MAHARSHI DAYANAND UNIVERSITY
Rohtak-124001, Haryana (INDIA)
(A State University established under Haryana Act No. XXV of 1975)
'A+' Grade University Accredited by NAAC

STANDARD OPERATING PROCEDURES(SOPs)

FOR

"HUMAN ETHICS COMMITTEE (HEC)"

(FOR BIOMEDICAL AND HEALTH RESEARCH INVOLVING HUMAN PARTICIPANTS)

Of

Maharshi Dayanand University, Rohtak Haryana (INDIA) -124001

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HEC- SOPs ESTABLISHMENT

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APPROVED BY	Prof. M.C. Gupta	Chairperson		11.05.2024

Date of implementation:**12.05.2024**
Version No.: **1.0**
Valid till:**11.05.2025**

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Human Ethics Committee for Research (for Biomedical and Health Research involving Human Participants) of Maharshi Dayanand University, Rohtak would be known as HEC in this document. It has been divided into different clauses and their sub clauses. It is recommended that these clauses should be referred as mentioned in this document. These Standard Operating Procedures are laid down in consensus following the regulations of New Drugs and Clinical Trials Rules, 2019 and 2022 (Amendment)&ICMR Ethical guidelines (2017). This document may be amended either after 1 year or after any specific requisite/regulatory requirement which might be considered relevant by the HEC.

1. PURPOSE

The following may be called“Standard Operating Procedures (SOPs) for the Human Ethics Committee (HEC) of Maharshi Dayanand University (MDU), Rohtak."SOPs provide and describe clear and unambiguous instructions on Terms of Reference (TOR), which present the framework for the constitution, scope, tenure, roles and responsibilities, and related activities of the Human Ethics Committee (HEC) in accordance with established ICMR ethical guidelines for biomedical research on human subjects.

2. ADOPTION AND OBJECTIVE

MDU Rohtak has adopted these written SOPs(Version No: 1.0) to ensure the protection of the rights and welfare of human participants in biomedical, health, behavioraland experimental research conducted therein.The SOPs would be updated periodically to reflect changing requirements. A copy of the latest version of SOPs would be made available to each member and they should be trained on the SOPs. The SOPs would be available in the secretariat of the HEC as both hard and soft copies.The objective of the SOPs is to maintain effective functioning of the HEC of MDU Rohtak and to ensure quality and technical excellence in reviewing of initial/approved biomedical and health research proposals/studies involving human participants including vulnerable, and keeping their dignity, rights and safety in accordance with the latest ICMR ethical guidelines.

3. SCOPE

The present SOPs apply to all activities performed by the HEC reviewing research studies on biomedical, health, social, behavioral,etceither initially submitted or ongoing/already approved conducted in India involving human participants including vulnerable, their biological material, and data in accordance with the ICMR ethical guidelines at MDU Rohtak, as well as those done at other locations under the guidance of a principle investigator or co-investigator employed at MDU Rohtak.The HEC would review scientific and ethical aspects of all such types of research studies involving Ph.D. work, M.Sc. dissertation work, and other research studies/projects including self-funded and sponsored projects, which are carried out in this institution by the staff members and students, and those carried out by institutional members in collaboration with other national or international institutions. SOPs may also state TORs for the ‘special situations’ (optional) as per ICMR latest guidelines,when required.

SOP/24/1/1:TERMS OF REFERENCE OF HEC

SOP/24/1/1.1:Authority under which the HEC has been constituted:

Maharshi Dayanand UniversityRohtak is the competent authority for the constitution of the Human Ethics Committee (HEC)as an independent body with respect to decision making and its working in order to provide public assurance of protection, reviewing and approving the biomedical and health research projects, the suitability of the investigator(s), facilities and the methods and material to conduct research.Head of Institution is competent authority to nominate the qualified and experienced persons as the members of HEC to review and evaluate research studies for biomedical and health research on human participantsas per recommended National ethical guidelines. Any change to HEC constitute would be approved by Headof Institution.The HEC would function in accordance with the relevant national law and regulations in force from time to time.Head of the Instituteas appellate has the power to dissolve the HEC or reconstitutethe HEC.

SOP/24/1/1.2:Administration and management support:

MDU would provide all administrative and reasonable financial support to the HEC activities which including training, resources and infrastructure at the same time. HEC would have full time secretariat including office and staff for safe archival of records and smooth functioning.There would be provision of funds for organizing workshop/conference/seminar etc., and contingencies for remuneration, honorarium, stationarycharges,telephonebills, and other requirements including accreditationprocess,as and when needed. The HECwouldworkonaNoprofitbasisandwouldalwaysuseits fund for continuous improvement and development of HEC, especially the trainingof membersin areasethical research. Remuneration for traveling expense, honorarium for attending the HEC meetings and /or honoraria would be given to the HEC members and other independent consultants or any other person authorized by authority and the HEC. HEC members would be paid remuneration and honorarium applicable as per university rules. AllpaymentswouldbereceivedbyHECas per university rules/guidelines. Allfinancialcommunicationsand procedures would adhere and comply to Institute's internal routine financial audits, asappropriate.Member Secretary of HEC would be accountable for all administrative matters. He wouldhavesupportfromadministrativestaffasnecessaryformanagementofvariousadministrative activities such as filing of HEC documents, distribution of dossiers, tracking HEC activities,and supportincoordinationof HEC meetings,ad-hoc support as needed.MemberSecretaryinconsultationwithHEC ChairpersonandothermemberswouldevaluatetheworkloadofHEConanongoingbasis.

SOP/24/1/1.3:Registration and accreditation of HEC:

The HEC should be located in India and registered with the relevant licensing and regulatory authority, wherever applicable. Efforts should be made to seek recognition/certification/accreditation from recognized national/international bodies.Such certification/accreditation are voluntary exercises and help in quality assurance and quality improvement to ensure that HECs follow best practices in protecting the dignity, rights, safety, and well-being of their participants. Any change in the membership or the constitution

of the registered HEC shall be intimated in writing to the licensing authority within thirty working days.

SOP/24/1/1.4:Basic Composition of HEC:

1) HECs should be multi-disciplinary and multi-sectoral.
2) There should be adequate representation of age and gender, one woman member is mandatory.
3) Preferably 50% of the members should be non-affiliated or from outside the institution.
4) The number of members in an EC should preferably be between 7 and 15.
5) A minimum of 5 members should be present to meet the quorum requirements.
6) The HEC should have a balance between medical and non-medical members/technical and non-technical members, depending upon the needs of the institution.

SOP/24/1/1.5:Tenure of HEC and its members:

1) HEC would perform working up to its validity period as per rules.
2) The duration of appointment of members would be 2-3 years. The duration of member could be extended.

SOP/24/1/1.6:Policy for removal, replacement, resignation procedure of HEC members:

A defined percentage of HEC members would be changed on aregular basis.The members who have resigned may be replaced at the discretion of the appointing authority for the same. Members who decide to resign must provide to the competent authority and HEC chairman, a written notification of their proposed resignation date at least 30 calendar days prior to the next scheduled meeting. In case of resignation, the Head of Institution would appoint a new member, falling in the same category of membership, that is, a Medical Scientist with a Medical Scientist. Appointment may be made in consultation with the Member Secretary and/or Chairperson. A member can be replaced by competent authority in the event of death or long-term non-availability or for any action not commensurate with the responsibilities laid down in the guidelines deemed unfit for a member. A member may be relieved of his/her membership in case of conduct unbecoming for a member of the Ethics Committee, long term inability to participate in the meetings, contribution is not adequate, on any reasonable grounds, especially relocation to another city. The membership shall be reviewed by the HEC, if the member is a regular defaulter. If deemed necessary, the HEC may decide to terminate the membership and recommendation can be made to the by the Institutional Head in office, by the Chairman HEC for necessary action.

SOP/24/1/1.7:Role and Responsibilities of HEC:

HEC would function as per written SOPs referring the ICMR guidelines for all biomedical and health research. The HEC is mandated to examine research proposals where research is to be wholly or partially carried out at MDU to ensure that research is carried out in accordance with ethical principles. To ensure that the research projects carried out at MDUare :-

- Sound in design, and in compliance with the ICMR guidelines.
- Do not compromise safety of the patients or volunteers.
- Are conducted under the supervision of persons with the required expertise.

It is the responsibility of the HEC members and the secretariat to read, understand, follow the established SOPs. The HEC would review all types of research proposals involving human participants with a view to safeguard the dignity, rights, safety and well being of all actual and potential research participants before approving the research proposals. The goals of research, however important, should never be permitted to override the health and well being of the research subjects. The HEC would ascertain whether all the cardinal principles of research ethics, Respect for Free and Informed Consent, Respect for Human Dignity, Respect for Vulnerable Persons, Respect for Privacy and Confidentiality and Justice are taken care of in planning, conducting and reporting of the proposed research. For this purpose, it would look into the aspects of protocol review, selection of participants, voluntary participation of potential participants, informed consent process, risk benefit ratio, distribution of burden and benefit, maintenance of privacy and confidentiality and provisions for appropriate compensations. It would review the proposals before the commencement of the study as well as review periodically until the completion of the study through appropriate well documented procedures. Such a review may be based on the periodic study progress reports furnished by the investigators and/or monitoring and internal audit reports furnished by the Sponsor and/or by visiting the study sites.

The mandate of the HEC shall be to review all research projects to be conducted at the Institution involving human beings directly or indirectly, irrespective of the funding agency. HEC would provide advice to the researchers on all aspects of the welfare and safety of the research participants after ensuring the scientific soundness of the proposed research through appropriate Scientific Review Committee/ Research Committee. In case an ethics committee revokes its approval accorded to a trial protocol, it would record the reasons for doing so and at once communicate such a decision to the Investigator as well as to the Licensing Authority. In case of serious adverse event of death, the ethics committee shall forward its report on the serious adverse event of death, after due analysis, along with its opinion on the financial compensation.

1. The basic responsibility of HEC is to ensure protection of the dignity, rights, safety and well-being of the research participants.
2. HEC must ensure ethical conduct of research by the investigator team.
3. HEC is responsible for declaration of conflicts of interest to the Chairperson, if any, at each meeting and ensuring these are recorded in the minutes.
4. HEC should perform its function through competent initial and continuing review of all scientific, ethical, medical and social aspects of research proposals received by it in an objective, timely and independent manner by attending meetings, participation in discussion and deliberations.
5. HEC must ensure that universal ethical values and international scientific standards are followed in terms of local community values and customs.
6. HEC should assist in the development and education of the research community in the given institute (including researchers, clinicians, students and others), responsive to local healthcare requirements.
7. The Secretariat should support the Member Secretary and Alternate Member Secretary (if applicable) in all their functions and should be trained in documentation and filing procedures under confidentiality agreement.

8. The HEC should ensure that privacy of the individual and confidentiality of data including the documents of HEC meetings is protected.
9. HEC reviews progress reports, final reports and AE/SAE and gives needful suggestions regarding care of the participants and risk minimization procedures, if applicable.
10. HEC should recommend appropriate compensation for research related injury, wherever required.
11. HEC should carry out monitoring visits at study sites as and when needed.
12. HEC should participate in continuing education activities in research ethics and get updated on relevant guidelines and regulations.
13. HEC may see that conduct of same/similar research by different investigators from same institution is harmonized. 'Me too' research (replicative) should not to be encouraged and submission of same research to different funding agencies should not be accepted.

SOP/24/1/1.8:Roles and Responsibilities of HEC members:

There would be one Chairperson and one Member Secretary in the HEC. The Chairperson would headthe committee. The Member Secretary would be the guardian of all documents and funds in thepossessionofthecommittee.OtherHECmemberswouldberegularcommitteememberswithequal ranking. Members of HEC are expected to attended all HEC meetings and prior information should be provided if a member is unable toattend meeting. Members cannot substitute for the role of any other member who is absent for a meeting. The role of Chairperson/Member Secretary/Alternative Member Secretary is an additional activity to their primary responsibility based on their qualifications.The role, qualification, and responsibilities for being HEC members as per ICMR guidelines are given in **Table 1.**

Table No. 1. Composition, Affiliations, Qualifications, Member Specific Roles and Responsibilities of HEC

Member	Qualifications	Responsibility
Chairperson (Non-affiliated)	A well-respected person from any background with prior experience of having served/ serving in an HEC	Conduct HEC meetings and ensure active participation of all members during meeting, Ratifyminutesofthepreviousmeetings, SeekCOIdeclarationfrommembersand ensurequorumandfairdecision making, Handlecomplaintsagainstresearchers, HEC members,conflictofinterestissuesand requests for use of HECdata,etc.
MemberSecretary (Affiliated)	Should be a staff member of the institution, Should	Organize an effective and efficient procedure for receiving, preparing, Circulating andmaintainingeachproposalfor review, Schedule HECmeetings,preparetheagendaandminutes, Organize HECdocumentation,communicationand archiving, Ensuretrainingof HECmembers, Ensure SOPs are updated as and when required & adherence of HEC functioning to the

	have knowledge and experience in clinical research and ethics, be motivated and have good communication skills	SOPs, Prepareforandrespondto auditsandinspections, Ensurecompletenessofdocumentationatthetimeof receipt andtimelyinclusioninagenda for HECreview, Assess the need for expedited review/ exemption from review or full review, Assess the need to obtain prior scientific review, Invite independent consultant, patient orcommunity representatives, Ensurequorumduringthemeetingandrecorddiscussions and decisions
Basicscientist (Affiliated/ non-affiliated)	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	Scientific and ethical review - emphasis on intervention, benefit-risk analysis,research design, methodology and statistics, continuing review process, SAE,protocoldeviation, progressand completionreport, drugsafetyand pharmacodynamicsincaseofclinicaltrials
Clinician (Affiliated/ non-affiliated)	Should be individual/s with recognized medical qualification, expertise and training	Scientific review of protocols including review of the intervention, benefit-riskanalysis, research design, methodology, sample size, site of study and statisticsOngoing review of the protocol (SAE, protocol deviation or violation, progress andcompletionreport), Reviewmedicalcare,facilityandappropriatenessoftheprincipalinvestigator,provisionfor medicalcare,managementand compensation, Thoroughreviewofprotocol,investigatorsbrochure & allotherprotocoldetails
Legalexpert (Affiliated/ non-affiliated)	Should have a basic degree in Law from	Ethicalreviewoftheproposal,ICDalongwithtranslations,MoU,ClinicalTrial Agreement (CTA), regulatory approval, insurance document, other site approvals,researcher'sundertaking,protocolspecificotherpermissions(NAC-SCRT,HMSC etc.) compliance with guidelines

	a recognized university, with experience, Desirable: Training in medical law.	etc.
Social scientist/philosopher/ethicist/ theologian Affiliated/ non-affiliated	Should be an individual with social/ behavioral 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	Ethicalreviewoftheproposal,ICDalongwiththetranslations, Assess impact on community involvement, socio–cultural context, religious or philosophical context,ifany Serve as a patient/participant/ societal / community representative and bring in ethicalandsocietalconcerns.
Layperson (Non-affiliated)	Literate person from the public or community, Has not pursued a medical science/ health related career in the last 5 years,	Ethicalreviewoftheproposal,ICDalongwithtranslation(s), Evaluatebenefitsandrisksfromtheparticipant'sperspectiveandopine whether benefits justifythe risks, Serve as a patient/participant/ community representative and bring in ethical and societal concerns. Assessonsocietal aspectsifany.

	May be a representative of the community from which the participants are to be drawn, Is aware of the local language, cultural and moral values of the community, Desirable: involved in social and community welfare activities	

SOP/24/1/1.9:Membership Requirements:

Members would be selected in their personal capacities based on their qualifications, experience, interest, commitment and willingness to volunteer the required time and effort for the HEC.

Every EC member must:

1. Provide a recent signed CV and training certificates on human research protectionand good clinical practice (GCP) guidelines, if applicable;
2. Either be trained in human research protection and/or GCP at the time of induction into the EC, or must undergo training and submit training certificates within 6 months of appointment (or as per institutional policy);
3. Be willing to undergo training or update their skills/knowledge during their tenure as an EC member;
4. Be aware of relevant guidelines and regulations;
5. Read, understand, accept and follow the COI policy of the EC and declare it, if applicable, at the appropriate time;
6. Sign a confidentiality and conflict of interest agreement/s;
7. Be willing to place her/his full name, profession and affiliation to the EC in the public domain; and
8. Be committed and understanding to the need for research and for imparting protection to research participants in research.

SOP/24/1/1.10:PeriodicassessmentofHECMembers

For the efficient functioning of ECs, it's very important to ensure all HEC members are assessed on their performance at least once a year. Chairperson should also carry out his/her own self-assessment every year.

