

f. Shredding of the closed files

The IEC staff will report to the Member Secretary and/or Chairperson. The office timings for the IEC staff will be as per GIMS rules and regulations. The staff will avail leave as per GIMS norms.

Finances Related to Ethics Committee Activities and Functioning

All research proposals/clinical trials funded/sponsored by Pharmaceutical companies/ Agencies/ Multinationals etc. will be charged an administrative fee/ processing fee of ***Rupees Twenty Five Thousand for fresh proposals and Rupees Twenty Five Thousand for annual follow-ups/renewal review proposals.***

All non funded/ funded (funded by organizations like ICMR, UGC, DST Government of India, State Science & Technology Department, UNICEF, WHO, USAID, Non Profitable Organizations etc) research proposals by Undergraduate students are charged an administrative fee/ processing fee of ***Rupees One Thousand for fresh proposals.*** Post graduate students and staffs of GIMS, Kalaburagi are charged an administrative fee/ processing fee of ***Rupees One Thousand five hundred for fresh proposals.***

Waiver of these fees is permissible for Post Graduate Synopsis of RGUHS and Under Graduate Students of GIMS, Kalaburagi for ICMR-STS projects. **Waiver of fees is at the discretion of Chairman-IEC and Member secretary-IEC, GIMS, Kalaburagi.**

Method of payment: The payment will be taken by cash or can be paid by cheque drawn in favour of " **Director, Gulbarga Institute of Medical sciences**". The review fee for pharmaceutical and government sponsored study will always be accepted through cheque.

Deposits and Accounting: The EC administrative staff shall collect the fees (cash or cheque). The deposits shall be made to the GIMS-IEC account (Gulbarga Institute of Medical sciences- Institutional ethics committee). The Account section, GIMS, Kalaburagi shall maintain deposit records according to policy. Annual compiled data related to finance of IEC shall be shared by Accounts section, GIMS, Kalaburagi.

Expenditure: The expenditure will be made from GIMS-IEC account towards following points-

a) Staff salary

b) Stationary expenses

c) Maintenance of IEC facility for eg. repair work, construction, pest control, fire proofing etc.

d) Making resources available for office for eg. purchase of computers, printers, scanners etc.

e) Paying fixed honorarium to external members of Rs. 300/- for each meeting attended.

f) SOP and GCP training programmes organized by IEC

g) Expenses towards organising IEC meetings

6. Initial Submission Procedure

1. All proposals should be submitted on any working day three weeks in advance of scheduled meeting. Copy of SOP of GIMS IEC will be given to PI / Co-PI if he/she has applied for review for the 1st time.

2. All relevant documents should be enclosed with application form.

3. Required number of copies (5 copies along with 1 CD) of the proposal along with the application and documents in prescribed format duly signed by the Principal Investigator (PI) and Co-investigators / Collaborators / Research Scholars shall be guided to the Chairperson GIMS IEC, through member secretary. In his absence via any person nominated by chairperson. Receipt of the application will be acknowledged by the IEC office.

4. The date of GIMS-IEC meeting will be intimated to the Principal Investigator to attend the meeting and to make a brief presentation of the proposal and to clarify the points raised by the members.

5. The decision of the committee on the proposal 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 or before the next meeting.

6. All research proposals/clinical trials funded/sponsored by Pharmaceutical companies, Agencies, Multinationals etc. will be charged an administrative fee/ processing fee as specified by the Research Secretariat / Office of IEC of GIMS.

Required documents submitted for Research Proposal:

1. Title of the research proposal

2. Name of the Principal Investigator with qualification and designation

3. Name of the Co-Investigator(s) with qualifications and designation

4. Name of the Institute / Hospital / Field area where research will be conducted

5. Forwarding letter from the Head of the Department / Institution / Guide.

6. Protocol of the proposed research:

- Research objectives,
- Rationale for undertaking the investigations in human participants in the light of existing knowledge
- Brief review of litterature which include all relevant pre-clinical animal data and clinical trial data from other centres within the country / other countries, if available and usefulness of the project / trial
- Precise description of methodology of the proposed research, including Inclusion and exclusion criteria for entry of participants, sample size (with justification), type of study design (observational, experimental, pilot, randomized, blinded etc.), intended intervention, dosages of drugs, route of administration, duration of treatment and details of invasive procedures if any, Plan to withdraw or withhold standard therapies in the course of research. Plan for statistical analysis of the study. Ethical issues in the study and plans to address these issues.

7. Proposal should be submitted with all relevant enclosures like proforma, case report forms, questionnaires, follow-up cards, participant recruitment procedures and brochures, if any, Informed consent process, including patient information sheet and informed consent form in English and local language(s). Investigator's brochure for trial on drugs/ devices/ vaccines/ herbal remedies and statement of relevant regulatory clearances. Source of funding and financial requirements for the project.

8. Explain all anticipated ‘risks’ (adverse events, injury, discomfort) of the project. Efforts taken to minimize the ‘risks’. Proposed compensation and reimbursement of incidental expenses and management of research related and unrelated injury/ illness during and after research period.

Resubmission of study with corrections as per IEC suggestions

- For resubmission- the PI will submit 3 copies of the amended study related documents along with justification for amendment or modification, and clearly highlighted/demarcated sections which have undergone change
- The IEC Secretariat will verify the completeness and reconfirm that the copies contains the modification highlighted with respect to the earlier submission
- The IEC Secretariat will perform the analysis. The unchanged study related documents need not be submitted.

7.Notification of Review Outcome

Review Procedure:

- The IEC will evaluate the possible risks to the subject with proper justifications, the expected benefit and adequacy of documentation for ensuring privacy, confidentiality and justice issue.
- The IEC review will be done through formal meetings and will not resort to decision through circulation of proposal.
- In making decision on application for the ethical review of any research proposal, IEC will consider the following;

  - Member having the conflict of interest will indicate to the chairman prior to their view of application and same will be recorded in the minutes.
  - Where there is conflict of interest, member will withdraw from the decision making procedure.
  - A decision will only be taken when sufficient time has been allowed for the review and discussion of an application and in absence of non members.
  - Decision will only be taken at meetings where a quorum is complete.
  - Decision will be taken only after reviewing a complete application with all the
  required documents necessary for proposal, consideration has been examined by IEC.
  - Only members who participated in review and discussion will participate in decision.
  - Wherever possible, the decision will be arrived through consensus not by vote, but when a consensus appears unlikely voting can be performed.

- Decision procedure will specify the conditional decision, with clear suggestions and re-review procedure.
- Negative decision will be supported by clearly stated reasons.

- In the case of a positive decision, the PI is notified of the following requirements through an approval letter:
  - Responsibilities of the PI
  - Submission of annual status reports/progress report(s) is decided on case to case basis, usually yearly.
  - The need to notify the IEC in the case of amendments to the recruitment material like 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
  - The information the IEC expects to receive in order to perform ongoing review
  - The final summary or final report
  - The schedule/plan of ongoing review by the DSMB of sponsored trials
- IEC shall intimate the licensing authority about the approval of clinical trials intended for academic purposes such as use of approved drug formulation to study new indication or new route of administration or new dose or new dosage .The IEC shall await for comments from the DCGI for a period of 30 days from the date of receipt of communication from the IEC. If no communication from DCGI is received in the specified time frame, IEC shall presume that no permissions are required from the licensing authority and will issue the final approval letter for the study.
- An IEC may decide to reverse its positive decision on a study if it receives information that may adversely affect the risk/ benefit ratio
- Any advice by the IEC that is non-binding will be appended to the decision
- In the case of a negative decision, the reasons should be clearly stated in the communication to the PI
- The PI will also be notified of the cap for accrual of number of participants
- All decision and approval letters will be signed by the Member Secretary, IEC or the nominated Secretary for that meeting.
- In case Member Secretary IEC is Principal Investigator, the decision letters will be signed by Chairperson IEC.

- The decisions letters will be communicated to the Principal Investigator and wherever required to the organizational offices and officials and other concerned authorities.
- Member Secretary, IEC/Chairperson IEC, will sign and date the approval certificate in the original research protocol.
- The letter will mention whether the decision has been arrived at by consensus unanimous or majority opinion amongst the voting members of IEC, or by voting.
- If the decision has been arrived by voting, the letter will state the number of votes for and against approval of the project.

8. Expedited Review

- The proposals presenting no more than minimal risk to research participants may be subjected to expedited review. The Member- Secretary and the Chairperson of the IEC may do expedited review only if the protocols involve -

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

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

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

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

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

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

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

5. When in emergency situations like serious outbreaks or disasters a full review of the research is not possible, prior written permission of IEC may be taken before use

of the test intervention. Such research can only be approved for pilot study or preliminary work to study the safety and efficacy of the intervention and **the same participants should not be included** in the clinical trial that may be initiated later based on the findings of the pilot study.

a. Research on interventions in emergency situation

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

- when consent of person/ patient/ responsible relative or custodian/ team of designated doctors for such an event is not possible. However, information about the intervention should be given to the relative/ legal guardian when available later;
- When the intervention has undergone testing for safety prior to its use in emergency situations and sponsor has obtained prior approval of DCGI;
- Only if the local IEC reviews the protocol since institutional responsibility is of paramount importance in such instances.
- If Data Safety Monitoring Board (DSMB) is constituted to review the data;

b. Research on disaster management

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

- Research planned to be conducted after a disaster should be essential culturally sensitive and specific in nature with possible application in future disaster situations.
- Disaster-affected community participation before and during the research is essential and its representative or advocate must be identified.

- Extra care must be taken to protect the privacy and confidentiality of participants and communities.
- Protection must be ensured so that only minimal additional risk is imposed.
- The research undertaken should provide direct or indirect benefits to the participants, the disaster-affected community or future disaster- affected population and *a prior* agreement should be reached on this, whenever possible, between the community and the researcher.
- All international collaborative research in the disaster-affected area should be done with a local partner on equal partnership basis.
- Transfer of biological material, if any, should be as per Government rules taking care of intellectual property rights issues.

