Institutional Human Ethics Committee
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STANDARD OPERATING PROCEDURES (Master SOP)

Institutional Human Ethics Committee (IHEC)

GMERS Medical College & Hospital, Gotri, Vadodara

Version 5

Effective from 8th December 2019

MEMBER SECRETARY
IHEC
GMERS Medical College
& Hospital
Gotri, Vadodara.

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Preface

In any biomedical research involving human beings, the study participants are the most vulnerable of the partners. They are at risk of physical and emotional exploitation. This is largely due to the high esteem in which health professionals and researchers are held by the lay public, which can easily be abused. In addition, there are special groups such as minors, refugees, mentally unsound etc. who are even more prone to exploitation in research.

This SOP states the procedures for constituting the Human Ethics Committee as well as the responsibilities of both the members as well as the principal investigators. I am confident that this SOP will help all the researchers for preparing the research protocols and ensure smooth functioning of the Institutional Human Ethics Committee. I hope this will not only facilitate and expedite project submission and approval but also ensure that no important facets of participants' safety and privacy are overlooked.

Chairman,
Institutional Human Ethics Committee,
GMERS Medical College & Hospital,
Gotri, Vadodara, Gujarat, India

Introduction

This SOP is applicable w.e.f. 8th December 2019 and valid for two years or till revised. This SOP is applicable for all research proposals submitted to Institutional Human Ethics Committee (IHEC), GMERS Medical College, Gotri, Vadodara, Gujarat - 390021.

Adoption of SOP: GMERS Medical College & Hospital, Gotri, Vadodara, Gujarat has adopted this written master Standard Operating Procedure (SOPs) which includes all SOPs

Purpose:

- To establish and constitute the Institutional Human Ethics Committee (IHEC) for GMERS Medical College & Hospital, Gotri, Vadodara, Gujarat
- To contribute to the effective functioning of the IHEC so that a quality and consistent ethical review mechanism for health and biochemical research is put in place for all proposals dealt by the committee as prescribed by ICMR - The ethical guidelines for biomedical research on human subjects, CDSCO, New drugs and clinical trial rules 2019, DCGI
- To describe the operating procedures for IHEC
- To ensure the safeguards of vulnerable population in clinical research

Responsibility: All members of IHEC and investigators are responsible for implementing these SOPs

Role of IHEC

- IHEC will review and approve all type of research proposals involving human participations with a view to safeguard the dignity, safety and well-being of all actual and potential research participants. The goals of research, however important, should never be permitted to override the health and well-being of the research subjects
- The IHEC will take care that all the cardinal principles of research ethics viz. Autonomy, Beneficence, Non- malfeasance and Justice are taken care of in planning, conduct and reporting of the proposed research. For this purpose, it will look into all the aspects of informed consent process, risk benefit ratio, distribution of burden and benefit and provisions for appropriate compensations wherever required
- It will review the proposals before start of the study as well as monitor the research throughout the study until and after completion of the study through appropriate well documented procedures for example annual reports, final reports and site visits etc.
- The committee will also examine compliance with all regulatory requirements, applicable guidelines and laws
- The mandate of the IHEC will be to review all research projects involving human subjects to be conducted at the institute by the investigator of this institute, irrespective of the funding agency. IHEC may consider the academic project and/or dissertation proposed to be conducted at GMERS Medical College & Hospital, Gotri from investigator outside of this institute. IHEC may also consider academic project and/or dissertation proposed to be conducted outside of this institute from investigator of this institute.

Applicable regulatory guidelines

- Good Clinical Practice (GCP) – Government of India
- Ethical Guidelines for Biomedical Research on Human Subject by ICMR
- International Conference on Harmonization (ICH) GCP guidelines
- New drugs and clinical trial rules 2019

SOP 1. Constituting the Institutional Human Ethics Committee (IHEC)

Scope:

- Dean of the GMERS Medical College & Hospital, Gotri will select and nominate the Chairperson of the IHEC
- The Chairperson of the committee will be from outside of the institute to maintain the independence of the committee
- Dean in consultation with chairperson will nominate the member secretary and other members of the IHEC, who have the qualification and experience to review and evaluate the scientific, medical and ethical aspects of the proposed study
- The member secretary will belong to the GMERS Medical College & Hospital, Gotri and will conduct the function of committee
- Chairperson of the committee will invite the members to join the committee by sending an official request letter
- Members will confirm their acceptance to the chairperson by providing all necessary information and documents
- The number of members in the committee will be minimum 7 to maximum 15 with at least one female member and 50% non-affiliated members
- Other members will be a mix of medical /non-medical, scientific and non-scientific persons /Gender /including lay public to reflect the differed viewpoints
- The Composition of the committee will be as follows
    - A chairperson (Outside of the institute)
    - A member secretary (From the institute)
    - Five to twelve members from different departments / specialties / disciplines or areas
        - Basic medical scientist
        - Clinician
        - Legal expert
        - Social scientist / person from N.G.O / philosopher
        - Lay person from community (Outside the institute)
- The committee may invite individuals/experts from other institutes or communities if required as its member
- There will be adequate representation of age, gender, community, etc. in the committee to safeguard the interests and welfare of all sections of the community / society
- All members should be aware of local, social and cultural norms, as this is the most important social control mechanism
- Chairperson will appoint joint secretary to help secretary if required

Quorum requirements

- The minimum of five members are required to compose the quorum
    - Basic medical scientist
    - Clinician
    - Legal expert
    - Social scientist / person from N.G.O / philosopher
    - Lay person from community

Tenure

- **Committee:** Three years
- **Chairperson:** Three years
- **Secretary:** Three years
- **Member:** Three years

Membership Requirements

- The duration of appointment is initially for period of three years
- Chairperson may renew the appointment on the basis of the member's participation
- Each member is required to sign the declaration and confidentiality agreement regarding IHEC activities
- IHEC members have to undergo orientation program in national and international developments in ethics on a regular basis as decided by Chairperson
- At the end of three years, as the case may be, the committee will be reconstituted, and 50% of the members will be replaced by a defined procedure
- A member can be replaced in the event of death or long-term non-availability (Three consecutive meeting) or transfer from the institution or for any action not commensurate with the responsibilities laid down in the guidelines deemed unfit for a member
- A member can tender resignation from the committee with proper reasons to do so with a notice period of one month
- All members should maintain absolute confidentiality of all discussions during the meeting and sign a confidentiality form
- Conflict of interest should be declared by members of the IHEC

Formation of Sub-Committee

- The IHEC may form sub-committee if they need
- The purpose of this committee will be to evaluate post graduate thesis, research project submitted by undergraduate students and residents & even minor academic projects of faculty members

Information to CDSCO in case of change in IHEC composition

- The change in composition may occur due to induction of new members, removal/resignation of members from IHEC, transfer of institutional members, tenure ending of members or reconstitution by head of the institute. Member secretary shall inform the CDSCO within 30 days period in case of changes in IHEC composition.