Parameter of Evaluation for HEC Members:

- Currenttenure
- Termsserved
- Trainingreceived
- Typeoftrainingreceived
- No ofmeetings attended
- No ofprojectsreviewedpermeetingasprimaryreviewer
- No ofprojectsreviewedper meetingassecondaryreviewer
- ParticipationinSAEreportreviewprocess-yes/no
- Participationinsitemonitoringvisits-yes/no
- Number and type of continuing training workshops organized for HEC members (applicabletoMember Secretary)
- Number and type of continuing training workshops organized for staff of the HEC MemberSecretary
- Anyothersignificantcontributionto thefieldofresearchethics
- RemarksbytheChairpersonontheassessment

PointsforSelf-assessmentforHECchairperson

- Currenttenure-
- Termsserved–
- Trainingreceived–
- Typeoftraining received–
- No.ofmeetings heldin current year –
- No ofmeetings attended-
- WhetherquorumrequirementfulfillmentensuredasperscheduleYinHECmeetings
- Whetherconsiderationsrelatedto conflictofinterestconsidered
- Anysignificantcontributiontothefieldofresearchethics
- Anyothercomments

SOP/24/1/2: CONFLICT OF INTEREST

Definition: A situation in which a person, such as a public official, an employee, or a professional, has aprivate or personal interest sufficient to appear to influence the objective exercise of his orher officialduties. Therearethreekeyelementsinthisdefinition:financialinterest,officialduties,andprofessionalinterest. It has been recognized that the potential for conflict of interest would always exist but has faith in the HEC and its Chairperson to manage the conflict issues so that the ultimate outcome is the protection of human subjects. When a member has a conflict of interest, the member should notify the Chairperson and may not participate in the proposal review or approval except to provide information requested by the Committee. If an applicant submitting a protocol believes that an HEC member has a potential conflict, the investigator may request that the member be excluded from the review of the

protocol. The request must be in writing and addressed to the Chairperson. The request must contain evidence that substantiates the claim that a conflict exists with the HEC member(s) in question. The committee may elect to investigate the applicant's claim of the potential conflict. Conflict of interest may arise through any of the following:

1) A member is involved in a potentially competing research program.
2) Access to funding or intellectual information may provide an unfair competitiveadvantage.
3) A member's personal biases may interfere with his or her impartial judgment.

TheappropriateConfidentialityandConflictofInterestAgreementFormwouldbeprovidedto the Institutional Human EthicsCommitteemembersandIndependentConsultants. Every member at beginning of the tenure and before he/she commences to reviewresearchprojectssubmittedtoInstitutional Human EthicsCommitteeandbeforehe/shestartsto function as Institutional Human Ethics Committee members and before he/she starts attendingInstitutional Human EthicsCommitteemeetingwouldreadtheConfidentialityandConflictofInterestAgreementFo rmcarefullyandthoroughly. Institutional Human Ethics Committee member; Independent Consultant would fill up the detailssuch as name, designation and would be provided it to Member Secretary of Institutional Human Ethics Committee. The newly appointed Institutional human Ethics Committee member, before the beginning oftheir tenure, and Independent Consultants would sign and date the document before amemberSecretary.Theywouldgive thesignedformback tothememberSecretary. The member Secretary keeps the original copies of the signed Agreements at the EthicsCommittee forResearchonHumanSubjectsofficeinthefile. ThememberSecretary wouldstorethefile inasecurecabinetwithlimitedkeyholders.

SOP/24/1/3:TRAININGON ETHICAL GUIDELINES:

Continuous training of the existing and newly added members along with the secretariat supporting staff of HEC will be mandatory as per national guidelines. In order to implement this, the following measures will be taken from time to time: -

1. Members should be trained in human research protection, EC functions and SOPs, and should be conversant with ethical guidelines, GCP guidelines (if applicable) and relevant regulations of the country.
2. EC members should undergo initial and continuing training in human research protection, applicable EC SOPs and related regulatory requirements. All trainings should be documented.
3. Any change in the relevant guidelines or regulatory requirements should be brought to the attention of all EC members.
4. EC members should be aware of local, social and cultural norms and emerging ethical issues.

Every HEC member must

a) Provide a training certificates on human research protection and good clinical practice (GCP) guidelines, if applicable;
b) Either be trained in human research protection and/or GCP at the time of induction into the EC, or must undergo training and submit training certificates within 6 months of appointment (or as per institutional policy);

c) Be willing to undergo training or update their skills/knowledge during their tenure as an EC member.

The Human Ethics Chairperson, Committee Member Secretary, and other members would be encouraged to receive continued training by participating in a workshop, conference and/ or retraining program related to research ethics, as a delegate, faculty, facilitator, etc. at least once every year. Institute will provide the financial support for these training programs. Chairperson and Member Secretary would organize workshops or training programs for the committee members. The Human Ethics Committee would conduct workshops on ethics in Biomedical, Health, Clinical research and Good clinical research practices from time to time to impart training to existing and newly added members of HEC. Chairperson and the Member Secretary would inform all the members about any updates on ethical and regulatory guidelines regularly during meetings.Likewise, the Member Secretary /other members of HEC, and workshop/seminar etc will also make the secretariat supporting staff conversant with the ethical guidelines/updates/amendments, if anywith help of timely briefing/extension lectures.

SOP/24/1/4:ETHICAL REVIEW PROCEDURES:

SOP/24/1/4.1:Types of Reviews

Exemption from review

Proposals with less than minimal risk where there are no linked identifiers, forexample;

- research conducted on data available in the public domain for systematicreviews or meta-analysis;
- observation of public behaviour when information is recorded withoutany linked identifiers and disclosure would not harm the interests of theobserved person;
- quality control and quality assurance audits in the institution;
- comparison of instructional techniques, curricula, or classroom managementmethods;
- consumer acceptance studies related to taste and food quality; and
- public health programmes by Govt agencies such as programme evaluationwhere the sole purpose of the exercise is refinement and improvement ofthe programme or monitoring (where there are no individual identifiers).

Expeditedreview

Proposals that pose no more than minimal risk may undergo expedited review,for example;

- research involving non-identifiable specimen and human tissue fromsources like blood banks, tissue banks and left-over clinical samples;
- research involving clinical documentation materials that are non-identifiable(data, documents, records);
- modification or amendment to an approved protocol includingadministrative changes or correction of typographical errors and change inresearcher(s);
- revised proposals previously approved through expedited review, fullreview or continuing review of approved proposals;

- minor deviations from originally approved research causing no risk orminimal risk;
- progress/annual reports where there is no additional risk, for exampleactivity limited to data analysis. Expedited review of SAEs/unexpected AEswould be conducted by SAE subcommittee; and
- formulticentre research where a designated main EC among theparticipating sites has reviewed and approved the study, a local EC mayconduct only an expedited review for site specific requirements in additionto the full committee common review.
- research during emergencies and disasters (ICMR guidelines Section 12).

Fullcommitteereview

All research proposals presenting more than minimal risk that are not coveredunder exempt or expedited review should be subjected to full committeereview, some examples are;

- research involving vulnerable populations, even if the risk is minimal;
- research with minor increase over minimal risk (ICMR guidelines Table 2.1);
- studies involving deception of participants (ICMR guidelines section 5.11 for furtherdetails);
- amendments of proposals/related documents (including but not limitedto informed consent documents, investigator's brochure, advertisements,recruitment methods, etc.) involving an altered risk;
- major deviations and violations in the protocol;
- any new information that emerges during the course of the research fordeciding whether or not to terminate the study in view of the alteredbenefit–risk assessment;
- research during emergencies and disasters either through an expeditedreview/ scheduled or unscheduled full committee meetings. This may bedecided by Member Secretary depending on the urgency and need;
- prior approval of research on predictable emergencies or disasters beforethe actual crisis occurs for implementation later when the actual emergencyor disaster occurs.

Emergency/ Interim review(wherever and whenever applicable)

SOP/24/1/4.2:Step-wise procedure for submission of Research Proposal for Review by HEC

Researchers should submit their research proposals in soft (hec.secretary@mdurohtak.ac.in) as well as hard copies to the Secretariat for review in the prescribed format and required documents as per HEC SOPs. The HEC should prepare a checklist for the required documents as given in Annexure-1-5. This list is subjected to modifications, depending on the type of research, HEC SOPs and institutional policies. Annexure for all kind protocols are available at website of ICMR. (https://main.icmr.nic.in/sites/default/files/guidelines/Common_Forms.pdf). Following steps would be followed right from the receipt up to decision on research proposal by the HEC: -

1. HEC meeting notification will be circulated amongst the faculties from time to time as per schedule. Researchers/Principal Investigators may also inquiry from the HEC office (01262293027/hec.secretary@mdurohtak.ac.in) regarding submission of research proposals and schedule of meeting etc.

2. Researcher/Principle Investigators shall forward their application to the Chairperson HEC, through Member Secretary and the receipt of the application would be acknowledged by the HEC office.
3. Principal Investigator is required to submit his/her application letter and 15 hardcopies of the proposal and soft copy of the same in .pdf format on hec.secretary@mdurohtak.ac.in at least 3 weeks before a scheduled meeting.
4. HEC Secretary shall screen the proposals for their completeness and depending on the risk involved categorize them into three types, namely, exemption from review, expedited review, and full committee review.
5. A researcher cannot decide that her/his proposal falls in the exempted, expedited or full review category.The decision on the type of review required rests with the HEC, and it would be decided on a case-to-case basis. Researchers can approach the HEC with appropriate justification for the proposal to be considered as exempt, expedited or if waiver of consent is requested.
6. In case of incomplete data, the investigators would be informed by the office after consulting the Member Secretary to make the necessary corrections and to resubmit the proposal.
7. Every application would be then allotted an HEC registration number to be used for all future correspondence and other references.
8. After the initial scrutiny by Member Secretary the proposals would be circulated to the HEC members.HEC members should be given enough time (at least 1 week) to review the proposal and related documents, except in the case of exempted/expedited review.
9. Expedited review can be conducted by Chairperson, Member Secretary and one or two designated members.
10. Approval granted through expedited review and the decisions of the SAE subcommittee must be ratified at the next full committee meeting.
11. All HEC members should review all proposals as per procedures for review of proposals in accordance with their SOPs/ICMR guidelines.
12. HEC may adopt a system for pre-meeting peer review by subject experts and obtain clarifications from the researchers prior to the meeting in order to save time and make the review more efficient during the full committee meeting, especially in institutions where there are no separate scientific review committees.
13. HEC may have a system of appointing primary and secondary reviewers. The Member Secretary should identify the primary and secondary reviewers for reviewing the scientific content and the ethical aspects in the proposal as well as the informed consent document, depending upon their individual expertise.
14. The Member Secretary may identify subject experts to review the proposal as per need.These experts may be invited to the EC meeting or join via video/tele conference but would not participate in final decision making.
15. HEC should meet regularly, adopt best practices, try to reduce turnaround time or have procedures in place for early decision making so that research is not delayed.
16. The designated (primary and secondary) reviewers and subject experts should conduct the initial review of the study protocol and study related documents as per the predefined study assessment form and for factors.

17. Date of HEC meeting would be intimated to the PI to attend the meeting and to make a brief presentation of the proposal and to clarify the points raised by the members. HEC can suggest for online meetings and virtual presentations of the investigators in special situations such as COVID-19 pandemic, etc.
18. If revision is to be made, the revised proposal in required number of copies should be submitted within a stipulated period of time as specified in the communication or before the next meeting.
19. Minutes of the HEC meetings, all the proceedings and deliberation would be documented. Signatures of the Chairman and the Member Secretary would be obtained on the minutes of the meeting document. The minutes would be circulated to he Researcher/PI/HODs in case of student proposals.
20. Independent experts may be invited to the meeting or to provide written comment, subject to applicable confidentiality agreement. They would not have a role in decision making.
21. In the absence of Chairperson (in hard pressed situation the inability to chair HEC meeting also in writing submission) an alternate Chairperson would be elected from the other members on the day of meeting (or Chairperson should nominate a committee member as Acting Chairperson for that meeting) by the members present, who would conduct the meeting. The alternate or acting chairperson should have the powers of the chairperson and should be non-affiliated person.
22. The Member Secretary is responsible for organizing the meetings, maintaining the records and communicating with all concerned. Member Secretary would prepare the minutes of the meetings and get it approved by the Chairperson and all the members.
23. In the absence of Member Secretary (in emergency situation with prior information to the Chairperson),Alternate Member Secretary among the members, would organize the HEC meeting.
24. The recommendations by the HEC would be communicated to all the PIs and guides/HODs in case of student's proposals. If required additional review meetings can also be conducted with a short notice period.

SOP/24/1/4.3:Review of multicentric research:

Multicentre research is conducted at more than one centre by different researchers usually following a common protocol. A large number of clinical trials, clinical studies and public health research including surveys are conducted at several research centres within the country or at international sites. Multicentric research studies are carried out with the primary aim of providing a sound basis for the subsequent generalization of its results. All sites are required to obtain approval from their respective ECs, which would consider the local needs and requirements of the populations being researched and safeguard the dignity, rights, safety and well-being of the participants. There are concerns, however, related to duplication of effort in the parallel review by the involved ECs, wastage of time and also those related to communication between the committees. Therefore, in multicentric studies using a common protocol the considerations mentioned in sections 4.10.1 and 4.10.2 of ICMR guidelines (or may be made).

SOP/24/1/4.4:Frequency HEC meetings:

- The Member Secretary in consultation with the Chairperson may convene the HEC meeting once in every three months,probably in January/April/July/October or earlier, if minimum of ten scientific proposals are received or as per any emergency situation.
- Meetings would be planned in accordance with the need of the work load.
- All the HEC meetings would be held regularly on scheduled dates that are announced and notified in advance.
- If there are more number of proposals for consideration per meeting either meetings may be more frequent or more EC's to be constituted as per requirement of the institution. Emergency meeting may also be conducted.

SOP/24/1/5:MEETING QUORUM(FOR FULL COMMITTEE REVIEW):

1. A minimum of five members present in the meeting room.
2. The quorum should include both medical, non medical or technical or/and non-technical members
3. Minimum one non-affiliated member should be part of the quorum.
4. Preferably the lay person should be part of the quorum.
5. The quorum for reviewing regulatory clinical trials should be in accordance with current CDSCO requirements.
6. No decision is valid without fulfillment of the quorum.

So as to maintain independence, the head of the institution should not be part of the HEC but should act as an appellate authority to appoint the committee or to handle disputes.

1) Chairperson and Member Secretary could have dual roles in the ethics committee. They could fulfill a role based on their qualifications (such as that of clinician, legalexpert, basic scientist, social scientist, layperson etc.) in addition to taking on the roleof Chairperson or Member Secretary.
2) HEC can also have a set of alternate members who can be invited as members withdecision-making powers to meet the quorum requirements. These members have thesame TORs as regular members and can attend meetings in the absence of regularmembers.
3) HEC can maintain a panel of subject experts who are consulted for their subjectexpertise, for instance, a pediatrician for research in children, a cardiologist for researchon heart disorders, etc. They may be invited to attend the meeting to give an expertopinion on a specific proposal but will not have decision making power/voting rights.
4) HEC may invite subject experts as independent consultants or include a representativefrom a specific patient group as a member of the HEC or special invitee, for opinion ona specific proposal, for example HIV, genetic disorders, or cancer, with appropriatedecision making power.
5) As far as possible a separate scientific committee should priorly also review proposalbefore it is referred to HEC. EC can raise scientific queries besides ethical ones as bothgood science and ethics are important to ensure quality of research and participantprotection.

In addition to this

1. The HEC may constitute one or more sub-committees of its members to assist in the functions assigned by it.
2. The HEC may associate such experts who are not its members, in its deliberations but such experts shall not have voting rights, if any.
3. All nominated members including the Member Secretary have the right to vote.
4. All members should maintain in absolute confidentiality of all discussions during the meeting. They have no rights to participate if they are principal investigator/ Co-investigator or any kind of conflict of interest with the proposed study.

SOP/24/1/5.1:ProcessforcallingexpertsforHECmeeting:

ItistheresponsibilityoftheChairperson/MemberSecretary/HECmember/stonominate thenameofoneormoreIndependentexperts.TheChairpersonisresponsibleforendorsing the choice of expert nominated by HEC Member Secretary/ HEC member/s. The administrativeproceduresregardingselection,confidentialityagreementandmaintenanc eofrosterofexpertswouldbecarriedoutbyadministrativestaffunderguidance from MemberSecretary.