6. Expedited review may also be taken up in cases of nationally relevant proposals requiring urgent review.

9. Elements of Review

The IEC, GIMS, Kalaburagi will substantially review research proposals and their supporting documents with special attention to the scientific validity, informed consent and submission form for the suitability and feasibility of the study.

The following will be considered as applicable:

1. **<u>Scientific Design and Conduct of the Study</u>**
   - Is the project original and innovative? e.g. Does the project challenge existing paradigms or clinical practice; address an innovative hypothesis or critical barrier to progress in the field? Does the project develop or employ novel concepts, approaches, methodologies, tools or technologies for this area?
   - Is this an attempt to validate, prove or disapprove the validity of existing knowledge?
   - Appropriateness of study design, work plan and structure to achieve the stated objectives: Are the conceptual or clinical framework, design, methods and analyses adequately developed, well integrated, well-reasoned and appropriate to the aims of the project?
   - Appropriateness of the study design in relation to the objectives of the study;

- The statistical methodology (including sample size calculation), and the potential for reaching sound conclusions with the smallest number of research participants;
- The justification of predictable risks and inconveniences weighed against the anticipated benefits for the research participants and the concerned communities;
- The justification for the use of control arms;
- Potential of the work that would be conducted to lead into a larger and high impact study;
- Criteria for prematurely withdrawing research participants, and criteria for suspending or terminating the research as a whole;
- The adequacy of provisions made for monitoring and auditing the conduct of the research;
- Investigator's capability, availability of infrastructure and scientific environment to conduct the study within the time frame and carry it forward;
- The adequacy of the site, including the support staff, available facilities, and emergency procedures;
- Study Reporting and publication of the research.

2. Care and Protection of Research Participants

- Required qualifications and experience of the investigators for the proposed study;
- Any plans to withdraw or withhold standard therapies for the purpose of the research, and the justification for such action;
- Plans to withdraw subjects from the study by the investigator;
- Medical care to be provided to research participants during and after the course of the research;
- Adequacy of medical supervision and psycho-social support for the research participants;
- Steps to be taken if research participants voluntarily withdraw during the course of the research;
- Criteria for extended access to, the emergency use of, and/or the compassionate use of study products;
- Arrangements, if appropriate, for informing the research participant's general practitioner or family doctor, including procedures for seeking the participant's consent to do so;

- Description of any plans to make the study product available to the research participants following the research and description of any financial costs to research participants
- Rewards and compensations for research participants (including money, services);
- Provisions for compensation/treatment in the case of the injury/disability/death of a research participant attributable to participation in the research (as per institutional policy/ICMR guidelines/existing national legislation (CDSCO,DCGI).
- Insurance and indemnity arrangements.

3. Protection of Research Participant Confidentiality

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

4. Informed Consent/ Consent Process

- Non-study-specific basic elements required
  - A statement that the study involves research.
  - An explanation of the extent of the confidentiality of records identifying the subject.
  - An explanation of any compensation and any available treatments if injury occurs during study participation.
  - An explanation of appropriate contact persons for answering pertinent questions about the study.
  - A statement that the subject's study participation is voluntary: (1) right of the subject to refuse from study participation and (2) right of the subject to discontinue from study participation at any time.
- Study-specific basic elements required
  - An explanation of the purposes of the study and the expected duration of the subject's participation.
  - A description of the procedures to be followed and identification of any procedures which are experimental.
  - A description of any foreseeable risks or discomforts to the subject.

- A description of any direct and/or indirect benefits to the subject.
- A disclosure of alternative procedures or courses of treatment, if any.

- Study-specific additional elements required
  - A statement of possibly unforeseeable risks to the subject or to the embryo or foetus.
  - An explanation of any anticipated circumstances under which the subject's participation may be terminated by the investigator without regard to the subject's consent.
  - A description of the anticipated expenses, if any, to the subject for study participation.
  - An explanation of the consequences of withdrawal from study participation by the subject.
  - A statement that, if any, significant new information that may be relevant to the subject's willingness to continue participation will be provided during the study.
  - The approximate number of subjects involved in the study.

5. **Community Considerations**

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

10. Review of informed consent documents

1. **Essential Elements:**

- Statement that the study involves research and explanation of the purpose of the research
- Statement that the study is approved by IEC
- Expected duration of the Subject's participation and total number of subjects that will be accrued on the study.
- Description of the procedures to be followed, including all invasive procedures
- Description of any reasonably foreseeable risks or discomforts to the Subject
- Description of any benefits to the Subject or others reasonably expected from research. If no benefit is expected Subject should be made aware of this.
- Disclosure of specific appropriate alternative procedures or therapies available to the Subject.
- Statement describing the extent to which confidentiality of records identifying the Subject will be maintained and who will have access to Subject's medical records
- Trial treatment schedule(s) and the probability for random assignment to each treatment (for randomized trials)
- Compensation and/or treatment(s) available to the Subject in the event of a trial-related injury
- An explanation about whom to contact for trial related queries in the event of any injury and rights of Subjects
- The anticipated prorated payment, if any, to the Subject for participating in the trial. In particular IEC review payments to determine that:
    - The amount of payment and the proposed method and timing of disbursement neither is coercive nor presents undue influence.
    - In case any amount paid as a bonus for completion is reasonable and not so large as to unduly induce participants to stay in the study when they would otherwise have withdrawn.
    - A description of acceptable and unacceptable payment arrangements for the sponsor, organization, researcher, and those referring research participants, if applicable:
    - Address the acceptability of payments in exchange for referrals of prospective participants ("finder's fees" or" referral fees").
    - Address payments designed to accelerate recruitment that are tied to the rate or timing of enrolment ("bonus payments").
- Subject's responsibilities on participation in the trial

- Statement that participation is voluntary, that the subject can withdraw from the study at any time and that refusal to participate will not involve any penalty or loss of benefits to which the Subject is otherwise entitled
- Any other pertinent information

2. <u>Additional elements, which may be required</u>

- Statement of foreseeable circumstances under which the Subject's participation may be terminated by the Investigator without the Subject's consent.
- Additional costs to the Subject that may result from participation in the study.
- The consequences of a Subject's decision to withdraw from the research and procedures for orderly termination of participation by Subject.
- Statement that the Subject or Subject's representative will be notified in a timely manner if significant new findings develop during the course of the research which may affect the Subject's willingness to continue participation will be provided.
- A statement that the particular treatment or procedure may involve risks to the Subject (or to the embryo or fetus, if the Subject is or may become pregnant), which are currently unforeseeable.
- Approximate number of Subjects enrolled in the study
    - A full description of the process for obtaining informed consent, including the identification of those responsible for obtaining consent
    - Adequacy, completeness and comprehension of written and oral information to be given to the research participants, and, when appropriate, their Legally Acceptable Representative(s) (LAR)
    - Clear justification for the intention to include research participants who cannot consent, and a full account of arrangements made to obtain their consent/authorisation/consent of LAR;
    - 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;
    - Provisions made for receiving and responding to queries and complaints from research participants or their representatives during the course of a research project.

11. Review of subject recruitment procedures

- The characteristics of the population from which the research participants will bedrawn (including gender, age, literacy, culture, economic status, and ethnicity)
- the means by which initial contact and recruitment is to be conducted;
- the means by which full information is to be conveyed to potential researchparticipants or their representatives;
- inclusion criteria for research participants;
- exclusion criteria for research participants;
- students or staff recruitment in research
- healthy volunteers.
- information contained in the advertisement and mode of its communication.
- final copy of printed advertisements.
- final audio or video taped advertisements.
- <u>Advertisements:</u>

  The IEC reviews advertising to ensure that advertisements:
  - DO NOT State or imply a certainty of favourable outcome or other benefits beyond what is outlined in the consent document and the protocol.
  - DO NOT Include exculpatory language.
  - DO NOT Emphasize the payment or the amount to be paid, by such means as larger or bold type.
  - DO NOT Promise “free treatment” when the intent is only to say participants will not be charged for taking part in the investigation.
  - Advertisements are limited to the information prospective participants need to determine their eligibility and interest, such as:
    - The name and address of the researcher or research facility.
    - The purpose of the research or the condition under study.
    - In summary form, the criteria that will be used to determine eligibility for the study.
    - A brief list of benefits to participants, if any.
    - The time or other commitment required of the participants.
    - The location of the research and the person or office to contact for further information.

12. Review of on-going studies

The purpose of continuing review is to monitor the progress of the study which was previously approved; not only for the changes but to ensure continued protection of the rights and welfare of research subjects.

It is the responsibility of the IEC secretariat to send reminders to PIs regarding the submission of Continuing Review Application/Annual Status Report.
All the approved studies will be reviewed atleast annually. IEC is responsible for determining the date of continuing review if the project will be reviewed more frequently in the year including specific criteria used to make these determinations (e.g., an IEC may set a shorter approval period for high-risk protocols or protocols with a high risk: potential benefit ratio). This decision is taken during the IEC meeting wherein the project is finally approved.
IEC is primarily responsible for reviewing the study progress, the occurrence of unexpected events or problems, and the rate of accrual of participants. The protocol, informed consent documents and assent documents are examined to ensure that the information remains accurate. The IEC has delegated this responsibility of initial detailed review of Continuing Review Application to GIMS-IEC. The IEC has the same options for decision making on a continuing review application as for an initial review application. The decision is made as, approved to continue the study; approved with modifications; or not approved.

Detailed Instructions

1. Determine the date of continuing review

- The secretariat will look through the master file of projects approved by the IEC for the due date of continuing reviews.
- The Secretariat should receive the continuing review application well in advance i.e. 10 months after IEC final approval and atleast annually.