SOP 2. Confidentiality / Conflict of Interest Agreement

- All appointed members or consultant reviewers shall:
  - Obtain the agreement from the Secretariat
  - Read through the context of the form very carefully and fill it
  - Ask questions, if any and the secretariat officer shall explain or clarify the context
  - Sign and date at the undersigned signature and give it back to secretariat
  - Keep a photocopy as their records
- The secretariat shall keep an original copy of the signed agreement as records in a confidentiality/ conflict of interest agreement file and store in a secure cabinet with limited access

SOP 3. Administration and Function of IHEC

Secretariat

- The secretariat of the IHEC shall comprise of the Chairperson, and Members Secretary and all members
- The IHEC shall have a permanent secretariat at GMERS Medical College & Hospital, Gotri manned by member secretary of IHEC and supporting staffs
- Institute shall also provide the necessary funding for the operations of the IHEC.

Functions of the Secretariat

- Organizing an effective and efficient tracking procedures for each proposal received
- Prepare, maintain and distribute study files
- Organize IHEC meetings regularly
- Prepare and maintain meeting agenda and minutes
- Maintain the IHEC documentation and archive
- Communicate with IHEC members and applicants
- Arrange for training of its members
- Organize the preparation, review, revision and distribution of SOPs and guidelines
- Provide the necessary administrative support for the IHEC related activities to chairperson of IHEC
- Provide updates on relevant and contemporary issues related to ethics in health research, as well as relevant contemporary literature to committee members

Responsibilities of Secretary

- The secretary shall be responsible for the oversight of committee documents, records and archives
- Perform a pre-review of each submission of the IHEC to ensure adherence to administrative submission requirements
- Undertake all administrative procedures in providing training and educational programs to new and continuing IHEC members
- Support the chairperson in preparing and providing a statement of assurance when required by the regulations guiding the establishment of the IHEC
- Design and disseminate templates for committee submission documents, including research protocols, informed consent materials, agreements and periodic and final reports
- Design and maintain a system for collecting and filling all committee documents, including meeting minutes, member qualifications, protocol submission versions, deviations from approved protocols, and periodic and final reports
- Assist the institution to recruit new Committee members
- Ensure that all required materials for submission are present and complete
- Create and distribute meeting agendas, and arrange meeting logistics
- Attend Committee meetings, take minutes during the meetings, and verify and distribute minutes in a timely manner
- Correspond with all submitting researchers at all times throughout the submission and review process, while remaining independent of the researcher's protocol operations. Advise submitting investigators on preparing and submitting protocols for review according to relevant SOPs
- Properly distribute and keep files of all correspondences
- Assist the chairperson to conduct committee meetings. Continually study and update staff about committee operational regulations

- Be available for and attend any outside investigations or audits of the Committee
- Comply with requests during an investigation or audit

Responsibilities of Joint Member Secretary (Whenever appointed)

- Support the Member Secretary in executing functions of the IHEC
- Perform the same functions of Member Secretary in his/her absence or when conflict of interest is declared by member secretary

Functions of the Chairperson

- Chair the committee meetings in accordance with all regulations
- Prepare and provide a statement of assurance when required by the regulations guiding the establishment of the committee
- Facilitate the provision of training and educational programs to new and continuing committee members. The training shall include programs about the basic principles of human subject protection, current literature, regulations and guidelines affecting the committee
- Review and accept revisions that were made as per the committee recommendation pending protocol approval
- Determine submissions that could be exempted from review, and notify the committee and the submitting investigator of such exemptions
- Assign responsibilities and duties to any other member in his or her absence
- Supervise the member secretary and ensure s/he is performing his/her task dutifully

Responsibilities of Member of the committee

- Review, discuss and consider research protocols submitted for evaluation to safeguard the rights and well-being of study participants
- Review progress reports and monitor ongoing studies as appropriate
- Evaluate final reports and outcomes
- Support the executive in the discharge of their duties when called upon
- Maintain confidentiality of documents and deliberations of the Committee meetings
- Declare conflict of interest
- Participate in continuing education activities in biomedical ethics and research
- Undertake duties assigned to them by the Chair
- Attend meetings regularly and participate actively during deliberations

Dissolving the Committee

- At any point in time, should IHEC cease to exist, the Committee is automatically dissolved

SOP 4. Conduction of meeting

- The chairperson shall lead all meetings of the IHEC
- If for reasons beyond control, the chairperson is not available, the committee will decide the chairperson for that particular meeting who will be from outside of the institute.
- In the case where the member secretary is unsuccessful in routing the materials to committee members, the member secretary shall at least notify the member(s) of the non-occurrence of the meeting, and shall arrange for alternative means of material distribution. Whenever possible, the member secretary shall distribute the materials electronically
- The member secretary shall notify all committee members and applicants of any changes in meeting time, date or agenda as soon as discovered

Meeting Procedure

- The chairperson or a delegated member of the committee shall call the meeting to order only when a quorum of members is present. If quorum is incomplete, the meeting shall be rescheduled
- The chairperson shall follow the agenda for the progress of the meeting. The meeting shall most likely follow the following order
  - Confirmation of minutes of the previous meetings
  - Matters arising from previous minutes
  - Discussion of new agendas
  - Action items (voting on protocols, acceptance of serious adverse events, periodic and annual reports, and final reports)
  - Other matters
- If the meeting is to review a new submitted protocol, the principal investigator of that protocol may be invited when deliberating on the protocol to answer questions that shall be raised by the committee but must go out when decisions are made on the protocol
- The meeting of the IHEC will be held quarterly (every 3 months) and as needed

Meeting Minutes

- During committee meetings, all deliberations shall be recorded in writing or recorded electronically
- The minutes shall include a list of attendees, actions taken by the committee, the decision or vote on those actions, including the number of members voting for, against and abstaining, the basis for requiring changes in or disapproving research, and a written summary of the discussion of issues and their resolution.
- The secretary shall also include a summary of each considered protocol in the minutes
- The secretary shall circulate the minutes with a copy of the next meeting's agenda to all committee members at least four days before the date of the subsequent meeting
- All committee members shall review the minutes for accuracy and completeness
- The committee members shall make recommendations to the minutes at the next committee meeting
- The chairperson shall confirm the accuracy and completeness and sign the minutes during the next meeting
- The secretary shall archive the official minutes with the meeting's agenda and all relevant attachments

SOP 5. Independent Consultants

IHEC may call upon subject experts as independent consultants who may provide special review of selected research protocols if needed. These experts may be specialists in ethical or legal aspects, specific diseases or methodologies, or represent specific communities; patient groups or special interest groups e.g. Cancer patients, HIV / AIDS positive persons or ethnic minorities. They are required to give their specialized views but do not take part in the decision making which will be made by the members of the IHEC. They will have to submit necessary documents viz. CV, MRC if related and sign a confidential agreement before given documents for review.