SOP/24/1/5.2:RecommendationofnamesofExpertsandmakingarosterofExpertsfortheHE C

- Chairperson/ Member Secretary/ HEC members would nominate the names of experts from differentspecialtiesof Medicine as&whenrequired.
- Member Secretary would issue an appointment letter to the expert after confirmingtheirwillingness throughtelephonic/electroniccommunication.
- After receiving written approval from experts, a list of experts would be maintained in the HEC records. The details of each expert (name, designation, specialty, affiliation,contactdetailsandupdatedcurriculumvitae)wouldbemaintainedintheHECre cords.

SOP/24/1/5.3:ConsultinganExpertduringHECreviewprocess

- AnHECmember/MemberSecretary/Chairpersonmaysuggestthattheopinionbesought from one or more expert(s) and may suggest the name of a particularexpert (s) from the list of experts maintained by the HEC or from outside the list.The experts shall be suggested from outside the list only if during the reviewprocessofanygivenresearchstudyitisfeltthatthestudyinvolvesproceduresorinfor mation that is not within the area of collective expertise of the HEC membersorall the expertsofthespecialtyisnotavailableforthe meeting.
  - TheMemberSecretaryinconsultationwithChairperson(oratfullboardmeeting;as deemed necessary) would decide to identify and select the experts outside therosterto beinvitedbasedonareaofexpertise,independence andavailability.
- Member Secretary on behalf of the HEC would invite expert(s) in writing to assist inthe review of the research study and provide his/ her independent opinion inwriting.Thismaybedoneafterseekingconcurrenceandconfirmingavailabilityofthe expert throughtelephonic/electroniccommunication.

SOP/24/1/5.4:CommunicationwithExperts

- The Member Secretary may request a copy of the updated curriculum vitae

oftheexpert(those outsideroster)forHECrecords andfuture reference.

- The Member Secretary would request expert to declare conflict of interest, if any,inwritingandsignconfidentialityandconflict ofinterestagreements.
- The Member Secretary would provide explanations/ clarifications (telephonically orin writing) to the expert(s) if any doubts or questions are raised. Any furtherexplanationscanbeprovidedbytheChairperson/HECmembers/Investigator.

SOP/24/1/5.5:Full committee meeting

1. All proposals that are determined to undergo full committee review must be deliberated and the decision about the proposal taken at a full committee meeting.
2. HECs should conduct regular full committee meetings to deliberate proposals in accordance with a pre-decided schedule.
3. A meeting would be considered valid only if the quorum is fulfilled. This should be maintained throughout the meeting and at the time of decision making.
4. If a member has declared a COI for a proposal then this should be submitted in writing to the Chairperson before beginning the meeting and should be recorded in the minutes.
5. The member who has declared COI should withdraw from the EC meeting (leave the room) while the research proposal is being discussed upon. This should be minuted and the quorum rechecked.
6. A list of absentee members as well as members leaving or entering in-between the meeting should be recorded.
7. Proposals should be taken up item-wise, as given in the agenda.
8. No of proposals reviewed in a meeting should justify that there is ample time devoted for review of each proposal. If there is more number of proposals for consideration per meeting either meetings may be more frequent or more EC's to be constituted as per requirement of the institution.
9. Time allotted for the meeting should be reasonable to allow ample discussion on each agenda item.
10. The minutes of the previous meeting and list of protocols that were exempt from review or underwent expedited review should be ratified.
11. The researcher may be called in to present a proposal or provide clarifications onthe study protocol that has been submitted for review but should not be present atthe time of decision making.
12. The primary and secondary reviewers can brief the members about the study proposaland review carried out.
13. The Member Secretary could present the comments of an independent consultant (if applicable) or subject experts could be invited to offer their views, but theyshould not participate in the decision-making process. However, her/his opinionmust be recorded.

14. Representative(s) of the study group population can be invited during deliberationsto offer their viewpoint but should not participate in the decision-making process.
15. The EC may utilize electronic methods such as video/conference calls for connectingwith other subject experts/independent consultants during the meeting.
16. All members of the EC (including the Chairperson and the Member Secretary) presentin the room have the right to vote/express their decision and should exercise thisright.
17. The decision must be taken either by a broad consensus or majority voteand should be recorded. Any negative opinion should be recorded with reasons.

SOP/24/1/5.6:HEC decision on proposal/s on review

1. HEC can give one of the following decisions:
   a) **Approval**
   b) **Approved with minor revision**
   c) **Major Modification**
   d) **Rejected**

1. If the study duration is less than a year, the approval will be valid for entire duration of the study and if the study duration is more than a year, the progress of the study would be reviewed after completion of a year and further extension will be provided.
2. Depending on the risk involved, the progress of the proposal may be monitored annually or at shorter intervals (quarterly, half yearly) as per HEC decision. Approval may be continued if progress is satisfactory.
3. HEC may decide to reverse its positive decision on a study if it receives information that may adversely affect the benefit-risk assessment.
4. The Member Secretary (assisted by the Secretariat) should record the discussions and prepare the minutes which should be circulated to all the members for comments before final approval by the Chairperson/Vice-Chairperson/designated member of the committee.
5. The decision of HEC should be communicated to the researcher along with suggestions, if any.
6. The researcher should have an opportunity to reply/clarify to HEC comments or to discuss or present her/his stand.
7. The researcher can also approach the head of the institute who serves as an appellate for HEC matters.

SOP/24/1/5.7:Agenda Preparation, Meeting Procedures, Recording of Minutes and communication by HEC

Preparation of the agenda, minutes and other record keeping, would be the responsibility of the Ethics Committee Member Secretary.

MeetingSchedule

The Institutional Human Ethics Committee would meet once in three months. Advance notice, 07days before each meeting would be sent out to the members, along with the agenda.Expedited meeting is possible on as and when needed basis; Ethics Committee

meetingcan be held earlier if required or postponed if there is no new/amended protocol and ifthere is no specific agenda for the meeting at the discretion of Member Secretory orChairman.

DecisionMaking:

- The Member secretary, designated by the Chairperson, would record the Minutes of themeetingandcirculatethesameto themembers withinone weeksofthe meeting.
- The Investigator/Co-investigator is called to the meeting to present the study or answerspecific queries. However, he / she would not participate in the decision making / votingprocess ofthatstudyevenifhe/she isaregularmemberoftheethicscommittee.
- A Study Team member including the Principal Investigator would be deemed an interestedpartywithregardtothereview.
- The Study Team Member's non participation in the decision making / voting process wouldberecordedintheresponseletterfromtheEthicsCommittee.OnlythoseEthicsCommitteemembers whoareindependentoftheinvestigatorandthesponsorofthetrialshouldvote/provideopinionon atrial-related matter.
- TheInstitutionalHuman EthicsCommitteemaycalluponsubjectexpertsasindependentconsultants who may provide special review of selected research protocols, if need be.Theseexpertsmaybespecialistsinethicalorlegalaspects,specificdiseasesormethodologies, or represent specific communities; patient groups or special interestgroups e.g. Cancer patients, HIV/AIDS positive person or ethnic minorities. They arerequiredtogivetheirspecializedviewsbutdonottakepartinthedecision-makingprocesswhichwould bemadebythemembers of the InstitutionalHuman Ethics Committee
- Thedecisionofthecommitteewouldtakebyamajorityvoteafterthequorumrequirementsare fulfilled to recommend / reject / suggest modifications for a repeat review or adviseappropriatesteps.
- If subject experts are invited to offer their views, they would not take part in the votingprocess. Accordingly, HEC wouldmake decision.

In case Institutional Human Ethics Committee revokes its approval accorded to a trial protocol, itmust record the reasons for doing so and at once communicate such a decision to theInvestigator. Inallcases,the studywouldbe unambiguouslyidentifiedbyprotocoltitleandnumber.

All documents reviewed would be listed in the response letter, which would also state the listofmembers presentanddateofthemeetingatwhichthe studywasreviewed.

Themember-secretarywouldconveythedecisionofthecommitteetothePrincipalInvestigator in writing. The response letter would include the signature and date by theInstitutionalHuman EthicsCommitteeMember Secretary.

Thedecisionlettermustcontainfollowinginformation:

a) DateandtimeofEthics Committeemeeting
b) Placeofthemeeting
c) NamesanddesignationoftheChairpersonandmemberswhoattendthemeeting.
d) TitleoftheResearchproposal
e) Nameofthe Chiefinvestigator
f) Listofdocuments(withdateandversionnumberwhereverpossible)reviewedby the InstitutionalEthicsCommittee
g) AclearStatementoftheDecisionReached.Anyadvice(non-binding)bytheInstitutionalEthicsCommittee
h) InthecaseofNegativedecision,reasonsfornotapprovingtheproposalmustbemen

tioned

i) Inthecaseof"approval"decision,theresponsibilitiesofthechiefinvestigator must becommunicated:

Should an amendment to a study related document be administrative in nature and notinvolving study design or safety criteria, it may be provisionally approved in writing, bythe Chairperson/Member-Secretary of the Institutional Human Ethics Committee without calling afull meeting.

The Chairperson/member-secretary would inform other members of the Institutional Human EthicsCommittee of amendment and his / her decision during the subsequent regular meetingofthecommittee.Thedecisionwould beratifiedandcommunicated.

Minutes of the HEC meetings, all the proceedings and deliberation would be documented.Memberhavingaconflictofinterestwouldindicatetothe Chairmanpriortotherevie wofapplication.Anycommitteemember withaconflictinginterestinaproposalwouldabstainfro mdeliberationsandinthedecision-makingprocessonthatproposal,excepttoprovideinformationasrequestedbythecommittee.Suc habstentionswouldberecordedintheminutes.

The meeting shall generally proceed in the order organized in the agenda. However, theChairperson may allow adjustments in the order of issues to be discussed depending onthe situation.

ItistheresponsibilityoftheMemberSecretarytoensureproperrecordinganddisseminationof theminutesafterthemeeting isover.

TheMemberSecretarywouldcomposethesummaryofeachmeetingdiscussionanddecision in a concise and easy-to-read style in the minutes within 7 working days of themeetingday.

The Member Secretary would make sure to cover all contents in each particular category toinclude thefollowing:

- Nameofpersonpreparingtheminutes
- Locationwherethe meetingwasheld(city,state)
- Meetingnumber,date/durationofthemeeting(timeofcommencementandend)
- NamesoftheHECmembersandguestsattendingthe meeting
- NameoftheindividualservingasChairpersonofthemeeting
- DeterminationofadulyconstitutedquorumbytheChairpersontoproceedwi ththe meeting

The Member Secretary would ask the members whether any points need to be discussedregarding minutes of the previous meeting. If no points are raised, the minutes would beconsideredasconfirmed.

TheChairpersonwouldreviewandfinallyapprovetheminutes.

Communicatingthedecision

Theschedule/planofongoingreviewbytheHECshouldbecommunicatedtothePI.

The Member Secretary would place the original version of the minutes in the minutes' file.AdecisionoftheHECwouldbecommunicatedtotheapplicantinwriting,within14daysof the meeting atwhichthedecisionwastaken.

An investigator is expected to submit reply to the letter of recommended modifications /queries sent by the HEC, within 30 days of date of receipt of the letter. If the investigatorfails to reply within this period, the file would be considered closed by the HEC and ethicsclearance approval letter would not be issued by HEC. The investigator would have to re-applyfortheEthicsCommitteeapproval.

Thecommunicationofthedecisionwouldinclude:

- DecisionwouldbecommunicatedbytheMemberSecretaryinwriting.

- Suggestionsformodifications,ifany,shouldbesentbyHEC.
- Name andaddressof HEC.
- Thedateandplaceofdecision
- Thenameanddesignationoftheapplicant.
- Titleoftheresearchproposalreviewed.
- The clear identification of proposal no., version no., date, amendment no., date.
- Aclearstatementofdecisionreached.
- AnyadvicebytheHECto theapplicant.
- In case of conditional decision, any requirement by HEC, including suggestions for revision, and the procedure for having the application re reviewed.
- In case of rejection of the proposal, reason(s) for the rejection would be clearly stated. Signature of the member secretary with date
- CommunicationtoInstitutionalofficialandtoRegulatoryagencieswouldbeperform edbyMemberSecretarywheneverrequirementariseas perbutnotlimitedto SOPofHEC.

SOP/24/1/6: REVIEWOFRESEARCH STUDYPROPOSAL:

1. The Study Protocol and other study related documents would be provided to expert for review
2. The expert would provide his assessment in writing to HEC whichwould become permanent part of the HEC documents.
3. The assessment feedback would be reviewed by Member Secretary in the HEC meeting when the concerned study is being discussed.
4. If deemed necessary, the Chairperson or Member-secretary may seek additional information or clarifications from the expert in writing. Additional Information provided by the expert would be considered as a part of the Assessment feedback.
5. If deemed necessary, the Chairperson or Member-secretary may invite the expert to attend an HEC meeting for providing additional information or clarifications that may be sought by HEC members or Chairperson. However, the expert would not participate in the decision-making process on the research study.
    1. Aletterofintentorproposalbythe Investigator
    2. Cover letter to the Member Secretary forwarded by Departmental Head/ Director
    3. Type of review requested
    4. Application form for review
    5. Clinical trial agreement between the sponsors, investigator and the head of the institution(s) (if applicable)
    6. Current curriculum vitae of all the study researchers
    7. GCP training certificate (preferably within 5 years) of investigators (clinical trials)
    8. Research protocol
    9. Protocol Amendment, if any.
    10. Investigator's Brochure.
    11. Subject recruitment procedures (e.g. Advertisements) Safety Reports
    12. Informed consent form, [English]
    13. Informed consent form, [English to Hindi translation].
    14. Patient/ volunteer information Leaflet [English]
    15. Patient/ volunteer information Leaflet [English to Hindi translation].
    16. Case record form/Questionnaire
    17. Any written information to be provided to subjects including patient emergency card, study related questionnaire

18. Import license, where applicable
19. MoU in case of studies involving collaboration with other institutions (if applicable)
20. Patient instruction card, diary, etc. (if applicable)
21. Investigator's brochure (as applicable for drug/biologicals/device trials)
22. Investigator's undertaking
23. Details of funding agency/sponsor and fund allocation (if applicable)
24. A statement on COI, if any
25. Any other research ethics/other training evidence, if applicable as per EC SOP
26. List of ongoing research studies undertaken by the principal investigator (if applicable)
27. Undertaking with signatures of investigators
28. Regulatory permissions (as applicable)
29. Relevant administrative approvals (such as HMSC approval for International trials)
30. Institutional Committee for Stem Cell Research (IC-SCR) approval (if applicable)
31. Documentation of clinical trial registration (preferable)
32. Insurance policy (it is preferable to have the policy and not only the insurance certificate) for study participants indicating conditions of coverage, date of commencement and date of expiry of coverage of risk (if applicable)
33. Indemnity policy, clearly indicating the conditions of coverage, date of commencement and date of expiry of coverage of risk (if applicable)
34. Any additional document(s), as required by HEC (such as other EC clearances for multicentric studies)

SOP/24/1/6.1:The protocol should include the following:

1. The face page carrying the title of the proposal with signatures of the investigators;
2. Brief summary/ lay summary;
3. Background with rationale of why a human study is needed to answer the research question;
4. Justification of inclusion/exclusion of vulnerable populations;
5. Clear research objectives and end points (if applicable);
6. Eligibility criteria and participant recruitment procedures;
7. Detailed description of the methodology of the proposed research, including sample size (with justification), type of study design (observational, experimental, pilot, randomized, blinded, etc.), types of data collection, intended intervention, dosages of drugs, route of administration, duration of treatment and details of invasive procedures, if any;
8. Duration of the study;
9. Justification for placebo, benefit–risk assessment, plans to withdraw. If standard therapies are to be withheld, justification for the same;
10. Procedure for seeking and obtaining informed consent with a sample of the patient/participant information sheet and informed consent forms in English and local languages. Av recording if applicable; informed consent for stored samples;
11. Plan for statistical analysis of the study;
12. Plan to maintain the privacy and confidentiality of the study participants;
13. For research involving more than minimal risk, an account of management of

risk or injury;

14. Proposed compensation, reimbursement of incidental expenses and management of research related injury/illness during and after research period;
15. Provision of ancillary care for unrelated illness during the duration of research;
16. An account of storage and maintenance of all data collected during the trial; and
17. Plans for publication of results – positive or negative – while maintaining confidentiality of personal information/ identity.
18. Ethical considerations and safeguards for protection of participants

SOP/24/1/6.2:Keyelementsforreviewincludefollowing:

ScientificDesignandConductoftheStudy

- The 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
- Criteria for prematurely withdrawing research participants
- Criteria for suspending or terminating the research as a whole
- The adequacy of the site, including the supporting staff, available facilities, and emergency procedures
- The manner in which the results of the research would be reported and published

ProtectionofResearchParticipantConfidentiality

- Adescriptionofthepersonswhowouldhaveaccesstopersonaldataoftheresearchpa rticipants,including medicalrecordsandbiological samples themeasurestakentoensuretheconfidentialityandsecurityofpersonalinformation concerning researchparticipants.