2. Notify the Principal Investigator or the study team

- Reminders in writing/email are sent from IEC secretariat to the Principal Investigators for submission of /Continuing review applications for projects
- Principal Investigator should submit three hard copies of the report (1+2) and a soft copy.

3. Manage continuing review application upon receipt

- The Secretariat will receive the Continuing Review Application submitted by the Principal Investigator for each approved study.
- Upon receipt of the Continuing Review Application, the Secretariat of the IEC will perform the following
- However IEC may verify from sources other than the investigators to ensure that no material changes had occurred since previous IEC review by conducting monitoring of the study.
- The projects for which this may be done includes complex projects involving unusual levels or types of risk to subjects; projects conducted by investigators who previously have failed to comply with the regulatory/IEC requirements, projects where concern about possible material changes occurring without IEC approval have been raised based upon information provided in previous continuing review reports or from other sources.

4. Verify the contents of the package

- The Secretariat will check for duly complete and signed application by Principal Investigator.
- An original copy with 2 photo copies and a soft copy will be submitted

5. Review of Continuing Review Application

- If IEC determines that a project needs verification from sources other than the investigators that no material changes have occurred since previous IEC review, including specific criteria used to make these determinations (e.g., such criteria could include some or all of the following:

  (a) randomly selected projects;

  (b) complex projects involving unusual levels or types of risk to subjects;

  (c) projects conducted by investigators who previously have failed to comply with the regulatory/IEC requirements ;

  (d) projects where concern about possible material changes occurring without IEC approval have been raised based upon information provided in continuing review reports or from other sources.)
- The DSMSC Secretary will review the Continuing review Application and will record his/her comments on the application and the same will be forwarded to the IEC Secretary

- In case any clarifications or queries are raised by the Secretary GIMS-IEC the same will be intimated to PI and reply will be awaited.
- The IEC Secretary will decide whether to discuss the application along with the comments of the GIMS-IEC and Principal Investigator's response in the next full board meeting or expedited review meeting.

6. Prepare meeting agenda

- The Secretariat will follow procedures on the preparation of meeting agenda and place the forwarded Annual Progress Report/Continuing Review.
- Application on the agenda for the full board/expedited review meeting of the IEC.

7.Review Process

- The IEC Chairperson/ Member Secretary/ members will use the Continuing Review Application Form to guide the review and deliberation process.
- The IEC members could arrive at any one of the following decisions at the IEC meeting: approval to continue the study, not approved or approved with modifications- - Studies for which modifications have been suggested by the IEC may not proceed until the conditions set by the IEC have been met. Studies should be amended and submitted to the IEC within one month for re-review
- The decision will also include any significant findings that have arisen during review process and this will be communicated to Principal Investigator.
- It is the responsibility of Principal Investigator to provide this information to the participants and once done submit the report to IEC.
- The decision regarding the approval / recommended modifications / disapproval will be noted and documented in the minutes of the meeting is recorded by the Member Secretary.
- The IEC Secretariat will maintain minutes of the meeting relevant to the continuing review as part of the official record of the review process.
- Continuing review of the study may not be conducted through an expedited review procedure, unless the study was eligible for, and initially reviewed by, an expedited review procedure; or the study has changed such that the only activities remaining are eligible for expedited review.
- Continuing review of research previously approved by the convened IEC (e.g., not originally subject to expedited review) may be eligible for expedited review:
- Where the research is permanently closed to the enrollment of new subjects; all subjects have completed all research-related interventions; and the research remains

active only for long-term follow-up of subjects; or Where no subjects have been enrolled and no additional risks have been identified; or Where the remaining research activities are limited to data analysis.

8. Store original documents

- The IEC secretariat will file the continuing review in master file of the research study.

9. Communicate the IEC decision to the Principal Investigator

- The Secretariat will notify the Principal Investigator of the decision.
- If IEC has recommended modifications, the decision will be notified to the Principal Investigator and he/she will be requested to resubmit the relevant documents within 1 month for the approval till then the subject recruitment or enrollment is suspended, however incase of safety concerns the project is completely suspended.
- Principal Investigator will be communicated about the decision within 15 working days after the minutes are finalized.

10. Lapses in IEC Approval

- Investigators must plan ahead to meet required continuing review dates.
- If an investigator fails to submit an electronic Continuing Review Application to the IEC or the IEC does not approve continuation of the research one year before the date of lapse, the research must stop.
- All of the following research procedures must stop:
    - Subject recruitment or enrollment
    - Collection of data/information
    - All research-related interventions or interactions with currently enrolled subjects
    - Data analyses involving subject identifiable data
- Exception: Research-related interventions or interactions with currently enrolled subjects can continue only if stopping the research would jeopardize the rights or welfare of current subjects.
- The IEC must make this determination and decide which subjects should continue with the intervention during the lapse.
- A request for such an exception must be made in the writing to the IEC by the PI.

13. Review of Protocol Deviation/Non-Compliance / Violation / Waiver

- The investigators/ trial sites should follow the procedures written in the approved protocol; comply with national / international guidelines / institutional guidelines or rules or procedures mandated by the IEC for the conduct of human research respond to the IEC requests regarding statutory, ethical, scientific or administrative matters.
- The IEC secretariat is responsible for receiving deviations /violations as per and waiver reports submitted by the Principal Investigator/others and placing it on the agenda of the meeting.
- The IEC secretariat is responsible for receiving noncompliance reports and taking the appropriate action.
- Reporting of deviation/ /violation in any other reporting format will not be accepted.
- IEC members should review and take action on such reports.

Detailed instruction

1.Protocol violation/s

- Definition: Divergence or departure from the expected conduct of an approved study not consistent with the current Institutional Ethics Committee approved version of the research protocol, consent document or addenda
- This usually constitutes a change in the conduct of the research that should have received prospective IEC review and approval prior to implementing the change; or has harmed or posed a significant risk of harm to a research subject or others; or has damaged the scientific integrity of the data collected or confounded the scientific analysis of the study results; or has resulted from willful or voluntary misconduct on the part of a Principal
- Investigator or a member of the research team. Examples:
    - patient being consented after the screening procedures are completed
    - patient being consented after the first dose of the drug has been given

2. Protocol deviation/s

- Definition: Divergence or departure from the expected conduct of an approved study not consistent with the current Institutional Ethics Committee approved version of the research protocol, consent document or addenda is a protocol deviation if it: has no substantive effect on the risk posed to a research subject or others; will not affect the subjects' willingness to participate in the study; has no substantive effect on the value of the data collected; does not confound the scientific analysis of the study results; and did not result from willful or voluntary misconduct on the part of an Investigator or a member of the Investigator's study team.

- Examples:
    - wrong version of the informed consent form being used
    - sample collections at different time points than specified in the protocol
    - patient following up on days not specified in the protocol

3. Protocol Waiver

- It is a prospective deliberate decision to deviate from the protocol that has been approved by the sponsor. Such waivers must be notified to and approved by IEC
- Member Secretary/Chairperson. **e.g.** Protocol Waiver means a prospective decision by a sponsor or investigator to permit accrual of a subject who does not satisfy the approved inclusion/exclusion criteria for enrollment (age, concurrent medication).
- When a deviation occurs it should be reported to the sponsor as well as the IEC.
- In some instances a sponsor will issue a waiver related to a specific subject, to continue the subject in the study
- Examples of sponsor waivers are: it is in the subject's best medical interest to remain on study exception to inclusion/exclusion criteria (age, concurrent medication) visits out of sequence or out of protocol "window" injection of study drug in left arm rather than right arm.

4.Non-compliance

- Noncompliance is defined as failure to comply with national regulations, IEC policy or the determinations or requirements of the IEC.
- Non serious and Non continuing noncompliance involves isolated incidents, e.g. an unintentional mistake, an oversight, or a misunderstanding.
- The issue is not serious or continuing in nature.
- Serious non-compliance: An action or omission, non-compliant with National regulations or IEC policy, taken by an investigator that any other reasonable investigator would have foreseen as increasing risks or compromising the rights and welfare of a participant or other persons.
- Continuing non-compliance: A pattern of repeated actions or omissions taken by an investigator that indicates a deficiency in the ability or willingness of an investigator to comply with National regulations, IEC policy or determinations or requirements of the IEC.
- Research Misconduct noncompliance that involves callous disregard for the protection of human participants or for the integrity of research may meet the

definition of research misconduct. Any fabrication, falsification, or plagiarism in proposing, performing, or reviewing research or reporting research results.

Detection of Protocol deviation/ non-compliance/ violation/waiver

- The IEC members performing monitoring of the project at trial site can detect a protocol deviation/non-compliance/violation if the project is not conducted as per protocol/ national/international regulations, while scrutinizing annual/ periodic reports/ SAE reports based on any other communication received from the Investigator/ trial site/ sponsor/ study monitor/ CRO.
- Additionally, information regarding noncompliance in studies that enroll human participants may come to the attention of the IEC through: continuing reviews
- For cause monitoring
    - audit reports
    - SAE reports
    - IEC minutes
    - Any other sources.
- The Secretariat can detect a protocol deviation/non-compliance/ violation from failure to: comply with statutory requirements; respond to requests from the IEC within a reasonable time limit; respond to communication made by the IEC,
- The PI himself/herself should forward protocol deviation / non- compliance /violation/waiver reports to the IEC within 10 working days of the PI's knowledge of the deviation/violation.
- Investigators, research staff, or other individuals affiliated with TMC are required to report all suspected noncompliance to the IEC
- Communication/ complaint/ information received from research participant who has been enrolled or any individual who has been approached for enrollment.
- Any report/ communication brought to the notice of member secretary /Chairperson of IEC.
- Communication received from the Director, TMC informing IEC about an alleged protocol violation/ non-compliance/ protocol deviation.