SOP 6. Procedure of Communication with IHEC

- All communication should be done to the secretariat office
- Secretariat office address:
  IHEC Office,
  Room No. 201, First Floor, College Building,
  GMERS Medical College & Hospital,
  Gotri, Vadodara, Gujarat.
- Email: ihecmcgv@gmail.com
- Secretariat office timing: 10 am to 5 pm
- All communications to be done through EC coordinator if appointed
- In emergency, member secretary may be contacted on his/her mobile

SOP 7. Application Procedures

Submission of a new protocol for review

- All proposals should be submitted to the secretariat in the prescribed application form (Annexure 1) and expedited review form (Annexure 2) if applicable along with the declaration by all investigators (Annexure 3)
- All relevant documents should be attached with application form
- For a thorough and complete review, all research proposals should be submitted with the following documents
  - Name of the applicant with designation
  - Name of the institute / hospital / field area where research will be conducted
  - Departmental presentation letter / scientific review committee presentation letter
  - Protocol of the proposed research as per format given in the Annexure 1
  - Ethical issues in the study and plans to address these issues
  - Proposal should be submitted in prescribed format with all relevant enclosures mentioned in the check list of form like case report forms, questionnaires, follow up cards etc.
  - Informed consent process, including patient information sheet and informed consent form in local language(s)
  - For any drug / device trial, all relevant pre-clinical animal data and clinical trial data from other centers within the country / countries, if available
  - Curriculum vitae of all the investigators
  - Any regulatory clearances required
  - Source of funding and financial requirements for the project
  - Other financial issues including those related to insurance
  - An agreement to report Serious Adverse Events (SAE) to IHEC
  - Statement of conflicts of interest, if any
  - Agreement to comply with the relevant national and international guidelines applicable
  - A statement describing any compensation for participation (including expenses and access to medical care) to be given to research participants; a description of the arrangements for indemnity, if applicable (in study related injuries); a description of the arrangements for insurance coverage for research participants, if applicable; 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) in the protocol made on that account. The reasons for negative decisions should be provided
  - Plans for publication of results "positive or negative" while maintaining the privacy and confidentially of the study participants
  - CTRI Registration number where applicable
  - Any other information relevant to the study
- The academic proposals after verification by secretariat shall be sent by investigator electronically (in single file pdf format only) to all members and secretariat along with one hard copy to secretariat at least 7 days before the schedule meeting
- Pharma sponsored protocols shall be sent by investigator to all members in hard copy at least 21 days before the meeting. Investigator shall also submit two hard copies and soft copy (CD/ DVD/ Pendrive/ External hard drive) to secretariat.
- Proposals along with the application and documents in prescribed format should be duly signed by the Principal Investigator (PI) and Co-investigations / Collaborators

- The date of meeting will be intimated to the researcher to remain present to offer clarifications if necessary
- The decision will be communicated in writing. If revision is to be made, the revised documents in required number of copies should be submitted within a stipulated period of time as specified in the communication or before the next meeting

Submission of amendments to Protocol

Amended protocol shall be submitted in two hard copies and one soft copy (CD/ DVD/ Pendrive/ External hard drive) to the secretariat with the following:

- Amended protocol
- Version change history
- Amendment history for protocol
- Amendment history for ICF
- Additional documents which require approval
- Submission letter

Submission of Additional/ Revised documents

One copy of all documents should be sent to the secretariat

Change in PI

In case of transfer of PI working on ongoing project approved by IHEC, it is the duty of PI to make alternate arrangement of PI and inform the IHEC.

SOP 8. Participation of Principal Investigator (PI) in IHEC meeting

- The Secretary shall notify all PIs of the meeting date and time at least four days before. The secretary shall also notify all PIs about their proposal's place in agenda. Co-Investigator (Co-I) may attend on the PI's behalf if necessary.
- The PI/Co-I may be invited into the meeting room during consideration of his or her proposal
- The PI/Co-I may be invited to make a 6 to 8 minutes presentation on the proposal under consideration. After presentation, PI shall remain in the meeting to answer any questions, concerns and suggestions from members
- After questions and answers session, PI/Co-I and any other persons with a potential conflict of interest with the proposal shall leave the meeting during the decision/ voting period

SOP 09. Elements of Review

- Scientific value
- Scientific design and conduct of the study
- Power of the study
- Appropriateness of the method
- Approval of appropriate scientific review committees if applicable
- Examinations of predictable risks/harms
- Examinations of potential benefits
- Method for selection of subjects, inclusion/exclusion criteria
- Management of research related injuries, adverse events
- Compensation provision
- Justification for placebo in control arm, if any
- Availability of products after the study, if applicable
- Patient information sheet and informed consent
- Protection of privacy and confidentiality
- Involvement of the community, wherever necessary
- Plans for data analysis and reporting
- Adherence to all regulatory requirements and applicable guidelines
- Competence of investigators, research and supporting staff
- Facilities and infrastructure at study sites
- Criteria for withdrawal of patients, suspension or termination of the study

SOP 10. Decision Making

- All decisions will be taken in meetings and not by circulations of project proposals
- Members will discuss the various issues before arriving at a consensus
- A member should withdraw from the meeting during the decision procedure where a conflict of interest arises and this should be indicated to the chairperson prior to the application and recorded in the minutes
- Decisions will be made only in meetings where the quorum is complete
- Only members can make the decision. The expert consultants will only offer their opinions.
- Decisions shall be arrived at through consensus, when a consensus is not possible, the IHEC shall vote and the majority decision shall prevail
- There should be provision of dissent note by the members
- Decision will be to approve, reject or revise the proposals. Specific suggestions for modifications and reasons for rejection will be given to PI/applicant
- In cases of conditional decisions, clear suggestions for revision will be given
- Modified proposals may be reviewed by an expedited review by identified members
- Procedure for appeal by the researcher will be clearly defined
- The decision will be recorded in the minutes of the meeting and Chairperson's approval will be taken in writing
- All present members should have to submit their opinion for all the submitted proposals
- Decision will be made by members only and invites will have no rights to take decision or voting
- Head of Institute (Dean) or Head of the hospital (Superintendent) will have no right of voting or decision making