SOP/24/1/6.3:CommunityConsiderations

- Theimpactandrelevanceoftheresearchonthelocalcommunityandontheconcerne dcommunitiesfrom whichtheresearchparticipants are drawn
- Thestepstakento consultwith theconcernedcommunitiesduringthecourseofdesigningtheresearch
- Theinfluenceofthecommunityontheconsentofindividuals
- Proposedcommunityconsultationduringthecourseoftheresearch
- The extent to which the research contributes to capacity building, such as theenhancement of local healthcare, research, and the ability to respond to publichealthneeds
- A description of the availability and affordability of any successful study productto theconcernedcommunitiesfollowingtheresearch
- The manner in which the results of the research would be made available to theresearchparticipantsandthe concerned communities.

SOP/24/1/6.4:RecruitmentofResearchParticipants

HECwouldcarefullyreview andensure:

- Thecharacteristicsofthepopulationfromwhichtheresearchparticipantswouldbedrawn(includinggender,age,literacy,culture,economicstatus,andethnicity)
- Themeansbywhichinitialcontactandrecruitmentistobe conducted
- Themeansbywhichfullinformationistobeconveyedtopotentialresearchparticipants ortheirrepresentatives
- Inclusioncriteriaforresearchparticipants
- Exclusioncriteriaforresearchparticipants.

In addition to its review for scientific merit and protection of subjects from unnecessaryresearch risks, the EC would evaluate all protocols for subject recruitment especially withrespect to women with childbearing potential, minority groups and children. Exclusion ofminorities, women or children would be recommended or approved, when inclusion isinappropriatewithrespectto thehealthofthe subjectsorthepurposeoftheresearch.

HECwouldalsoevaluaterecruitmentmethodologiesthatareinvolvedtorecruitpatientsintothe studies. HECwould discuss this in detail with Principal Investigator of the study. Themethods by which patients can be recruited are out patient or inpatient department andconsultation,referralfromdoctorswithinandoutsideInstitution,throughcamps,database reviewetc.

SOP/24/1/6.5:Human EthicsCommitteeexpectsfromtheprincipalinvestigatortobeinformed about:

1) Theinitiationofthestudy/randomizationofthefirstpatient(inthestatusreport),
2) Theprogressofthestudyatintervalofevery One year,
3) Any Serious Adverse Events occurring in the course of the study within 24 hoursof their occurring. In case Member Secretary is not available personally due toweekend or any other condition, it can be notified to Ethics Committee membersecretarybyemailathec.secretary@mdurohtak.ac.in,whichwouldbefollowedbysignature of MembersecretaryorChairmanwithin7days.
4) Anychangesintheprotocolandpatientinformation/informedconsentdocuments,priortotheirimplementation.
5) Amendments/revisions to any study-related document as well as patient safetyrelatedinformation
6) Studycompletionanddiscontinuationwithreasons
7) Justificationforapprovaltorestartstudiesdiscontinuedearlier

Thefinalreport ofthe studyshallbe submittedtotheHuman EthicsCommitteein allcases,evenwhen thestudyabandonedforanyreason(s).

SOP/24/1/6.6:Review for protocolresubmittedpackage:
CheckttheReceivedPackagesfor:

- MinutesofpreviousHECmeeting
- ResponsetothecommentsbyInvestigatorsChecklist
- Revisedversionofprotocolandrelateddocumentssuchastheinformedconsent document, data collection or case report forms, diary sheets,etc. are included as part of thepackage.

- Changes made to the documents should be bold and the deleted matter should be made strikethrough for easy verification of the corrections done by the investigators.
- Putthestamp,writedateandacknowledgethereceiptoftheprotocol.

ReviewtheRevisedProtocol

- ChecktherecievedprotocolasperChecklist(annexure attached)
- Refertothemeetingminutesasguidanceforthereview.
- Ensure that the response to comments of HEC members as mentioned in the minutes is given by the investigator and page numbers where changes are made are mentioned in the proposal.
- Makefurthercommentsiftheresponseisnotsatisfactoryandthechanges havenotbeen incorporated in the study proposal.
- Internal reviewers would write the comments on the Project Review Report form and would put signature with date.
- NotifytheHECMember Secretary.
- Inform thePrincipalInvestigatortomakethenecessaryrevisions.
- Send the resubmitted proposal with incorporated changes to reviewers /full board as per the decision in the minutes.
- Iftheproposalhasonlyminormodificationsasdecidedinthepreviousfullboard meeting, the proposal with incorporated changes is sent to external reviewers.

SOP/24/1/6.7:HECmeeting:

If the HEC previously decided that major modifications to be made in the proposal, thentherevision would be processed as:

- The primary reviewer presents a brief oral or written summary of the study designand his/her comments to the HEC members.
- TheChairpersonentertainsdiscussionontheprotocolrevision.
- Further recommendations for modifications to the protocol, consent form as requested bythe Committee are noted in the meeting minutes as 'with modifications made by HEC and would be communicated to the investigator.
- TheChairpersontakesaconsensusoftheHECmembersontherevisiontoeither and make decision on the protocol/s.

1. Member(s)ofthecommitteewhois/arelistedasinvestigator(s)onaresearchpr oposal and having conflict of interest shall declare conflict of interest and would not vote on the proposal and would opt out from all deliberations on the proposal byleaving the meeting room.
2. An investigator or study team member invited for the meeting would not vote or participate in the decision-making procedures of the committee.
3. An independent consultant invited for the meetingto provide opinion would not vote or participate in the decision-making procedures of the committee.
4. If the HEC decision is **'Approved'**, without implies the approval of the study as it is presented with no revision/clarification/modifications and the study can be initiated.
5. If the HECdecision is **approved with minor revision,** it implies that the

study can be initiated only after PI response/s and with supportive documents/clarifications are reviewed and approved by member secretary of HEC.

6. If the HEC decision is **major modification**, it implies the PI should resubmit with the major modification for reconsideration of proposal by full board review.
7. If the HEC decision is **Rejected,**thecommittee willclearly defined reasons must be given for not approving/terminating/revoking of permission.

SOP/24/1/6.8:WrittenCommunicationoftheDecision:

1. The Member SecretarythenpreparestheApprovalletterandgetsthemember'sorChairperson 'ssignature.
2. If thestudyis approved, theCommitteedetermines thefrequencyofContinuingReview for each study site (usually it should be once a year).
3. The Member Secretary sends an Approval letter to the investigator notifying the HEC decision and schedule of continuing review.
4. The letter contains, at a minimum, a listing of each document approved, the date set by the Committee for frequency of continuing review, and a review of other obligationsand expectations from the investigator throughout the course of the study.
5. If the Committeerequiresmodificationstoanyof thedocuments, theMember Secretarysendsa writtenrequestofthespecificchangestotheinvestigatortomakethenecessary changes

SOP/24/1/6.9:Review of Protocol Amendments

- Any revision to an approved research protocol or written consent form if proposed, must be brought to the attention of the committee for approval.
- Amendments to approved protocols and other study related documents should not be initiated until the committee approval has been obtained.
- All deviations from the study protocol should be documented in the original records along with the reasons for doing so.
- In case of any adverse event the same along with the remedial measures taken must be reported by the investigator(s) immediately to the Chairperson and the Member Secretary besides making a note of it in the study documentation.

SOP/24/1/6.10:ContinuingReviewofStudyProtocols

ItistheresponsibilityoftheHECMemberSecretarytoremindthePIsregardingcontinue dreview of protocols at the correct interval. All the approved protocols would be reviewedannually. It is the responsibility of the Member Secretary to ensure a decision regardingwhethertheprojectneedstobereviewedmorefrequentlyistakenduringtheHE

Cmeetingin which the project is finally approved. This must be recorded in the minutes if there isany change from annual review. A fresh decision to increase review may be taken ifrequiredbasedontheSAEreports,monitoringreports,orsafetyconcerns.Thisisresponsibilityof theMemberSecretary.
TheHECisresponsibleforreviewingtheprogressmadeintheprotocol(numberofpatientsrecruited, dropped out, reasons for drop-out), the occurrence of unexpected events orproblems,andcompliance oftheinvestigatorregardingHECcommunication.

SOP/24/1/6.11:Determiningdateofcontinuingreview

- Thedateofthecontinuingreviewwouldalways be atleastonce intheyear.
- TheHECmayrecommendmorereviewsduringtheapprovalprocess dependingonthe levelof risk.Thiswouldbedocumentedintheminutes.
- TheMemberSecretarywouldinspecttheminutesofmeetingtosetatimetableforcontinuingreview.
- TheMemberSecretarywouldidentifyandrecordtheduedatesforeachproject

SOP/24/1/6.12:ContentofStatusReport

The Member Secretary would receive a letter submitted by the PI for continuing review ofeachapprovedprotocol.OnlyonesetofStatusReport(continuingreviewreport)shall besubmittedbythe PI to theHECwhichshouldcontainsfollowingpoints:

- No.ofparticipantsscreened
- No.ofrecruitedparticipants
- No.ofongoingparticipants
- No.ofcompletedparticipants
- Noofparticipantswithdrawnfromstudy
- Hasanyinformationappearedintheliterature,orevolvedfromthisorsimilarresearch that might affect the HEC/HEC's evaluation of the risk/benefit analysis ofparticipants involved inthisprotocol?
- DetailsofSAE
- DetailsofPDs/PVs

SOP/24/1/6.13:Reviewprocess

The Continuing review submission may undergo expedited review or full board review asdeemedappropriate bytheHECChairperson/MemberSecretary.
TheHECChairperson/MemberSecretary/Member/swouldusetheStatusReport(continuingreviewreport)toguide thereviewanddeliberation process.
TheHECChairperson/MemberSecretary/Member/scouldreachoneofthefollowing decisions afterreview:

- Noted-TheHECapprovesthecontinuationoftheprojectwithoutanymodifications.
- Modificationsrecommended:Thestudyprotocolsthathavebeensuggestedmodifications by the HEC may not proceed until the conditions set by the HEC in thedecision have been met. The amendments and the required documents should beamendedandsubmitted to theHECwithinone monthforre-review.
- The project cannot be continued: The reasons for discontinuation of the projectshouldbementionedintheletternotifyingthedecisiontothePrincipalInvesti

gator.

The HEC Chairperson would sign and date the HEC decision on minute of meeting after adecisionhasbeenreached.

ThedecisiononcontinuingreviewtakenbytheChairperson/MemberSecretary/Member/swoul dbe informedto allHECmembers atthe nextfullboardmeeting.

The Status Report (continuing review report) may be discussed at full board if deemednecessarybyChairperson/MemberSecretary.

TheHECMemberSecretarywouldmaintainandkeeptheHECminutesofthemeetingrelevant to the continuing review as part of the official record of the review process in the projectfile.

SOP/24/1/6.14:CommunicatingHECDecisiontothePI

The Member Secretary would notify the PI of the decision within 14 days of the meeting atwhich the report was discussed or of the date of review by the Chairperson/ MemberSecretary/HEC Member/s.

Non-submissionofcontinuingreviewreportbyprincipalinvestigatorbeforeduedate

If a PI fails to submit the continuing review report within one month of the due date (i.e.11thmonthsfromthedateofapproval,orearlieronthedatesasspecified),theMe mberSecretarywouldsendatelephonicand/oremailreminderatleast15dayspriort oduedateof review. If there is no response, the HEC Member Secretary would put up the matter fordiscussionattheforthcomingfullboardmeetingforappropriateactionwhichma yconsistofbut not limitedtosending:

I. A reminderletteragain
II. AletteraskingexplanationfornON-submission
III. AletteraskingthePItoputrecruitmentofnewparticipantsonholdtillr eportissubmitted
IV. AnyotheractionasdeemedappropriatebyHEC

Final Reporting

The Committee must be notified of the trials completed or terminated (wherever applicable). A copy of the final report should be submitted as soon as it is available. Statement of PI regarding conclusion/ completion/ termination/ abandonment of the study must be submitted as soon as the study is terminated.

SOP/24/1/7:REVIEWOFSERIOUSADVERSEEVENT(SAE)REPORTS:

TheHECMemberSecretarywouldreceivethefollowingdocumentswithinthespeci fiedtimeframe ifanSAEisexperiencedbyanyresearchparticipant:

- InitialSAEreporttobesubmittedbythePrincipalInvestigator(PI)within24hours of occurrence
- DueanalysisshouldbesubmittedbythePIwithin14daysfromtheoccurrence oftheSAE
- DueanalysiswouldalsobesubmittedbythesponsorwithIn14daysintheformat
- Thefollow upreportsofallon-siteSAEtilltheeventis resolved.

TheHECMemberSecretarywouldverifythatthereportiscompleteinallrespectsandthat ithasbeenreceivedat the HEC officewithinthespecifiedtimelines.The HEC Member Secretary would sign and write the date on which the report is received.

SOP/24/1/7.1:ReviewandDecisiononSAEReportsandCommunicationtoPIandRegulator

yAuthority by HEC

MemberSecretaryoftheSAEwouldreviewtheSAEreportandpresenttothefullboard/SAEsubcommittee for review and opinion. An emergency HEC meeting (full board or SAEsubcommittee)would bescheduledwithin7days forthesame.

AtthemeetingofHEC,theSAEreportswouldbereviewedwithaspecialfocusonrelatednessto the clinical trial, medical management and financial compensation to be given to theresearchparticipants.

The applicable formulae and guidelines from the regulatory authority would be used duringthis discussionNew Drugs and Clinical Trials Rules, 2019.[http://cdsco.nic.in/writereaddata/GSR%2053(E)%20dated%2030.01.2013.pdfhttp://www.iscr.org/pdf/Gazaate_notification.PDF dated 12th December 2014,Formula for calculating amount of compensation study related death,http://www.cdsco.nic.in/writereaddata/formula2013SAE.pdf]and for study related injury other than deathhttp://www.cdsco.nic.in/writereaddata/uploaded_for_website1_final2014.pdf].

The decision can be arrived at by consensus. If not agreed by consensus, the issue wouldbeputforvoting.(amajorityvoteforadecisionis2/3rdmajorityofthememberspresentandvoting). The minutes of the HEC meeting would include the information on SAE at the site along with the opinionontheabovepoints ontheonsite SAE.

ParticipantID	Letterno./anddateofreporting	TypeofReport(I/FU)	Date ofonset	whetherstudydrug withheld	SAE Outcome	Causalityintheopinion of PI	Recommendation(s)bythe HEC

I-initial,FU-Follow-Up

The HEC Member Secretary would draft a formal letter to the concerned PI and inform him/her about the HEC decision. This letter would be signed and dated by the Member-Secretaryor Chairperson (HEC) and would be sent to the PI within a period of 7 days from the date ofthe HEC meeting.

The PI would be requested to reply to the query letter on the SAE report within 7 workingdays.

The opinion regarding relatedness, medical management and compensation for researchrelated injury would be communicated to the Licensing authority (DCGI) within 30 calendardays of the occurrenceofthe SAE incaseof regulatoryclinical trials.The Member Secretory would file a copy of these letters in the study file.

SOP/24/1/7.2:Reports of SAEOccurringatotherSites

TheinvestigatorwouldneedtosubmittheSAEsoccurringatothersites(CIOMSandSUSARS)in the form of hard or soft copies along with the appropriate covering letter (hard copy)mentioningthetotal numberof reports.

TheSAEsoccurringatothersiteswouldbereviewedbytheSecretaryoftheHECinformedto other members and discussed in the forthcoming scheduled meeting. The agenda andminutes ofthemeetingwould include theinformationonSAEs atothersites.

SOP/24/1/7.3:OnsiteAdverse Event

TheHECMemberSecretarywouldreceivethefollowingdocumentspertainingtoAEexperiencedbythe researchparticipants forresearchproposals approvedbythe HEC:

- Onsite AE reports to be submitted by the PI annually in the continuing reviewreport.
- In view of the risk assessment of a given research proposal the HEC can

requestadverse events to be reported earlier, if deemed necessary at specified timelinesintheproject approval letter.

- TheHECMemberSecretarywouldverifythatthereportiscompleteinallrespectsandsignedand dated by the PI and that it has been received at the HEC office within the specifiedtimelines.Ifthereporthasbeenreceivedbeyondthespecifiedtime,it wouldbeconsideredas deviation.
- Member Secretary of HEC may put the AE reports for discussion at full board if deemednecessary.
- Queries, if any on the report would be communicated to the PI by the Member Secretary ofHECfollowing full boardmeeting.

SOP/24/1/7.4:DecisionofHEConSAEreview

The HEC may take one or more of the following decisions on review of the SAE reports. Type of Actions Taken by HEC on Review of SAE Report:

Following detailed review of the SAE reports and related documents, the HEC can suggest one of the following actions:

- NotetheinformationabouttheSAEinrecordsforfuturereference.
- Requestfurtherfollowupinformationand/oradditionaldetails.
- Askforperiodicfollow-upoftheresearchparticipanttillSAEis resolved
- Dependingoncomplexitiesofissue,HECmaydecidetoseekopinionofoutsideexpertconsultantwho is requestedto respondwithin14workingdays.
- Providerecommendationsregarding/raisequeriesrelatedtocompensationforstudyrelated injuryanddeath
- Suggestchanges/amendmentsinprotocol,PatientInformationSheet/InformedConsentDocument/Investigators'Brochure/anyotherstudyrelateddocuments.
- Suspendthestudytilladditionalinformationisavailable.
- Suspend the study till review is completed (safety monitoring of ongoing patientsto becontinued).
- Suspendthestudytillamendments requestedforbythe HECare carriedout.
- Suspendenrollmentofnewparticipants.
- Suspendcertainactivitiesundertheprotocol.
- Direct the PI to inform participants already enrolled in the study about the AEsand if required obtain their consent again (re-consent) regarding continuation inthe researchtrial.
- DirectthePItoinformparticipantsalreadyenrolledinthestudyabouttheAEandrequestthemtoundertakeadditionalvisits,additionalprocedures,additionalinvestigations,etc.asprescribedintheamendment
- Terminatethestudy.
- Anyotherappropriateaction.

Thedecisionshallberecordedintheminutes ofthefullboardHECmeeting. If the recommendation from the HEC includes suspension of the study or suspension ofanyoneormoreofthestudy-relatedproceduresoractivities,amendmentsintheprotocolorotherstudy-relateddocuments(excludingInvestigators'brochure),re-consenting of research participants, the decision would be conveyed to the PI throughtelephone, fax or email within 24 hours. Such a communication would be documented bythe HEC Member-Secretary in the study file. A formal letter to the PI informing about theHEC recommendations in such situations would be sent within 5 working days of the HECmeetinghaving takenplace.

SOP/24/1/7.5:Management of Premature Termination, Suspension,Discontinuation of the Study

Protocols may be terminated/suspended/discontinued at the recommendation of the HEC, Principal Investigator (PI), Sponsor, Regulator or other authorized bodies wherein participant enrolment and follow-up are discontinued before the scheduled end of the study.

It is the responsibility of the HEC to manage the termination of any study (recommended for termination by Monitoring Board, Principal Investigator, Sponsor or other authorized bodies or by the HEC) that the HEC has previously approved. The Member Secretary is responsible for management of the premature termination/ suspension/discontinuation process.

Recommendation for Termination/ Suspension/ Discontinuation

By PI / Sponsor

An investigator/ Sponsor may put on hold a previously approved research when in the judgment of investigator/ Sponsor this is appropriate to protect the rights or welfare of participants or when new safety information has appeared in the literature, or evolved from this or similar research.

By HEC

HEC members/Chairperson can prematurely terminate/ suspend/ discontinue the study in the following situations:

Protocol non-compliance/violation following which HEC decides in full board meeting to terminate/ suspend/ discontinue the study.

1) SAEs occurring at trial site may require the study to be prematurely terminated for the safety of the patients.
2) When research is not conducted in accordance with HEC policies, is not in compliance with the local regulations or that has been associated with unexpected serious harm to participants.
3) Zero accrual for 1-2 years or long-term, low accrual.

Suspended protocols remain open and require continuing review.

HEC may revoke approval and recommend stopping permanently all activities in previously approved research protocol. Terminated protocols are considered closed and no longer require continuing review.

In case the study is terminated by PI/QCO (Quality Control Officer) should give a written explanation to the HEC in one month.

SOP/24/1/7.6:Detailed instructions

Receipt of Recommendation for Study Termination.

- Member Secretarywould receive study protocol termination/suspension/discontinuation report submitted by PI and verify the contents of report for completeness (Appendix) and/or other documents (letter from PI / sponsor).

Review by the HEC

- Member Secretarywould inform Chairperson and Additional Member Secretary regarding recommendation for premature termination/ suspension/ discontinuation of study protocol and termination/ suspension/ discontinuation report within 3 working days of receipt of report.
- Member Secretary/Additional Member Secretary / Chairperson shall review the report and either call for an**EMERGENCY**

MEETINGor discuss the report at the regular full board meeting.

- Member Secretarywould arrange for an Emergency meeting/ keep matter for discussion at fullboard meeting as per SOPs& superseded by National Ethical Guidelines for Biomedical and Health Research Involving Human Participants, 2017 and amended time to time.
- Member Secretary/Additional Member Secretary in the meeting would inform members of the premature termination/suspension/ discontinuation of the project and the reasons for the same.
- If the premature termination/ suspension/discontinuation report is unclear or more information is required from the PI, the Chairperson shall instruct the Member Secretary to seek clarifications/ additional information from the Principal Investigator.
- Chairperson shall sign and date the study termination/ suspension/ discontinuation report in acknowledgement.
- If the HEC has revoked approval/suspended the study, regulatory authorities and Head of the institution must be informed within 14 working days of the full board meeting.

SOP/24/1/7.7:Notifying the Principal Investigator

- Member Secretarywould prepare a notification letter and send to the PI within 14 working daysafter the meeting acknowledging the approval of termination/ letter seekingclarifications/information regarding the premature termination.
- In case a letter is sent seeking clarifications/information regarding the prematuretermination/suspension/discontinuation, the PI shall send a written response within 60days of receiving the letter.
- If the PI does not comply, the matter would be put to the full board meeting for discussion.
- The investigator may appeal or respond to the convened HEC in writing.

SOP/24/1/7.8:Store the Protocol Documents

- The Member Secretarywould keep the original version of the Premature Termination Report in theProtocol file and send the file to archive.

- The protocol documents would be stored for a period of 5 years from the date of projecttermination
- Any protocol amendment likely to affect rights, safety or well-being of research subject of conduct of study.
- Serious or unexpected ADR related to study or product, action taken by Investigator, Sponsor and Regulatory Authority.
- Any event or information that may affect the benefit/risk ratio of the study.
    1) A decision of a follow up review would be issued and communicated to the applicant indicating modification/suspension/termination /continuation of the project.
    2) In case of premature suspension /termination, discontinuation of study the applicant must notify the HEC of the reasons for suspension/termination with a summary of results.
    3) Applicant must inform the time of completion of study and must send the result summary to HEC.
    4) HEC must receive a copy of final summary of study completed

from the applicant.

SOP/24/1/8:REVIEW OF INFORMED CONSENT DOCUMENT (SUBJECT INFORMATION SHEETANDINFORMEDCONSENTFORM)ANDINFORMEDCONSENTPROCESS :

PatientinformationsheetandinformedconsentforminEnglish/Hindiandlocallanguage(s) should be enclosed. The patient information sheet should provide adequateandcompleteinformationinunderstandablelanguage.Itshouldalsoassurethatanynewinformationthatbecomesrelevantduringthetrialandisrelatedtotheirparticipationwouldbe given to them. The consent form should be as per schedule Y and its subsequentamendmentpublishedinGazetteofIndia.RequirementofAudio-Visualinformedconsent/Audioinformedconsent/onlywritteninformedconsentwouldbediscussedduringeachinitialstudyreview aspertheapplicableregulationspublishedinGazette ofIndia.

Followingpointswouldbeconsideredwhilereviewinginformedconsent:

- Understandablelanguage
- Statementthatstudyinvolves research
- Sponsorofstudy
- Purposeandprocedures
- Risks&discomforts
- Benefits
- Compensationforparticipation
- Compensationforstudyrelatedinjury
- Alternatives toparticipation
- Confidentialityofrecords
- StatementthatconsentisvoluntaryRighttowithdrawReviewofProtocolDeviations/Violations

SOP/24/1/8.1:DetectionofProtocoldeviation/violation

Protocoldeviation/violationProtocoldeviation/violationmaybedetectedinonethefollowingways(butnot limitedto thoselistedbelow):

Protocoldeviation/violationreportbytheMemberSecretary

Protocoldeviation/ violationmaybedetectedinonethefollowing ways(butnotlimited to thoselisted below):

I. Protocol deviation/ violation may be reported by Investigator/ study site/ sponsor/Contract-ResearchOrganization totheHEC.
II. TheHECmembersperformingmonitoringoftheprojectattrialsitemaydetectprotocol deviation/violation if the project is not being conducted as per protocol/national/international regulations.
III. TheMemberSecretarymaydetectprotocoldeviation/violationfromfailuretocomply with statutory requirements/ failure to respond to requests from HEC withinreasonable time limit/failureto respondtocommunicationmade byHEC.
IV. The HEC members may detect protocol deviation/ violation when scrutinizing annual/periodicreports/SAEreports/anyothercommunicationreceivedfromt

heInvestigator/trialsite/sponsor/studymonitor/contractresearchorganization
.

V. The HEC Member Secretary and/ or HEC members may become aware of a protocoldeviation/ violation while reviewing study-related documents including reports filedinbythePrincipal Investigator (PI)
VI. Communication/ complaint/ information received from a research participant whohasbeenenrolledoranyindividualwho has beenapproachedforenrolment.
VII. Anyreport/communicationbroughttothenoticeofMember,Secretary/Jt.Secretary/Chairpersonof HECbyanindependentperson.
VIII. Communication received from the Head of the Institution informing HEC about anallegedprotocol violation/protocoldeviation.

SOP/24/1/8.2:Actionstobe taken

1. Theactionofthe HECwouldbe basedon:
   - Thenatureandseriousnessofthedeviation/violation.
   - Frequencyofdeviation/violationinthestudyinthe past.
   - Frequency of deviation/ violation in previous studies conducted by the samePI/Co-PIorinthesamedepartment.
2. Member Secretary would decide on the impact of the protocol deviation / violationand act accordingly. Depending upon the seriousness, the HEC shall do the following (notlimitedtotheseactions):
   - AskPIforwrittenclarificationassoonasthe deviationis received.
   - If the impact is serious, this report would be shared with the Chairperson andtwoormoreHECmembersdesignatedbythe Chairperson.
   - IftheimpactoftheprotocoldeviationisseriousenoughtheMemberSecretary would schedule a full-board meeting specifically to discuss the issuewithin7working days of theinitial scrutiny
   - TheMemberSecretarywouldputuptheinformationandcommunicationat thenextfull boardmeeting fordiscussion.
3. The Member Secretary in consultation with HEC members would review the informationavailable anddeliberate onit.
4. TheChairpersonwouldtakeafinaldecisiondependingontheseriousnessofthe violation. The decision would be taken to ensure that the safety and rights of theresearchparticipantsaresafeguarded.Thedecisionwouldbetakenbyvoting.Amajorityvote for approval, disapproval or request for modifications of a study suspension orterminationofanongoingstudyisdefinedas2/3rdofthevotingmemberspresentatthe meeting.
5. ThedecisiontakenbyHECcouldinclude oneormoreofthefollowing:
   - Determinethatnofurtheractionisrequired,ortakeotheractionsasappropriate.
   - InformthePIthattheHEChasnotedtheviolation/deviation,andinstructthe PItoensurethatdeviations/violationsdonotoccurinfutureandtofollowHECrecommendations.
   - Enlist measures that the PI would undertake to ensure that such deviations /violations donot occurinfuture.

- Observetheresearchorconsentprocess(dependingonthenatureandfrequencyof thedeviation).
- Suggestmodificationstotheprotocol.
- Alter the interval for submission of the continuing review/ annual projectstatus.
- Ask for additional training of the investigator and study team of ReprimandthePI.
- SeekadditionalinformationfromthePI.
- Conductauditoftrialbythe HEC.
- Suspendthestudytilladditionalinformationismadeavailableandscrutinized.o Suspend the study till recommendations made by the HEC are implementedbythePI andfoundtobesatisfactorybythe HEC.
- Suspendthe studyforafixeddurationoftime.
- Suspensionorterminationofthestudy.
- Revokeapprovalofthecurrentstudy.InformDCGI/otherrelevantregulatoryauthorities.
- Keep other research proposals from the PI/ Co-PI under abeyance. Reviewand/orinspect otherstudies undertakenbyPI/Co-PI.
- This final decision would be recorded on minutes of the meeting by the Member Secretary.

SOP/24/1/8.3:ProcedureforNotifyingthePIandOtherConcerned Authorities

TheMemberSecretarywoulddraftanotificationletter.

- The signed letter by Member Secretary would be sent to the PI and Institutional Officials (ifrequired oncase-to-casebasis).
- The HEC Member Secretary would send a copy of the notification to the relevantnationalauthorities(ifrequiredoncase-to-casebasis)andinstitutes(ifrequiredoncase-to-casebasis incaseof multi-centrictrials).

SOP/24/1/8.4:RecordsandfollowuptobekeptbyHECMemberSecretary

TheMemberSecretarywouldkeepacopyofthenotificationletterinthe respective project file.

SOP/24/1/9:POLICYFORSTUDIESONVULNERABLEPOPULATION:

ThepurposeofthissectionistodetailtherequirementsforInstitutionalHuman EthicsCommitteeapproval of research involving vulnerable populations. Vulnerable populations must begivenspecialconsideration.

SOP/24/1/9.1:ExamplesofVulnerablePopulations: -

I. **Handicapped persons:** Persons with mental or physical handicaps are consideredto bea vulnerablepopulation.
II. **Elderlypersons**
III. **Researchonpersonsbelow 18yearsofAge**
IV. **Subordinate Individuals:** Subordinate relationships can be unduly influenced bytheirsuperior.The following are examplesofsuchrelationships:

V. **Employer/employee**

VI. **Militaryofficer/soldier**

VII. **Personswithmentalhealthconditions**

VIII. **Traumatic or emergency situations:** Individuals who are in the midst of atraumatic or emergency situation or otherwise under emotional duress can bepotentiallyvulnerable.

IX. **Low Socioeconomic Status:** Low socioeconomic status can create a vulnerabilityof subjects resulting from unique socioeconomic factors. For example, an offeroffinancialcompensation for participation in research may be interpreted as exploitivewhendirectedtowardimpoverished subjects.

X. **Incurabledisease:**Thefollowingareexamplesofsuchdisease:
-CancerPatientwithnocuretherapyisavailable-HIVetc.

XI. **Researchonpregnantwomen,fetusesandneonates**

SOP/24/1/9.2:SpecialConsiderationsandProceduretoreviewstudiesonVulnerable

Theinclusionofcertaingroupsofparticipantswhomaybevulnerabletoundueinfluenceor coercion may require additional protections. When the Ethics Committee reviewsresearch involving vulnerable populations, the Ethics Committee applies any additionalIndianregulations,ScheduleYrequirements,asapplicable.TheEthicsCommitteeeval uates whether additional safeguards have been included in the study to protect therights and welfare of participants who may be vulnerable to undue influence. The HECrequiresatleastoneormoreindividualswhoareknowledgeableaboutorhaveexperience inworkingwiththese participants arepartofthereview process.

TheHECwould reviewresearchinvolvingvulnerablepopulationsaccordingtoapplicablerequirementsandguidel inesandwould makesdecisions. Iftheresearchincludesavulnerable population that does not have additional protections, the Ethics Committeewould evaluate the research proposal to ensure that precautions are taken to protect theparticipants.

The Institutional Human Ethics Committee must consider risks to participants when reviewingproposed research. There are risks to vulnerable populations that would not normallyneedconsideration,suchasthefollowing:

A. **Towhatrisks, uniquetotheirstatus,wouldparticipantsbeexposed?**
B. **Whatprotectionswouldbemadeto mitigaterisks?**
C. **Aresubjectscapableofprovidingconsent?**

If the Institutional Human Ethics Committee determines that a legal representative isappropriate, such as when the subject is an adult with a cognitive disability, theHECwouldworktogetherwithitslegaladvisortodeterminewhoismostappropriateaccord ing to Indian Regulations and state law to provide legally effective consentonbehalfof thesubject.

D. **Researchinvolvingchildren**

- Where possible, parent/guardian consent should be accompanied by

assentfrom the child showing them to be a willing participant in the research project. Itis recommended that the assent of the child be sought when deemedappropriatebythestudyteam

- ParticipantInformationSheetsandConsent/Assentformsmustbepresentedi naform and language that is understandable by a child of 10 years of age (that is, toafifth-gradelevel)

Alsobasedontherequirementoftheresearchareasuchas HIV,Geneticdisorderetc.specificpo pulationgroupmayalso berepresented inethicscommittee.Avulnerablecategoryofsubjectsincludeschildren,prisoners,pregna ntwomen,handicappedor mentallydisabledpersons,refugees,displacedpersonsandeconomicallyoreducationall ydisadvantaged persons, who are likely to be vulnerable to coercion orundue influence. Projects that involve vulnerable population and special groups should be subjected to full review by all the members.

Compensation: If a participant volunteers to involve him/her in the study. If the study requires more than one hour of his time, he/she has to be compensated with suitable compensation. No study should involve financial burden to the participant. All financial expenditure shouldbe included in the project proposal.

SOP/24/1/9.3:SupplementReviewofresearchproposals involvingvulnerable population

Vulnerablepersonsarethoseindividualswhoarerelativelyorabsolutelyincapableofprotecting their own interests and providing valid informed consent. Include economically and socially disadvantaged; children (up to 18 years);women in special situations; tribals and marginalized communities; refugees, migrants, homeless, persons or populations in conflict zones, riot areas or disaster situations; afflictedwithmentalillnessandcognitivelyimpairedindividuals,differently abled –mentally and physically disabled; terminally ill or are in search of new interventions having exhausted all therapies; suffering from stigmatizing or rare diseases; or have diminished autonomy due to dependency or being under a hierarchical systemand unduly influenced either by the expectation of benefits or fear of retaliation in case of refusal to participate which may lead them to give consent.

HECsshouldcarefullydeterminethebenefitsandrisksofthestudyand examinethe justification provided and risk minimization strategies. Additionalsafetymeasures should bestrictlyreviewed and approved bytheHEC.HECmustensurethatthe informedconsentprocess shouldbewelldocumentedandrecordingof assent in case of research studies involving children aged 7 to 18 years and reconsent, when applicable.Informedconsentfromvulnerablepopulationsmaybeobtainedfrom LAR(Legallyauthorized representative) in presence of impartial witness after through explanation of risks and benefits.

SOP/24/1/9.4:AudioVisualRecordingoftheInformedConsent Process

The purpose of this SOP is to describe the procedures for Audio-Visual (AV) recording, storage and archival of the informed consent and assent process for

regulatory studies.

This SOP applies to all those regulatory clinical trials approved by the DCGI, which require documenting of the written informed consent and assent process.

- An audio-video recording of the informed consent process in case of vulnerable subjects in clinical trials of NewChemical Entity or New Molecular Entity including procedureofprovidinginformationtothesubjectandhisunderstandingonsuch
- consent,shall bemaintained bytheinvestigatorforrecord:
- Provided that in case of clinical trial of anti-HIV and anti-leprosy drugs, only audio recording of the informed consent process of individual subject including the procedureofprovidinginformationtothesubjectandhisunderstandingonsuch
- consentshall bemaintained bytheinvestigatorforrecord.
- StatementthatthereisapossibilityoffailureofIPtoprovideintendedtherapeutic effect
- StatementthatincaseofPlacebocontrolledtrials,theplaceboadministeredtothe subjects shall not have any therapeutic effect
- Anyotherpertinent information

Responsibilities:

i) HECwouldensurethat Principalinvestigator wouldconduct AV recordingoftheinformed consent process, store and archive without violating the participant confidentiality as detailed below in section 6.
ii) HECwouldspecificallyaskforconsent forAVConsentinginaddition totheICF
iii) AVrecordings maybereviewed periodicallybyHECmembers

Applicablerules,regulationsandguidelines:

i. Order from Director General of Health Services (DGHS), Ministry of Health and Family Welfare, Office of Drugs Controller General (India), F.No. X.11014/1/2012- DFQC dated 31st July 2015 Schedule Y (Jan 2005).
ii. National EthicalGuidelinesforBiomedicaland Health ResearchonHumanParticipants, ICMR2017
iii. International Conference on Harmonization; Good Clinical Practice Guidelines: May 1996
iv. As perthe DCGIofficeorderdated 25Aug2015G.S.R.611. (E)A-Vrecordingof ICF Process in case of Vulnerable Subjects Anti-HIV and Anti Leprosydrugs, onlyAudio recording of the ICF Process.

DetailedInstructions forPI to follow:

All basic principles and procedures for the administration and documentation of the informed consent process are described in SOP Initial review of submitted protocol.

1) If the participant is unable to give consent for medical or legal reasons, the

consent should be taken from the legally acceptable representative (LAR) and the process recorded.

2) If the participant/LAR is illiterate then an impartial witness is needed. This person should also be in the frame for the entire duration of the consent process.
3) AVrecordingshouldbedoneofassentwhereverapplicable
4) Ensure the following infrastructure is available prior to counseling of potential participant:
   a. The informed consent process should be carried out in the designated area when the following conditions should be met) that is -

i. Freefrom disturbance
ii. Well lit
iii. Ensuresprivacyfortheparticipant
iv. Participantshouldbe comfortable

b. Camerahavingvideofacilitywith

- Goodresolution(at least1280x720pixels)
- Sufficientmemory(atleast 4 GB)
- Sufficientbatterybackup(atleast2hours)
- Shownon-editabledate &timeonvideo(preferably)

a) Mikesystem
b) Computer/laptopwithCD/DVDwriter
c) BlankCDs/DVDswithcover
d) External Harddisk(atleast 500GBto1 TB)

5) Beforestartingthe informedconsent process(and theAVrecordingofthesame)
   i. Ensurethatall thenecessaryequipmentmentionedaboveisfunctional.
   ii. The potential participant/LAR/ Impartial witness should be informed that the whole process of taking the consent is being recorded as per Govt. of India notification to ensure that he/she has understood all the potential risks and benefits involved in the study including failure of the IMP, study details and his/her rights for the purpose of documentation and the confidentiality of the same is assured.
   iii. The potential participant/LAR/ impartial witness should be made aware that his/her recording may be shown to government agencies or members from the HEC and independent auditors.
   iv. His/her consent should be documented in a separate ICD that states the same.The process of obtaining signatures of the potential participant/LAR/ impartial witness & Principal Investigator or her designee on this Audio-video consent form should be carried out as per specified in Annexure AF/HEC/04/08/V-8.0 of SOP/08/V-8.0.

ActualAVrecording process:

i. The PI/Co-I/medically qualified person delegated by the PI and the

potential participant/LAR(andifneedbe,theimpartialwitness)shouldsitcomfortablyfacingeach other / side-by-side in such a way that their faces would be captured in the frame simultaneously.

ii. The PI/Co-I/medically qualified person delegated by the PI should introduce himself/herself by name, designation and his/ her role in the research, and state the current date and time.

iii. Participant/LARshould be requested to introduce his/her name, age and address and in case of LAR, he/she should clearly state relation to actual participant as well as the reason why the participant cannot give consent. Participant/LAR should also state the language he/she understands best and is literate in. The PI/Co-I/medically qualified person delegated by the PI may facilitate this process to ensure all above points are captured in the recording.

iv. In case participant/LAR is illiterate and an impartial witness is needed, the impartial witness should be requested to introduce him/her, give his/her address and state the language that he/she is literate in.

v. The Participant/LAR should state that he has been informed about the fact that the entire consent process is being recorded and that he/she has agreed for the same.

vi. The Informed Consent Process should be carried out as per SOP 08/V-8.0: Administering and documenting informed consent.

vii. The participant should be allowed to read the consent document (and this process should be recorded)

viii. The PI/Co-I/medically qualified person delegated by the PI should explain all the elements of the approved ICF in the language best understood by the potential participant

ix. Explanation or narration given by the PI/Co-I/medically qualified person delegated by the PI, all the questions asked by the potential participant/LAR and answers given to them should be clearly audible and recorded.

x. At any point during the consent process, if the participant wishes to take more time to read/ understand the consent document, including, for example, take it home to discuss with relatives the recording shall be stopped mentioning the time of stopping.

xi. The participant/LAR (wherever applicable) should be invited to sign the consent form onlyafter satisfactory answers (in the investigator's judgement) have been given bythe participant/ LAR to all the above-mentioned questions.

xii. Participant/LAR should read out all the statementsmentionedinICFasper Schedule-Y and state whether he/she agrees or not for each statement and affix signature/thumb print at the end

xiii. Theactual signingprocessshould berecorded.

xiv. The impartial witness should be requested to enter the name and details

of the participant and the date the consent is documented. The impartial witness would also be requested to sign and date the consent form.

xv. The PI/Co-I/medically qualified person delegated by the PI would also sign and date the consent form at the end of the process.

xvi. Therecordingwouldbestopped afterthankingtheparticipant.

- The recording should be checked for completeness and clarity of both audio and video recording.
- No editingshould be done on the recordingso as to maintain authenticity.
- The computer/laptop should be password protected. The password would be known only to the PI and members of the study team as designated by the PI. A register should be maintained wherein, each time the data is accessed, the details of who accessed thedata, date and reasons for the same this should be entered into the designated register.
- The recording should be then transferred to a CD labeled according to study name, unique identifier assigned to the participant, date and time of the recording, no. of recordings (applicable during re-consenting) and archived in the external Hard drive. The CD should be filed in the participant binder.
- The study participants should be informed that there is possibility of failure of investigational product to provide intended therapeutic effect.
- In case of placebo-controlled trial, the placebo administered to the subjects shall not have any therapeutic effect.

Archival

a. The soft copies of the recordings should be stored in a password protectedexternal hard drive for minimum of five years.

b. Theoriginalrecordinginthecomputer/laptopwouldbedeleted whenstudyisclosed out.

SOP/24/1/9.5:ReviewofAmendedProtocolsandProtocol-relatedDocuments:

- ItistheresponsibilityoftheHECMemberSecretarytoensurethecompletenessofthe documentssubmittedtotheHEC.
- A re-submitted protocol and related documents may be reviewed by either theChairpersonandtwoormoreHECmembersdesignatedbytheChairperson/Member secretary (in expedited review meeting), or all the HEC members as perHECdecisiondeterminedbytheHECatthetimeoftheinitialreviewoftheproject during the full board HEC meeting. This information would be recorded in theminutes of themeetings.

Theamendedprotocol/protocolrelateddocumentwouldrequireFullBoardreviewifanyofthe followingcriteria aremet:

TheProtocolamendmentchangestherisk-benefitassessmentsuchas

- Achangeinstudydesign,
- Additionaltreatmentsorthedeletionoftreatments
- Changesininclusion/exclusioncriteria.
- Changeinmethodofdosageformulation,suchas,oralchangedtointravenous
- Asignificantchangeinthenumberofresearchparticipants(ifthedecrease/increase in the number of research participants alters the fundamentalcharacteristics of thestudy,itissignificant)
  - For regulatory studies, a protocol amendment with above changes wouldrequire DCGI Approval
- In the case of an amended study protocol and related documents, the membersecretary/chairpersonwoulddecidewhetherthepropose dprotocolamendment(s)needstoundergoafullboardreview orexpeditedreview.Iftheamendment(s)is /areofadministrativenaturethemembersecretary/chairpersoncanrecommend an expedited review, while if the amendment/s relate to participantsafetyordatacapture,itshouldberecommendedforfullboardreview. Additionally, primary reviewers who had reviewed the initial submission may beaskedtoreviewtheresubmitted protocol.

Detailedinstructions

- The Member Secretary for summarizing and including it on the agenda for fullboard discussion in the forthcoming meeting if the decision on the protocol was‘to bediscussed at full board’
- The designated HEC members if the decision on the protocol was ‘to be reviewedbytwoormoreHECmembers’
- TheChairperson/MemberSecretaryifthedecisionontheprotocolwas‘Approved withrecommendationssubjecttoreviewbyChairperson/MemberSecretaryonly ’as perHEC DecisionForm.

ReviewofrevisedprotocolbyHECmember/MemberSecretary/Chairperson

- In case the decision is to discuss the revised protocol at the full board meeting,the Member Secretary would present a brief oral summary of the study design andthecommentsoftheHECmembers/Chairpersoninthe HECFullBoardmeeting.
- The Chairperson shall entertain discussion on the protocol revision from all theHECmembers.
- Thefinaldecisionregardingtheresearchprojectshallbereachedbyvoting(2/3rd majorityofthememberspresentandvoting)andshallincludeoneofthefollowing:
  a) Approved
  b) Modifications to items noted at the convened meeting and follow-up by theChairperson/ Member Secretary /HEC members after receipt of the requestedmodifications:
  c) Disapprovedgivingreasonsfordisapproval

Thefinaldecisionregardingtheresearchprojectshallbereachedbyvoting (2/3rdmajorityofthememberspresentandvoting)andshallincludeoneof thefollowing:

- Approvetheprotocolamendment
- Require a modification to the proposed amendment or informed consentdocuments, stating the reason and action required to sustain the studywitha follow-upfull HEC review/HECreview.
- Not approve the amendment request, stating the reason – but allow thestudytocontinueaspreviouslyapproved.
- Suspendthestudy,untilfurtherinformationisobtained

SOP/24/1/9.6:PolicyforExpeditedreview

Allrevisedproposals,epidemiologicaland/orAcademicproposalunless specificallyrequired to go to the main committee, would be examined in a meeting of identifiedmembers convened by the Chairman to expedite decision-making. Expedited review mayalsobeorderedbytheChairmanand/orMemberSecretaryincasesofn ationallyrelevantproposals requiring urgent review.

SOP/24/1/9.7:Patient Charter – Rights and Responsibilities of ResearchParticipants

RightsofResearchParticipant

- Subject should be given enough time to decide whether or not to be in theresearchstudy;
- Research Participant Is allowed make that decision without any pressure fromthe peoplewhoareconductingtheresearch
- Understands his/her right to refuse to be in the study at all, or to stopparticipatingat anytime afterbeginning the study
- Research Participant should be told the purpose of the study, what would happenduring the research, and what the participant would be asked to do if he/she is inthe studyina levelof language that is easilyunderstood
- Research Participant should be told about known and reasonably foreseeablerisks of being in the study, including the chances of experiencing those risks andthe possibleseverityof therisks
- Research Participant should be told about the possible benefits of being in thestudy.
- Research Participant should be told whether there are any

costs associated withbeing in the study and whether the participant would be compensated forparticipatinginthestudy

- ResearchParticipantshouldbetoldwhowouldhaveaccesstoinformationcollected during or after the study, to what extent confidentiality can be assured,andhowhis/herconfidentialitywould beprotected
- Research Participant should be told who to contact with questions about theresearch, who to tell about a research-related injury, and who to ask abouthis/herrightsasa researchparticipant
- Ifthe studyinvolvestreatmentortherapy:
  - Research Participant should be told about other non-research treatmentchoices;and
  - Research Participant should be told where treatment is available should aresearch-related injury occur, and who would pay for research-relatedtreatment.

ResponsibilitiesofResearchParticipant

- Completely read the consent form and ask the Principal Investigator (PI)questions, if any. Participant should understand what would happen to him/herduringthestudybeforehe/she agreesto participate.
- Knowthedateswhenstudyparticipationstartsandends.
- Carefullyweighthepossiblebenefits(ifany)andrisksofbeinginthestudy.
- Talk to the Principal Investigator (PI; the person in charge of the study) if he/shewants tostopbeing part oftheresearchstudy.
- Contact the PI and/or the EC with complaints or concerns about participation inthe study.
- Report to the PI immediately any and all problems he/she may be having withthe studydrug/procedure/device.
- Fulfil the responsibilities of participation as described on the consent formsunless he/sheisstoppinghis/herparticipation inthestudy.
- Inform the PI or the person responsible study when reimbursement have beenreceivedthat was promised forparticipating inthestudy.
- Askfortheresultsofthestudy
- Keepacopyoftheconsentformforrecords

Subject'sparticipationandwithdrawal

- Participants always have the right to withdraw from their participation inresearch at any time and for any reason

without penalty or loss of benefits towhichthey wouldotherwisebeentitled.

PatientFeedback:

- Patient feedback can be collected on ad hoc basis to evaluate the subject'sunderstanding for clinical Research. Appendix 11 covers the form for researchfeedback frompatient.

SOP/24/1/9.8:CorrectiveandPreventiveActions(CAPA)Process:

Any issues that are identified by HEC during initial and ongoing review of studiesshould be brought to the attention of Investigator and site team and appropriateresponseshouldbesought.Forissuesthatconsideredrepetitive,serious anddirectlyaffects study conduct, HEC should request Investigator to perform route causeanalysisandimplementCAPA andsubmit adetailedreporttoHEC.The Drugs Controller General India (DCGI) in its gazette notification GSR72E, dated08th February 2013, 122DD states, 'The Ethics Committee shall allow inspectors ofofficials authorized by the Central Drugs Standard Control Organization to enter itspremisestoinspectanyrecord,dataoranydocumentrelatedto clinicaltrial andprovide adequate replies to any query raised by such inspectors or officials, as thecase may be,inrelation to theconductofthetrial.'

SOP/24/1/9.9:Correctionofdeficienciesobserved ataudit/inspection

- Member Secretary/ designated HEC member/ Member Secretary would review commentsandrecommendationsoftheauditor/inspect or.
- On receipt of Audit/ Inspection Report the Chairperson should implement correctiveand preventive measures and set the timeline for implementation of corrections asstatedby theauditor/inspector
- Action plan should be communicated by the Member Secretary/ designated HECmembertotheauditor/inspectorafterseekingapproval of theChairperson.
- A review date for an internal follow-up audit would be decided by the Chairperson (ifapplicable).

SOP/24/1/9.10:SiteMonitoringandPost-MonitoringActivities

1. It is recommended that HEC should systematically monitor the approved study site until completion of the research to check for compliance or improve the function.
2. Monitoring can be routine or "for cause" and must be decided at a full committee meeting. For research that involves higher risk or vulnerable participants or if there is any other reason for concern, HEC at the time of initial review or continuing review can suggest that routine monitoring may be conducted at more frequent intervals. Some causes for monitoring are as under: -

- high number of protocol violations/deviations;
- large number of proposals carried out at the study site or by the same researcher;
- large number of SAE reports;
- high recruitment rate;
- complaints received from participants;
- any adverse media report;
- adverse information received from any other source;
- non-compliance with EC directions;
- misconduct by the researcher; and
- any other cause as decided by the HEC.

It is the responsibility of the Full Board or Chairperson and Member Secretary todecidetoconducton-sitemonitoring.ItisfurtherthereresponsibilityofthedesignatedHECmember(s)toperformon-sitemonitoring:

- Routine monitoring for the site may be decided at the time of approval of the projectbythe Full Board.
- Thisisrecordedinthe HECminutes.
- "For-cause monitoring" would be performed at the site for reasons identified by anymemberofthe HEC, after approvalby theChairperson.
- The reasons for identifying for "for-cause monitoring" could include any one or more of thefollowing:
  - Highnumberofprotocolviolations,
  - Largenumberofstudiescarriedoutbytheinvestigator,
  - LargenumberofSeriousAdverseEvents(SAE)reports,
  - Highrecruitmentrate,orLarge numberofProtocoldeviations,
  - Complaints receivedfromparticipantsoranyotherperson,
  - Frequentfailuretosubmittherequireddocuments
  - Anyother causeasdecidedby HEC.

Beforethevisit

- Irrespective of the cause for conducting monitoring the following procedure would be followed
- The Chairperson would identify and select one or more HEC members (henceforth referredtoasmonitors) toconductmonitoringofthesite.
- Theselected memberswouldbegivenanappointmentletter inthis regard.
- The agenda of monitoring would be decided by the identified monitors in consultation withtheMember Secretary andChairperson
- The Member Secretary would decide the date of the monitoring in consultation with themonitorsandthePI.
- The final date would be communicated to the PI (with a request to be available) and monitors.
- The monitor would receive from Member Secretary and review the

relevant project documentsandmakeappropriatenotes.

- The Member Secretary provided Monitors with relevant reference material /documentsrelatedtotheproject

Duringthevisit

TheMonitorwould follow thechecklistand:

- Checkthelogofdelegationofresponsibilitiesofstudyteam,
- Check if the site is using latest HEC approved current versions of the protocol,informedconsentdocuments,caserecordforms,diaries,advertisements,etc.
- Observe the informed consent process, if possible, review randomly selectedparticipants' files to ensure that participants are signing the correct informedconsent
- Check investigational product accountability is adequately controlled anddocumented throughout the product flow at the study site (arrival, dispensing, use,returnfromthesubjectandreturn/destructionafter the study)
- Check for storage times, conditions and expiry dates to be acceptable and sufficient supplies available,wherever applicable
- Verify that the investigator follows the approved protocol and all approved amendment(s),if any
- Ensure that the investigator and the investigator's trial staff are adequately informed aboutthetrial
- Verify that the investigator and the investigator's trial staff are performing thespecified study functions, in accordance with the approved protocol and any otherwritten agreement between the sponsor and the investigator/institution, and have notdelegatedthesefunctions tounauthorized individuals
- Verify that theinvestigatoris enrollingonlyeligible subjects
- Determine whether all SAEsare appropriately reported within the time as per theapplicable regulatory requirement(s). Case record forms would be checked to reviewthe safety data i.e. Adverse Events (AEs) and SAEs for the volume or severity ofadverseevents
- Review the project files of the study to ensure that documentation is filed appropriately
- Reviewthe sourcedocumentsfortheircompleteness
- Collectviewsofthestudyparticipants, ifpossible.

Afterthevisit

- The Monitor would submit the report to the HEC Member Secretary within 7 working daysofconductinga sitemonitoringvisit.

- Thereport shoulddescribethefindingsofthemonitoringvisit.
- The Member-Secretary would present the monitoring report at the next full board HECmeeting and the concerned Monitor would provide additional details/ clarifications tomembers,asrequired.
- The HEC would discuss the findings of the monitoring process and take appropriatespecificactionbyvotingorcombinationofactions,so meofwhichare listedbelow:
  - ✓ Continuationoftheprojectwithorwithoutchanges
  - ✓ Restrictionsonenrollment
  - ✓ Recommendationsforadditionaltraining
  - ✓ Recruitingadditionalmembersinthestudyteam

Revising/ providing qualifications/ experience criteria for members of the studyteam,terminationofthe study

- Suspensionofthestudy,etc.
- If the Monitor has findings that impact on safety of the participant the Monitor wouldinform the Member Secretary on the same day. The Member Secretary would discusswiththeChairpersonandany oneoftheactionsdescribed abovewould betaken.
- Thefinal decisiontakenatthefullboardHECmeetingby theChairpersonin MoM
- The Member Secretary would convey the decision to the Principal Investigator inwritingwithin14workingdaysof themeeting.
- TheMemberSecretarywouldplace the copyofthereportinthe protocolfile.

SOP/24/1/9.11:Dealing with Participants' Requests and/or Complaints toInstitutional Human Ethics Committee

- Arequest,complaintorquery,fromaresearchparticipantwouldbeaccepted bytheMemberSecretary
- TheMemberSecretarywouldadditionallyascertaindetailsoftherequest/co mplaintbyexaminganyrelevantdocumentsandbyinterviewingthepartic ipantifnecessary. If required, the Member Secretary would call for additional relevantinformationanddocumentsfrom thePrincipalInvestigator (PI).
- The Member Secretary would inform the Chairperson about the request, query orcomplaintreceivedfromtheresearchparticipant.
- IncaseofarequestforadditionalinformationorclarificationtheMemberSe cretaryinconsultationwiththeChairpersonwouldprovidetheinformation

himself / herself or would designate one or more HEC member(s) to provide suchinformation

- Incaseofacomplaintreceivedfrom aresearchparticipant:
  - The Member Secretary, in consultation with the Chairperson would initiate aprocess to address any injustice that may have occurred. Depending on theseriousness of the matter, the Chairperson would direct the Member Secretaryto:
    - AppointasubcommitteeoftwoormoreHECmembersforenquiryin orderto resolvethematter.
    - CallanemergencymeetingoftwoormoreHECmembers fordiscussionor Considerthematterfordiscussionatthenextfullboardmeeting
  - TheChairperson/MemberSecretary/designatedHECmemberswould assessthesituation and mediate a dialogue between the research participant and PI inanattempt toresolvethematter.
  - The HEC would insist on factual details to determine gap, if any, between truthandindividual perception.

- The final decision would be taken by the Member Secretary in consultation with theChairperson based on the recommendation of any one of the above and it would beinformedto the researchparticipantandthe PIbythe Member Secretary.
- The HEC members would be informed about the action taken and the outcomes in the forthcoming HEC meeting (in case of requests/ complaints not discussed in full board meeting) and minutes.
- The Member Secretary would place all documents in the relevant study file.

SOP/24/1/9.12:Emergency Meeting

- The Member Secretary in consultation with the Chairman may convene the HEC meeting once in every three months or earlier if minimum of ten scientific proposals are forwarded. The member-secretary with the help of the technical staff (EDP section) has the responsibility of intimating all the members and investigators.
- Additional review meetings can also be held with short notice as and when required.
- Based on necessity, emergency meetings can be called on the request of the office head of institute. The member-secretary in consultation with the Chairperson would decide on calling such meetings. Expedited meeting would be conducted as per the procedures discussed in ICMR National Ethical Guidelines and New Drugs and Clinical Trials Rules 2019.
- The Chairperson would direct the Member Secretary to consider the matter with in two weeks for discussion at a full board meeting or to call an emergency meeting of 2 or more HEC members for discussion or to appoint a subcommittee

of 2 or more HEC members for “due analysis” in order to resolve the matter.

SOP/24/1/10:OFFICIAL RECORD KEEPING AND ARCHIVING

1) All documentation and communication of an EC should be dated, filed and preserved according to written procedures.
2) Confidentiality should be maintained during access and retrieval procedures by designated persons.
3) All active and inactive (closed) files should be appropriately labeled and archived separately in designated areas.
4) Records can be maintained in hard copies as well as soft copies.
5) All records must be archived for a period of at least three years after the completion/termination of the study.
6) Documents related to regulatory clinical trials must be archived for five years after the completion/termination of the study or as per regulations.
7) Records may be archived for a longer period, if required by the sponsors/regulatory bodies.
8) HEC records should be accessible for inspection by authorized representatives of regulatory agencies
9) HECs may adopt methods for electronic storage of records wherever feasible.

SOP/24/1/10.1:CorrespondenceRecord Keeping

- CorrespondencebetweentheInstitutional HumanEthicsCommitteeandthePrincipalInvestigator/studyteamandotherrelevantrecords(responseletter,minutesofmeetings, membership list composition etc.) would be retained for minimum period of 5years aftercompletionofthetrial.
- The Institutional Human Ethics Committee would review all research projects and also the on-goingresearchprojectsatintervalsappropriatetothedegreeofrisk tothestudysubjects.
- Thecommitteewouldmaintainalistofprojectssubmitted,approved/disapprovedandtheoutcome of each project including subject in formation, relevant correspondence and allstudyrelated documents.

SOP/24/1/10.2:Documentation and Records

The proceedings of all meetings shall be documented and shall be kept in confidence.The release of the detailed documentation to non-committee members can only be made in case of exceptional circumstances, which shall be verified either by court orders or by affirmative opinions by the Chairperson and the Member Secretary. Minutes of the meeting shall be circulated by Member Secretary for verification by the Chairperson and members present during the discussion. After verification, the Member Secretary shall communicate final decisions regarding protocols to the investigator(s). All documentation sample for different kinds of studies and must be retained ordinarily for five years after the completion of the study.

SOP/24/1/10.3:**The following records should be maintained by the HEC office:**

1. The Constitution and composition of the HEC
2. Signed and dated copies of the curriculum vitae of all HEC members with records of training if any
3. Standard Operating Procedures of the HEC and modifications approved from time to time.
4. National and International guidelines
5. Copies of protocols submitted for review
6. All correspondence with the members of the Board, and investigators regarding application, decision and follow up;
7. Notice and agenda of all HEC meetings;
8. Minutes of all HEC meetings with signatures of the Member Secretary and the Chairperson.
9. Copies of decisions communicated to the applicants;
10. Record of all notifications issued for premature termination of a study with a summary of the reasons;
11. Final report of the study including microfilms, CDs and Video recordings/samples for different kinds of studies. PI may be asked to report completion of the study.

SOP/24/1/10.4:RecordMaintenance

- AllthedocumentsandcommunicationsofHECwouldbedated,filedandarchivedina secureplace.
- Onlythemembersecretaryorpersons,whoareauthorizedbytheChairmanofHECwouldhave theaccesstothevarious documents.
- Allthedocumentsrelatedtoresearchproposalswouldbearchivedforaminimumperiodof 5 years intheInstitute,followingthecompletion/terminationofthestudy.
- Nodocument(exceptagenda)wouldberetainedbyanyHECmember.
- At the end of each meeting, every member must return the CD/DVD containing all theresearch proposals and documents to HEC Member Secretary. They would archive one copyinHEC officeandothercopies would bedestroyed.

Followingdocumentswouldbefiledandarchivedwithproperlabelonthetopoffile foreasyidentification:

1. ConstitutionandcompositionofEthicsCommittee
2. CVofthecommitteemember
3. EthicsCommittee SOPandtheirSubsequentchanges
4. Copiesofdocumentssubmittedforreview includedbutnotlimitedtoProtocol,IB
5. Agendaof allEthicsCommitteemeetings
6. MoMwith signatureofChairman
7. Copiesof decisioncommunicated tothe applicants
8. RecordsofallcorrespondencewithEthicsCommitteebyapplica

ntincludingstatusreport,SAEnotification, reasonfor premature terminationofthestudy.

SOP/24/1/10.5:Maintenance of Active Study Files

Alldocumentationandcommunicationofan HECaretobedated,filedandpreservedaccordingtowrittenprocedures.Strictconfidentialityistobemaintainedduringaccessandretrievalprocedures.Thefollowingrecordsshouldbemaintainedforthefollowing:

i. Alldocumentationandcommunicationofan ECshouldbedated,filedandpreservedaccordingtowritten procedures.
ii. Confidentialityshouldbemaintainedduringaccessandretrievalproceduresbydesignatedpersons.
iii. Allactiveandinactive(closed)filesshouldbeappropriatelylabelledandarchivedseparately in designated areas.
iv. Recordscanbemaintainedinhardcopiesaswellassoft copies.
v. Allrecordsmustbearchivedforaperiodofatleast3yearsafterthecompletion/terminationof thestudy.
vi. Documents relatedtoregulatoryclinicaltrialsmustbearchivedfor5yearsafterthecompletion/terminationofthe studyorasper regulations.
vii. Records may be archived for a longer period, if required by the sponsors/regulatorybodies.
viii. HECshould describe archival and retrieval mechanisms in SOPs.
ix. HECrecordsshouldbeaccessibleforinspectionbyauthorizedrepresentativesofregulatory agencies.
x. ECs may adopt methods for electronic storage of records wherever feasible. Table 2 givesexamples of records thatcan bemaintained.