Noting protocol deviation / non-compliance / violation/waiver by the Secretariat

- The IEC members who have performed monitoring of a particular trial and detect protocol deviations/non-compliance/violations will inform the Secretariat in writing.
- Whenever a protocol deviation / non-compliance / violation has been observed the Secretariat will ensure that the issues as well as the details of noncompliance involving research investigators are included in the IEC meeting agenda.
- The deviations/violations will be scrutinized for gravity and implications in the formal full board IEC meeting. The IEC decision will be communicated to the PI.

Procedures for Handling Suspected Noncompliance

- Upon receipt of an allegation, Member Secretary IEC in consultation with Chairperson, IEC will review the allegation and determine if it is valid. If the allegation is valid, then will undertake an inquiry. Chairperson, IEC may temporarily suspend the study, pending review in IEC.
- Member Secretary IEC in consultation with Chairperson, IEC undertakes an inquiry of the allegations within 7 week days of the suspected noncompliance.
- The purpose of the inquiry is fact-finding, and may involve examination of study records and discussion with the research team, other personnel, research participants, witnesses, the complainant (if not anonymous), and others as appropriate.
- Qualified IEC staff documents and compiles the information and Member Secretary IEC presents the findings to the IEC.
- IEC determines whether the allegation is (1) non-serious and non-continuing or (2) serious or continuing noncompliance that warrants investigation by the IEC or (3) has no basis in fact.
- IEC determines if immediate suspension of study procedures and/or study enrollment is required for the project in question, as well as for other projects under the same investigator.
- This initial decision is based on preliminary review of available information, communication with the principal investigator(s) involved in alleged noncompliance activities, and the seriousness of the allegations.
- The principal investigator(s) involved in the allegations and associated research staff personnel, appropriate Department Head(s), and Institutional Head are notified in writing about any suspension.
- National regulatory agencies are notified, if applicable.

- In case of externally funded studies, notice is sent to the sponsor and to the concerned regulatory bodies.
- If a study is suspended, further fact-finding and a timely review by a convened IEC determines the length of any suspension.
- If the noncompliance activity is determined to be non-serious and non-continuing: The issue is resolved by a subcommittee of IEC (comprising of member Secretary, IEC, DSMSC Secretary, one IEC member). Principal investigator(s), and concerned staff may be called for the discussion.
- Member Secretary IEC documents the outcome of all communications in writing.
- This report includes any sanctions or corrective actions required on the part of the investigator and the timelines for resolution.
- A copy of this report is sent to the principal investigator(s) involved in the noncompliance activities, associated research staff and others as deemed appropriate within 21working days.
- A written response from the principal investigator acknowledging the report and describing corrective actions is required within 7 working days from the date of the corrective report.
- The complainant will be provided information as deemed appropriate by the IEC Chair.
- All communication is documented in a restricted IEC confidential file.
- If during the inquiry of a non-serious or non-continuing noncompliance is determined that the noncompliance is serious or continuing, the matter will be referred to the full board IEC for their investigation.
- If the noncompliance activity is determined to be a serious or continuing, the matter is forwarded to the IEC Secretariat for their investigation: IEC Chair(s) and member Secretary IEC, readdresses the possible need for suspension of study procedures and/or study enrollment for the project in question, as well as for other projects under the same investigator, pending a timely review by a convened Institutional Review Board.
- If research activity suspension is warranted: The principal investigator(s) involved in the noncompliance activities and associated research staff, Department Head(s) and Institutional Officials are notified in writing about any suspension.

- Concerned National regulatory agencies are notified, if applicable In case of national externally funded studies, notice is sent to the sponsor and to the concerned regulatory bodies.
- The issue is presented to the next appropriate convened IEC. For urgent issues, member Secretary IEC may convene an emergency meeting of the IEC.
- The IEC will receive a copy of the most recently approved consent form, any necessary sections from the IEC approved protocol and all documented communications and discussions concerning the noncompliance from the inquiry phase.
- The complete IEC protocol will be available at the IEC meeting.
- The Principal Investigator will be invited to attend the meeting and provided a opportunity to respond to the allegation(s).
- The IEC may also meet with the complainant (if no anonymous) and others as needed.
- After the IEC has completed the investigation, the IEC will determine the appropriate course of actions, such as:

  Modification of the research protocol;

  Modification of the informed consent form or process;

  Additional information provided to past participants;

  Notification of current participants (required when such information may related to participants' willingness to continue to take part in the research;

  Requirement that the current participants re-consent to participation;

  Modification of the continuing review schedule;

  Monitoring of research;

  Monitoring of the consent process;

  Suspension of the research;

  Termination of the research;

  Obtaining more information pending a final decision;

  Referral to other organizational entities (e.g., legal counsel, risk management, institutional official, etc.);

  Requirement of additional training or re-training;

  Other appropriate actions
- A copy of IEC report is sent to the principal investigator(s) involved in the noncompliance activities, associated research staff and others as deemed appropriate within 21working days. ***Board discussion, Decision and Action***

- If a protocol deviation / non-compliance / violation is detected by an IEC member during a monitoring visit, he/she will present the monitoring report which will be discussed at the full board meeting.
- If detected by the Secretariat/forwarded by Principal Investigator, the Secretary will present the protocol deviation / non-compliance / violation/waiver information.
- Each allegation is taken seriously and reviewed in a consistent, prompt, and professional manner. Additionally, care is taken to maintain confidentiality.
- The Chairperson/IEC members will review the information available and take a decision depending on the seriousness of the violation.
- The decision will be taken to ensure that the safety and rights of the research participants are safeguarded.
- The decision will be taken by consensus and if no consensus is arrived at, voting will be conducted.
- The actions taken by the IEC could include one or more of the following:
    - Determine that no further action is required, or take other actions as appropriate.
    - Inform the PI that the IEC has noted the violation/ noncompliance/ deviation, and instruct the PI to ensure that deviations/noncompliance/ violations do not occur in future and to follow IEC recommendations.
    - Enlist measures that the PI would undertake to ensure that such deviations/noncompliance/violations do not occur in future.
    - Observe the research or consent process,(depending on the nature and frequency of the deviation)
    - Suggest modifications to the protocol
    - Alter the interval for submission of the continuing review/annual project status
    - Require additional training of the investigator and study team
    - Reprimand the PI.
    - Seeking additional information from the Principal Investigator.
    - Audit of trial by the IEC.
    - Suspend the study till additional information is made available and is scrutinized.
    - Suspend the study till recommendations made by the IEC are implemented by the

- PI and found to be satisfactory by the IEC.
- Suspend the study for a fixed duration of time.
- Suspension or termination of the study
- Revoke approval of the current study.
- Inform DCGI/ other relevant regulatory authorities.
- Keep other research proposals from the PI/ Co-PI under abeyance.
- Review and/ or inspect other studies undertaken by PI/Co-PI.

Procedure for notifying the investigator and other concerned authorities

- The IEC secretariat records the IEC decision.
- The Member Secretary drafts a notification letter.
- The signed letter by Member Secretary is sent to the Principal Investigator and Department Head(s) and Institutional Officials (if required)
- The IEC secretariat sends a copy of the notification to the relevant national authorities and institutes if applicable, as in the case of a multi-centric trial.

Records and follow up to be kept by IEC secretariat

- The IEC secretariat:
  - Keeps a copy of the notification letter in the respective project file.
  - Stores the file on the shelf with an appropriate label.
  - Follows up the action after a reasonable time.

14. Policy for financial declaration of payments

- Administrative officer of GIMS-IEC is responsible for managing adequate finance, human resource allocation for administrative work and record keeping.
- Member Secretary will oversee the administrative activities.
- Administrative officer of GIMS-IEC , Kalaburagi, shall be maintaining financial transparency of ethics committee payments.
- The IEC of GIMS maintains financial records which include the committee fees for their services, an honorarium payment to each of the members and all other expenses incurred.

- All the IEC members are given honorarium as per decision taken by the Director and administrative officer of GIMS.
- The subject experts/independent consultant if invited shall be given remuneration & Conveyance allowance as decided by the GIMS-IEC.
- **All other expenses**
    - The conveyance allowance of approximately Rs. 300/- will be provided to the chairperson.
    - All expenditure of IEC is managed through payment received as fee.
    - All expenditure including meeting arrangement cost, travel arrangement to chairperson and external members, Ethics Committee Member Training arrangement, stationary and other infrastructure requirements.
- **Procedure to maintain financial record**
    - IEC coordinator will submit all payment cheque/DD to account department of the institute.
    - All payment received are separately maintained.
    - All financial payments received and disbursed shall be reviewed by member secretary at end of every financial year.
    - All financial transactions are liable under Institute's internal audit yearly.
- **Deposits and Accounting:** The EC administrative staff shall collect the fees (cash or cheque). The deposits shall be made to the GIMS-IEC account (Gulbarga Institute of Medical sciences- Institutional ethics committee). The Account section, GIMS, Kalaburagi shall maintain deposit records according to policy. Annual compiled data related to finance of IEC shall be shared by Accounts section, GIMS, Kalaburagi.

15. Mechanism for examination of SAEs and recommendations for payment of Compensation

- The primary responsibility of the GIMS-IEC is to review and address SAE and unexpected events involving risks to research participants. In addition, the committee is authorized to offer mediation under appropriate circumstances.

IEC should also make sure that researchers are made aware of the policies and procedures concerning reporting and continuing review requirements.