SOP 11. Communicating the decision

- Decision will be communicated by the member secretary in writing preferably within 7 working days
- Suggestions for modifications, if any, will be sent by IHEC
- Reasons for rejection will be informed to the researchers
- Approval letter will be issued by the member secretary in 7 working days

SOP 12. Review of Protocol Amendment

- The PI shall prepare the amendment package and submit to the Secretariat of the IHEC
- Upon receipt of the amendment package, the Secretariat shall inform the Chairperson of the Committee verbally and in writing and send the request for amendment memorandum and the protocol and related documents to the chairperson within two working days of receipt of the secretariat.
- After review of the materials, the chairperson shall determine whether the protocol requires expedited or full review and decision should be sent to member secretary within two working days
- On receiving approval from the chairperson, member secretary will send approval letter to the PI within seven working days
- If the chairperson decides the protocol requires full committee approval, the Secretariat shall:
  - Place the protocol amendment request on the agenda for the next convened meeting and
  - Distribute to each committee member the amendment's revision documents to clearly identify each change and requested changes to the consent form, if applicable.

SOP 13. Expedited Review

- All revised proposals, unless specifically required to go to the main committee, will be examined in a meeting of selected members identified by the chairperson to expedite decision making
- Expedited review may also be taken up in cases of nationally relevant proposals requiring urgent review
- The proposals involving no more than minimal risk to research participants
- An expedited review may be conducted, only if the protocols involve
  - Revised proposal previously approved through full review by the IHEC or continuing review of approved proposals where there is no additional risk or activity is limited to data analysis or health record research
  - Anonymous surveys and retrospective studies
  - Analysis of stored pathological specimens / paraffin blocks without personal identifiers
  - Research activities that involve only procedures listed in one or more of the following categories
    - Clinical studies of drugs and medical devices only when
      - Research is on already approved drugs **except** when,
        - Study of drug interaction
        - Conducting trial on vulnerable population
      - Adverse Event (AE) or unexpected Adverse Drug Reaction (ADR) of minor nature is reported
    - Research involving clinical materials (data, documents, records, or specimens) that have been collected for non-research (clinical) purposes
  - Other documents which would be considered for expedited review are as follows but may not restrict to
    - Minor deviations from originally approved research during the period of approval (usually of one year duration)
    - Change in the name, address of sponsor
    - Change in contact details of Principal Investigator (PI) and IHEC
    - Change in PI or hand over of trials or projects
    - Inclusion or deletion of name/s of co-investigator/s
    - Request for change in PI, Co-I, change in any member involved in the research
    - Minor amendments in the protocol, case record form
    - Minor corrections in budget
    - Other administrative changes in the investigator's brochure, informed consent form, etc

SOP 14. Follow up procedures

- The schedule for periodical review of ongoing approved projects will be communicated to the PI at least two weeks before
- All SAEs and the interventions undertaken should be intimated
- Annual Status Reports for periodical review should be submitted in prescribed format (Annexure 4)
- Protocol deviation, if any, should be informed with justifications
- Any amendment in the protocol should be submitted for approval
- Change of investigators should be notified
- Premature termination of study should be notified in given format (Annexure 5)
- Final closure report should be submitted at the end of study in given format (Annexure 6)

SOP 15. Documentations & Archiving

- The Member Secretary is responsible for implementing this SOP
- All the documents and communications of IHEC will be dated, filed and archived in a secure place
- All the documents related to research proposals will be archived for a minimum period of 5 years in the Institute, following the completion /termination of the study.
- Following documents will be filed and archived with proper label on the top of file for easy identification of proposal
    - The constitution, written standard operating procedures of the IHEC, and regular (annual) reports
    - The curriculum vitae of all IHEC members
    - A record of all income and expenses if any, of the IHEC, including allowances and reimbursements made to the secretariat and IHEC members
    - The published guidelines for submission established by the IHEC
    - The agenda of the IHEC meetings
    - The minutes of the IEC meetings duly signed by Chairperson
    - One copy of all materials submitted by an applicant
    - A copy of the decision and any advice or requirements sent to an applicant
    - All written documentation received during the follow up
    - Copy of all correspondence with members, researchers and other regulatory bodies
    - Copy of all existing relevant national and international guidelines on research ethics and laws along with amendments
    - The notification of completion, premature suspension, or premature termination of study
    - The final summary or final report of the study
    - Hard copy of all the communication done electronically
- All of above document's soft copy shall also be saved on external hard drive and shall be archived in a secure place

SOP 16. Review of serious adverse event reports

- Purpose
  - The purpose of this SOP is to highlight procedure for the review of serious adverse event reports (SAEs) for all the research projects and clinical trials approved by IHEC, Gotri
- Scope
  - This guideline is applicable for all the research projects and clinical trials approved by IHEC, Gotri

- **Responsibility**

Chairperson:

- Ensure all reported SAEs are discussed during the EC meeting.
- Opinion to DCGI on SAE compensation in timely manner.
- Ensure appropriate management of SAE by researcher/applicant.
- Ensure subjects or their nominee are receiving compensation and medical management as applicable.
- Ensure all reporting timelines are met if not then appropriate justification should be documented.
- Ensure causal relationship are established for each SAE by IHEC, Gotri.

Member Secretary/ EC coordinator:

- Ensure all relevant data for SAEs are submitted to IHEC, Gotri.
- Ensure SAEs are communicated with Chairperson and Other members as applicable.
- Filing of SAE records at IHEC, Gotri office.
- To send compensation opinion letter to DCGI on each SAE reported.
- Communication with researcher/applicant in case need of further information related to SAE

SAE review subcommittee

- SAE review subcommittee shall be consists of two clinician members and basic medical scientists. Member Secretary/Joint member secretary shall be the member of this subcommittee to facilitate its smooth functioning and co-ordinate with Chairperson. The presence of one clinician and one Basic Medical Scientist (Pharmacologist) is must to conduct the review of SAE. SAE subcommittee may invite investigator to provide any clarifications.
- This subcommittee shall review all trial related documents, source documents, SAE reports by principle investigator, SAE reports by sponsor, medical management related documents It will suggest the relation of causality with trial medications and required compensations to the Chairperson for its submission to CDSCO. The recommendations of SAE review subcommittee and report to CDSCO shall be ratified in the next IHEC full committee meeting.