Table2DocumentstobemaintainedbyECforrecord

Typeofdocument	Document specifics

Administrative Documents	• ConstitutionandcompositionoftheEC • Appointment letters • SignedanddatedcopiesofthemostrecentcurriculumvitaeofallEC members • Signed confidentiality agreements • COI declarations of members • Trainingrecords of EC members • FinancialrecordsofEC • Registration/accreditationdocuments,asrequired • Acopyofnationalandinternationalguidelinesandapplicable regulations • Regulatory notifications • Meeting-related documents
Proposal-RelatedDocuments	• Agenda and minutes • Allcommunications receivedor madebytheEC • SOPs • Onehardcopyandasoftcopyoftheinitialresearchproposalandall related documents • Decision letters • Any amendments submitted for review and approval • Regulatory approvals • SAE,AE reports • Protocoldeviations/violations • Progress reports, continuing review activities, site monitoring reports • AllcorrespondencebetweentheECandresearchers • Recordofnotificationissuedforprematureterminationofastudywith asummary ofthereasons • Finalreportofthestudy • Publications, if any

SOP/24/1/10.6:Maintaining of confidentiality of EC's Documents

The proceedings of all meetings shall be documented and shall be kept in confidence. Therelease of the detailed documentation to non-committee members can only be made in case of exceptional circumstances, which shall be verified either by court orders or by affirmative opinions by the Chairperson and the Member Secretary. Minutes of the meeting shall be circulated by Member Secretary for verification by the Chairperson and members present during the discussion. After verification, the Member Secretary shall communicate final decisions regarding protocols to the investigator(s). All documentation sample for different kinds ofstudies and must be retained ordinarily for five years after the completion of the/study

14. FLOW CHARTS

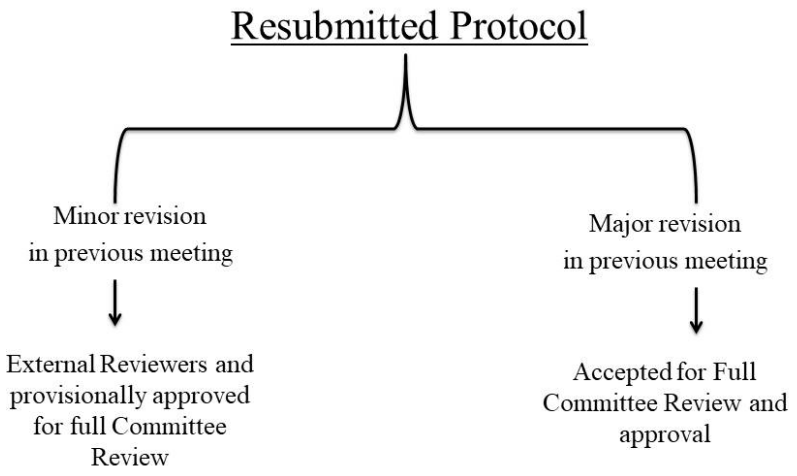

Fig. 1: Procedure for the Resubmitted Review

Fig. 2: Stepwise Overview of Application Procedure

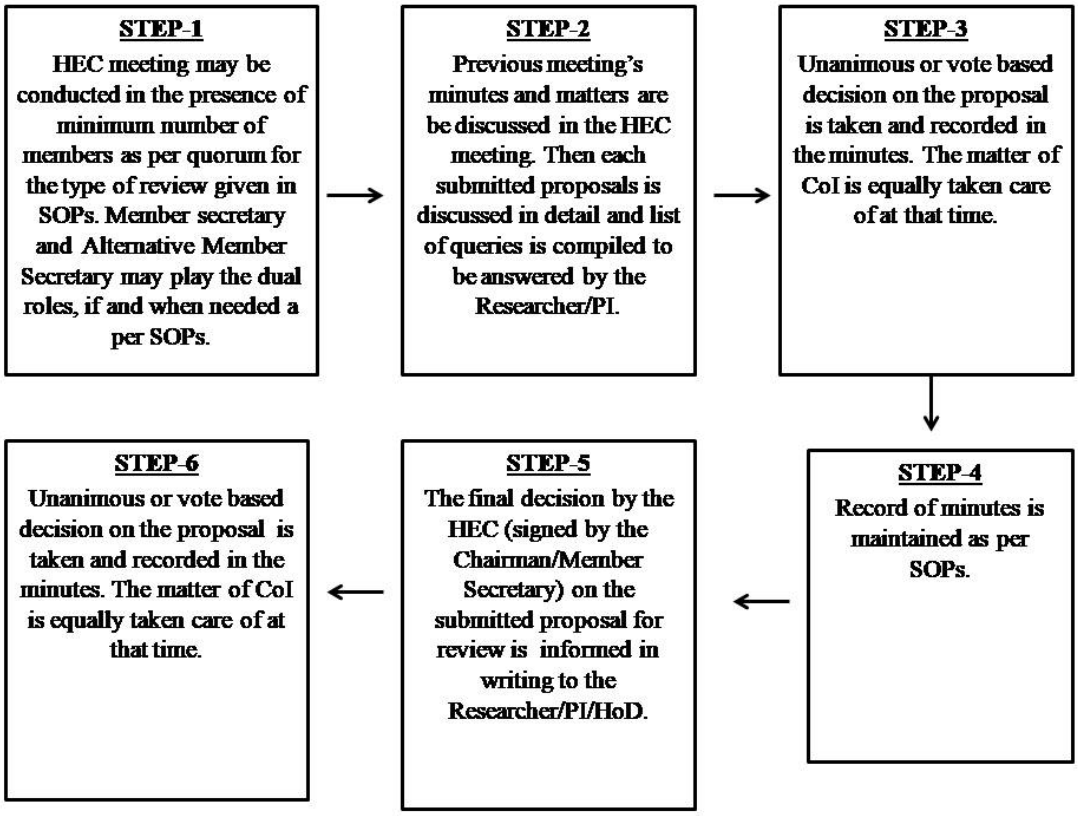

Fig. 3: Committee Meeting Procedures & Circulation of Decision

15. References

1. National Ethical Guidelines For Biomedical And Health Research Involving Human Participants Indian Council Of Medical Research 2017 [Compiled & Edited by: Dr. RoliMathur Head, ICMR Bioethics Unit NCDIR, Bengaluru Published by: Director-General Indian Council of Medical Research New Delhi 110 029 www.icmr.nic.in ISBN: 978-81-910091-94 October, 2017 [Indian Council of Medical Research] https://ethics.ncdirindia.org/asset/pdf/ICMR_National_Ethical_Guidelines.pdf
2. EXTRAORDINARY, PART II—Section 3—Sub-section (i), MINISTRY OF HEALTH AND FAMILY WELFARE (Department of Health and Family Welfare) NOTIFICATION New Delhi, the 19th March, 2019 https://cdsco.gov.in/opencms/export/sites/CDSCO_WEB/Pdf-documents/NewDrugs_CTRules_2019.pdf
3. https://ethics.ncdirindia.org/Common_forms_for_Ethics_Committee.aspx
4. https://naitik.gov.in/DHR/Downloads

ANNEXURE -1 (A1/SOP/24/1)

Details of documents to be submitted for HEC review

1. Cover letter to the Chairman HEC
2. Type of review requested
3. Application form for initial review
4. The correct version of the informed consent document (ICD) in English and Hindi language(s).
5. Case record form/questionnaire
6. Recruitment procedures: advertisement, notices (if applicable)
7. Participant/Patient form/instruction card, diary, etc. (if applicable)
8. Investigator's brochure (as applicable for drug/biological/device trials)
9. Details of funding agency/sponsor and fund allocation (if applicable)
10. Brief curriculum vitae of all the study researchers
11. A statement on COI, if any
12. GCP training certificate (preferably within 5 years) of investigators (clinical trials)
13. Any other research ethics/other training evidence, if applicable as per HEC SOP
14. List of ongoing research studies undertaken by the principal investigator (if applicable)
15. Undertaking with signatures of investigators
16. Regulatory permissions (as applicable)
17. Relevant administrative approvals (such as HMSC approval for International trials)
18. Institutional Committee for Stem Cell Research (IC-SCR) approval (if applicable)
19. MoU in case of studies involving collaboration with other institutions (if applicable)
20. Academic Clinical trial agreement between the sponsors, investigator and the head of the institution(s) (if applicable)
21. Documentation of Academic clinical trial registration (preferable)
22. Insurance policy (it is preferable to have the policy and not only the insurance certificate) for study participants indicating conditions of coverage, date of commencement and date of expiry of coverage of risk (if applicable)
23. Indemnity policy, clearly indicating the conditions of coverage, date of commencement and date of expiry of coverage of risk (if applicable)
24. Protocol details/synopsis
25. Research study approval, if applicable
26. Any additional document(s), as required by HEC (such as other HEC clearances for multicentric studies)

ANNEXURE -2(A2/SOP/24/1)

Details of documents to be included in the protocol

The protocol should including the following:

1. the face page carrying the title of the proposal with signatures of the investigators;
2. brief summary/ lay summary;
3. background with rationale of why a human study is needed to answer the research question;
4. justification of inclusion/exclusion of vulnerable populations;
5. clear research objectives and end points (if applicable);
6. eligibility criteria and participant recruitment procedures;
7. detailed description of the methodology of the proposed research, including sample size (with justification), type of study design (observational, experimental, pilot, randomized, blinded, etc.), types of data collection, intended intervention, dosages of drugs, route of administration, duration of treatment and details of invasive procedures, if any; duration of the study;
8. justification for placebo, benefit–risk assessment, plans to withdraw. If standard therapies are to be withheld, justification for the same;
9. procedure for seeking and obtaining informed consent with a sample of the patient/participant information sheet and informed consent forms in English and local languages. AV recording if applicable; informed consent for stored samples;
10. plan for statistical analysis of the study;
11. plan to maintain the privacy and confidentiality of the study participants;
12. for research involving more than minimal risk, an account of management of risk or injury;
13. proposed compensation, reimbursement of incidental expenses and management of research related injury/illness during and after research period;
14. provision of ancillary care for unrelated illness during the duration of research;
15. an account of storage and maintenance of all data collected during the trial; and
16. plans for publication of results – positive or negative – while maintaining confidentiality of personal information/ identity.
17. ethical considerations and safeguards for protection of participants.

ANNEXURE -3(A3/SOP/24/1)

Informed Consent Document must contain

ParticipantInformationSheet (PIS)

1. Statement that the study involves research and explanation of the purpose of the research, in simple language
2. Expecteddurationoftheparticipationof subject.
3. Descriptionoftheproceduresto befollowed,includingallinvasive procedures.
4. Descriptionof anyreasonablyforeseeable risks ordiscomforts to the Subject.
5. Descriptionofanybenefitstotheparticipantorothersreasonablyexpectedfromresearch.Ifno benefit is expected participants should be made aware of this.
6. Disclosureofspecificappropriatealternative proceduresortherapiesavailabletotheparticipant.
7. Statementdescribingtheextenttowhichconfidentialityofrecordsidentifyingthe participant would be maintained and who would have access to participant's medical records.
8. Trialtreatmentscheduleandtheprobabilityforrandomassignmenttoeachtreatment(for randomized trials).
9. Statementdescribingthefinancialcompensationandthemedicalmanagementasunder:
10. In case of an injury occurring to the subject during the research/clinical trial, free medical managementshallbegivenaslongasrequiredortillsuchtimeitisestablishedthattheinjury is not related to the clinical trial, whichever is earlier.
11. In the event of a trial related injury or death, the sponsor or his representative or the investigatoror Centre,asthecasemaybe,inaccordancewiththerule39,as thecasemaybe, shall provide financial compensation for the injury or death.
12. Anexplanationaboutwhotocontactfortrialrelatedqueries,rightsofSubjectsandintheevent of any injury.
13. Theanticipatedproratedpayment,if any,tothe participant forparticipatinginthetrial.
14. Responsibilitiesofsubjectonparticipationin thetrial.
15. Statement that participation is voluntary, that the subject can withdraw from the study at any timeandthat refusaltoparticipatewouldnotinvolveanypenaltyorlossofbenefitstowhichthesubject is otherwise entitled.
16. Statementthatthereisapossibilityoffailureofinvestigationalproducttoprovideintended therapeutic effect.
17. Statementthatinthecaseofplacebo-controlledtrial,theplaceboadministeredtothesubjects shall not have any therapeutic effect.
18. Anyotherpertinentinformation.

Additional elements, which may be required:

1. Statementofforeseeablecircumstancesunder whichtheparticipationofthesubjectmaybe terminated by the Investigator without his or her consent.

2. Additionalcosts tothe participantthat mayresultfrom participationin thestudy.
3. Theconsequencesofaparticipant'sdecisiontowithdrawfromtheresearchandprocedu resfor orderly termination of participation by Subject.
4. StatementthattheParticipantorparticipant'srepresentativewouldbenotifiedinatimel ymannerif significantnew findingsdevelopduringthecourseoftheresearchwhichmayaffecttheparticipant's willingness to continue participation would be provided.
5. Astatementthattheparticulartreatmentorproceduremayinvolveriskstothe participant(orto the embryo or fetus, if the participant is or may become pregnant), which are currently unforeseeable.
6. Approximatenumber ofparticipantsenrolledinthestudy.

ANNEXURE -4(A4/SOP/24/1)

InformedConsentForm (both in English and Hindi)

Participant's Initials: _____
Participant's Name: _____ Date of Birth/Age: _
Address of
Participant _____Qualification _____
Occupation:StudentorSelf-EmployedorServiceorHousewifeorOthers(Pleaseclickas appropriate).
Annual Incomeofthesubject:_____
Nameandaddressofthenomineesandhisrelationtothesubject(forthepurposeofcompensationin case of trial related death).
PlaceInitialbox (Subject)

- Iconfirm thatIhave read andunderstood theinformation []

Sheet dated _____forthe abovestudyandhave had theopportunityto askquestions.

- Iunderstand that myparticipationin thestudyis voluntaryand []
- that Iamfreetowithdrawatanytime,withoutgivinganyreason, without mymedicalcareorlegal rights being affected.
- I understand that the Sponsor of the research/clinical trial, others working on the Sponsor's behalf, the Human Ethics Committee and the regulatory authorities would not need my permission to look at my health recordsbothinrespectofthecurrent studyand anyfurtherresearchthatmaybeconductedin relation to it, even if I withdraw from the trial. I agree to this access. However, I understand that my identity would not be revealed in any information released to third parties or published. [ ]
- Iagreenottorestricttheuseofanydataorresultsthatarise fromthisstudyprovidedsuchause is only for scientific purposes [ ]
- Iagreeto takepart intheabovestudy. []

Signature(orThumbimpression)oftheSubject/LegallyAcceptable Representative: Date: _____/ _____/

Signatory's Name: _____

Signature of the Investigator: _____Date: _____/ _____/

Study Investigator's Name: _____

Signature of the Witness _____

Date: _____

Name of the Witness:_____

ANNEXURE –5(A5/SOP/24/1)

UndertakingbytheInvestigator

- Fullname,addressandtitleofthePrincipalInvestigator(orInvestigatorswhenthereisno Principal Investigator).
- Name and address of the Institute/medical college/hospital or other facility where the researchwould be conducted: Education,training&experiencethatqualifythe Investigatorfortheresearch study/academic clinicaltrial(Attach details including Medical Council registration number, or any other statements of qualifications)
- Nameandaddressofalllaboratoryfacilities tobeusedin thestudy.
- NameandaddressoftheEthicsCommitteethatisresponsibleforapprovalandcontinuingre view of the study.
- Namesoftheothermembersoftheresearchteam(Co-orsub-Investigators)whowouldbeassisting the Investigator in the conduct of the investigations.
- ProtocolTitleandStudynumber (ifany)of theresearch/academic clinical trialto beconductedbytheInvestigator.

Commitments:

- ✓ Ihavereviewedtheclinicalprotocolandagreethatitcontainsallthenecessaryinformationto conduct the study. I would not begin the study until all necessary ethics committee and regulatory approvals have been obtained. I inform that no work has been started for this research yet.
- ✓ I agree to conduct the study in accordance with the current protocol. I would not implement any deviation from or changes of the protocol without agreement by the Sponsor and prior review and documented approval or favorable opinion from the ethics committee of the amendment, except wherenecessarytoeliminatean immediatehazardtothetrialsubjectorwhenthechangesinvolved are only logistical or administrative in nature.
- ✓ Iagreeto personallyconduct or supervisetheresearch/academic clinical trial at mysite.
- ✓ Iagreetoinform alltrialsubject,thatthedrugsarebeingusedforinvestigationalpurposes and I would ensurethat the requirements relatingto obtaininginformed consent and ethics committeereview andapproval specifiedintheNewDrugsandClinicalTrialsRules,2019andGoodClinicalPractices guidelines are met.
- ✓ I agree to report to the Sponsor all adverse experiences that occur in the course of the investigation(s)inaccordancewiththeregulatoryrequirementsandGoodClinicalPractices guidelines.
- ✓ IhavereadandunderstoodtheinformationintheInvestigator'sbrochure,includingthepotential risks and side effects of the drug.
- ✓ I agree to ensure that all associates, colleagues and employees assisting in the conduct of the studyare suitablyqualifiedandexperienced

andtheyhavebeeninformedabouttheirobligationsin meeting their commitments in the trial.

- ✓ Iagreetomaintainadequateandaccuraterecordsandtomakethoserecordsavailableforaudit or inspection by the Sponsor, ethics committee, Central Licensing Authority or their authorized representatives, in accordancewith regulatoryprovisions and the Good Clinical Practices guidelines. I would fully cooperate with any study related audit conducted by regulatory officials or authorized representatives of the Sponsor.
- ✓ Iagreetopromptlyreporttotheethicscommitteeallchangesintheresearch/clinicaltrialactivitiesa nd all unanticipated problems involving risks to human subjects or others.
- ✓ IagreetoinformallseriousadverseeventstotheCentralLicensingAuthority,sponsoraswellas the ethics committee within twenty-four hours of their occurrence. In case, of failure to do so, I shall furnish the reason for the delay to the satisfaction of the Central Licensing Authority along with the report of the serious adverse event.
- ✓ Thereport of the serious adverse event, after due analysis, shall also be forwarded byme to the Central LicensingAuthority,theChairpersonofthe ethicscommitteeandtheHeadoftheinstitution where the trial has been conducted within fourteen days in accordance with the regulatory requirements.
- ✓ Iwouldmaintainconfidentialityoftheidentificationofallparticipatingsubjectsandassure security and confidentiality of study data.
- ✓ Iagreetocomplywithallotherrequirements,guidelinesandstatutoryobligationsasapplicable to clinical Investigators participating in clinical trials.

(SignatureofInvestigatorwithdate)