Detailed instructions

A. <u>On site SAEs</u>

(i) Instructions for PI

- **The initial reports of all serious adverse event of Death/ other than death** should be reported by the PI along with the justification for the causality assessment **within 24 hours** of the occurrence to-

➢ IEC

➢ Sponsor or its representative

➢ CDSCO (in case of studies that require approval of the CDSCO)

- **The follow up report of the serious adverse event of Death/ other than death** along with the justification for the Principal Investigator's causality assessment shall be forwarded by the Investigator within **fourteen calendar days** of the occurrence of the serious adverse event of death to-

➢ IEC

➢ Sponsor or its representative

➢ CDSCO (in case of studies that require approval of the CDSCO)

➢ Head of the Institution (in case of studies that require approval of the CDSCO)

➢ ICMR (in case of studies that require approval of the ICMR)

- In case the event is Death due to disease progression, the event should be notified in the SAE reporting format unless it is specified in the IEC approved protocol that such events will not reported.
- If the patient is out of trial and on survival follow up the event should be notified unless it is specified in the IEC approved protocol that such events will not be reported
- SAE reports are received by GIMS - 01 signed hard copy (original) + softcopy
- Serious Adverse Event should be graded as per Common Terminology Criteria for Adverse Events (CTCAE) Ver. 5.0
- Follow-up reports on the SAEs should be submitted within 14 calendar days of the initial report or when any additional information regarding the event is available, whichever is earlier.

(ii) SAE related activities before IEC meeting

- One signed hard copy and a soft copy of the SAE report must be submitted to the GIMS Office.

- The IEC Secretariat will verify if the reports are complete, signed and dated by the PI/Co-PI/Co-I and will check for dates and typo errors in the SAE report such as SAE description, SAE term and CTCAE grading
- In case the IEC Secretariat notes that the report is incomplete or incorrect, the report will be returned to the PI with the consent of Secretary, GIMS
- The IEC secretariat should receive the reports of all SAEs including deaths for IEC approved studies within 24 hours of the occurrence of the SAE.
- In case of public holidays or weekends or any other justified reasons, SAEs may be reported as email notifications or soft copy attachment of SAE form in order to meet SAE reporting timelines. Email notifications should include patient trial id, patient case number, SAE event and a brief description of the SAE.
- However duly signed hard copies of the SAEs along with the email notification(hard copy) should be submitted to GIMS office on the next working day.
- The SAE reported for death will be stamped “Death” on the right corner of the1st page of SAE form for easy / immediate identification.

(iii) Actions to be taken by Member Secretary, IEC

- The Member Secretary will review the SAE Report, write comments and forward it to the Secretary, GIMS, immediately.
- If the SAE reported is “Death or outcome of any SAE reported is ‘death’, the Member Secretary, IEC, will review the SAE report (either hard copy or softcopy) and forward it to Secretary, GIMS within 1 working day for immediate action either as hard copy or via email.
- If deemed necessary, Member Secretaries of IECs and Secretary, GIMS will review the SAE death, either in person or by e-mail/ telephone and inform the Chairperson, IEC.
- Any queries raised are emailed to the PI for action
- In case of urgency or if a particular significant trend in serious unexpected and related or unrelated events is observed on any trial a meeting may be held.
- Based on discussion, necessary action may be taken by the Secretary/IEC Member Secretary
- SAEs received from 1st – 31st of every month are reviewed in the schedule GIMS meeting

- Two lead discussants are assigned by Secretary GIMS for SAE review. It is ensured that the lead discussant is not a part of the study team and has no conflict of interest.
- Agenda is sent to Secretary, GIMS for finalization and signature
- The original signed hard copy of agenda is filed. The soft copies of meeting agenda and SAE reports are sent to GIMS members via email for review.

(iv) After the GIMS-IEC review of SAE

- After the GIMS-IEC meeting, the Minutes are finalized by the Secretary, GIMS.
- A formal letter signed by GIMS Secretary will be sent to the investigator/s with instructions for specific actions as per the GIMS decision.
- In case a PI fails to respond to the GIMS-IEC letter, the matter will be discussed at the next full board IEC meeting and a decision will be taken for specific action
- The IEC secretariat will send the letter to the PI and file a copy of the letter in the master file of the research protocol.
- The original signed hard copy of Minutes of meeting is filed in the 'GIMS-IEC Agenda and Minutes file'
- Minutes are ratified in the next GIMS meeting.
- PI should respond to GIMS-IEC queries within 07 working days from the receipt of the IEC query letter. The PI response to GIMS queries are reviewed by Secretary GIMS. These replies get discussed in the next scheduled GIMS meeting and may be forwarded to IEC in case further opinion is required.
- The Member Secretary will table the SAEs and the GIMS minutes in the next earliest full board meeting of respective IEC.

(v) Responsibilities of the IEC in case of studies that are approved by licensing authority (DCGI):

- In case of SAE (any) report, IEC after due analysis will send its opinion on compensation to the licensing authority within 30 calendar days of the occurrence of the serious adverse event

(vi) During the IEC meeting

- The Secretary, GIMS will discuss the SAEs and actions taken in the IEC meeting.
- The minutes of GIMS meeting will be discussed. If appropriate, specific action or combination of actions will be taken, based on the consensus decision of the IEC. Some of which are listed below:

➢ Note the SAE report in the IEC records if information submitted is found to be adequate.

➢ Direct the PI to inform participants already enrolled in the study about the SAE and request them to undertake additional visits, additional procedures, additional investigations, etc. as per recommendation.

➢ Direct the PI to re-evaluate the event as to whether it is AE/SAE and report to IEC.

➢ Direct the PI to inform participants already enrolled in the study about the SAE and obtain their consent regarding continuation in the research study, if necessary.

➢ Request further follow up information

➢ Request additional details

➢ Recommend an amendment to the protocol, the ICD, Participant information sheet, investigator brochure and/ or any other document.

➢ Recommend whether or not compensation should be paid to the patient /his nominee for trial related injury / death as per institutional policy.

➢ Suspend certain activities under the protocol (while going on with activities intended to protect the safety, well-being of participants who have already been enrolled);

➢ Suspend enrolment of new research participants;

➢ Suspend the study till amendments requested for by the IEC are accepted

➢ Suspend the study for a fixed duration of time;

➢ Suspend the study till additional information is obtained;

➢ Suspend the study till review is completed;

➢ Terminate the study;

➢ Any other action

(vii) Actions to be taken by Chairperson

- The Chairperson, IEC on the basis of the information and comments received from the Member Secretary IEC and Secretary GIMS, and applying his/ her judgment will direct the IEC Secretariat to any one or more actions listed below, but are not limited to:

➢ Soliciting opinion of one or more expert in writing. The information can be provided to expert after he/ she/ they agree(s) to the confidentiality clause and abide by the rules and regulations of IEC. The expert would be requested to provide an opinion in writing within 2-14 working days, depending upon the gravity and seriousness of the matter.

➢ Calling for an emergency review by full board.

- This review should be initiated within 48 working hours (2 working days) of receipt of information.
- This review could be done through a meeting, teleconference, email or telephonic conversation.
- The IEC Secretariat will take appropriate steps to ensure that IEC members are informed about this full board meeting.
- Depending upon the complexity of the issue(s) involved, the Chairperson could direct the Member Secretary, IEC, to invite one or more experts whose opinion would be valuable. These experts could participate after they agree to the confidentiality clause and abide by the rules and regulations of IEC.
- For-cause monitoring

➢ Suspend trial-related procedures as listed by the secretariat

➢ Suspending all trial related procedures (except those intended for safety and wellbeing of the participant) till further review by the IEC

➢ Suspending enrolment of new research participants till further review by the IEC

B. <u>Off site SAEs</u>

(i) Off Site SAEs

- where adverse event reports that are serious, unexpected and related (definitely, probably and possibly) to the drug need prompt reporting to the IEC.
- The SAEs that are expected (if listed in the informed consent) or unexpected but unrelated to the drug have to be logged by the PI and to be submitted timely The following log has to be maintained continuously until the end of the study.

- Those off site SAEs which qualify for prompt reporting, will be reported to IEC Secretariat, and forwarded to Member Secretary, IEC and Secretary, GIMS-IEC.
- If the IEC and GIMS-IEC need to review the offsite SAE reports, the committee will request copies of SAE reports at any time, as and when necessary.
- If a trend is observed in SAEs by PI, such a trend needs to be reported by the PI and action on such reports will be taken by the Member Secretary, IEC and Secretary GIMS-IEC.
- The IEC Secretariat will timely accept the complete set of "Off site SAE reports" and/ or the log.

(ii) Off site SAEs (PSUR)

- The PSUR/Line listings submitted by PI on a monthly/quarterly/biannual basis are filed by GIMS-IEC as a detailed review of the same is out of the scope of IEC/GIMS-IEC.
- It is the PI's responsibility to review the listings in detail and report if a trend is observed and communicate the same to GIMS-IEC.
- The offsite SAEs are received in the format as per SOP and one copy is acknowledged and returned back to PI
- The soft copy is saved
- The same is entered in the Offsite SAE entry book by IEC secretariat
- The SAEs are checked and stamped 'For GIMS-IEC/Noted & File' and then forwarded to IEC for signature/review
- Any queries raised by the IEC Secretary are sent to PI by email or letters as applicable; else the Offsite SAEs are filed in the respective project files.
- Depending on the trend observed by the PI, if appropriate, specific action or combination of actions will be taken. Some of which are listed below:

➢ Note the SAE report in the IEC records

➢ Direct the PI to inform participants already enrolled in the study about the SAE and request them to undertake additional visits, additional procedures, additional investigations, etc. as prescribed in the amendment.

➢ Direct the PI to inform participants already enrolled in the study about the SAE and obtain their consent regarding continuation in the research trial, if necessary.