- **Handling of serious adverse event:**
  - The researcher/investigator is responsible for reporting all SAEs to the IHEC, Gotri within 24 hours of knowledge. Reporting of SAE may be done through email communication (including on non-working days).
  - Sponsor (applicant) and Investigator after due analysis will send detailed SAE reports to IHEC, Gotri in the reporting format of CDSCO within 14 calendar days of occurrence.
  - IHEC, Gotri will send its recommendation on compensation for SAE to the DCGI within 30 calendar days of occurrence.

- The financial compensation will be over and above any expenses incurred on the medical management of the subject.
- Chairman may call for IHEC meeting to discuss about handling and management of reported SAE. The investigator may be called in the meeting to offer clarification.
- The chairman of the committee will have the right to suspend temporarily any research activities in the purview of the committee if untoward or unexpected adverse events occur. If this occurs, the proposal must be re-evaluated by the full committee at its next meeting and a decision whether to continue the study must be reached.

- **Compensation for research-related harm**
  Sponsor shall provide the compensation as defined by CDSCO

- **Compensation receipt by research particpaints:**
  - IHEC, Gotri should ensure that receipt of payment by the subjects in timely manner.
  - Site should notify payment order from competent authority and subject's acknowledgement post compensation given to subject.
  - In case of death or disability IHEC, Gotri should ensure that compensation given to the subject's nominee (i.e. nominee as per detail provide under Informed consent form).

SOP 17. Conduction of research on vulnerable population

- **Vulnerable subjects:** A vulnerable category of subjects includes members of a group with hierarchical structure (e.g. prisoners, armed forces personnel, staff and students of medical, nursing and pharmacy academic institutions), patients with incurable diseases, unemployed or impoverished persons, patients in emergency situation, ethnic minority groups, homeless persons, nomads, refugees, minors or others incapable of personally giving consent

- **Review Procedure**
  - Conduction of trial on vulnerable population can never be given exemption from review and cannot be passed through expedited review
  - All research that involves vulnerable population and special groups should be subjected to full review by all the members
  - Audio-visual consent is mandatory for regulatory trials involving vulnerable populations

- **Elements for review of research involving vulnerable subjects**
  - Strategic issues include inclusion and exclusion criteria for selecting and recruiting participants, informed consent and willingness to volunteer; coercion and undue influence; and confidentiality of data
  - The IHEC must carefully consider group characteristics, such as economic, social, physical, and environmental conditions, to ensure that the research incorporates additional safeguards for vulnerable subjects
  - The investigators must not over-select or exclude certain groups based on perceived limitations or complexities associated with those groups. For example, it is not appropriate to target staff and students as research subjects merely because they are a readily available "captive" population
  - Research should be according to ICMR guidelines, Schedule Y and other local statutory guidelines if any
  - Just as in providing medical care, research studies that plan to involve any potentially vulnerable populations must have adequate procedures in place for assessing and ensuring each subject's capacity, understanding, and informed consent and assent
  - In certain instances, it may be possible for researchers to enhance understanding for potentially vulnerable subjects. Examples include
    - Depute someone not involved in the research to obtain the consent, for e.g., inclusion of a consent monitor, a subject advocate, interpreter for hearing-impaired subjects
    - A translator of informed consent forms into the language subject understands, and read the consent form to subject slowly and ensuring his understanding paragraph by paragraph
  - The IHEC may require additional safeguards to protect potentially vulnerable populations. For instance
    - The IHEC may direct the investigator to submit each signed informed consent form to the IHEC
    - Someone from the IHEC may oversee the consent process
    - A waiting period of few days to establish initial contact and enrollment to allow time for family discussion and questions

- **Children Involved as Subjects in Research**
  - Children are persons who have not attained the legal age for consent to treatments or procedures involved in the research under the applicable jurisdiction in which the research will be conducted
  - The proposed research must fall within one of two categories
    - Research not involving greater than minimal risk
    - Research involving greater than minimal risk, but presenting the prospect of direct benefit to the individual subjects
  - It is the general position of IHEC that children will not be included in research in one of the following categories
    - Research involving greater than minimal risk, but likely to yield knowledge that can be generalized about the subject's disorder or condition
    - Research not otherwise approvable, which presents an opportunity to understand, prevent, or alleviate a serious problem affecting the health and welfare of children
  - Specific explanation in protocol must be required for the enrollment of children
  - **Parental Permission**
    - Permission of one parent is sufficient for research involving less than minimal risk to the children. Permission of both the parents is required for any research involving more than minimal risk to the children. IHEC will not allow inclusion of any children in clinical trials where parental permission is not possible (for example, neglected or abused children). No consent waiver will be given
  - **Assent of the Child**
    - Assent must be obtained when the child is capable of giving it. The IHEC should consider the age, maturity, and psychological state of the child involved. Assent form should be tailored for the child, with respect to his or her level of understanding. For young children, especially, the assent form should be designed as a one-page document, with simple, age-appropriate language, and presented in a manner understandable by the child
    - The IHEC may determine that the assent of the child is not necessary if and only if **all three** of the following conditions are satisfied
      - The research offers possible direct benefit to the child
      - The benefit is important to the health or well-being of the child; and
      - The benefit is available only in the context of the research
    - IHEC must take great care in approving research where the child is suffering from a life-threatening illness with little chance of therapeutic benefit
    - IHEC must also be cautious in allowing parents to overrule a child's dissent where experimental therapy has little or no reasonable expectation of benefit

- **Research on Pregnant Women, Fetuses and Human in Vitro Fertilization**
  - Research involving pregnant women and fetuses should involve the least possible risk. The IHEC must document specific findings to minimize the potential for risk or harm to the fetus, and additional attention must be given to the conditions for obtaining informed consent. The IHEC must be familiar with the requirements of the following conditions
    - Research involving pregnant women
    - Research directed towards the fetus in utero
    - Research involving the fetus ex utero; and
    - Research involving dead fetuses, fetus material, or placenta
  - Specific explanation in protocol must be required for the enrollment these group

- Pregnant women only be involved in clinical research where the "purpose of the activity is to meet the health needs of the mother". A purpose of treating the "health needs" alone of the pregnant woman is not ethical when the benefits to her are greatly outweighed by the risks to fetus and offspring
- Where the purpose of clinical research involving a pregnant woman is not to meet her health needs, she may participate only if "the risk to the fetus is minimal"
- Research can only be permitted with the fetus as subject when "the purpose of the activity is to meet the health needs of the particular fetus and the fetus will be placed at risk only to the minimum extent necessary to meet such needs"
- Non-therapeutic research is not permitted in fetus
- Subject expert should have been called for the research involving pregnant women and fetus