➢ Request further follow up information

- Request additional details
- Recommend an amendment to the protocol, the ICD, Participant information sheet, investigator brochure and/ or any other document.
- Suspend certain activities under the protocol (while going on with activities intended to protect the safety, well-being of participants who have already been enrolled);
- Suspend enrolment of new research participants;
- Suspend the study till amendments requested for by the IEC are accepted
- Suspend the study for a fixed duration of time;
- Suspend the study till additional information is obtained;
- Suspend the study till review is completed;
- Terminate the study;
- Any other action

C. DCGI Query on Serious Adverse Events:

1. DCGI queries on SAEs which were already discussed in GIMS-IEC and ratified in previous IEC meetings will be answered based on the opinion and findings of the GIMS-IEC and IEC at that time. IEC discussion or opinion at that time will be conveyed to DCGI and Principal Investigator.
2. In potentially contentious issues, Member Secretary, IEC will inform Chairperson.
3. Chairperson may use his/her discretion to bring it to the full board IEC meeting. The reply to DCGI is sent with a copy of same to Principal Investigator.

16. Site Monitoring Policies

The purpose of this Standard Operating Procedure (SOP) is to provide the policies for site monitoring.

Scope

This SOP applies to any visit and/or monitoring of IEC approved study protocols. Clinical trials sponsored by external funding sources and industry are continually audited for compliance and monitored for progress by the external monitors. Institutional clinical studies without outside sponsorship are the focus of the monitoring system of this committee.

However, if any of the aforementioned studies require a “for cause” monitoring, as thought necessary by the IEC, these SOPs will also apply to the same.

Responsibility

IEC is charged with the mission of developing and enacting quality assurance procedures to monitor the overall progress of institutional clinical trials and for ensuring adherence to clinical trial and procedural requirements.

This includes review of the overall progress of each study to insure the safety of participants, validity of data, that the projected accrual goals are met on a timely basis, that excess accrual is avoided, that eligibility and evaluability rates do not fall below minimum acceptable standards, that risks are not excessive, that adverse events are appropriately monitored and reported to the appropriate agencies. Inherent in this process is the goal of enhancing the quality of the research by providing the investigator with constructive criticism.

The GIMS-IEC Secretary assigns the GIMS-IEC members /independent experts to monitor the trials.

The monitoring is conducted by at least 2 members of the GIMS-IEC who have enough expertise and understanding of the clinical aspects of the disease/ patient population being studied, with an adequate understanding of relevant biostatistics and clinical trial conduct and methodology.

Detailed instructions

A. Selection of study

- Investigator initiated studies will be identified for routinely monitored (at least annually) by the degree of intervention, sample size, complexity of the study and risk involved.
- Principal Investigator should intimate the IEC after accrual of first 10 participants in the study or after 6 months of initiation of study whichever is earlier.
- Pharma sponsored studies are not routinely monitored but for cause monitoring may be conducted.
- For cause monitoring will be performed for the study for reasons identified by any member of IEC, approved by Chairperson. For cause monitoring could be initiated, in any of the following conditions but not limited to:
    - For high number of protocol violations
    - Too many studies carried out by a Principal Investigator

- High number of SAE reports
- High recruitment rate
- Non-compliance or suspicious conduct
- Any complaints related to the research
- Any other cause as decided by IEC

B. Before the visit

- For cause/routine monitoring of the project, the IEC Chairperson/ Secretary will inform GIMS-IEC to perform the task of monitoring during discussion of the study, on receipt of annual status reports or review of SAEs.
- Two members of the GIMS-IEC who have enough expertise and understanding of the clinical aspects of the disease/ patient population being studied, with an adequate understanding of relevant biostatistics and clinical trial conduct and methodology willbe allocated the task of monitoring a particular trial
- The Secretariat will intimate the PI regarding the scheduled monitoring visit. GIMS-IEC and PI will coordinate the monitoring visit
- A request regarding the monitoring visit will be sent to the monitor along with a copy of the monitoring visit form
- The monitor will also:
    - Notify the Principal Investigator about the scheduled visit.
    - The monitor will review the study project files and make appropriate notes.
    - The monitor may carry copy of documents from the IEC approved project files fo rverification and Study Monitoring Visit Report Form

C. During the visit

The monitor will –

- Review the informed consent document to make sure that the PI is using the current, approved version
- Review randomly the participant's source files for proper informed consent
- documentation. (usually about 10%, or maybe higher)
- Observe the informed consent process, if possible,
- Check investigational product accountability is adequately controlled and documented throughout the product flow (arrival, dispensing, use, return from the participant and

return/destruction after the study). Storage times, conditions and expiry dates mustalso be acceptable and sufficient supplies available wherever applicable.

- Observe laboratory and other facilities necessary for the study, if possible.
- Review the study/ source files to ensure appropriate documentation
- Verifying that the investigator follows the approved protocol and all approved
- amendment(s), if any.
- Ensuring that the investigator and the investigator's trial staff are adequately informed about the trial
- Verifying that the investigator and the investigator's trial staff are performing the specified study functions, in accordance with the approved protocol and any other written agreement between the sponsor and the investigator/institution, and have not delegated these functions to unauthorized individuals.
- Verifying that the investigator is enrolling only eligible participants.
- Verifying that source documents and other study records are accurate, complete, kept up-to-date and maintained.
- Checking the accuracy and completeness of the CRF entries, source documents and other study related records against each other.
- Determining whether all Serious Adverse Events (SAEs) are appropriately reported within the time periods required by GCP/ Regulatory agencies, the protocol, the IEC/IEC, the sponsor, and the applicable regulatory requirement(s). Case record forms would be checked to review the safety data i.e. Adverse Events (AEs) and Serious Adverse Events (SAEs) for the volume or severity of adverse events.
- Collect views of the study participants, if possible.
- Fill the Study Monitoring Visit Report Form and write the comments.

D. After the visit

- The monitor will complete the report describing the findings of the monitoring visit and submit the same to the GIMS-IEC office. After the form is received at GIMS-IEC office, it is checked for completeness. The preliminary comments will be shared with the PI.
- Form is reviewed by GIMS-IEC secretary, and the form is forwarded to IEC Secretary for action
- The IEC Secretary/GIMS-IEC member representative/lead discussant for the project presents the monitoring visit findings including briefing about the study protocol,

performance, SAE and previous monitoring reports if any in the IEC full board meeting.

- The Secretariat will place the report in the correct files.
- Full board recommendations to change the study/ premature termination/ continuation of the project will be informed to the Principal Investigator in writing within **14 days of the meeting**.
- Grounds for recommending suspension or termination of a clinical trial to the IEC include, but are not limited to:
  - Zero accrual for 1-2 years or long-term, low accrual.
  - Stopping rule violations.
  - Major violations in the conduct of the study (including serious IEC violations) that
  - result in an unacceptable audit rating.
  - Safety issues
  - Compliance issues
- The decision to recommend suspension or termination of a clinical trial is
- carefully considered and takes into account whether corrective actions had been requested at previous reviews and were not implemented.
- If the decision is made to recommend suspension or termination of a clinical trial, there commendation will be sent to IEC. IEC has the ultimate authority to effect termination or suspension of a clinical trial.

17. Revision of timeline for archival of documents after completion or termination of study and timeline for submission of application along with study protocol by researcher as per Indian GCP.

To provide guidelines for preparation and maintenance of study files and other related documents for all IEC approved ongoing projects as well as storage/archival/disposal of study files and other study related documents for projects which are completed and closed.

Scope

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

Responsibility

It is the responsibility of IEC staff to ensure that all study files are prepared, maintained, and kept securely for the complete period of the study and for five years after the closure of the project (under a proper system that ensures confidentiality and facilitates retrieval at any time).

Active study files maintenance & archival of closed files

A Study Master File is the file comprising of all essential documents and correspondence related to the study/protocol. Study master file should be established at the time of initial submission in the IEC office.

•The study files are assigned unique identifiers (serial project no.)

•All documents related to the study file are gathered, classified and combined together appropriately.

•All active files are kept in a secured file cabinet with controlled access. Only authorized individuals' i.e. IEC Secretariat will have access to the files. The study files are maintained in an easily accessible and secure place for complete period of the study and at least 5 years after the study closure.

•All closed study files are separately archived.

•IEC staff will archive the closed project files once the completion/status reports are reviewed by the IEC. The completed/closed project files are clearly labelled and stored in the archival room. Only the IEC Secretariat, auditors and the regulatory authorities would have access to these files.

•The records are stored by ITS on servers and are backed-up at regular intervals. Documentation of back-up for the IEC database and electronic files is kept by IT programmer.

Disposal of closed files and copies of protocols and documents submitted for IEC review.

The trial master file will be maintained in the IEC office for complete period of the study and for five years following closure of the study. After completion of the archival period the closed files will be shredded and disposed off in the central shredding facility. However, all the copies of the research projects and documents submitted for IEC review will be shredded by the authorized IEC personnel after the IEC meeting without any notification to the Principal Investigator. A log book of disposed documents will be maintained.

Accessibility / Retrieval

Master files will be made available for inspection and copying by authorized representatives of regulatory authorities after receiving the request in writing.

In case any investigator needs a copy of any document from the master file, he/she should make a written request. The IEC staff will furnish a copy of the required document within a week with the IEC Secretary's consent. The IEC will issue a copy of the requested documents on formal written request.

For administrative purposes, the IEC Secretariat can retrieve archived file(s) without requiring the Chairperson's approval. For this purpose, the IEC Secretary can authorize a staff member of the IEC secretariat to physically retrieve a file.

Final Disposal of Master files

The master files will be disposed off by the IEC secretariat after the archival period of 5 years. A formal written off register will be maintained, providing details of the documents being written off / disposed off.

TIMELINE FOR SUBMISSION OF APPLICATION & STUDY PROTOCOL

1. Purpose

This SOP is designed to describe and act as a guideline for the IEC Secretariat to manage research study submissions

2. Scope

The scope includes the following -

•Submission for initial review

•Resubmission of study with modifications

•Submission of protocol amendments and any other amendments.

•Submission of status reports/continuing review of the study

•Submission of Serious Adverse Events and Deviations/Violations

•Submission of study completion/termination report

•Submission of any other study related documents

3.Responsibility

It is the responsibility of the IEC secretariat to receive record and distribute the study documents for IEC review.

4. Detailed process

A. Receive submitted packages

For the initial review of study, investigators should submit all study related documents to the IEC, no fewer than fourteen (14) days before the next scheduled meeting. The PI should submit research proposal to the IEC for review and approval under any of the 5 sections mentioned below:

- Initial Review Application
- Resubmission of Study with Corrections
- Protocol Amendment or any other amendments
- Annual Status Reports /Continuing Review of the study
- Study Completion / Termination
- Submission of Serious Adverse Events and Deviations/Violations

- Any other documents

The IEC will accept new submissions from Principal Investigators only after ensuring that continuing review applications/status reports of the previously approved studies have been submitted by the Principal investigator in a timely manner. The IEC shall not process a new research proposal from the PI unless the PI has submitted continuing review application/status reports for ongoing IEC approved studies.

B. On receipt of the study related documents the IEC will scrutinize the documents for the completeness of the submission. The scope of administrative review is as enlisted:

- *Check* the submissions for initial review to ensure that all mandatory forms and documents are submitted.
- Submission should include
  - Project submission Form
  - Study protocol
  - Other related documents necessary for initial review
- *Notify* the investigators, if the IEC form is incorrectly filled and/or the submission is incomplete.
- Upon satisfactory submission of research proposals by investigators, The PI is required to obtain permission from the Head of the concerned department, the DMG convener (if applicable) and all investigators who makes up the study team.
- *Check* completeness of hard copy of the research proposal submitted with necessary information and signatures at all designated places in the submission form.
- *Stamp*, sign & date on the cover letter confirming receipt of the documents.
- *Record* the completeness of submission on document receipt form and inform the investigators for necessary action
- *Ensure* payment of Institutional Ethics Committee processing fees for all
- Pharmaceutical sponsored clinical trials.
- *Store* the hard copies and soft copy of the research project. The hard copies will be stored under controlled access storage in IEC office. The soft copy of the study accepted will be stored electronically.
- Additional hard copies if required should be submitted by the PI.

- Soft copy of vernacular versions the ICFs and questionnaires uploaded online shall be accepted only in pdf format
- The running project number, study title, principal investigator, type of study and duration of project will be labelled on each project file.
- All correspondence from and with the IEC Secretariat, for the project, should quote the running project number i.e.211 (unique identity number).

5. Detailed description of Study Project Submission

The study protocol should be accompanied with the following relevant supporting documents for scientific and ethical review.

(i) Project Submission Form

- Grouping of Project
- Project Fact Sheet
- Investigator Declaration and Study Team Undertaking with Duties &Delegation
- Financial Disclosure
- Project Submission Overview
- Budget Sheet for the Proposed Study

(ii) Essential Documents

- Study protocol
- Lay Summary-Provide a non-scientific summary of the proposal, including a statement about the importance of the question the research application will address, the relevance of the research to your country or region, and the potential impact of the study results.
- Case Record Form
- Informed Consent Documents- Participant Information Sheet & Informed Consent Forms (ICFs) for adults. For studies involving children, parent information sheet and consent form and child information sheet and assent form are mandated in case of children between age 7-18 years of age.
- English, & Kannada ICDs are to be mandatorily submitted to IEC. ICDs in other languages may be submitted if required by the study
- Application for waiver of consent (if applicable)
- Audio video informed consent (if applicable)

- Investigator's Brochure (if applicable)
- Package insert/product insert (if applicable)
- Questionnaires (if applicable)
- Agreement to comply with national and international GCP protocols for clinical trials
- Regulatory clearance from appropriate regulatory authorities i.e. Drugs Controller General India (DCGI) approval/ICMR/Health Ministry Screening Committee(HMSC)(if applicable)
- For national/international collaborative study Draft/Final Memorandum of
- Understanding (MoU) between the collaborating institutes
- Draft/Final Clinical Trial Agreement (CTA) (if applicable)
- Draft/Final Material Transfer Agreement(MTA) if applicable
- Insurance/Indemnity policies, indicating who are covered (if applicable)
- Participant recruitment and enrollment procedures/advertisement (if any)
- Documentation of clinical trial registration (if applicable)
- Decision of other Ethics Committees (If required / asked for)
- One page, recent, signed and dated curriculum vitae of the investigators indicating qualifications and relevant experience.
- MMC registration certificate of the investigators (if applicable)
- Good Clinical Practice Certificate/Training certificate in clinical research
- Any other important information relevant to the study
- Cover letter enlisting all the documents submitted.

6. Minor revisions of study after initial review for approval

•Minor modifications submitted after initial review of the research proposal that do not alter the risk-benefit assessment for the research and do not require substantial changes in protocol and informed consent document fall under the category of IEC decision **"revision with minor modifications/amendments**"

•PI will submit 1 copy of the revised study related documents along with justification for modification, and clearly highlighted / demarcated sections which have undergone change. The additional hard copies if required should be submitted by the PI.

•The IEC Secretariat will verify the completeness and reconfirm that the copies

contains the revisions highlighted with respect to the earlier submission.

7. Major revisions of study after initial review for approval

•Major modifications submitted after initial review of the research proposal that may alter the risk-benefit assessment for the research and require substantial changes in protocol and informed consent document fall under the category of IEC decision **"revision with major modifications for resubmission"**

PI will submit 1 copy of the revised study related documents along with justification for modification, and clearly highlighted / demarcated sections which have undergone change. The additional hard copies if required should be submitted by the PI.

•The IEC Secretariat will verify the completeness and reconfirm that the copies contain the revisions highlighted with respect to the earlier submission

8. Post approval- Research Protocol Amendments and other study related documents

•Investigators who may wish to modify or amend their approved protocols and/or other study related documents must seek IEC approval

•The PI should submit 1 hard copy + soft copy of the amended documents. Additional hard copies if required should be submitted by the PI.

•The IEC Secretariat will verify the completeness of the submission.

•The PI should highlight the modification/s in the amendment, and provide a summary of changes. PI should also indicate whether these changes would entail change in the ICF as per the form.

•The Member Secretary in consultation with Chairperson will decide whether to initiate:

- Full board review or
- Carry out an expedited review in case of minor administrative amendment

9. Annual Continuing Reviews of Approved Research Studies

•The GIMS-IEC will send reminders for annual report to individual PI at least 90 days prior to lapse of approval.

•The GIMS-IEC will receive a copy of Annual Status/ Continuing Review Report in the prescribed format and related documents for the approved research study.
•The IEC Secretariat will verify the completeness of the Progress report. The IEC Secretariat will sign and date the documents.
•The progress or continuing review application will be discussed in the Full Board meeting of IEC or expedited review meeting of the IEC.

10. Research study Completion/ Premature Termination / Suspension / Discontinuation of the study

•The GIMS-IEC on behalf of the IEC will send reminders for annual status report to Individual Principal Investigators
•The IEC will receive a copy of Study Completion Report / Premature Termination / Suspension / Discontinuation of the study
•The IEC Secretariat will verify the completeness of the Study Completion / Premature Termination / Suspension / Discontinuation of the study filled by the PI.
•The Study Completion / Premature Termination / Suspension / Discontinuation of the study report will be discussed in Full Board/ Expedited meeting of IEC.

11. Submission of Serious Adverse Events and Deviations/Violations

•The IEC secretariat will receive a copy of SAE and Deviations and Violations in the prescribed format
•The IEC Secretariat will verify the completeness of the SAE/Deviations and Violations filled by the PI.
•The SAEs will be discussed in the GIMS-IEC meeting and the Minutes of the GIMS-IEC meeting will be forwarded to the IECs.
•The SAE and Deviations and Violations will be discussed in the Full Board meeting of IEC for further action

ANNEXURE -1

GULBARGA INSTITUTE OF MEDICAL SCIENCES, KALABURAGI
Institutional ethics committee

Initial Review Submission Form for Research Proposal

1. Title of the research proposal

2. Name of the Principal Investigator with qualification and designation

3. Name of the Co-Investigator(s) with qualifications and designation

4. Name of the Institute / Hospital / Field area where research will be conducted

5. Forwarding letter from the Head of the Department / Institution / Guide.

6. Protocol of the proposed research: (includes and not limited to) clear research objectives, rationale for undertaking the investigations in human participants in the light of existing knowledge, inclusion and exclusion criteria for entry of participants. Precise description of methodology of the proposed research, including sample size (with justification), type of study design (observational, experimental, pilot, randomized, blinded etc.), intended intervention, dosages of drugs, route of administration, duration of treatment and details of invasive procedures if any, Plan to withdraw or withhold standard therapies in the course of research. Plan for statistical analysis of the study. Ethical issues in the study and plans to address these issues.

7. Proposal should be submitted with all relevant enclosures like proforma, case report forms, questionnaires, follow-up cards, participant recruitment procedures and brochures, if any, Informed consent process, including patient information sheet and informed consent form in English and local language(s). Investigator's brochure for trial on drugs/ devices/ vaccines/ herbal remedies and statement of relevant regulatory clearances. Source of funding and financial requirements for the project.

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

9. Usefulness of the project / trial

10. Expected ‘benefits’ to volunteers / community. ‘Benefits’ to other categories if any

11. Explain all anticipated ‘risks’ (adverse events, injury, discomfort) of the project. Efforts taken to minimize the ‘risks’. Proposed compensation and reimbursement of incidental expenses and management of research related and unrelated injury/ illness during and after research

period. Description of the arrangements for indemnity, if applicable in study-related injuries and description of the arrangements for insurance coverage for research participants, if applicable.
12. Agreement to report all Serious Adverse Events (SAE) to GIMS -IEC.