- **Research involving students and staff of GMERS Medical College, Gotri**
  - **"Student"** means any individual who is enrolled at GMERS Medical College, Gotri and those individuals who are in training as, Residents, Fellows, or Postdoctoral trainees, including individuals enrolled at a training facility other than GMERS Medical college, Gotri training or work program
  - **"Staff"** mean all GMERS Medical College, Gotri and GMERS General Hospital, Gotri, employees, including faculty and out sourced contractual employee
  - GMERS Medical College, Gotri and GMERS General Hospital, Gotri students and staff have the same rights as any other potential subject to participate in research project, irrespective of the degree of risk, provided all of the following conditions exist
    - The research must not bestow upon any academic or occupational advantage to participating students or staff subjects over other students or staff who does not volunteer, and the researchers must not impose any academic or occupational penalty on those students or staff who does not volunteer
    - Students and staff must not be systematically treated differently from non- students or staff subjects as part of the project
    - Due to the potential for perceived or real coercion to participate students and staff (especially those under the direct supervision of the PI or co-investigators) must be reviewed by Head of the institute

- **Research Involving Decisionally-Impaired Subjects**
  - Decisionally-impaired individuals are those who have a diminished capacity for judgment and reasoning due to psychiatric, organic, developmental, or other disorder that affects cognitive or emotional functions. Other individuals, who may be considered decisionally-impaired, with limited decision making ability, are individuals under the influence or dependent on drugs or alcohol, those suffering from degenerative diseases affecting the brain, terminally ill patients, and persons with severely disabling physical handicaps
  - As with all subjects the IHEC must carefully consider selection issues, privacy and confidentiality, coercion and undue influence, and risk-benefit analysis. Additional safeguards should be considered by the IHEC to protect these subjects
  - Specific explanation in protocol must be required for the enrollment these group
  - The proposed research must fall within one of two categories
    - Research not involving greater than minimal risk

- Research involving greater than minimal risk, but presenting the prospect of direct benefit to the individual subjects

- It is the general position of IHEC that individuals with decisional impairment will not be enrolled in research in one of the following categories
  - Research involving greater than minimal risk, but likely to yield knowledge that can be generalized about the subject's disorder or condition
  - Research not otherwise approvable, which presents an opportunity to understand, prevent, or alleviate a serious problem affecting the health and welfare of individual
- If the research subject is unable to consent, the individual's assent, and particularly his dissent, should be considered. The process by which one determines whether an individual is capable of providing assent must be included in the research protocol
- If the research subject cannot give his consent, and has not expressed his dissent, then a surrogate decision maker must be found to consent in the subject's place. Consent from one of the family members: competent spouse, competent parent, or adult child (in order of preference) should be taken in this situation

- **Research on ethnic minority groups, homeless persons, nomads, refugees**
  - As with all subjects the IHEC must carefully consider selection issues, privacy and confidentiality, coercion and undue influence, and risk-benefit analysis. Additional safeguards should be considered by the IHEC to protect these subjects
  - Specific explanation in protocol must be required for the enrollment these group
  - The proposed research must fall within one of two categories
    - Research not involving greater than minimal risk
    - Research involving greater than minimal risk, but presenting the prospect of direct benefit to the individual subjects
  - It is the general position of IHEC that ethnic minority groups, homeless persons, nomads, refugees will not be enrolled in research in one of the following categories
    - Research involving greater than minimal risk, but likely to yield knowledge that can be generalized about the subject's disorder or condition
    - Research not otherwise approvable, which presents an opportunity to understand, prevent, or alleviate a serious problem affecting the health and welfare of individual

- **Research Involving Prisoners and armed forces personnel**
  - It is the general position of IHEC that prisoners and armed forces should not be involved in research

SOP 18. Fee Structure

- Fee is applicable for sponsored protocols only
- For Review
  - Fee paid is for the review process only, i.e. it shall be read by all members, discussed in the meeting, clarifications sought and conveyed to the PI/Sponsor
  - Various administrative charges include honorarium paid to IHEC members as fixed by IHEC from time to time, coordinator honorarium, postal handling and courier charges, stationary and various other charges.
  - It does not ensure that approval shall be definitely granted. Any protocol which is rejected shall be done so after review, no fee will be refunded.
  - Receipt of payment of IHEC fees must be submitted by PI along with initial submission of documents.
  - On receiving payment IHEC secretariat will issue a receipt to PI
  - IHEC will issue the following if required
    - Invoice
    - Photocopy of cancelled cheque
    - Photocopy of PAN card of IHEC
    - GST declaration
  - Information for payment of IHEC fee
    - Bank: State Bank of India, Natubhai Circle Branch, Vadodara
    - PAN Number: AAAAI7573B
    - Account Number: 00000033521872385
    - IFSC Code: SBIN0060195
  - Protocol base fee structure for review process (Excluding TDS & other applicable taxes)
    - For new pharma sponsored protocol - Rs. 50,000/-
    - Emergency meeting for pharma sponsored protocol - Rs. 80,000/- (Emergency meeting can be arranged after 3 weeks of submission of proposal however prior permission should be taken)
    - Amendments after one year – Rs. 20,000/-
  - On receiving payment IHEC secretariat will issue a receipt to PI

SOP 19. Revision of SOP

The purpose of this SOP is dedicated to address when and how SOPs shall be reviewed and revised if the IHEC wishes to revise or update the SOP.

- The SOP shall be evaluated for accuracy and timeliness in an annual review and the secretary shall alert the IHEC of an annual review requirement
- The IHEC, secretary or an assigned member can review and revise the SOPs. S/He shall ensure that the SOP reflects the most current outline of procedures.
- After revision, SOP shall be accepted by Chairperson of IHEC

SOP 20. Distribution of SOP

This describes how to distribute and limit the distribution of IHEC approved SOPs.

- The master SOP is property of the institute and shall be kept confidential in a safe place. It shall not be disclosed without permission from IHEC.
- However sometimes SOP and annexures should be made available for non-members
- The master SOP shall only be disclosed to members after obtaining confidentiality agreement
- It is the responsibility of member secretary to distribute SOPs to all committee members and PIs, archive the electronic copy and hard copy.
- All requests for extra copy of master SOP or part of it should be made to and fulfilled by member secretary
- Member secretary shall keep a log of distribution of SOP

SOP 21. Internal Audit of IHEC

- Aim of the Audit
  - To review compliance with SOP
  - To take feedback
- Scope of the Audit
  - Review of Responsibilities, Composition, functions and operations
  - Review of meeting minutes, documentation process, meeting quorum,
  - Review of listed protocols as per Agenda
  - Review of decision-making process and documentation
  - Review of safety reporting, tracking follow-ups
  - Review of archival process and records
- Appointment of Internal Auditor
  - All members of IHEC shall take the responsibility of conducting Internal Audits by turns. Chairperson will appoint one member as Auditor for each quarter
- Audit Report
  - Audit findings shall be discussed and a formal report filed in the subsequent EC meeting by the internal auditor
  - Areas of improvement shall be discussed and suitable action planned by the Chairperson

SOP 22. Audio-Visual Consent

Purpose

To describe the procedure for taking Audio Video (AV) recording of Informed Consent Process

Scope

This guideline is applicable for all the research projects and clinical trials where Audio-Visual consent has to be taken.

The following procedures have to be followed for taking Audio-Visual Consent

- AV recording should be done for research purpose only
- When making or using recording, Principal Investigator / designee (Co-investigator or medically qualified person) should respect patient's privacy, confidentiality, dignity and their right to make decisions.
- PI/designee should give subject, the information they want or need about the purpose of the recording.
- PI/designee should ensure that subject is under no pressure and undue influence to give their consent for the recording to be made.
- Prior written consent for AV recording should be taken.
- Investigator should ensure the following infrastructure is available and instruments are working
  - Room is free from disturbance
  - Ensure privacy of the participant
  - Participant should be comfortable
  - Camera should have adequate resolution
  - Camera should have sufficient memory
  - Camera with inbuilt showing date and time is preferable if possible
  - Camera should have sufficient battery backup
  - Facility of CD/DVD writer
  - Banner mentioning full name and details of research project with name & details of principal investigator and sponsor
- Informed consent process should be done one to one interaction with PI/designee and subject
- The PI/designee and subject / LAR (if need to be impartial witness) should sit comfortable in such a way that their faces will be captured in frame simultaneously
- Complete procedure should be recorded right from starting till entering details of subject/LAR/IW, signing the informed consent form and at the end signing by PI/designee. Time and date should be noted. Recording should be clearly audible.
- PI/designee should introduce himself/herself by name, designation and his/her role in the research
- Subject/LAR should be requested to introduce himself/herself, his/her name, age, address and in case of LAR, he/she should clearly state relation as well as the reason why the subject cannot provide written consent. Subject/LAR should also state the language he/she understands best and is literate in.
- In order to identify the subject/LAR/IW, his/her photo ID should be recorded and documented.
- PI/designee should provide the subject with the information in a language that is non-technical and understandable by the study subjects and same should be recorded
- Explanation or narration given by PI/designee, all the questions asked by the subject/LAR and answers given to them should be recorded.
- PI/designee should give ample of time to read and understand the information sheet given to the subject

- At any point during the consent process, if the participant wishes to take more time to read/discuss with relatives the recording should be stopped mentioning the time of stopping. When he/she returns, a date and time of new recording, short introduction, and history of prior recording should be mentioned.
- If PI/designee does not know the language of subject/LAR/IW, a member of the study team who understand the language will become interpreter.
- PI/designee should ask the questions and document their answers before starting signing process
- Videographer to monitor video for an uninterrupted recording of consent process is allowed
- The recorded data should be copied into a dedicated computer. A password protected study folder should be created and recorded data to be stored.
- The recording should be checked for completeness and clarity of both audio and video recording by study team
- Each file should be assigned a unique reference number without disclosing identity of subject.
- The CD should be prepared subject wise and stored in cabinet under lock and key.
- No editing should be done on the recording so as to maintain authenticity
- Access to the recording can be provided only in a court of law or in cases may be required to communicate to regulatory agency.
- IHEC will have the rights to access the recording
- AV recording must be done on any re-consenting procedure followed.
- AV recording should be done of assent wherever applicable.

SOP 23. Protocol deviation/ non-compliance/ violation review and management

Purpose

To provide instructions for taking action(s) when investigator(s)/trial site(s) fail(s) to: follow the procedures written in the approved protocol and comply with national and/ or international guidelines, statutory provisions, institutional guidelines or rules or procedures for the conduct of human research;

Scope

This guideline is applicable for all the research projects and clinical trials approved by IHEC, Gotri

Responsibility

Chairperson:

- To ensure appropriate corrective and preventive action for non-compliance reported.
- To ensure corrective actions are informed to Researcher as applicable.
- For cause visit/unplanned visit to study site for review of actions taken by researcher for non-compliance reported.

Member Secretary/ EC coordinator:

- Documentation of corrective and preventive action for non-compliance reported.
- Communication Researcher/investigator for IHEC, Gotri opinion or feedback on non-compliance reported.
- To document the facility report for site visit conducted by IHEC, Gotri.
- Filing of records at IHEC, Gotri office.

Detection of Protocol Deviation/ Non-Compliance/ Violation

Protocol Deviation/Non-Compliance/Violation may be detected in one the following way (but not limited to those listed below):

- The Principal Investigator (PI) himself/ herself may forward protocol deviation/non-compliance/violation reports to inform the IHEC, Gotri.
- Protocol deviation/ non-compliance/ violation detected by IHEC, Gotri member
    a. after due enquiry of PI/study site or
    b. during monitoring of the project at trial site or
    c. during scrutinizing annual/ periodic reports/ SAE reports/ any other communication received from the Investigator/ trial site.
- Allegation of protocol deviation/ non-compliance/ violation reported to the IHEC, Gotri: 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 IHEC, Gotri.

Management of Protocol Deviation / Non-Compliance / Violation

- Upon receipt/notice of non-compliance its impact (i.e. impact of non-compliance to patient right, safety and well-being) shall be assessed by Member Secretary in consultation with Chairperson. This discussion can be meeting or telephonic.
- Followed by seriousness of the violation/non-compliance decision shall be taken to

- call expedite meeting of members or
- can be discussed telephonic with other relevant members or
- notification to IHEC, Gotri is sufficient and no further action is expected from PI/Site.

- If reported/observed non-compliance is related to SAE or AE then clinician members to be mandatorily contacted to take their opinion. If it is related to legal and social then respective IHEC, Gotri members to be contacted for their opinion.
- In case of expedite meeting required then member secretary planned un-schedule meeting for discussion on non-compliance reported with available members however not necessary to ensure quorum. Members related to type of non-compliance should be part of meeting. During the meeting non-compliance and management of non-compliance shall be discussed in detail. If IHEC, Gotri requires further information related to non-compliance shall be asked from PI/Site. The recommendation/suggestion shall be given via recommendation or observation letter to the PI.
- If require IEC members can plan for cause assessment visit at study site.
- Discussion during the meeting shall be documented in the form of minutes of meeting and same will be approved by the chairperson of the meeting.
- PI shall be followed up to get the responses on the submitted suggestion or observation letter.
- If un-schedule meeting is not required for non-compliance observed at site during monitoring then shall be notify and discussed in the subsequent regular meeting of the ethics committee.
- If non-compliance identified during Member's facility visit to study site then same shall be discussed with Authorized signatory available at site and appropriate response shall be obtained. He/she has to convey this information to Member Secretary or Chairperson (telephonic or during meeting based on seriousness of non-compliance).
- IHEC, Gotri should maintain record of all such non-compliance notified or received from study site along with actions suggested and taken by the study site.

IHEC, Gotri Decision Making and Action

- Direct the PI to ensure that deviations/non-compliances/violations do not occur in future and follow IECBPH recommendations.
- Reasonable time shall be given to the PI to respond IHEC, Gotri's observation.
- Enlist measures that the PI would undertake to ensure that deviations/noncompliance/violations do not occur in future.
- Call for additional information.
- Suspend the study till additional information is made available and is scrutinized based on seriousness of non-compliance.
- Inform the Institutional Head/Dean/Medical Superintendent.
- Revoke approval of the current study.
- Inform DCGI/ Other relevant regulatory authorities.
- Refuse to review subsequent applications from an investigator cited for noncompliance for a specified duration of time.
- Any other action considered appropriate by the IEC for safeguarding the interests of the research participants participating in the current trial or in future trials.
- **Note:** All IHEC, Gotri records (minutes of meeting, decisions etc. shall be archive as per archive procedure)

SOP 24 Procedure to be followed for site monitoring visit

Purpose

The purpose of this Standard Operating Procedure (SOP) is to provide the procedures for selection and monitoring of the study site for the research projects and clinical trials approved by IHEC, Gotri

Scope

This guideline is applicable for the study site of all the research projects and clinical trials approved by IHEC, Gotri

Responsibility

Chairperson:

- To identify the need of site visit conducting research projects and clinical trials approved by IHEC, Gotri.
- To ensure timely visits are conducted at site for efficient oversight of IHEC, Gotri.
- To ensure visit reports are prepared and communicate with researcher in timely manner.
- To ensure closure of actions by the researcher.
- To decide the action against researcher in case failure of closure of actions.

Member Secretary:

- To coordinate study site visit with site and members.
- Preparation of study site visit report.
- Follow-up with principle investigator (PI) for closure of actions (if any).

EC Members:

- To perform study site visit as per site monitoring check-list.
- To comply procedure, define in the SOP.

Site Selection:

Based on the following pre-requisites, Chairperson and/or Member Secretary shall identify a particular site for 'monitoring' (but not limited to below);

1. New Investigational site
2. High recruitment
3. Major Non-compliance/protocol deviation
4. Interim site visit (shall be annually or as and when require)
5. For cause visit: shall be performed at sites for reasons identified by any members of the IHEC, Gotri, after approval by the Chairperson.

Before Site Visit:

- The Chairperson shall identify and select two or more IHEC, Gotri members (monitors) to conduct monitoring of a study site.
- The final date shall be communicated to the PI (with a request to be available) and monitors by the IHEC, Gotri member secretary.
- The agenda for site visit/ monitoring shall be prepared by member secretary and shall be circulated to the designated IHEC, Gotri members and shall be notified to PI via email communication.

- The IHEC, Gotri members shall carry with them the site monitoring checklist collected from the member secretary.

During Site Visit:

- Upon arrival at the study site, the monitors shall begin with the opening meeting with PI and initiate the process of site monitoring. If the PI shall unavailable then a designated person with appropriate authority shall receive the monitors and fulfill with all the requirements.
- During site monitoring the monitors shall follow the checklist along with other applicable processes.
- The monitors shall check (but not limited to below):
    - In of new site, infrastructure, facility areas along with the initial site documents
    - The log of delegation of responsibilities of study team
    - Whether the site is using latest IHEC, Gotri approved version of the protocol, informed consent documents (ICD), case record forms (CRF), diaries, advertisements, etc.
    - That the investigator is enrolling only eligible subjects.
    - ICD process (if possible) & documentation
        - Ensure audio-visual recording of consent
        - Ensure AV recording of the informed consent process storage and archival without violating the participant confidentiality.
        - Ensure the following infrastructure is available at the time of counseling of study participant;
          i. Free from disturbance
          ii. Well lit
          iii. Ensures privacy and comfort for the participant
    - Recruitment strategy & patient counseling process
    - That the subject or the subject's legally acceptable representative is informed in a timely manner if new information becomes available that may be relevant to the subject's willingness to continue participation in the trial. The communication of this information is documented or not.
    - Randomly-selected participant files to ensure that the documentation is as per standards laid down in applicable regulatory guidelines and that the participants are signing the informed consent forms.
    - Investigational product (IP) accountability is adequately controlled and documented throughout the product flow at the study site (including IP arrival, dispensing, use, return from the subject and return/destruction after the study)
    - Whether the investigator is following the approved protocol and all approved amendment(s), if any and are performing the specified study functions, in accordance with the approved protocol
    - Whether the investigator protected and ensured access to medical care necessitate for participation, initiation, continuation and post completion of the study.
    - Whether the investigator is failed to adhere the protocol (that may consider a failure to protect the rights, safety, and welfare of subjects) and is documented and reported to the IECBPH and applicable regulatory body in timely manner
    - Whether all serious adverse events (SAEs) are appropriately reported within the time as per the applicable regulatory requirement(s)
    - Noncompliance with the protocol, SOPs, GCP, and/or applicable regulatory requirement(s) by an investigator/institution
    - Case record forms shall be checked to review the adverse events (AEs) and SAEs for safety evaluation.

- Payment process to participants (If applicable)
- Review of non-compliances/complaints in the study approved by IECBPH (If applicable)
- The study files to ensure that documentation is filed appropriately
- The source documents for their completeness
- The views of the study participants, if possible
- Members may interact with Research participant / patient during their site visit. Based on participants/patient feedback Chairperson/ Member secretary shall initiate necessary actions (if applicable) and shall record in the Site Monitoring Report.

After Site Visit:

- The monitors shall submit the completed site monitoring report to the IHEC, Gotri member secretary within 7 working days of conducting the monitoring visit.
- The member secretary shall prepare the site monitoring report (the findings of the monitoring visit).
- IHEC, Gotri members shall discuss the findings from the site monitoring process.
- Chairperson shall be responsible for final decision taken and approval of Site Visit/ Monitoring Report.
- The member secretary shall convey the decision of the IHEC, Gotri to the PI in writing within 14 working days of the site visit.
- The member secretary shall keep the copy of the report in the IHEC, Gotri file.