13. Other financial issues including those related to insurance.

14. An account of storage and maintenance of all data collected during the trial.

15. Research proposals approval by scientific advisory committee

16. For international collaborative study details about foreign collaborators and documents for review of Health Ministry's Screening Committee(HMSC) or appropriate Committees under other agencies/ authority like Drug Controller General of India (DCGI)

17. For exchange of biological material in international collaborative study a MoU/ Material Transfer Agreement between the collaborating partners.

18. Statement of conflicts of interest, if any.

19. Agreement to comply with the relevant national and applicable international guidelines, Good Clinical Practices (GCP) protocols for clinical trials.

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

21. A statement on, probable ethical issues and steps taken to tackle the same like justification for washout of standard drug, or the use of placebo control.

22. Curriculum vitae of all the investigators with relevant publications in last five years.

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

24. Any other information relevant to the study.

25. Signature of the Principal Investigator with date.

Note: The above information and enclosures should be furnished wherever necessary depending upon the nature of study proposal

ANNEXURE-2

FORMAT FOR SUBMISSION OF PROJECTS INVOLVING RESEARCH IN HUMAN SUBJECTS FOR CLEARANCE BY ETHICS COMMITTEE OF GIMS, KALABURAGI.

- Submit five (5) copies of the Research Project along with Covering letter and 'soft copy' on email ***gimspharmacology@gmail.com*** along with a blank CD with the following information to the Member Secretary, Institution Ethics Committee at Room No. ____, _____GIMS , Tel No**.____ .** The Principle Investigator must submit protocol forwarded through the Head of Department.
- No research project shall be / can be started unless ethics clearance/approval is obtained. Please bear in mind that no retrospective / post facto ethical clearance can be provided to research projects which were neither submitted nor wetted by the Institution Ethics Committee.
- All submissions should be made in the prescribed Format of the **Institution Ethics Committee** with signatures of all the investigators. The submission must be accompanied with *Participant Informed Consent Form* (PICF) and *Participant Information Sheet* (PIS), both in English and Kannada/Concerned local Language, **in a simple layman's language, in a narrative form, directed to Participant /LAR, covering all the points given on the website,** before it can be considered for placing before the Institution Ethics Committee. Also ensure that all the pages are numbered.
- **Project Submission Time**: Submissions will be received on all working days.proposals should be submitted before the given last date. All meetings of Institution Ethics Committee will be held as far as possible on first Monday of Jan, March, May, July, September, and November. The frequency will change depending upon the Load .
- While submitting replies raised by the Institution Ethics Committee, the candidates are advised to mention the Institution Ethics Committee reference number/s and also attach a copy of the comments of the Institution Ethic Committee. Moreover if the approval is required in a particular format, the same may be submitted in a CD.
- **Amendment Submission:** While submitting amendments in protocols a covering letter should be provided clearly stating the changes and a certificate by the PI that the changes made in the protocol will not hamper the safety of the subject in anyway.

ANNEXURE-3

Gulbarga Institute of Medical Sciences, Kalaburagi
Institutional ethics committee

Ongoing Approved Research Review Submission Form

1. Reference number
2. Month / Year of approval
3. Number of ongoing review
4. Title of the research proposal
5. Name of the Principal Investigator (PI) with qualification and designation
6. Name of the Co-investigator(s) (Co-PI) with qualification and designation
7. Duration of the Project
8. Source of funding & financial allocation for the project / trial
9. Has subject recruitment begun?
10. If subject recruitment has not begin, give reasons and proceed to No:20
11. How many subjects have been screened?
12. How many subjects have been recruited?
13. How many more to be recruited
14. Is subject recruitment continuing?
15. Are there any ‘drop outs’?
16. Are subjects still receiving active intervention?
17. Have there been any adverse events? If yes, give details
18. Have there been any Serious Adverse Events adverse events? If yes, give details.
19. Have there been any unanticipated study-related problems?
20. Is there any new risk or benefit information? If yes, give details.
21. Are there any interim changes to the protocol or consent form? If yes, give details including submission of revised protocol and consent form for approval

22. Does the scientific literature indicate changes in knowledge relevant to the conduct of the study?

23. List of attachments for review, if any

24. Remarks, if any

25. Signature of the Principal Investigator with date.

Note: The above information and enclosures should be furnished wherever necessary depending upon the nature of study proposal.

ANNEXURE-4

Guideline for preparation of the informed consent form

While submitting your project to the IEC, ensure that you have included an informed consent form that is prepared as per the guidelines for ICMR ethical guidelines.

Kindly note:

i. Informed consent forms in English, Kannada, and Hindi are mandatory and any Language if applicable

ii. Font: Times Roman or Arial or Kannada/ Regional laguage

iii. Size: 12

iv. All the consent forms must have Version No, Date, Page no **in the footer**

v. Separate forms should be prepared when minors (children) are study participants; assent form for the mature minors (age 7-18 years) and consent form for the parents

The consent form template describes the minimal requirements. You are free to add additional information you wish to

Participant Information Sheet & Informed Consent Form

[The simplified title of the project as per the project submission form with names of Principal Investigator and all other investigators.]

Introduction:

You are invited to participate in a study/research/experiment. This document gives you a description of the study/trial in which you are being asked to participate. Your participation in this study is voluntary, and you can enquire about all details before giving your written consent to participate in the study.

Purpose:

The purpose of this study is to

……

Information:

List all procedures, which will be carried out in the study. Clearly state experimental procedures and explain technical and medical terminology in simple, non-technical & direct language. Graphics could be used if helpful in making the text meaningful to the research subject.

If this is a randomized trial, details of both arms of the trial must be explained

State the amount of time required by the subject for the study with clearly stating the total duration of the study.

Clearly state:

i. The number of participants who will take part in the research

ii. Information concerning taping or filming (If applicable)

iii. If case tissues or biological samples, are being retained for research, describe what will be done to the tissues in simple lay person's terms. (If applicable)

Also mention that the many of the most effective treatments used today are the result of clinical trials done in the past.

Confidentiality

The information in the study records will be kept confidential and the clinical charts will be housed (specify the location). Data will be stored securely and will be made available only to persons conducting the study and to the regulatory authorities. The data will not be made available to another individual unless you specifically give permission in writing. No reference will be made in oral or written reports which could link you to the study. Result of the study will not be communicated to the subject unless deemed necessary.

Compensation for study related Injury

Compensation of subjects for disability or death resulting from such research related injury;

Describe the details of compensation or insurance for study related injury to the trial subject.

Explain who will bear the cost in case of trial related injury?

Research subjects who suffer physical injury as a result of their participation in the research study are entitled to financial or other assistance to compensate them equitably for any temporary or permanent impairment or disability subject to confirmation from IEC. In case of death, their dependents are entitled to material compensation.

Statement describing the financial compensation and medical management as under

1. In the event of an injury occurring to the clinical trial subject, such subject shall be

provided free medical management as long as required.

2. In the event of a trial related injury and death, the sponsor or his representative, whosoever has obtained permission from the Licensing Authority for the conduct of clinical trial, shall provide financial compensation for the injury or death

(**As per the DCGI directive,** it is mandatory for sponsors to comply to the following requirement : incase of study related injury, sponsor should provide completed medical care as well as compensation for the injury (Death)as per the provisions of law and same should be included in ICF)

Contact

If you have questions at any time about the study or the procedures, (or you experience adverse effects as a result of participating in this study,) you may contact the researcher, [PI Name], at [Office Address], and [Office Phone Number].

If you have any questions about the informed consent process or your rights as a participant, contact the Member Secretary, IEC [Name], at [Office Address], and [Office Phone Number].

Participation

Your participation in this study is voluntary; you may decline to participate at any time without penalty and without loss of benefits to which you are otherwise entitled.

If you withdraw from the study prior to its completion, you will receive the usual standard of care for your disease, and your non participation will not have any adverse effects on your subsequent medical treatment or relationship with the treating physician

If you withdraw from the study before data collection is completed, your data will not be entered in the study report.

If staff /student is involved - Your participation in this research will not bestow upon you any competitive academic or occupational advantage over other students or staff who do not volunteer, and we will not impose any academic or occupational penalty on those students or staff who do not volunteer."

Informed Consent Form

Participant's Initials: _____ Participant's Name: _____

Date of Birth / Age: _____

Title of the study:.....

(i) I confirm that I have read and understood the information sheet dated _____ [ ]
for the above study and have had the opportunity to ask questions.

(ii) I understand that my participation in the study is voluntary and that I am free [ ]
free to withdraw at any time, without giving any reason, without my medical
care or legal rights being affected.

(iii) I understand that the study investigator and study team, the Ethics Committee and [ ]
the regulatory authorities will not need my permission to look at my health records
both in respect of the current study and any further research that may be conducted in
relation to it, even if I withdraw from the study. I agree to this access. However, I
understand my identity will not be revealed in any information which may get
published.

(iv) I agree not to restrict the use of any data or results that arise from this study provide [ ]
such a use is only for scientific purpose(s).

(v) I agree to take part in the above study. [ ]

I have read the above information and agreed to participate in this study.

Sign/Thumb Impression of the Participant Date

ANNEXURE-5

ASSENT FORM

Subject Title:

1) Patient's Name:

2) Patient's Date of Birth/ Age: 3) Sex:

4) Name of Consenting:

5) Relationship to Patient:

6) Patient's Diagnosis:

i. I have been explained about the study in detail in the language I understand, and I have clarified all my doubts.

ii. I certify that the determination for the proposed health caredecision was made in accordance with the known wishes of the patient, or the patient'sbest interest, as the wishes of the Patient are unknown or unclear.

iii. I agree not to restrict the use of any data or results that arise from this study provided such a use is only for scientific purpose.

iv. I understand that the Patient is unable to consent because of incapability and therefore I consent on the Patient's behalf.

Signature / thumb impression of guardian Date:

Signature of witness Date:

Signature of the investigator Date: