Government of Karnataka

Hassan Institute of Medical Sciences

Autonomous Institution of Govt of Karnataka

Institutional Ethics Committee

'STANDARD OPERATING PROCEDURES'

HIMS IEC SOP Version 1, 2021

Prepared by

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LIST OF SOPS OF THE INSTITUTIONAL ETHICS COMMITTEE

	Hassan Institute of Medical Sciences Institutional Ethics Committee				
	Standard Operating Procedure				
	SOP No	**Version No**	**Revision No**	**Issue date**	**Valid till**
	HIMS IEC/SOP-01	**01**	**R0**	**28-07-2021**	**27-07-2023**
Title: Writing, Reviewing, Distributing and Amending Standard Operating Procedures for ECs					

Writing, Reviewing, Distributing & Amending the SOP

- The procedure for writing, reviewing, distributing and amending the existing SOP to conduct activities of the HIMS IEC in accordance with National Ethical Guidelines for Biomedical and Health Research involving Human Participants by New Drugs and Clinical Trial Rules (2019), ICMR (2017), International Conference on Harmonization - Good Clinical Practice (ICH - GCP) and Indian GCP has been described.

- Any member of the IEC can request for revision of SOP if she / he notices an inconsistency / discrepancy / has any suggestions on how to improve the existing SOP or finds the need to design an entirely new SOP. A person who is not a member of the IEC can make a request through an IEC member.

- It is the responsibility of the Chairperson of the IEC to appoint the SOP team to formulate the SOP. The SOP team will be formed as and when required to amend the existing SOP. The SOP team would be selected from the existing IEC members.

- The SOP shall be reviewed and revised at least once during the term of the committee or within a period of two years from the last revision, whichever is earlier.

- The SOP team will prepare the draft SOP. The draft SOP will be reviewed and approved by the IEC members at the full board meeting. Once approved, it will be notified by the Member Secretary for immediate implementation. The SOP team would stand automatically dissolved once the IEC full board approves the SOP

- Any Full Committee Meeting approved changes to the SOP shall be filed as Amendments to the Current SOP giving a specified Amendment number (in the format xx / Meeting Date / Year) and an appropriate SOP item number (in the format x.xx.xx.xx). When 5 Amendments accrue, it will be considered as a Revision. Any major change to the SOP will be a Version change. When the Version change of SOP is being done, all Amendments and Revisions shall be incorporated into the new Version.

- The SOP shall have a summary of Amendments and Revisions made to the earlier Version, filed at the beginning of the document.

- The approved SOP will be implemented from the issue date. The SOP will be identified by a Version number, Revision number and Issue date. When a revised version of the SOP is implemented (from the issue date), the old version will no longer be effective. A copy of the old version will be archived in the IEC Secretariat

- One Master Document (complete, original set with signatures affixed) of current SOP will be maintained by the IEC Secretariat in the SOP Master File. Another controlled copy will be made available to the Institutional Head of HIMS (Director). An uncontrolled copy of the current SOP will be available in the IEC office for use during the regular full board IEC meeting and reference. An uncontrolled copy of the SOP in PDF format will also be uploaded and displayed on the institutional webpage.

A. Authority under which HIMS IEC is constituted

- The Institutional Head of HIMS (Director) constitutes the IEC. The members will be appointed on the basis of their competencies and integrity and could be drawn from a private or public domain of disciplines. The Institutional Head of HIMS (Director) shall also designate a Chairperson and Member Secretary for the IEC.

B. Composition of IEC

1. The Ethics Committee shall have a minimum of seven members from medical, non-medical, scientific and non-scientific areas with at least
   (i) One lay person
   (ii) One woman member
   (iii) One legal expert
   (iv) One independent member from any other related field such as social scientist or representative of non-governmental voluntary agency or philosopher or ethicist or theologian.
2. The Ethics Committee shall consist of at least fifty percent of its members who are not affiliated with the institute or organization in which such committee is constituted.
3. One member of the Ethics Committee who is not affiliated with the institute or organization shall be the Chairperson, and shall be appointed by such institute or organisation.
4. One member who is affiliated with the institute or organization shall be appointed as Member Secretary of the Ethics Committee by such Institute or organization.
5. The committee shall include at least one member whose primary area of interest or specialisation is non-scientific and at least one member who is independent of the institution.

6. The members of the Ethics Committee shall follow the provisions of these rules, Good Clinical Practices Guidelines and other regulatory requirements to safeguard the rights, safety and well-being of trial subjects.
7. Every member of the Ethics Committee shall be required to undergo such training and development programmes as may be specified by the Central Licencing Authority from time to time
8. Minimum of five members will be present to meet the quorum requirements.
9. The EC will have a balance between medical and non-medical members, technical and non-technical members, depending upon the needs of the institution.

C. Composition, affiliations, qualifications, member specific roles and responsibilities.

Sl no	Members of HIMS IEC	Definition/Description
1	**Chairperson/** **Vice Chairperson** (optional) Non-affiliated. Qualifications - A well-respected person from any background with prior experience of having served/ serving in an EC	Conduct EC meetings and be accountable for independent and efficient functioning of the committee • Ensure active participation of all members (particularly non-affiliated, non-medical/ non- technical) in all discussions and deliberations • Ratify minutes of the previous meetings • In case of anticipated absence of both Chairperson and Vice Chairperson at a planned meeting, the Chairperson should nominate a committee member as Acting Chairperson or the members present may elect an Acting Chairperson on the day of the meeting. The Acting Chairperson should be a non-affiliated person and will have all the powers of the Chairperson for that meeting. • Seek COI declaration from members and ensure quorum and fair decision making.

		• Handle complaints against researchers, EC members, conflict of interest issues and requests for use of EC data
2	**Member Secretary/ Alternate Member Secretary** (optional) Affiliated. Qualifications - • Should be a staff member of the institution • Should have knowledge and experience in clinical research and ethics, be motivated and have good communication skills Should be able to devote adequate time to this activity which should be protected by the institution	Organize an effective and efficient procedure for receiving, preparing, circulating and maintaining each proposal for review • Schedule EC meetings, prepare the agenda and minutes • Organize EC documentation, communication and archiving • Ensure training of EC secretariat and EC members • Ensure SOPs are updated as and when required • Ensure adherence of EC functioning to the SOPs • Prepare for and respond to audits and inspections • Ensure completeness of documentation at the time of receipt and timely inclusion in agenda for EC review. • Assess the need for expedited review/ exemption from review or full review. Assess the need to obtain prior scientific review, invite independent consultant, patient or community representatives. • Ensure quorum during the meeting and record discussions and decisions.
3	**Basic Medical Scientist(s)** Affiliated Qualifications - • Non-medical or medical person with qualifications in basic medical sciences • In case of EC reviewing clinical trials with drugs, the basic medical scientist should preferably be a pharmacologist	Scientific and ethical review with special emphasis on the intervention, benefit-risk analysis, research design, methodology and statistics, continuing review process, SAE, protocol deviation, progress and completion report • For clinical trials, pharmacologist to review the drug safety and pharmacodynamics.

4	**Clinician(s)** Affiliated Qualifications - • Should be individual/s with recognized medical qualification, expertise and training	Scientific review of protocols including review of the intervention, benefit-risk analysis, research design, methodology, sample size, site of study and statistics • Ongoing review of the protocol (SAE, protocol deviation or violation, progress and completion report) • Review medical care, facility and appropriateness of the Principal investigator, provision for medical care, management and compensation. • Thorough review of protocol, investigators brochure (if applicable) and all other protocol details and submitted documents.
5	**Legal expert/s** Non-affiliated Qualifications - • Should have a basic degree in Law from a recognized university, with experience • Desirable: Training in medical law	Ethical review of the proposal, ICD along with translations, MoU, Clinical Trial Agreement (CTA), regulatory approval, insurance document, other site approvals, researcher's undertaking, protocol specific other permissions, such as, stem cell committee for stem cell research, HMSC for international collaboration, compliance with guidelines etc. • Interpret and inform EC members about new regulations if any
6	**Social scientist/ philosopher/ ethicist/theologian** Non-affiliated Qualifications - • Should be an individual with social/behavioural science/philosophy/ religious qualification and training and/or expertise and be sensitive to local cultural and moral values. Can be from an NGO involved in health-related activities	Ethical review of the proposal, ICD along with the translations. • Assess impact on community involvement, socio–cultural context, religious or philosophical context, if any • Serve as a patient/participant/ societal /community representative and bring in ethical and societal concerns.
7	**Lay person(s)** Non-affiliated. Qualifications -	Ethical review of the proposal, ICD along with translation(s). • Evaluate benefits and risks from the

	• Literate person from the public or community • Has not pursued a medical science/ health related career in the last 5 years • May be a representative of the community from which the participants are to be drawn • Is aware of the local language, cultural and moral values of the community • Desirable: involved in social and community welfare activities	participant's perspective and opine whether benefits justify the risks. • Serve as a patient/participant/ community representative and bring in ethical and societal concerns. • Assess on societal aspects if any.

D. Requirements for EC members

Every EC member must

1. provide a recent signed CV and training certificates on human research protection and 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 Conflict of Interest (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

E. Procedure for resignation, replacement and removal of members

A. Resignation

- An IEC member may resign from membership by submitting a letter of resignation to the Chairperson. The member may or may not assign reasons for resignation. The resignation will become effective from the day it is accepted by the Chairperson.
- An IEC member is deemed to be relieved from the duties of being the IEC member once he / she completes the term of IEC re registration validity from the date of appointment unless his / her term is extended by another term.
- Affiliate members will be deemed to have resigned from the Institutional Ethics Committee from the date of their superannuation or resignation to the Institution.

II. Replacement

- The tenure of IEC will be for a continuous period of re registration validity.
- The tenures of the IEC may be extended to one more term depending upon institutional requirements and regulatory policies from time to time.
- Extension of membership may be considered due to non-availability of members of similar stature, qualification and intent to contribute to ethical human research.

III. Removal/Disqualification for conduct unsuitable of an IEC member

- A member may be disqualified from continuance should IEC determine by a three-fourth majority specifically called for the purpose that the member's conduct has been inappropriate of an IEC member.
    i. The process will be initiated if IEC Chairperson or Member-secretary receives a communication in writing (provided by IEC

member or a member of the public) alleging misconduct by a member.

ii. The Chairperson will satisfy himself / herself that a prima facie case exists before initiating action. If, in the opinion of the Chairperson, the matter is of grave significance where integrity of IEC could be questioned, the Chairperson may suspend the membership of the concerned IEC member till final decision is taken by IEC. During the period of suspension, the concerned individual will not have any rights, privileges or responsibilities of an IEC member and will not perform any duties of IEC member.

iii. The Chairperson may call for a meeting of the IEC specifically to discuss this issue or the matter will be taken up for discussion. The meeting convened will follow the usual rules of quorum. The allegation will be discussed at the IEC meeting and the member alleged of misconduct will be provided adequate opportunity to defend himself / herself.

iv. The member would stand disqualified, if members present approve of disqualification by voting (voting by 2/3rd of majority of members present in the meeting and voting). The Chairperson will convey the disqualification to the concerned member through a written communication.

- Disqualification for not attending IEC meetings: A member may be disqualified from IEC membership if the member fails to attend more than 3 regular consecutive IEC meetings without prior intimation. The process conducted will be as follows:

i. The Member Secretary will inform Chairperson, in writing, if a member has not attended more than three consecutive regular meetings of the IEC without prior intimation to the IEC.

ii. The Chairperson will initiate the process of review of membership of such a member by including the matter in the Agenda of the next regular IEC meeting.

iii. A written communication will be sent to the concerned IEC member informing him/ her that the issue of disqualification

would be discussed at the meeting inviting the member to be present at the meeting to put up his/ her case. Alternately, the concerned IEC member will be allowed to state his/ her arguments regarding unauthorized absence in writing by a letter addressed to the Chairperson.

iv. The matter will be discussed and reviewed at the IEC meeting. The concerned member will be provided adequate opportunity to represent his/ her case. A written communication, if received from the concerned member will be read and reviewed at the meeting.

v. The Chairperson or Member-Secretary will inform the IEC members about the cessation of membership by a confidential written communication to other members of IEC or at the next meeting of IEC.

- Privacy is the right of an individual to control or influence the information that can be collected and stored and by whom and to whom that information may be disclosed or shared. Confidentiality is the obligation of the researcher/research team/organization to the participant to safeguard the entrusted information. It includes the obligation to protect information from unauthorized access, use, disclosure, modification, loss or theft.
- The researcher should safeguard the confidentiality of research related data of participants and the community.
- Potential limitations to ensure strict confidentiality must be explained to the participant. Researchers must inform prospective participants that although every effort will be made to protect privacy and ensure confidentiality, it may not be possible to do so under certain circumstances.
- Any publication arising out of research should uphold the privacy of the individuals by ensuring that photographs or other information that may reveal the individual's identity are not published. A specific re-consent would be required for publication, if this was not previously obtained.
- Some information may be sensitive and should be protected to avoid stigmatization and/or discrimination (for example, HIV status; sexual orientation such as lesbian, gay, bisexual, and transgender (LGBT);

genetic information; or any other sensitive information).

- While conducting research with stored biological samples or medical records/data, coding or anonymization of personal information is important and access to both samples and records should be limited.
- Data of individual participants/community may be disclosed in certain circumstances with the permission of the EC such as specific orders of a court of law, threat to a person's or community's life, public health risk that would supersede personal rights to privacy, serious adverse events (SAEs) that are required to be communicated to an appropriate regulatory authority etc.
- Statement describing the extent to which confidentiality of records identifying the Subject will be maintained and who will have access to Subject's medical records.
- Investigators will maintain confidentiality of the identification of all participating subjects and assure security and confidentiality of study data

Confidentiality Agreement Form for IEC Members

In recognition of the fact, that I (*Member's name, and his/her affiliation)* herein referred to as the "undersigned", have been appointed as a member of the IEC and have been asked to assess research studies involving research participants in order to ensure that they are conducted in a humane and ethical manner, adhering to the highest standards of care as per the national, and local regulations and institutional policies and guidelines and international and national guidelines;
Whereas, the appointment of the undersigned as a member of the IEC is based on individual merits and not as an advocate or representative of a home province, territory or community nor as a delegate of any organization or private interest;

Whereas, the fundamental duty of an IEC member is to independently review both scientific and ethical aspects of research protocols involving human subjects and make a determination and the best possible objective recommendations, based on the merits of the submissions under review;

Whereas, the IEC must meet the highest ethical standards in order to merit the trust and confidence of the communities in the protection of the rights and well-being of research participants;

The undersigned, as a member of the IEC, is expected to meet the same high standards of ethical behavior to carry out its mandate.

This Agreement thus encompasses any information deemed Confidential or Proprietary provided to the Undersigned in conjunction with the duties as a member of the IEC. Any written information provided to the undersigned that is of a Confidential, Proprietary, or Privileged nature shall be identified accordingly.

As such, the undersigned agrees to hold all Confidential or Proprietary trade secrets ("information") in trust or confidence and agrees that it shall be used only for contemplated purposes and shall not be used for any other purpose or disclosed to any third party. Written Confidential information provided for

review shall not be copied or retained. All Confidential information (and any copies and notes thereof) shall remain the sole property of the IEC.

The Undersigned agrees not to disclose or utilize, directly or indirectly, any Confidential or Proprietary information belonging to a third party in fulfilling this agreement. Furthermore, the Undersigned confirms that his/her performance of this agreement is consistent with the institute's policies and any contractual obligations they may have to third parties Agreement on Confidentiality

Please sign and date this Agreement, if the Undersigned agrees with the terms and conditions set forth above. The original (signed and dated Agreement) will be kept on file in the custody of the IEC. A copy will be given to you for your records.

In the course of my activities as a member of the IEC, I may be provided with confidential information and documentation (which we will refer to as the Confidential Information; subject to applicable legislation, including the Access to "Confidential Information"). I agree to take reasonable measures to protect the Information Act, not to disclose the Confidential Information to any person; not to use the Confidential Information for any purpose outside the Committee's mandate, and in particular, in a manner which would result in a benefit to myself or any third party; and to destroy all Confidential Information (including any minutes or notes I have made as part of my duties) to the Chairperson upon termination of my functions as a Committee member

I, _____ (name of the member) have read and accept the aforementioned terms and conditions as explained in this Agreement.

_____ _____
Signature Date

_____ _____
Chairperson's Signature Date

I acknowledge that I have received a copy of this Agreement signed by the IEC Chairperson and me.

_____ _____
Signature Date

Confidentiality Agreement Form

For Guest / Observer Attendees to IEC Meetings I, (name), understand that I am being allowed to attend the Institutional Ethics Committee meeting scheduled _____on at_____ am/ pm as a Guest. The meeting will be conducted in Hassan Institute of Medical Sciences, B G Nagara-571448. In the course of the meeting of the Institutional Ethics Committee some confidential information may be disclosed or discussed. Upon signing this form, I ensure to take reasonable measures to keep the information as confidential.

Signature of the Guest and Date	
Chairperson of IEC and Date	

I, _____ (name) acknowledge that I have received a copy of this Agreement signed by the IEC -Chairperson and me.

_____ _____

Signature of the Guest **Date**

Confidentiality Agreement Form for Independent Consultants/ Independent Monitors

I,_____
_____ (Name and Designation) as a non- member of Institutional Ethics Committee (IEC) understand that the copy / copies given to me by the IEC is/are confidential. I shall use the information only for the indicated purpose as described by the IEC and shall not duplicate, give or distribute these documents to any person(s) without prior permission from the IEC. Upon signing this form, I agree to take reasonable measures and full responsibility to keep the information as Confidential

Signature of the recipient and date	
Chairperson of IEC	

I, _____(name) acknowledge that I have received a copy of this Agreement signed by the Chairperson of the IEC and me

_____ _____

Signature Date

- COI refers to a set of conditions whereby professional judgement concerning a primary interest, such as participant's welfare or the validity of research either is, or perceived to be unduly influenced by a secondary interest. The secondary interest may be financial or non-financial, personal, academic or political. This is not inherently wrong, but COI can influence the choice of research questions and methods, recruitment and retention of participants, interpretation and publication of data and the ethical review of research. It is, therefore, necessary to develop and implement policies and procedures to identify, mitigate and manage such COI which can be at the level of researcher, ethics committee or at the level of institution.

A. Research institutions must

- develop policies and SOPs to address COI issues that are dynamic, transparent and actively communicated;
- implement policies and procedures to address COI and conflicts of commitment, and educate their staff about such policies;
- monitor the research or check research results for accuracy and objectivity; and
- not interfere in the functioning and decision making of the EC.

B. Researchers must

- ensure that documents submitted to the EC include disclosure of COI (financial or non-financial) that may affect their research;
- guard against conflicts of commitment that may arise from situations that place competing demands on researchers' time and loyalties; and
- prevent intellectual and personal conflicts by ensuring they do not serve as reviewers for grants and publications submitted by close colleagues, relatives and/or students.

C. ECs must

- evaluate each study in light of any disclosed COI and ensure appropriate action is taken to mitigate this; and
- require their members to disclose their own COI and take appropriate measures to recuse themselves from reviewing or decision making on protocols related to their COI; and
- make appropriate suggestions for management, if COI is detected at the institutional or researcher's level.
- Members are required to sign the conflict of interest and financial disclosure agreement at the start of their term. All IEC members shall disclose in writing to the IEC all conflicts of interest for themselves
- Member of the IEC may also be one of the investigators in a project submitted for review to the IEC. However, the member-as-investigator cannot participate in the review and approval process for any project in which he or she is present as a PI or Co-I or has any other potential conflict of interest except to provide information requested by the IEC
- Non-financial conflict of interest that require disclosure include but are not limited to:
    - Participation in the research project as PI or Co-Investigator
    - Co-author in a publication of the research project's results
    - Other relationships which may influence judgment of the IEC member in reviewing the research project:
        i. has family relation to a researcher whose project is under consideration
        ii. is a direct supervisor / mentor or trainee of the researcher(s)
        iii. has a prominent role in a directly competing research team or product
        iv. has a close personal relationship with a researcher or for other reasons feels unable to render a fair and unbiased review

- No member of an Ethics Committee, having a conflict of interest, shall be involved in the oversight of the clinical trial or bioavailability or bioequivalence study protocol being reviewed by it and all members shall sign a declaration to the effect that there is no conflict of interest.
- While considering an application which involves a conflict of interest of any member of the Ethics Committee, such member may voluntarily withdraw from the Ethics Committee review meeting, by expressing the same in writing, to the Chairperson.

- The details in respect of the conflict of interest of the member shall be duly recorded in the minutes of the meetings of the Ethics Committee
- In case the member secretary of the IEC has a conflict of interest, the discussion and decision-making process for that study shall be convened by the Deputy Member Secretary

Conflict of Interest Form/ Declaration for IEC Members

I _____ am aware of the policy of the IEC regarding conflict of interest and that no reviewer may participate in the review, comment or participate in decision making of any activity in which he/she has actual/potential conflict of interest except to provide information as requested by the IEC.

I declare (actual or potential COI) in relation to the proposal entitled "_____"submitted for review to the IEC. The reason for COI is_____. I will refrain from the review process and /or discussion at the IEC meeting / and also will not take part in ongoing and periodic review and monitoring of this study.

_____ Signature of IEC Member
_____ Date

_____ Chairperson's Signature
_____ Date

Conflict of Interest Form/ Independent consultants

I _____am aware of the policy of the IEC regarding conflict of interest and that no reviewer may participate in the review, comment or participate in decision making of any activity in which he/she has actual/potential conflict of interest except to provide information as requested by the IEC.

I declare _____ (actual or potential COI) in relation to the proposal entitled "_____"submitted for review to the IEC. The reason for COI is_____. I will refrain from the review process and /or discussion at the IEC meeting / and also will not take part in ongoing and periodic review and monitoring of this study.

_____ Signature of IEC Member _____ Date

_____ Chairperson's Signature _____ Date

[The original (signed and dated Agreement) will be kept on file in the custody of the IEC. A copy will be given to you for your records]

- 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 regulatory training and development programmes as may be specified by the Central Licencing Authority from time to time of the country.
- EC members should undergo initial and continuing training in human research protection, applicable EC SOPs and related regulatory requirements. All training should be documented.
- Any change in the relevant guidelines or regulatory requirements should be brought to the attention of all EC members.
- EC members should be aware of local, social and cultural norms and emerging ethical issues
- Training should be internal and external.
- Internal training will be by members themselves.
- External training would be conducted by experts from outside the institution.
- If any members of ethics committee fails to successfully complete such training and developmental programmes, shall be disqualified to hold the post of member of the Ethics Committee and shall cease to be a member of such committee.

- An expert who gives advice, comments and suggestions to the EC and has no affiliation to the institute or researchers proposing the research protocols. This individual has no voting power for decision making.
- The EC may invite subject experts as independent consultants or include a representative from a specific patient group as a member of the EC or special invitee, for opinion on a specific proposal, for example HIV, genetic disorders, or cancer, with appropriate decision-making power.
- The comments of an independent consultant (if applicable) could be presented by the Member Secretary or subject experts could be invited to offer their views, but they should not participate in the decision-making process. However, her/his opinion must be recorded.
- The EC may utilize electronic methods such as video/conference calls for connecting with other subject experts/independent consultants during the meeting.
- Member secretaries will Assess the need to obtain prior scientific review, invite independent consultants, patient or community representatives.

Confidentiality Agreement Form for an Independent Consultant

I,_____

(Name and Designation) as a non-member of Institutional Ethics Committee (IEC) understand that the copy / copies given to me by the IEC is/are confidential. I shall use the information only for the indicated purpose as described by the IEC and shall not duplicate, give or distribute these documents to any person(s) without prior permission from the IEC. Upon signing this form, I agree to take reasonable measures and full responsibility to keep the information as Confidential.

_____ _____

Signature of the Consultant Date

_____

Chairperson of IEC

_____

Date

Confidentiality Agreement Form

For Guest / Observer Attendees to IEC Meetings I, (name), understand that I am being allowed to attend the Institutional Ethics Committee meeting scheduled _____on at_____ am/ pm as a Guest. The meeting will be conducted in Hassan Institute of Medical Sciences, B G Nagara-571448. In the course of the meeting of the Institutional Ethics Committee some confidential information may be disclosed or discussed. Upon signing this form, I ensure to take reasonable measures to keep the information as confidential.

Signature of the Guest and Date	
Chairperson of IEC and Date	

I, _____ (name) acknowledge that I have received a copy of this Agreement signed by the IEC -Chairperson and me.

_____ _____

Signature of the Guest **Date**

- I understand that it is the policy of the IEC that no reviewer may participate in the review, comment or approve of any activity in which he/she has a conflict of interest except to provide information as requested by the IEC.
- I do not have any actual or potential conflict of interest in relation to the particular proposal submitted for review by the IEC to me.
- In the event that I develop any conflict of interest in relation to the particular proposal during the review process, I will declare it to IEC and refrain from reviewing it.

I, _____ (name) have read and accept the aforementioned terms and conditions as explained in this Agreement.

Signature of IC	Date
Chairperson's Signature	Date

I acknowledge that I have received a copy of this Agreement signed by the IEC Chairperson and me.

Signature	Date

[The original (signed and dated Agreement) will be kept on file in the custody of the IEC. A copy will be given to you for your records]

- It is responsibility of Member Secretary in consultation with Chairperson to decide whether a guest / observer may be allowed to visit the IEC Office or attend an IEC meeting.
- It is the responsibility of the guest/observers intending to attend an IEC meeting to read, understand, accept and sign the agreement contained in the Confidentiality form prior to visiting IEC/ attending an IEC meeting.
- The Secretariat will ensure that the Confidentiality Form is duly signed and dated by the guest or observer for IEC / IEC meeting and will file it in IEC records.
- Confidentiality Agreement Form will be provided to the guest attendee/observer on the day of visit/ at the time of meeting.
- The guest/ observer will read the form carefully before visit / or before commencement of the meeting and follow it.

Confidentiality Agreement Form for Guest / Observer Attendees to IEC/ IEC Meetings

I, _____ (name), understand that I am being allowed to visit IEC office facility / attend the IEC meeting on _____ at _____am as a Guest. The venue of the IEC meeting will be _____.

I may become aware of some confidential information during my visit to IEC / during the course of the IEC meeting. Upon signing this form, I ensure to take reasonable measures to keep the information as confidential.

Signature of the Guest	Date
Chairperson of IEC	Date

I, _____ (name) acknowledge that I have received a copy of this Agreement signed by the IEC -Chairperson and me.

Signature of the Guest	Date

A. **Initial Full Committee Review of New Research Protocols**

All research proposals presenting more than minimal risk that are not covered under exempt or expedited review should be subjected to full committee review, some examples are

1. Research involving vulnerable populations, even if the risk is minimal.
2. Research with minor increase over minimal risk.
3. Studies involving deception of participants.
4. Research proposals that have received exemption from review, or have undergone expedited review/undergone subcommittee review should be ratified by full committee, which has the right to reverse/or modify any decision taken by subcommittee or expedited committee.
5. Amendments of proposals/related documents (including but not limited to informed consent documents, investigator's brochure, advertisements, recruitment methods, etc.) involving an altered risk.
6. Major deviations and violations in protocol
7. Any new information that emerges during course of research for deciding whether or not to terminate study in view of altered benefit-risk assessment.
8. Research during emergencies and disasters either through an expedited review/scheduled or unscheduled full committee meetings. This may be decided by Member Secretary depending on urgency and need.
9. Prior approval of research on predictable emergencies or disasters before actual crisis occurs for implementation later when actual emergency or disaster occurs.

B. **Expedited Review of Research Protocols**

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

1. Research involving non-identifiable specimen and human tissue from sources like blood banks, tissue banks and left-over clinical samples.
2. Research involving clinical documentation materials that are non-identifiable (data, documents, records)
3. Modification or amendment to an approved protocol including administrative changes or correction of typographical errors and change in researcher
4. Revised proposals previously approved through expedited review, full review or continuing review of approved proposals.
5. Minor deviations from originally approved research causing no risk or minimal risk.
6. Progress/annual reports where there is no additional risk, for example activity limited to date analysis. Expedited review of SAEs/unexpected AEs will be conducted by SAE subcommittee and
7. For multi-centre research where a designated main EC among the participating sites has reviewed and approved the study, a local EC may conduct only an expedited review for site specific requirements in addition to full committee common review.
8. Research during emergencies and disasters.

C. **Exemption from Ethics Review of Research Protocols**

Proposals with less than minimal risk where there are no linked identifiers, for example

1. Research conducted on date available in public domain for systematic reviews or meta-analysis
2. Observation of public behaviour when information is recorded without any linked identifiers and disclosure would not harming interest of participant
3. Quality control and quality assurance audits in institution
4. Comparison of instructional techniques, curricula or classroom management methods
5. Consumer acceptance studies related to taste and food quality and
6. Public health programs by Govt. agencies such as program evaluation where sole purpose of exercise is refinement and improvement of program or monitoring.

A. Chairperson will

- Conduct EC meetings and be accountable for independent and efficient functioning of the committee
- Ensure active participation of all members (particularly non-affiliated, non-medical/ non- technical) in all discussions and deliberations
- Ratify minutes of the previous meetings
- In case of anticipated absence of both Chairperson and Vice Chairperson at a planned meeting, the Chairperson should nominate a committee member as Acting Chairperson or the members present may elect an Acting Chairperson on the day of the meeting. The Acting Chairperson should be a non-affiliated person and will have all the powers of the Chairperson for that meeting.
- Seek COI declaration from members and ensure quorum and fair decision making.
- Handle complaints against researchers, EC members, conflict of interest issues and requests for use of EC data

B. Member secretary will

- Organize an effective and efficient procedure for receiving, preparing, circulating and maintaining each proposal for review
- Schedule EC meetings, prepare the agenda and minutes
- Organize EC documentation, communication and archiving
- Ensure SOPs are updated as and when required
- Ensure adherence of EC functioning to the SOPs
- Assess the need for expedited review/ exemption from review or full review.
- Assess the need to obtain prior scientific review, invite independent consultant, patient or community representatives.

- Ensure quorum during the meeting and record discussions and decisions

C. Basic Medical Scientist will be responsible for

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

D. Clinician is responsible for

- Scientific review of protocols including review of the intervention, benefit-risk analysis, research design, methodology, sample size, site of study and statistics
- Reviewing medical care, facility and appropriateness of the Principal investigator, provision for medical care, management and compensation
- Thorough review of protocol, investigators brochure (if applicable) and all other protocol details and submitted documents

E. Legal expert is responsible for

- Ethical review of the proposal, ICD along with translations, MoU, Clinical Trial Agreement (CTA), regulatory approval, insurance document, other site approvals, researcher's undertaking, protocol specific other permissions, such as, stem cell committee for stem cell research, HMSC for international collaboration, compliance with guidelines etc
- Interpret and inform EC members about new regulations if any

F. Social scientist/ philosopher/ethicist/theologian is responsible for

- Ethical review of the proposal, ICD along with the translations.
- Assess impact on community involvement, socio–cultural context, religious or philosophical context, if any

- Serve as a patient/participant/ societal /community representative and bring in ethical and societal concerns.

G. Lay person is responsible for

- Ethical review of the proposal, ICD along with translation(s).
- Evaluate benefits and risks from the participant's perspective and opine whether benefits justify the risks.
- Serve as a patient/participant/ community representative and bring in ethical and societal concerns.
- Assess on societal aspects if any

H. Full Committee Meeting.

- 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.
- ECs should conduct regular full committee meetings to deliberate proposals in accordance with a pre-decided schedule, as described in the SOPs.
- A meeting will be considered valid only if the quorum is fulfilled. This should be maintained throughout the meeting and at the time of decision making.
- 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.
- 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.
- A list of absentee members as well as members leaving or entering in-between the meeting should be recorded.
- Proposals should be taken up item-wise, as given in the agenda.
- No of proposals reviewed in a meeting should justify that there is ample time devoted for review of each proposal. 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.

- Time allotted for the meeting should be reasonable to allow ample discussion on each agenda item.
- The minutes of the previous meeting and list of protocols that were exempt from review or underwent expedited review should be ratified.
- The researcher may be called in to present a proposal or provide clarifications on the study protocol that has been submitted for review but should not be present at the time of decision making.
- The primary and secondary reviewers can brief the members about the study proposal and review carried out as per EC SOPs.
- The comments of an independent consultant (if applicable) could be presented by the Member Secretary or subject experts could be invited to offer their views, but they should not participate in the decision-making process. However, her/his opinion must be recorded.
- Representative(s) of the study group population can be invited during deliberations to offer their viewpoint but should not participate in the decision-making process.
- The EC may utilize electronic methods such as video/conference calls for connecting with other subject experts/independent consultants during the meeting.
- All members of the EC (including the Chairperson and the Member Secretary) present in the room have the right to vote/express their decision and should exercise this right.
- The decision must be taken either by a broad consensus or majority vote (as per SOP) and should be recorded. Any negative opinion should be recorded with reasons.

The decisions may be as shown in the following box:

An EC can give one of the following decisions:

- approved – with or without suggestions or comments;
- revision with minor modifications/amendments – approval is given after examination by the Member Secretary or expedited review, as the case may be;
- revision with major modifications for resubmission – this will be placed before the full committee for reconsideration for approval; or
- not approved (or termination /revoking of permission if applicable) – clearly defined reasons must be given for not approving/terminating/revoking of permission.

- Approval may be granted for the entire duration of the proposed research or can be subject to annual review depending on the type of study. The EC

should review the annual report (counted from the day of approval or date of actual start of the study) for continuation as per SOP.

- Depending on the risk involved, the progress of the proposal may be monitored annually or at shorter intervals (quarterly, half yearly) as per EC decision. Approval may be continued if progress is satisfactory.
- An EC may decide to reverse its positive decision on a study if it receives information that may adversely affect the benefit-risk assessment.
- 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.
- The decision of the EC should be communicated to the researcher along with suggestions, if any.
- The researcher should have an opportunity to reply/clarify to EC comments or to discuss or present her/his stand.
- The researcher can also approach the head of the institute who serves as an appellate for EC matters.
- The head of the institute as appellate has the power to dissolve the EC or reappoint an EC.

- A medical device is defined as a medical tool which does not achieve its primary intended action in or on the human body by pharmacological, immunological, or metabolic means but which may be assisted in its intended function by such means. It may be an instrument, apparatus, appliance, implant, material or other article, whether used alone or in combination, including a software or an accessory, intended by its manufacturer to be used specially for human beings or animals for one or more of the specific purposes of:
  - (i) detection, diagnosis, prevention, monitoring;
  - (ii) treatment or alleviation of any physiological condition or state of health, or illness;
  - (iii) replacement or modification or support of the anatomy or congenital deformity;
  - (iv) supporting or sustaining life;
  - (v) disinfection of medical devices; or control of conception

- Clinical trials should be conducted in accordance with the ethical principles described in these guidelines, Indian GCP as well as applicable regulations for medical and medicated devices, that is, GSR 78 (E) dated 31.1.2017 or as per amendments/modifications issued from time-to-time.
- Safety data of the medical device in animals should be obtained and likely risks posed by the device should be considered in the same way as for a new drug under the Drugs and Cosmetics Rules, 1945.
- Apart from safety considerations of the device, the procedures to introduce

medical device in the patient should also be evaluated for safety.

- Devices should be provided free of cost or, if expensive, at feasible reduced rates.
- Avoid therapeutic misconceptions.
- Any AE/SAE should be reported within timelines as per the schedule for a new drug. Here user error could also be the cause of AE/SAE.
- If the participant wants to withdraw from a trial, it may not be possible to remove the internal device. This must be explained to the participant before enrolling her/him. The participant, however, should be allowed to opt out of continuing in the trial without prejudice to her/his ongoing treatment.
- If feasible, post-trial obligations should be emphasized with the sponsor.
- The duration of follow-up should be long enough to detect late onset adverse reactions, especially when the device is implanted within the body.
- Devices could be used internally or externally for diagnosis, treatment, mitigation or prevention of disease or disorder. Depending upon risks involved, devices (other than in vitro diagnostic devices) are classified as given in Table.

Class	Level of risk	Device examples
A	Low	Thermometers/ bandages /tongue depressors
B	Low–moderate	Hypodermic needles /suction equipment
C	Moderate–high	Lung ventilator /bone fixation plate
D	High	Heart valves/implantable defibrillator

- Devices used for in vitro diagnosis could be a reagent, calibrator, control material, kit, instrument, apparatus, equipment, system, or specimen receptacle, whether used alone or in combination with any other such devices, that is intended by its manufacturer to be used in vitro for examination of any specimen, including any blood or tissue donation derived from the human body solely or Principally for the purpose of providing information. The information could be related to:

  (i) a physiological or pathological state;

  (ii) congenital deformity;

(iii) determining the safety and compatibility of any blood or tissue donation with a potential recipient thereof; or

(iv) monitoring of therapeutic measures.

- Diagnostics devices can be notified and non-notified. Notified are in vitro diagnostic devices for testing HIV, HBsAg, HCV and blood grouping. Non-notified are those for testing malaria, TB, dengue, chikungunya, typhoid, syphilis, cancer markers, etc

- Amendments of proposals/related documents (including but not limited to informed consent documents, investigator's brochure, advertisements, recruitment methods, etc.) involving an altered risk will be subjected to full committee review

- Major deviations and violations in the protocol will be subjected to full committee review

	Hassan Institute of Medical Sciences Institutional Ethics Committee				
	Standard Operating Procedure				
	SOP No	**Version No**	**Revision No**	**Issue date**	**Valid till**
	HIMS IEC/SOP-12	**01**	**R0**	**28-07-2021**	**27-07-2023**
Title: Review of protocol amendments					

- Any change in protocol and documents from that of previously IEC approved protocol/document. This applies to amended study protocols/ documents and letters that are submitted for IEC approval. Amendments made to protocols or any other amendments related to the study may not be implemented until reviewed and approved by the IEC
- The Member Secretary, IEC, classifies the amendments into minor or major.
- Minor amendments include those that do not increase the risk or decrease the potential benefit to subjects and minor changes in previously approved research during the period covered by the original approval. Minor amendments may be reviewed by the expedited review process. Minor notifications may be noted by the Member Secretary and not tabled in IEC meeting. This may include but may not be restricted to: Renewed insurance policy DCGI approvals, permission letters for Government authorities, schools' Administrative notes Documents of administrative nature.
- The major amendments are reported on the agenda of the subsequent scheduled IEC meeting. If the amendments and other documents which need full board review, they will be processed as per the process described for full board review.
- Amendments of proposals/related documents (including but not limited to informed consent documents, investigator's brochure, advertisements, recruitment methods, etc.) involving an altered risk will be subjected to full committee review
- Protocol amendments, if become necessary before initiation or during the course of a clinical trial, all such amendments should be submitted to the Central Licencing Authority in writing along with the approval by the ethics committee, if available, which has granted the approval for the study.

- Ongoing research should be reviewed at regular intervals, at least once a year, (or more often, if deemed necessary depending on the level of risk) or as may be specified in the SOP of the EC and at the time of according approval, and as indicated in the communication letter.
- The EC should continually evaluate progress of ongoing proposals, review SAE reports from all sites along with protocol deviations/violations and non-compliance, any new information pertaining to the research and assess final reports of all research activities.
- Clinical trials under the purview of a licensing authority must comply with all regulations applicable to SAEs. The EC should also ensure compliance by the researcher. For academic and other trials, an institutional policy should be established.
- The EC should examine the measures taken for medical management of SAEs. Participants should not have to bear costs for the management of study-related injury whether they are in the intervention arm or the control arm.
- Compensation must be given for research-related injuries if applicable, as determined by the EC and as per regulatory requirement (if applicable).
- For protocol deviations/violations the EC should examine the corrective actions. If the violations are serious the EC may halt the study. The EC may report to the institutional head/government authorities where there is continuing non-compliance to ethical standards.
- Reports of monitoring done by the sponsor and DSMB reports may also be sought.

- The EC reviews progress reports, final reports and AE/SAE and gives needful suggestions regarding care of the participants and risk minimization procedures, if applicable.
- The EC should continually evaluate progress of ongoing proposals, review SAE reports from all sites along with protocol deviations/violations and non-compliance, any new information pertaining to the research and assess final reports of all research activities.

Structure, Content and Format for Clinical Trial Report

1. Title Page: This page should contain information about the title of the study, the protocol code, name of the investigational product tested, development Phase, indication studied, a brief description of the trial design, the start and end date of patient accrual and the names of the Sponsor and the participating Institutes (Investigators).

2. Study Synopsis (1 to 2 pages): A brief overview of the study from the protocol development to the trial closure should be given here. This section will only summarise the important conclusions derived from the study.

3. Statement of compliance with the Good Clinical Practices Guidelines.

4. List of abbreviations and definitions

5. Table of contents

6. Ethics Committee: This section should document that the study was conducted in accordance with the ethical principles of Declaration of Helsinki. A detailed description of the Ethics Committee constitution and dates of approvals of trial documents for each of the participating sites should be provided. A declaration should state that Ethics Committee (EC) notifications

as per Good Clinical Practice Guidelines and Ethical Guidelines for Biomedical Research on Human Subjects, issued by Indian Council of Medical Research have been followed.

7. Study Team: Briefly describe the administrative structure of the study (Investigators, site staff, Sponsor or designates, Central laboratory etc.).

8. Introduction: A brief description of the product development rationale should be given here.

9. Study Objective: A statement describing the overall purpose of the study and the primary and secondary objectives to be achieved should be mentioned here.

10. Investigational Plan: This section should describe the overall trial design, the Subject selection criteria, the treatment procedures, blinding or randomisation techniques if any, allowed or disallowed concomitant treatment, the efficacy and safety criteria assessed, the data quality assurance procedures and the statistical methods planned for the analysis of the data obtained.

11. Trial Subjects: A clear accounting of all trial Subjects who entered the study will be given here. Mention should also be made of all cases that were dropouts or protocol deviations. Enumerate the patients screened, randomised, and prematurely discontinued. State reasons for premature discontinuation of therapy in each applicable case.

12. Efficacy evaluation: The results of evaluation of all the efficacy variables will be described in this section with appropriate tabular and graphical representation. A brief description of the demographic characteristics of the trial patients should also be provided along with a listing of patients and observations excluded from efficacy analysis.

13. Safety Evaluation: This section should include the complete list

13.1 all serious adverse events, whether expected or unexpected and

13.2 unexpected adverse events whether serious or not (compiled from data received as per Table 5 of this Schedule). The comparison of adverse events across study groups may be presented in a tabular or graphical form. This section should also give a brief narrative of all important events considered related to the investigational product.

14. Discussion and overall Conclusion: Discussion of the important conclusions derived from the trial and scope for further development.

15. List of References:

16. Appendices: List of Appendices to the Clinical Study Report

(a) Protocol and amendments

(b) Specimen of Case Record Form

(c) Investigators' names with contact addresses, phone, e-mail etc.

(d) Patient data listings

(e) List of trial participants treated with investigational product

(f) Discontinued participants

(g) Protocol deviations

(h) Case Record Forms of cases involving death and life threatening adverse event cases

(i) Publications from the trial

(j) Important publications referenced in the study

(k) Audit certificate, if available

(l) Investigator' certificate that he/she has read the report and that the report accurately describes the conduct and the results of the study.

	Hassan Institute of Medical Sciences Institutional Ethics Committee				
	Standard Operating Procedure				
	SOP No	**Version No**	**Revision No**	**Issue date**	**Valid till**
	HIMS IEC/SOP-15	01	R0	**28-07-2021**	**27-07-2023**
Title: Review of Serious Adverse Events (SAE) reports					

- SAE is defined as an Adverse Event or Adverse Drug Reaction that is associated with death, inpatient hospitalisation (in case the study was being conducted on out-patients), prolongation of hospitalisation (in case the study was being conducted on in-patients), persistent or significant disability or incapacity, a congenital anomaly or birth defect, or is otherwise life threatening.
- The Principal Investigator should submit within 24 hours Initial SAE report or the unexpected adverse event report to the Sponsor, IEC, DCGI and Head of the Institution through hard copies or by mail. In case, of failure to do so, Principal Investigator shall furnish the reason for the delay to the satisfaction of the Central Licencing Authority along with the report of the serious adverse event.
- The report of SAE of due analysis shall be forwarded by the Investigator to IEC, DCGI, sponsor and Head of the institution within 14 calendar days of occurrence SAE.
- IEC members will review the PI submitted SAE Documents and submitted in the Full board Meeting and IEC opinion/Minutes will be communicate with the DCGI and PI within 30 days of SAE Occurrence.
- The sponsor or his representative shall pay the compensation in case of clinical trial related Injury or death within 30 days of the receipt of such an order from Licensing Authority.

Data Elements for reporting serious adverse events occurring in a clinical trial

1. Patient Details
   - Initials & other relevant identifier (hospital/OPD record number etc.)*
   - Gender
   - Age and/ or date of birth
   - Weight
   - Height

2. Suspected Drug(s)
   - Generic name of the drug *
   - Indication(s) for which suspect drug was prescribed or tested
   - Dosage form and strength
   - Daily dose and regimen (specify units - e.g., mg, ml, mg/kg)
   - Route of administration
   - Starting date and time of day
   - Stopping date and time, or duration of treatment

3. Other Treatment(s)
   - Provide the same information for concomitant drugs (including non-prescription/ OTC drugs) and non-drug therapies, as for the suspected drug(s).

4. Details of Suspected Adverse Drug Reaction(s)
   - Full description of reaction(s) including body site and severity, as well as the criterion (or criteria) for regarding the report as serious. In addition to a description of the reported signs and symptoms, whenever possible, describe a specific diagnosis for the reaction.*
   - Start date (and time) of onset of reaction.
   - Stop date (and time) or duration of reaction.
   - Dechallenge and rechallenge information.
   - Setting (e.g. hospital, out-patient clinic, home, nursing home).

5. Outcome

- Information on recovery and any sequelae; results of specific tests and / or treatment that may have been conducted.
- For a fatal outcome, cause of death and a comment on its possible relationship to the suspected reaction; Any post mortem findings.
- Other Information: anything relevant to facilitate assessment of the case, such as medical history including allergy, drug or alcohol abuse; family history, findings from special investigations etc.

6. Details about the Investigator*
   - Name
   - Address
   - Telephone number
   - Profession (speciality)
   - Date of reporting the event to Licensing Authority:
   - Date of reporting the event to Ethics Committee overseeing the site:
   - Signature of the Investigator

Checklist for Serious Adverse Event (SAE) submission (For Onsite SAE)

Sl no	**Details**		
1	Country (Name of the country should be specified)		
2	SAE report of death or other than death, Please tick (✓)	Death	Other than Death
		☐ Yes ☐ No	Page No.
3	In case of Serious Adverse Event(SAE), please specify if there is any injury to the participant (Please specify Yes/No) in the box		
4	Protocol Title		
5	Protocol Study No./ ID /Code		
6	Copy of Clinical Trial permission obtained from CDSCO		
7	CTRI Registration No. (Mandatory for Clinical Trial Permitted after 15/06/09)		
8	Sponsor(Address with contact no and Email)		
9	CRO (Address with contact no and Email)		

10		Initial / Follow-up (FU)		
11		In case of follow-up: Date & Diary no of initial or recently submitted report information		
12		Patient Details		
	a	Initials & other relevant identifier (hospital/OPD record number etc.)		
	b	Gender		
	c	Age and/or date of birth		
	d	Weight		
	e	Height		
13		Suspected Drug(s)		
	a	Generic name of the drug		
	b	Indication(s) for which suspect drug was prescribed or tested		
	c	Dosage form and strength		
	d	Daily dose and regimen (specify units - e.g., mg, ml, mg/kg)		
	e	Route of administration		
	f	Starting date and time of day		
	g	Stopping date and time, or duration of treatment		
14		Other Treatment(s)		
	a	Provide the same information for concomitant drugs (including non-prescription/OTC Drugs) and non-drug therapies, as for the suspected drug(s).		
15		Details of the events		
	a	Full description of event (s) including body site and severity, as well as the criterion (or criteria) for regarding the report as serious. In addition to a description of the reported signs and symptoms, whenever possible, describe a specific diagnosis for the reaction.		
	b	Start date (and time) of onset of reaction.		
	c	Stop date (and time) or duration of reaction.		
	d	Dechallenge and rechallenge information.		
	e	Setting (e.g., hospital, out-patient clinic, home, nursing home).		
16		Outcome		

	a	Information on recovery and any sequelae; results of specific tests and/or treatment that may have been conducted.		
	b	For a fatal outcome, cause of death and a comment on its possible relationship to the suspected reaction; any post-mortem findings.		
	c	Other information: anything relevant to facilitate assessment of the case, such as medical history including allergy, drug or alcohol abuse; family history; findings from special investigations etc		
17		Details about the Investigator		
	a	CT Site Number, if any		
	b	Name		
	c	Address		
	d	Telephone/Mobile Number & Email		
	e	Profession (speciality)		
	f	Date of reporting the event to Licensing Authority:		
	g	Date of reporting the event to Ethics Committee overseeing the site:		
		Signature of the Investigator		
18		Details about the Ethics Committee		
	a	Name & Address		
	b	Name of Chairman & Address		
	c	Telephone/Mobile Number		
	d	Email		
19		Adverse Event Term/ Details of SAE		
20		Causality Assessment (Related/Unrelated) by Investigator.		
21		Causality Assessment (Related/Unrelated) bySponsor/CRO		
22		Details of compensation provided for injury or death. In case no compensation has been paid, reason for the same :		
23 a		Duly filled SAE Form as per Appendix XI of Schedule Y		
		Laboratory investigations report /Discharge summary (if available and applicable)		

	Post-mortem report (if applicable)/ Any additional documents)		

Note: Information not relevant to a particular SAE should be marked with NA

Serious Adverse Event (SAE) Analysis Report
(For Onsite SAE)

Sl no	**Details**		
1	Country (Name of the country should be specified)		
2	SAE report of death or other than death, Please tick (✓)	Death ☐ Yes ☐ No	Other than Death Page No.
3	In case of Serious Adverse Event(SAE), please specify if there is any injury to the participant (Please specify Yes/No) in the box		
4	Protocol Title		
5	Protocol Study No./ ID /Code		
6	Copy of Clinical Trial permission obtained from CDSCO		
7	CTRI Registration No. (Mandatory for Clinical Trial Permitted after 15/06/09)		
8	Sponsor(Address with contact no and Email)		
9	CRO (Address with contact no and Email)		
10	Initial / Follow-up (FU)		
11	In case of follow-up: Date & Diary no of initial or recently submitted report information		
12	Patient Details		
a	Initials & other relevant identifier (hospital/OPD record number etc.)		
b	Gender		
c	Age and/or date of birth		
d	Weight		
e	Height		

13		Suspected Drug(s)		
	a	Generic name of the drug		
	b	Indication(s) for which suspect drug was prescribed or tested		
	c	Dosage form and strength		
	d	Daily dose and regimen (specify units - e.g., mg, ml, mg/kg)		
	e	Route of administration		
	f	Starting date and time of day		
	g	Stopping date and time, or duration of treatment		
14		Other Treatment(s)		
	a	Provide the same information for concomitant drugs (including non-prescription/OTC Drugs) and non-drug therapies, as for the suspected drug(s).		
15		Details of the events		
	a	Full description of event (s) including body site and severity, as well as the criterion (or criteria) for regarding the report as serious. In addition to a description of the reported signs and symptoms, whenever possible, describe a specific diagnosis for the reaction.		
	b	Start date (and time) of onset of reaction.		
	c	Stop date (and time) or duration of reaction.		
	d	Dechallenge and rechallenge information.		
	e	Setting (e.g., hospital, out-patient clinic, home, nursing home).		
16		Outcome		
	a	Information on recovery and any sequelae; results of specific tests and/or treatment that may have been conducted.		
	b	For a fatal outcome, cause of death and a comment on its possible relationship to the suspected reaction; any post-mortem findings.		
	c	Other information: anything relevant to facilitate assessment of the case, such as medical history including allergy, drug or alcohol abuse; family history; findings from special investigations etc		
17		Details about the Investigator		

a	CT Site Number, if any		
b	Name		
c	Address		
d	Telephone/Mobile Number & Email		
e	Profession (speciality)		
f	Date of reporting the event to Licensing Authority:		
g	Date of reporting the event to Ethics Committee overseeing the site:		
	Signature of the Investigator		
18	Details about the Ethics Committee		
a	Name & Address		
b	Name of Chairman & Address		
c	Telephone/Mobile Number		
d	Email		
19	Adverse Event Term/ Details of SAE		
20	Causality Assessment (Related/Unrelated) by Investigator.		
21	Causality Assessment (Related/Unrelated) by Sponsor/CRO		
22	Details of compensation provided for injury or death. In case no compensation has been paid, reason for the same :		
23 a	Duly filled SAE Form as per Appendix XI of Schedule Y		
b	Laboratory investigations report /Discharge summary (if available and applicable)		
c	Post-mortem report (if applicable)/ Any additional documents)		

Details of payment for medical management of SAE? (please give information who paid how much was paid, to whom, with evidence of the same)

What is the investigator's assessment for the amount of compensation to be paid?

What is the sponsor's assessment for the amount of compensation to be paid?

Has the participant made a claim? ☐ Yes ☐ No

If yes, for how much amount _____ If no, please ensure that the participant / nominee have been made aware of his/her' rights regarding compensation. Please submit documentation regarding the same
Signature of the Principal Investigator : Date:

SEVENTH SCHEDULE (See rules 39, 40, and 42) FORMULAE TO DETERMINE THE QUANTUM OF COMPENSATION IN THE CASES OF CLINICAL TRIAL RELATED INJURY OR DEATH

1. Formula in case of clinical trial related death: Compensation = (B x F x R) / 99.37 Where, B = Base amount (i.e. 8 lacs) F = Factor depending on the age of the trial subject as per Annexure 1 (based on Workmen Compensation Act) R = Risk Factor depending on the seriousness and severity of the disease, presence of co-morbidity and duration of disease of the trial subject at the time of enrolment in the clinical trial between a scale of 0.5 to 4 as under:

1) 0.5: terminally ill patient (expected survival not more than (NMT) 6 months)
2) 1.0: Patient with high risk (expected survival between 6 to 24months)
3) 2.0: Patient with moderate risk
4) 3.0: Patient with mild risk
5) 4.0: Healthy Volunteers or trial subject of no risk.

However, in case of patients whose expected mortality is 90% or more within 30 days, a fixed amount of Rs. 2 lacs should be given.

2. Formula in case of clinical trial related injury (other than death): For calculation of quantum of compensation related to injury (other than death), the

compensation shall be linked to the criteria considered for calculation of compensation in cases of death of the trial subject as referred to in section of this Schedule. The quantum of compensation in case of Clinical Trial related SAE should not exceed the quantum of compensation which would have been due for payment in Case of death of the trial subject since the loss of life is the maximum injury possible. As per the definition of SAE, the following sequelae other than death are possible in a clinical trial subject, in which the trial subject shall be entitled for compensation in case the SAE is related to clinical trial.

i. A permanent disability: In case of SAE causing permanent disability to the trial subject, the quantum of compensation in case of 100% disability shall be 90% of the compensation which would have been due for payment to the nominee (s) in case of death of the trial subject. The quantum for less than 100% disability will be proportional to the actual percentage disability the trial subject has suffered. Accordingly, following formula shall be applicable for determination of compensation: Compensation = (C x D x 90) / (100 x 100) W h e r e : D = Percentage disability the trial subject has suffered. C = Quantum of Compensation which would have been due for payment to the trial subject's nominees) in case of death of the trial subject.

ii. Congenital anomaly or birth defect: The congenital anomaly or birth defect in a baby may occur due to participation of anyone or both the parent in clinical trial. Following situations may arise due to congenital anomaly or birth defect.

    a. Still birth;
    b. Early death due to anomaly;
    c. No death but deformity which can be fully corrected through appropriate intervention;
    d. Permanent disability (mental or physical). The compensation in such cases would be a lump sum amount such that if that amount is kept by way of fixed deposit or alike, it shall bring a monthly

interest amount which is approximately equivalent to half of minimum wage of the unskilled worker (in Delhi). The quantum of compensation in such cases of SAE shall be half of the base amount as per formula for determining the compensation for SAE resulting into death. In case of birth defect leading to sub-clause (c) and (d) of this clause to any child, the medical management as long as required shall be provided by the Sponsor or his representative which will be over and above the financial compensation.

iii. Chronic life-threatening disease; and

iv. Reversible SAE in case it is resolved.

In case of clinical trial related SAE causing life-threatening disease and reversible SAE in case it is resolved, the quantum of compensation would be linked to the number of days of hospitalisation of the trial subject. The compensation per day of hospitalization shall be equal to the wage loss. The wage loss per day shall be calculated based upon the minimum wage of the unskilled worker (in Delhi). Since, in case of hospitalisation of any patient not only the patient loses his/her wage, there will be direct or indirect losses of various kind including inconvenience, wage loss of attendant, etc. The compensation per day of hospitalisation in such case shall be double the minimum wage. Accordingly, following formula shall be applicable for determination of compensation: Compensation = 2 X W X N. Where, W = Minimum wage per day of the unskilled worker (in Delhi) N = Number of days of hospitalization

Factor (F) for calculating the amount of compensation

Age	Factor
Not more than...	
16	228.54
17	227.49
18	226.38
19	225.22
20	224.00
21	222.71
22	221.37
23	219.95
24	218.47
25	216.91
26	215.28
27	213.57
28	211.79
29	209.92
30	207.98
31	205.95
32	203.85
33	201.66
34	199.40
35	197.06
36	194.64
37	192.14
38	189.56
39	186.90
40	184.17
41	181.37
42	178.49
43	175.54
44	172.52
45	169.44
46	166.29
47	163.07
48	159.80
49	156.47
50	153.09
51	149.67
52	146.20
53	142.68
54	139.13
55	135.56
56	131.95
57	128.33
58	124.70
59	121.05
60	117.41
61	113.77
62	110.14
63	106.52
64	102.93
65 or more	99.37

	Hassan Institute of Medical Sciences Institutional Ethics Committee				
	Standard Operating Procedure				
	SOP No	**Version No**	**Revision No**	**Issue date**	**Valid till**
	HIMS IEC/SOP-16	01	R0	**28-07-2021**	**27-07-2023**
Title: Review of Study Completion Reports					

This SOP applies to the review of the Study Completion Report which is a written report of every completed study submitted by the Principal Investigator (PI).

- The Member Secretary will review the Study Completion Report, confirm that it is complete and present it at the next full board meeting.
- The Member Secretary will present the report and members can discuss as needed.
- Following the discussion, the Chairperson may take one of the following decisions:
  noted / approved, request for additional information / clarification
- The decision is noted in the meeting minutes
- The Member Secretary will draft a letter to the PI conveying decision on the study completion report.
- The study shall be considered as closed if the decision by IEC is "Noted" or "Approved".
- The entire study will be archived for a period of 5 years from the date of completion of the project if the decision is noted and closed.

- It is the responsibility of the IEC to manage the termination of any study (recommended for termination by Data Safety and Monitoring Board, Principal Investigator, Sponsor or other authorized bodies or by the IEC) that the IEC has previously approved.
- The IEC is responsible for reviewing the progress made in the protocol (number of patients recruited, dropped out, reasons for drop-out), the occurrence of unexpected events or problems, and compliance of the investigator regarding IEC communication.
- An investigator/ Sponsor may put on hold a previously approved research when in the judgment of the 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
- IEC members/Chairperson can prematurely terminate/ suspend/ discontinue the study in the following situations:

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

  ii. SAEs occurring at trial site may require the study to be prematurely terminated for the safety of the patients.

  iii. When research is not conducted in accordance with IEC policies, is not in compliance with the local regulations or that has been associated with unexpected serious harm to participants.

  iv. Zero accrual for 1-2 years or long-term, low accrual.

- Records relating to any order issued for premature termination of study with a summary of the reasons thereof.
- Suspended protocols remain open and require continuing review.
- The IEC may revoke approval and recommend stopping permanently all activities in a previously approved research protocol. Terminated protocols are considered closed and no longer require continuing review
- In case of studies prematurely discontinued for any reason including lack of commercial interest in pursuing the new drug application, a summary report should be submitted by sponsors within 3 months. The summary report should provide a brief description of the study, the number of patients exposed to the drug, dose and duration of exposure, details of adverse drug reactions, if any, and the reason for discontinuation of the study or non-pursuit of the new drug application.

- The researcher can apply to the EC for a waiver of consent if the research involves less than minimal risk to participants and the waiver will not adversely affect the rights and welfare of the participants.
- The EC may grant consent waiver in the following situations:

i. research cannot practically be carried out without the waiver and the waiver is scientifically justified;

ii. retrospective studies, where the participants are de-identified or cannot be contacted;

iii. research on anonymized biological samples/data;

iv. certain types of public health studies/surveillance programmes /programme evaluation studies;

v. research on data available in the public domain; or

vi. research during humanitarian emergencies and disasters, when the participant may not be in a position to give consent. Attempt should be made to obtain the participant's consent at the earliest.

- The work of every clinical trial site shall be overseen by the Ethics Committee before initiation and throughout the duration of conduct of such trial.
- Ethics committee will make at appropriate intervals, an ongoing review of the trials for which they have reviewed the protocol. Such review may be based on the periodic study progress reports furnished by the investigators or monitoring and internal audit reports furnished by the sponsor or visiting the study sites.
- EC will monitor clinical trial study sites at appropriate intervals depending upon the duration and type of clinical study until completion of the research to check for compliance or improve the function.
- 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, the EC at the time of initial review or continuing review can suggest that routine monitoring may be conducted at more frequent intervals.
- Examples of "for cause" monitoring
- The following situations may justify "for cause" monitoring high number of protocol violations/deviations
    i. large number of proposals carried out at the study site or by the same researcher
    ii. large number of SAE reports
    iii. high recruitment rate
    iv. complaints received from participants
    v. any adverse media report
    vi. adverse information received from any other source
    vii. non-compliance with EC directions
    viii. misconduct by the researcher and
    ix. any other cause as decided by the EC.

- EC will monitor the study site using the forms below:

GCP INSPECTION CHECKLIST
Central Drugs Standard Control Organization

(This list is not all inclusive; item may be added &/or deleted as per the Study/Site/Sponsor/Lab)

I. General		
1.	Name and address of theclinical trial site	
2.	Date of Inspection	
3.	Inspection Team Members:	
4.	Personnel present during Inspection (with name and role/designation.)	
5.	Address & Contact details ofInvestigator:	
6.	Name & address of the Sponsor	
7.	Name & address of clinical trialNOC holder	
8.	Name & address of EC	

9.	Protocol Title	
10.	Protocol Number Version/date Protocol amendments, if any.	
11.	Investigational Product	
12.	Stage of study: (Mark the relevant)	(A) Before Trial Commencement ☐ (C\B) During Conduct of the trial ☐ (C) After Completion of Trial ☐
13.	Type of Inspection:	Surveillance ☐ For Cause ☐

II.LEGAL & ADMINISTRATIVE ASPECTS:					
S. no.	**Item**	**Yes**	**No**	**NA**	**Remark**
1	Clinical trial NOC from O/o DCGI (Note: mention along with Protocol no., Ver.,date)				
2	NOC for subsequent protocol				

	amendments,if any from O/o DCGI				
3	Ethics Committee approval date (Note: mention along with Protocol no., Ver.,date)				
3	Appendix VII as per Sch.-Y (mention revision(s) and notification to O/oDCGI, if any)				
4	Whether valid financial agreement between the Sponsor, Investigator & Institution available.				
5	Whether liability of involved parties (Investigator, Sponsor and Institution) clearly agreed.				
6	Is the valid clinical trial Insurance available?				
7	Site Initiation date				
8	Date of screening of first subject,				
9	Date of signing ICF by the first subject				
10	Date of Last Patient-Last Follow-Up (ifapplicable)				
11	Whether SOP for various activities areestablished and documented.				

12	Verify, whether the hospital/institute/site has adequate emergency care facilities to handle emergency situation.				
III Organisation & Personnel					
1	Assure that signed & dated, Curriculum Vitae is available for the Investigator, SubInvestigator /Co-Investigator				
2	Confirm the educational qualification of theInvestigator with registration by Medical Council of State/India.				
3	Confirm the GCP, Schedule Y and protocolspecific training of Investigator, Sub-Investigator/Co-Investigator and its team.				
4	Determine whether authority for conducting various clinical trial activities were delegatedproperly by Investigator to competent personnel (obtain the list of personnel and duty delegation log).				
5	Check whether the person whom the authority is delegated is adequately qualifiedand trained for the activity/activities assigned.				

6	Obtain the list of all clinical trials performedby Investigator (Preferably for last three years)				
7	Ensure that the Investigator is involved in conduct of not more than three clinical trialsat a time.				
IV Conduct of Trial					
A.	**Screening of subjects:**				
1	Check and review the informed consent forthe screening of the subjects.				
2	Check site screening log & enrolment logand obtain authenticated copy.				
3	**Check whether the subjects are meeting the inclusion/exclusion criteria as per the approvedprotocol w.r.t review of source documents &/or CRF.**				
3.1	Clinical Examination by Investigator (Check patient file/Source documents)				
3.2	Verify ,Clinical Laboratory Evaluation (Check Blood Cell Counts, Biochemical test, Urine analysis etc.as required by protocol)				

3.3	Verify X-Ray, MRI, ECG, USG or any other technique required to ascertain the inclusion/exclusion criteria.				
3.4	Verify, Whether all conditions of Clinicaltrial NOC are followed or not?				
B. Subject record and Informed consent:					
1	Whether ICF have all the elements enlistedin Appendix V of Schedule Y.				
	Whether ICF is approved by Ethics Committee prior to consent process.				
2	Whether IC has been obtained from each subject prior to participation of the subject inthe study.				
3	Whether signature/thumb impression of thesubjects/legal representative have been affixed with date.				
4	Whether in case of illiterate subjects or illiterate representative of a subject, there aresignature and details of an impartial witness.				

5	Have witness/ signature being personallydated.(If applicable).				
6	Have patient/witness signature been personally dated?				
7	Has the dated signature of the designated person for administering informed consent (IC) been affixed?				
8	Is the designated person for administering ICmedically qualified?				
9	If IC has been administered by a designatedperson who is not medically qualified, is there evidence that subject's queries of a medical nature were answered by a medically qualified person or the investigator?				

10	Is the completed ICF signed and dated by theinvestigator?				
11	Check weather re-consenting is done forchanges in ICF, if any.				
B.1	**Audio-Visual recording of Informed Consent Process(For 'vulnerable population' in 'New Chemical Entities (NCEs) clinical trial' only & Anti HIV & Anti-Leprosy patients only Audio recording)** (Verify as per GSR 611(E) dated 31.07.2015)				

1	Whether audio-visual recording is performedfor all subjects, independently.				
2	Is audio-visual recording conducted in a room conducive to recording of disturbancefree audio and video of the consent process?				
3	Check whether the video recording is free from disturbance to ensure that the image is recognizable and the audio is clearly audible.				
4	Check whether the recording of informedconsent process is preserved safely.				
C. Source Documents and Case Record Form					
1	Verify condition, completeness, legibility, accessibility of the investigators source datafile. (source data includes study subject's files, recording from automated instruments,tracings, X-ray and other films, laboratory notes, photograph negatives, magnetic media, hospital records, clinical and office charts, subject's diaries, evaluation checklistsand pharmacy dispensing records)				

2	Whether subject received the test drug withrespect to dose and frequency according to the protocol;				
3	Determine whether safety/ efficacy end pointdata(Clinical, laboratory examination results) were collected and reported in accordance with the protocol				
4	Does medical record mentions subject ID/ name /hospital registration number / and indication that subjects are participating in aclinical trial				
5	Compare the source document with CRF anddetermine whether source data have been correctly transcribed in CRF;				
6	Verify the drop-outs and reason for drop-outof subject is appropriately recorded.				
7	Whether the withdrawal of subject from thestudy is recorded and appropriately justifiedin accordance with approved protocol.				

8	Verify whether Standard Operating Procedure of handling of Serious Adverse Event occurred in clinical trial is available.				
9	Verify whether all SAE's have been reportedto the sponsor, EC and Licensing authority asper the timelines in accordance with Schedule Y. (Verify as per GSR 53(E) dated 30.01.2013& GSR 889 (E) dated 12.12.14 effective from 12.06.2015)				
10	Verify Whether SOP for medical care duringserious adverse event is available or not.				
11	Verify whether adequate medical care havebeen given to the subject especially in the event of inter current illness, adverse eventsincluding abnormal lab parameters;				
12	Verify whether all study related activities areperformed at site approved by O/o DCGI.				
VI.				**Sponsor**	

1	Whether investigator maintain copies of allreport submitted to the sponsor;				
2	Whether all CRF were submitted to sponsorafter completion of study;				
3	Determine whether all dropout and reasonthereof were reported to sponsor;				
4	Determine the method and frequency of monitoring the progress of the study by the sponsor and corrective action by site.				

5	Whether sponsor appointed a monitor withappropriate qualification and experience to monitor trial at the site.				
6	Whether a log of onsite monitoring visit ismaintained at the site.				
7	Is monitor submits visit report withdeviations if any to the sponsor.				

8	Whether sponsor performed an audit as a partof QA in order to independent and separate from routine monitoring of quality control function.				
9	In case the investigator and sponsor agreesto prematurely terminate or suspend the study for any reason, whether it was promptly informed to study subjects, EthicsCommittee and Licensing Authority.				
VII. Investigational Product					
1	Review individual subject record to verify the correct dose administration with respectto dose, frequency, route of administration				
2	Determine whether unqualified /unauthorisedpersons administered/dispensed the test drug				
3	Determine whether adequate record of quantity of test drug received , dispensed is maintained.(Check the test drug reconciliation and verify the leftover drug orbalance on the day of inspection).				

4	Determine whether storage condition/monitoring method are as perprotocol/recommendation;				
5	Whether trial medication are maintained insecured manner with controlled access;				
6	Have un-used trial medications been returnedto the sponsor or disposed of according to protocol?				
7	Are the drugs dispensing records beingmaintained properly?				
8	Whether the records for reconciliation of allIP's are maintained?				
9	Are electronic or hand-written temperaturelogs available for the storage area of the investigational products?				
10	Verify that investigation product is appropriately labelled. (For clinical trial useonly).				
VIII. Ethics Committee					
1	Identify the name, address of the EC/ IEC inthe approval letter and compare it with one stated in Investigator Undertaking.				

2	Verify the Status of EC-whether Institutionalor Independent, Check Registration certificate (Verify as per GSR 72(E) dated 08.12.2013)				
2	Verify if EC approval letter mention studycode , title and version number of the protocol, list of other documents reviewed, list of members present at the meeting, quorum of five members as specified in Schedule Y satisfied, date, time , venue of the meeting, signature and date of membersecretary / Chairman.				
3	Verify whether the EC recorded minutes ofmeeting.				
4	Verify whether EC is performed on site monitoring of the clinical trial approved. (Frequency and SOP)				
5	Verify whether EC members have conflict ofinterest in the approved trial, if yes then the member should abstain from such approval meeting.				

6	Verify whether the communications between Investigator and EC are available for changes, Serious Adverse Event and deviations occurred in clinical trial.				
7	Verify whether EC is function in accordancewith conditions of registration by LA.				
IX Pathology Laboratory (for Screening/ Assessment)					
1	Name and address of the clinical laboratoryused in the study. (Local and Outside).				
2	Whether financial & Confidentiality agreement with Investigator and concerned laboratory (ies) in place.				
3	Is investigator/Sponsor verified the accreditation status and adequacy of the facilities to perform the specified tests as per protocol.				
4	Verify whether the SOP for sample preparation, handling and transportation is available. Verify the appropriateness of theSOP.				
X Quality Assurance					

1	Verify whether SOP for all proceduresconducted at site are available i.e. have a copy of Site Specific and Trialspecific SOPs				
2	Verify the essential components of SOP likewho prepared, checked, authorized and when, frequency of SOP revision				
3	Whether SOPs for all operation likescreening and Informed consent Process, AVrecording of ICP of vulnerable population in NCE-CTs, SAEs & its Management, Communication with EC/Sponsor/CDSCO, GCP/Sch.Y, training to trial team, training assessment				
4	Whether SOPs for all operation like IP handling and distribution to study subjects, blood samples collection, processing preservation and transportation to local laboratory.				
5	Whether SOPs for all operation of storage cabinets, refrigerators/deep freezers used to store samples and IP are available.				
6	Verify, whether records for job description/responsibilities, qualification andtraining for all				

	personnel involved in the clinical trial is maintained and stored.				
7	Verify whether the activities performed arein compliance with duty delegated by Investigator.				
8	Verify whether concern staff is adequatelytrained and records maintained there of				
9	In case of vaccines, are a spillage SOP available and the study team trained to handle such an incidence?				
XI	**Record keeping and data handling**				
1	Is adequate space available for documentretention?				
2	Determine whether documents are maintained properly and for the period asspecified.				
3	Whether necessary measures have been takento prevent accidental or premature destruction.				
4	Whether the archival access controlled orrestricted to authorized personnel.				
5	Weather SOP available to document all stepsin data management in order to allow				

	step bystep retrospective assessment of data quality and study performance.				
6	Whether corrections in documents carry the date and initials of Investigators and authorized person.				
XI-a	**Electronic data processing**				
1	Is electronic data processing is done byauthorized person?				
2	Verify whether list of authorized persons tomake changes is maintained				
3	Verify if provision for recording of trail ofchanges and deletions made is available.				
4	Whether the hardware and software use fordata recording and processing is validated				

Collect authenticated copies as exhibit wherever any Critical &/or Major non-compliance has been observed.

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	Hassan Institute of Medical Sciences Institutional Ethics Committee				
	Standard Operating Procedure				
	SOP No	**Version No**	**Revision No**	**Issue date**	**Valid till**
	HIMS IEC/SOP-20	01	R0	**28-07-2021**	**27-07-2023**
Title: Dealing with the Participants' Requests and Complaints					

- The Member Secretary may receive a request, complaint or query directly from the participant.
- The Member Secretary will additionally ascertain details of the request/ complaint by examining any relevant documents and by interviewing the participant if necessary. If required, the Member Secretary will call for additional relevant information and documents from the Principal Investigator (PI).
- In case of a request for additional information or clarification, the Member Secretary in consultation with the Chairperson will provide the information himself / herself or will designate one or more IEC member(s) to provide such information.
- In case of a complaint received from a research participant, Member Secretary in consultation with the Chairperson will initiate a process to address any injustice that may have occurred. Depending on the seriousness of the matter, the Chairperson will direct the Member Secretary to appoint a subcommittee of two or more IEC members for enquiry in order to resolve the matter or Call an emergency meeting of two or more IEC members for discussion or Consider the matter for discussion at the next full board meeting
- The Chairperson/ Member Secretary/ designated IEC members will assess the situation and mediate a dialogue between the research participant and PI in an attempt to resolve the matter.
- The IEC will insist on factual details to determine gap, if any, between truth and individual perception.
- The final decision will be taken by the Member Secretary in consultation with the Chairperson based on the recommendation of any one of the above and it will be informed to the research participant and the PI.

	Hassan Institute of Medical Sciences Institutional Ethics Committee				
	Standard Operating Procedure				
	SOP No	**Version No**	**Revision No**	**Issue date**	**Valid till**
	HIMS IEC/SOP-21	01	R0	**28-07-2021**	**27-07-2023**
Title: Emergency Meetings					

- An IEC meeting that is scheduled outside of a normally scheduled meeting to review study activities that require full IEC review and approval. In order to hold an emergency meeting, a quorum must be maintained throughout the entire discussion. Emergency meetings may be held via teleconference, if applicable
- Emergency meetings may be scheduled to approve safety / life threatening issues, SAE and other study activities that require Full Board review.
- It is responsibility of the Member Secretary in consultation with Chairperson to call an emergency meeting
- The Chairperson/ Member Secretary will decide to call an emergency meeting for any one or more of the following reasons:
- Urgent issues (which, if not decided upon early could adversely affect or have adverse impact on patient safety, public safety or national economy etc.)
- Occurrence of unexpected serious adverse event(s).
- A matter of life and death for the patients continuing in the trial.
- Other reasons, as deemed appropriate by the Chairperson
- For the purpose of calling an emergency meeting, contact by telephone or email to the email address provided by the member would be considered as sufficient.
- The Chairperson/Member Secretary will determine if there is a quorum.
- If a quorum is not met, the meeting will be postponed for 15 minutes. However, if there is no quorum at the end of 15 minutes; the meeting would be held without a quorum provided at least three members (other than Chairperson and including at least one scientific member) are present, given the urgency of the matter under consideration.
- The IEC members will act according to the relevant IEC SOPs (Expedited Review, SAE review, Review of Protocol deviations/violations etc.) for discussion and decision-making on the matter under consideration. The minutes of the emergency meeting would be prepared, distributed, approved and filed as described in the steps above for regular full board meeting.

- IEC communications refer to documented communications and can be in the form of hard copy letters or emails. It is encouraged that all IEC communications, received and issued, are in this form to facilitate documentation of all actions, instructions, and even responses to queries.
- **Log of protocol submissions should have at least the following elements:**
  i. Date of communication/submission
  ii. Name of IEC party contacted
  iii. Study information, i.e., sponsor, protocol number, Principal investigator, etc.
  iv. Content of communication or submission
  v. Notation of any follow-up necessary
  vi. Type of submission (if communication refers to a submission)
  vii. Contact information (address, telephone number, and e-mail) of sending party Name and signature of individual who received the communication and completed the record.

- **A copy of the communication/submission is filed in the:**
  i. Protocol file folder
  ii. IEC Communications folder
  iii. Others, as appropriate

- The contents of the proposed protocol for conducting clinical trials has to be submitted by the Principal investigator as below.

Submission of Documents to the IEC:

Researchers should submit research proposals as soft or hard copies to the Secretariat for review in the prescribed format and required documents as per EC SOPs. The EC should prepare a checklist for the required documents. This list is subject to modifications, depending on the type of research, EC SOPs and institutional policies.

1. Cover letter to Member Secretary.
2. Type of review requested.
3. Application form for initial review.
4. Correct version of the informed consent document (ICD) in English and local language. Translation and back translations certificates
5. Case record form/questionnaire.
6. Recruitment procedures: advertisement, notices (if applicable)
7. Patient instruction card, diary. (if applicable)
8. Investigator's brochure (as applicable for drug/biologicals/device trials)
9. Brief curriculum vitae of all study researchers.
10. Details of funding agency/sponsor and fund allocation. (if applicable)
11. A statement of Conflict of Interest.
12. GCP training certificate (preferable within 5 years) of investigators. (Clinical Trials)
13. Any other research ethics/other training evidence.
14. List of ongoing research studies undertaken by 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 approval. (if applicable)
19. MoU in case of studies involving collaboration with other institutions. (if applicable)
20. Clinical trial agreement between sponsor, investigator and head of the institutions. (if applicable)

21. Documentation of 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 conditions of coverage, date of commencement and date of expiry of coverage of risk. (if applicable)
24. Any additional documents as required by EC. (such as other EC clearances for multi-centric studies)
25. Protocol.

CONTENTS OF THE PROPOSED PROTOCOL FOR CONDUCTING CLINICAL TRIALS

Title Page

(a) Full title of the clinical study,

(b) Protocol, Study number, and protocol version number with date. (c) The Investigational New Drug (IND) name/number of the investigational drug.

(d) Complete name and address of the Sponsor and contract research organization if any.

(e) List of the investigators who are conducting the study, their respective institutional affiliations and site locations

(f) Name of clinical laboratories and other departments and/or facilities participating in the study.

Table of Contents

1. Background and introduction

(a) Preclinical experience

(b) Clinical experience

Previous clinical work with the new drug should be reviewed here and a description of how the current protocol extends existing data should be provided. If this is an entirely new indication, how this drug was

considered for this should be discussed. Relevant information regarding pharmacological, toxicological and other biological properties of the drug/biologic/medical device, and previous efficacy and safety experience should be described.

2. Study rationale: This section should describe a brief summary of the background information relevant to the study design and protocol methodology. The reasons for performing this study in the particular population included by the protocol should be provided.

3. Study objective (primary as well as secondary) and their logical relation to the study design.

4. Study design–

(a) Overview of the study design: Including a description of the type of study (i.e., double-blind, multicentre, placebo controlled, etc.), a detail of the specific treatment groups and number of study Subjects in each group and investigative site, Subject number assignment, and the type, sequence and duration of study periods.

(b) Flow chart of the study

(c) A brief description of the methods and procedures to be used during the study.

(d) Discussion of study design: This discussion details the rationale for the design chosen for this study.

5. Study population: the number of subjects required to be enrolled in the study at the investigative site and by all sites along with a brief description of the nature of the subject population required is also mentioned.

6. Subject eligibility

(a) Inclusion criteria

(b) Exclusion criteria

7. Study assessments – plan, procedures and methods to be described in detail.

8. Study conduct stating the types of study activities that would be included in this section would be: medical history, type of physical examination, blood or urine testing, electrocardiogram (ECG), diagnostic testing such as pulmonary function tests, symptom

measurement, dispensation and retrieval of medication, Subject cohort assignment, adverse event review, etc.

Each visit should be described separately as Visit 1, Visit 2, etc. Discontinued subjects: Describes the circumstances for Subject withdrawal, dropouts, or other reasons for discontinuation of Subjects. State how drop outs would be managed and if they would be replaced describe the method of handling of protocol waivers, if any. The person who approves all such waivers should be identified and the criteria used for specific waivers should be provided. Describes how protocol violations will be treated, including conditions where the study will be terminated for noncompliance with the protocol.

9. Study treatment-

(a) Dosing schedule (dose, frequency, and duration of the experimental treatment) Describe the administration of placebos and/or dummy medications if they are part of the treatment plan. If applicable, concomitant drug(s), their doses, frequency, and duration of concomitant treatment should be stated.

(b) Study drug supplies and administration: A statement about who is going to provide the study medication and that the investigational drug formulation has been manufactured following all regulations Details of the product stability, storage requirements and dispensing requirements should be provided.

(c) Dose modification for study drug toxicity: Rules for changing the dose or stopping the study drug should be provided.

(d) Possible drug interactions

(e) Concomitant therapy: The drugs that are permitted during the study and the conditions under which they may be used are detailed here. Describe the drugs that a Subject is not allowed to use during parts of or the entire study. If any washout periods for prohibited medications are needed prior to enrolment, these should be described here.

(f) Blinding procedures: A detailed description of the blinding procedure if the study employs a blind on the Investigator and/or the Subject

(g) Un-blinding procedures: If the study is blinded, the circumstances in which un-blinding may be done and the mechanism to be used for un-blinding should be given

10. Adverse Events: Description of expected adverse events should be given. Procedures used to evaluate an adverse event should be described.

11. Ethical considerations: Give the summary of:

(a) Risk/benefit assessment:

(b) Ethics committee review and communications

(c) Informed consent process

(d) Statement of subject confidentiality including ownership of data and coding procedures.

12. Study monitoring and supervision:

A description of study monitoring policies and procedures should be provided along with the proposed frequency of site monitoring visits, and who is expected to perform monitoring.

Case Record Form (CRF) completion requirements, including who gets which copies of the forms and any specific required in filling out the forms Case Record Form correction requirements, including who is authorized to make corrections on the Case Record Form and how queries about study data are handled and how errors, if any, are to be corrected should be stated. Investigator study files, including what needs to be stored following study completion should be described.

13. Investigational Product Management:

(a) Give investigational product description and packaging (stating all ingredients and the formulation of the investigational drug and any placebos used in the study)

(b) The precise dosing required during the study

(c) Method of packaging, labelling, and blinding of study substances (d) Method of assigning treatments to subjects and the subject identification code numbering system.

(e) Storage conditions for study substances

(f) Investigational product accountability: Describe instructions for the receipt, storage, dispensation, and return of the investigational products

to ensure a complete accounting of all investigational products received, dispensed, and returned or destroyed.

(g) Describe policy and procedure for handling unused investigational products.

14. Data Analysis: Provide details of the statistical approach to be followed including sample size, how the sample size was determined, including assumptions made in making this determination, efficacy endpoints (primary as well as secondary) and safety endpoints. Statistical analysis: Give complete details of how the results will be analysed and reported along with the description of statistical tests to be used to analyse the primary and secondary endpoints defined above. Describe the level of significance, statistical tests to be used, and the methods used for missing data; method of evaluation of the data for treatment failures, non-compliance, and Subject withdrawals; rationale and conditions for any interim analysis if planned. Describe statistical considerations for Pharmacokinetic (PK) analysis, if applicable.

15. Undertaking by the Investigator

16. Appendices: Provide a study synopsis, copies of the informed consent documents (patient information sheet, informed consent form etc.); Case Record Form (CRF) and other data collection forms; a summary of relevant pre-clinical safety information and any other documents referenced in the clinical protocol.

UNDERTAKING BY THE INVESTIGATOR

1. Full name, address and title of the Principal Investigator (or Investigators when there is no Principal Investigator).

2. Name and address of the medical college, hospital or other facility where the clinical trial will be conducted: Education, training & experience that qualify the Investigator for the clinical trial (Attach details including Medical Council registration number, or any other statements of qualifications)

3. Name and address of all clinical laboratory facilities to be used in the study.
4. Name and address of the Ethics Committee that is responsible for approval and continuing review of the study.

5. Names of the other members of the research team (Co-or sub-Investigators) who will be assisting the Investigator in the conduct of the investigations. 6. Protocol Title and Study number (if any) of the clinical trial to be conducted by the Investigator.

7. Commitments:

(i) I have reviewed the clinical protocol and agree that it contains all the necessary information to conduct the study. I will not begin the study until all necessary ethics committee and regulatory approvals have been obtained.

(ii) I agree to conduct the study in accordance with the current protocol. I will not implement any deviation from or changes of the protocol without agreement by the Sponsor and prior review and documented approval or favourable opinion from the ethics committee of the amendment, except where necessary to eliminate an immediate hazard to the trial subject or when the changes involved are only logistical or administrative in nature.

(iii) I agree to personally conduct or supervise the clinical trial at my site.

(iv) I agree to inform all trial subject, that the drugs are being used for investigational purposes and I will ensure that the requirements relating to obtaining informed consent and ethics committee review and approval specified in the New Drugs and Clinical Trials Rules, 2019 and Good Clinical Practices guidelines are met.

(v) I agree to report to the Sponsor all adverse experiences that occur in the course of the investigation(s) in accordance with the regulatory requirements and Good Clinical Practices guidelines.

(vi) I have read and understood the information in the Investigator's brochure, including the potential risks and side effects of the drug.

(vii) I agree to ensure that all associates, colleagues and employees assisting in the conduct of the study are suitably qualified and experienced and they have been informed about their obligations in meeting their commitments in the trial.

(viii) I agree to maintain adequate and accurate records and to make those records available for audit or inspection by the Sponsor, ethics committee, Central Licencing Authority or their authorised representatives, in accordance with regulatory provisions and the Good Clinical Practices guidelines. I will fully cooperate with any study related audit conducted by regulatory officials or authorised representatives of the Sponsor.

(ix) I agree to promptly report to the ethics committee all changes in the clinical trial activities and all unanticipated problems involving risks to human subjects or others.

(x) I agree to inform all serious adverse events to the Central Licencing Authority, sponsor as well as 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 Licencing Authority along with the report of the serious adverse event.

(xi) The report of the serious adverse event, after due analysis, shall also be forwarded by me to the Central Licencing Authority, the Chairperson of the ethics committee and the Head of the institution where the trial has been conducted within fourteen days in accordance with the regulatory requirements.

(xii) I will maintain confidentiality of the identification of all participating subjects and assure security and confidentiality of study data.

(xiii) I agree to comply with all other requirements, guidelines and statutory obligations as applicable to clinical Investigators participating in clinical trials.

8. Signature of Investigator with date.

INVESTIGATOR'S BROCHURE

The Investigator's Brochure should contain the version number, release date along with the following sections, each with literature references where appropriate:

1 Table of Contents

2 Summary: A brief summary (preferably not exceeding two pages) should be given, highlighting the significant physical, chemical, pharmaceutical, pharmacological, toxicological, pharmacokinetic, metabolic, and clinical information available that is relevant to the stage of clinical development of the investigational product.

3 Introduction: A brief introductory statement should be provided that contains the chemical name (and generic and trade name when approved) of the investigational product, all active ingredients, the investigational product pharmacological class and its expected position within this class (e.g. advantages), the rationale for performing research with the investigational product, and the anticipated prophylactic, therapeutic, or diagnostic indication. Finally, the introductory statement should provide the general approach to be followed in evaluating the investigational product.

4 Physical, Chemical, and Pharmaceutical Properties and Formulation: A description should be provided of the investigational product substance (including the chemical or structural formula), and a brief summary should be given of the relevant physical, chemical, and pharmaceutical properties. To permit appropriate safety measures to be taken in the course of the trial, a description of the formulation to be used, including excipients, should be provided and justified if clinically relevant. Instructions for the storage and handling of the dosage form should also be given. Any structural similarities to other known compounds should be mentioned.

5 Nonclinical Studies

5.1 Introduction: The results of all relevant nonclinical pharmacology, toxicology, pharmacokinetic, and investigational product metabolism studies

should be provided in summary form. This summary should address the methodology used, the results, and a discussion of the relevance of the findings to the investigated therapeutic and the possible unfavourable and unintended effects in human. The information provided may include the following, as appropriate, if known or available:

• Species tested

• Number and sex of animals in each group

• Unit dose (e.g., milligram/kilogram (mg/kg))

• Dose interval

• Route of administration

• Duration of dosing • Information on systemic distribution

• Duration of post-exposure follow-up

• Results, including the following aspects:

− Nature and frequency of pharmacological or toxic effects

− Severity or intensity of pharmacological or toxic effects

− Time to onset of effects − Reversibility of effects

− Duration of effects

− Dose response

Tabular format or listings should be used whenever possible to enhance the clarity of the presentation. The following sections should discuss the most important findings from the studies, including the dose response of observed effects, the relevance to humans, and any aspects to be studied in humans. If applicable, the effective and nontoxic dose findings in the same animal species should be compared (i.e., the therapeutic index should be discussed). The relevance of this information to the proposed human dosing should be

addressed. Whenever possible, comparisons should be made in terms of blood/tissue levels rather than on a mg/kg basis.

(a) Nonclinical Pharmacology: A summary of the pharmacological aspects of the investigational product and, where appropriate, its significant metabolites studied in animals, should be included. Such a summary should incorporate studies that assess potential therapeutic activity (e.g. efficacy models, receptor binding, and specificity) as well as those that assess safety (e.g., special studies to assess pharmacological actions other than the intended therapeutic effect(s)).

(b) Pharmacokinetics and Product Metabolism in Animals: A summary of the pharmacokinetics and biological transformation and disposition of the investigational product in all species studied should be given. The discussion of the findings should address the absorption and the local and systemic bioavailability of the investigational product and its metabolites, and their relationship to the pharmacological and toxicological findings in animal species.

(c) Toxicology: A summary of the toxicological effects found in relevant studies conducted in different animal species should be described under the following headings where appropriate:

− Single dose

− Repeated dose

− Carcinogenicity

− Special studies (e.g. irritancy and sensitization)

− Reproductive toxicity

− Genotoxicity (mutagenicity)

6 Effects in Humans:

(a) A thorough discussion of the known effects of the investigational products in humans should be provided, including information on pharmacokinetics,

metabolism, pharmacodynamics, dose response, safety, efficacy, and other pharmacological activities. Where possible, a summary of each completed clinical trial should be provided. Information should also be provided regarding results of any use of the investigational products other than from in clinical trials, such as from experience during marketing.

(b) Pharmacokinetics and Product Metabolism in Humans A summary of information on the pharmacokinetics of the investigational products should be presented, including the following, if available: − Pharmacokinetics (including metabolism, as appropriate, and absorption, plasma protein binding, distribution, and elimination). − Bioavailability of the investigational product (absolute, where possible, or relative) using a reference dosage form. − Population subgroups (e.g., gender, age, and impaired organ function). − Interactions (e.g., product-product interactions and effects of food). − Other pharmacokinetic data (e.g., results of population studies performed within clinical trial(s).

(c) Safety and Efficacy: A summary of information should be provided about the investigational product's or products' (including metabolites, where appropriate) safety, pharmacodynamics, efficacy, and dose response that were obtained from preceding trials in humans (healthy volunteers or patients). The implications of this information should be discussed. In cases where a number of clinical trials have been completed, the use of summaries of safety and efficacy across multiple trials by indications in subgroups may provide a clear presentation of the data. Tabular summaries of adverse drug reactions for all the clinical trials (including those for all the studied indications) would be useful. Important differences in adverse drug reaction patterns/incidences across indications or subgroups should be discussed. The Investigators Brochure IB should provide a description of the possible risks and adverse drug reactions to be anticipated on the basis of prior experiences with the product under investigation and with related products. A description should also be provided of the precautions or special monitoring to be done as part of the investigational use of the products.

(d) Marketing Experience: The Investigator's Brochure should identify countries where the investigational product has been marketed or approved. Any significant information arising from the marketed use should be summarised (e.g., formulations, dosages, routes of administration, and adverse product reactions). The Investigator's Brochure should also identify all the countries where the investigational product did not receive approval or registration for marketing or was withdrawn from marketing or registration.

7 Summary of Data and Guidance for the Investigator: This section should provide an overall discussion of the nonclinical and clinical data, and should summarise the information from various sources on different aspects of the investigational products, wherever possible. In this way, the investigator can be provided with the most informative interpretation of the available data and with an assessment of the implications of the information for future clinical trials. Where appropriate, the published reports on related products should be discussed. This could help the investigator to anticipate adverse drug reactions or other problems in clinical trials. The overall aim of this section is to provide the investigator with a clear understanding of the possible risks and adverse reactions, and of the specific tests, observations, and precautions that may be needed for a clinical trial. This understanding should be based on the available physical, chemical, pharmaceutical, pharmacological, toxicological, and clinical information on the investigational products. Guidance should also be provided to the clinical investigator on the recognition and treatment of possible overdose and adverse drug a reaction that is based on previous human experience and on the pharmacology of the investigational product.

INFORMED CONSENT

1. Checklist of informed consent documents for clinical trial subject,–

1.1 Essential elements:

(i) Statement that the study involves research and explanation of the purpose of the research.

(ii) Expected duration of the participation of subject.

(iii) Description of the procedures to be followed, including all invasive procedures.

(iv) Description of any reasonably foreseeable risks or discomforts to the Subject.

(v) Description of any benefits to the Subject or others reasonably expected from research. If no benefit is expected Subject should be made aware of this.
(vi) Disclosure of specific appropriate alternative procedures or therapies available to the Subject.

(vii) Statement describing the extent to which confidentiality of records identifying the Subject will be maintained and who will have access to Subject's medical records.

(viii) Trial treatment schedule and the probability for random assignment to each treatment (for randomized trials).

(ix) Statement describing the financial compensation and the medical management as under:

> (a) In case of an injury occurring to the subject during the clinical trial, free medical management shall be given as long as required or till such time it is established that the injury is not related to the clinical trial, whichever is earlier. (b) In the event of a trial related injury or death, the sponsor or his representative or the investigator or centre, as the case

may be, in accordance with the rule 39, as the case may be, shall provide financial compensation for the injury or death.

(x)An explanation about whom to contact for trial related queries, rights of Subjects and in the event of any injury.

(xi) The anticipated prorated payment, if any, to the subject for participating in the trial.

(xii) Responsibilities of subject on participation in the trial.

(xiii) Statement that participation is voluntary, that the subject can withdraw from the study at any time and that refusal to participate will not involve any penalty or loss of benefits to which the subject is otherwise entitled.

(xiv) Statement that there is a possibility of failure of investigational product to provide intended therapeutic effect.

(xv) Statement that in the case of placebo controlled trial, the placebo administered to the subjects shall not have any therapeutic effect.

(xvi) Any other pertinent information. 1.2 Additional elements, which may be required:

(a) Statement of foreseeable circumstances under which the participation of the subject may be terminated by the Investigator without his or her consent.

(b) Additional costs to the subject that may result from participation in the study.

(c) The consequences of a Subject's decision to withdraw from the research and procedures for orderly termination of participation by Subject.

(d) Statement that the Subject or Subject's representative will be notified in a timely manner if significant new findings develop during the course of the research which may affect the Subject's willingness to continue participation will be provided.

(e). A statement that the particular treatment or procedure may involve risks to the Subject (or to the embryo or foetus, if the Subject is or may become pregnant), which are currently unforeseeable.

(f) Approximate number of Subjects enrolled in the study.

Format of informed consent form for Subjects participating in a clinical trial – Informed Consent form to participate in a clinical trial Study

Title:

Study Number:

Subject's Initials: _____

Subject's Name: _____

Date of Birth/Age: _____

Address of the Subject ___

Qualification _____

Occupation: Student or Self-Employed or Service or Housewife or Others (Please click as appropriate) .

Annual Income of the subject:

Name and address of the nominees and his relation to the subject (for the purpose of compensation in case of trial related death).

(i) I confirm that I have read and understood the information Sheet dated _____ for the above study and have had the opportunity to ask questions.
(ii) I understand that my participation in the study is voluntary and that I am free to withdraw at any time, without giving any reason, without my medical care or legal rights being affected.

(iii) I understand that the Sponsor of the clinical trial, others working on the Sponsor's behalf, the Ethics Committee and the regulatory authorities will not need my permission to look at my health records both in respect of the current study and any further research that may be conducted in relation to it, even if I withdraw from the trial. I agree to this access. However, I understand that my identity will not be revealed in any information released to third parties or published.

(iv) I agree not to restrict the use of any data or results that arise from this study provided such a use is only for scientific purposes

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

Signature (or Thumb impression) of the Subject/Legally Acceptable Representative:

Signatory's Name:

_____

Signature of the Investigator: _____

Date: ____ / ____ /

Study Investigator's Name: ___ _____

Signature of the Witness _____

Date: ____ / ____ /

Name of the Witness:_____

Copy of the Patient Information Sheet and duly filled Informed Consent Form shall be handed over to the subject his or her attendant.

Format for according approval to clinical trial protocol by the ethics committee

To

Dr.

Dear Dr._____ The Institutional ethics committee or independent ethics committee (state name of the committee, as appropriate) reviewed and discussed your application to conduct the clinical trial entitled "……..." on……. (date).

The following documents were reviewed:

(a) Trial protocol (including protocol amendments), dated…….version No.(s) ……

(b) Patient information sheet and informed consent form (including updates, if any) in English or vernacular language.

(c) Investigator's brochure, dated ....., Version no…… Proposed methods for patient accrual including advertisements etc. proposed to be used for the purpose.

(d) Principal investigator's current Curriculum Vitae.

(e) Insurance policy or compensation for participation and for serious adverse events occurring during the study participation.

(f) Investigator's agreement with the sponsor.

(g) Investigator's undertaking.

The following members of the ethics committee were present at the meeting held on (date, time, place). ……

Chairperson of the ethics committee; …….

Member-Secretary of the ethics committee; …….

Name of each member with designation;

We approve the trial to be conducted in its presented form.

The ethics committee to be informed about the progress of the study, any Serious Adverse Events (SAE) occurring in the course of the study, any changes in the protocol and patient information or informed consent and to be provided with a copy of the final report.

Yours sincerely,

Member Secretary, Ethics Committee

- A study master file is the file comprising all essential documents and correspondence related to the study. This should be created for all proposals at the time of initial submission to the IEC office.
- All related documents of the approved study will be gathered, classified appropriately and placed in the study master file: These could include copies of
  i. All original research proposals reviewed and approved,
  ii. Reviewer's assessment forms
  iii. Study approval letter
  iv. Reviewed and approved consent documents,
  v. Amendments and any other correspondence
  vi. Study progress reports and interim reports,
  vii. Serious adverse event report forms submitted by investigators,
  viii. Any other reports
  ix. IEC correspondence
- Strict confidentiality will be maintained for the contents of the files
- All active files will be kept secured in a file cabinet with controlled access.
- All records must be archived for a period of at least 3 years after the completion/ termination of the study.
- Documents related to regulatory clinical trials must be archived for 5 years after the completion/termination of the study or as per regulations.
- Records may be archived for a longer period, if required by the sponsors/regulatory bodies.
- Maintenance of records by Ethics Committee for clinical trial.—
  (1) The Ethics Committee shall maintain data, record, registers and other documents related to the functioning and review of clinical trial or bioavailability study or bioequivalence study, as the case may be, for a period of five years after completion of such clinical trial.
  (2) In particular and without prejudice to the generality of the sub-rule (1), the

Ethics Committee shall maintain the following records for a period of five years after completion of every clinical trial or bioavailability study or bioequivalence study, namely:-

(i) the constitution and composition of the Ethics Committee;

(ii) the curriculum vitae of all members of the Ethics Committee;

(iii) standard operating procedures followed by the Ethics Committee;

(iv) national and international guidelines followed by the Ethics Committee;

(v) copies of the protocol, data collection formats, case report forms, investigators brochures, etc., submitted for review;

(vi) all correspondence with committee members and investigators regarding application, decision and follow up;

(vii) agenda of all Ethics Committee meetings and minutes of all Ethics Committee meetings with signature of the Chairperson;

(viii) copies of decisions communicated to applicants;

(ix) records relating to any order issued for premature termination of study with a summary of the reasons thereof;

(x) final report of the study including microfilms, compact disks or video recordings;

(xi) recommendation given by Ethics Committee for determination of compensation;

(xii) records relating to the serious adverse event, medical management of trial subjects and compensation paid.

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

Documents to be maintained by EC for record

Administrative documents

- Constitution and composition of the EC
- Appointment letters
- Signed and dated copies of the most recent curriculum vitae of all EC members
- Signed confidentiality agreements
- COI declarations of members
- Training records of EC members
- Financial records of EC
- Registration/accreditation documents, as required
- A copy of national and international guidelines and applicable

regulations
- Regulatory notifications
- Meeting-related documents
- Agenda and minutes
- All communications received or made by the EC
- SOPs

Proposal-related documents

- One hard copy and a soft copy of the initial research proposal and all related documents
- Decision letters
- Any amendments submitted for review and approval
- Regulatory approvals
- SAE, AE reports
- Protocol deviations/violations
- Progress reports, continuing review activities, site monitoring reports
- All correspondence between the EC and researchers
- Record of notification issued for premature termination of a study with a summary of the reasons
- Final report of the study
- Publications, if any

- It is the responsibility of Member Secretary to ensure that all active study files and IEC records are prepared, maintained during the study period and kept securely for a period of five years after the closure/ termination of the project.

- Vulnerable persons are those individuals who are relatively or absolutely incapable of protecting their own interests because of personal disability; environmental burdens; social injustice; lack of power, understanding or ability to communicate or are in a situation that prevents them from doing so.
- **Individuals may be considered to be vulnerable if they are**

i. socially, economically or politically disadvantaged and therefore susceptible to being

ii. exploited;

iii. incapable of making a voluntary informed decision for themselves or whose autonomy is compromised temporarily or permanently, for example people who are unconscious, differently abled;

iv. able to give consent, but whose voluntariness or understanding is compromised due to

v. their situational conditions; or

vi. unduly influenced either by the expectation of benefits or fear of retaliation in case of

vii. refusal to participate which may lead them to give consent.

- The key principle to be followed when research is planned on vulnerable persons is that others will be responsible for protecting their interests because they cannot do so or are in a compromised position to protect their interests on their own.
- **Following are some examples of vulnerable populations or groups**

i. Economically and socially disadvantaged (unemployed individuals, orphans, abandoned individuals, persons below poverty line, ethnic

minorities, sexual minorities – lesbian/ gay/bisexual and transgender (LGBT), etc.);

ii. 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;

iii. children (up to 18 years);

iv. women in special situations (pregnant or lactating women, or those who have poor

v. decision-making powers/poor access to healthcare);

vi. tribals and marginalized communities;

vii. refugees, migrants, homeless, persons or populations in conflict zones, riot areas or disaster situations;

viii. afflicted with mental illness and cognitively impaired individuals, differently abled mentally and physically disabled;

ix. terminally ill or are in search of new interventions having exhausted all therapies;

x. suffering from stigmatizing or rare diseases; or

xi. have diminished autonomy due to dependency or being under a hierarchical system (students, employees, subordinates, defence services personnel, healthcare workers, institutionalized individuals, under trials and prisoners).

- **Principles of research among vulnerable populations**

i. Vulnerable populations have an equal right to be included in research so that benefits accruing from the research apply to them as well.

ii. If any vulnerable group is to be solely recruited then the research should answer the health needs of the group.

iii. Participants must be empowered, to the maximum extent possible, to enable them to decide by themselves whether or not to give assent/consent for participation

iv. In vulnerable populations, when potential participants lack the ability to consent, a LAR should be involved in decision making

v. Special care must be taken to ensure participant's privacy and

confidentiality, especially because breach of confidentiality may lead to enhancement of vulnerability

vi. If vulnerable populations are to be included in research, all stakeholders must ensure that additional protections are in place to safeguard the dignity, rights, safety and well- being of these individuals.

vii. Additional Safeguards/Protections Mechanisms

viii. When vulnerable individuals are to be recruited as research participants additional precaution should be taken to avoid exploitation/retaliation/reward/credits, etc., as they may either feel intimidated and incapable of disagreeing with their caregivers, or feel a desire to please them. In the first case, they may be subjected to undue pressure, while in the second, they may be easily manipulated. If they perceive that their caregivers want them to participate in research, or if the caregiver stands to benefit from the dependent's participation, the feeling of being pressed to participate may be irresistible which will undermine the potential voluntariness of the consent to participate.

ix. Researchers must justify the inclusion of a vulnerable population in the research.

x. ECs must satisfy themselves with the justification provided and record the same in the proceedings of the EC meeting

xi. Additional safety measures should be strictly reviewed and approved by the ECs.

xii. The informed consent process should be well documented. Additional measures such as recording of assent and reconsent, when applicable, should be ensured.

xiii. ECs should also carefully determine the benefits and risks of the study and examine the risk minimization strategies

xiv. As potential participants are dependent on others, there should be no coercion, force, duress, undue influence, threat or misrepresentation or incentives for participation during the entire research period.

xv. Vulnerable persons may require repeated education/information

about the research, benefits, risks and alternatives, if any

xvi. Research on sensitive issues such as mental health, sexual practices/preferences, HIV/ AIDS, substance abuse, etc. may present special risks to research participants

xvii. Researchers should be cognizant of the possibility of conflicting interests between the prospective participant and LAR and should be more careful.

xviii. Participants may be prone to stigma or discrimination, specifically when the participant is enrolled as a normal control or is recruited from the general population in certain types of research.

xix. Efforts should be made to set up support systems to deal with associated medical and social problems

xx. Protection of their privacy, confidentiality and rights is required at all times – during conduct of research and even after its completion

xxi. Whenever possible, ancillary care may be provided such as setting up of a facility, school for unattended children of the participants or a hospital, or counselling centre.

xxii. An audio-video recording of the informed consent process in case of vulnerable subjects in clinical trials of New Chemical Entity or New Molecular Entity including procedure of providing information to the subject and his understanding on such consent, shall be maintained by the investigator for record: 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 procedure of providing information to the subject and his understanding on such consent shall be maintained by the investigator for record.

xxiii. The ethics committee should exercise particular care to protect the rights, safety and well-being of all vulnerable subjects participating in the study, e.g., members of a group with hierarchical structure (e.g. prisoners armed forces personnel, staff and students of medical, nursing and pharmacy academic institutions), patients with incurable

diseases, unemployed or impoverished persons, patients in emergency situation, ethnic minority groups, homeless persons, nomads, refugees, minors or other incapable of personally giving consent.

Obligations/duties of stakeholders

- **Researchers**

i. Recognize the vulnerability of the participant and ensure additional safeguards are in place for their protection.
ii. Justify inclusion/exclusion of vulnerable populations in the study.
iii. COI issues must be addressed.
iv. Have well defined procedures (SOPs) to ensure a balanced benefit-risk ratio.
v. Ensure that prospective participants are competent to give informed consent.
vi. Take consent of the LAR when a prospective participant lacks the capacity to consent.
vii. Respect dissent from the participant.
viii. Seek permission of the appropriate authorities where relevant, such as for institutionalized individuals, tribal communities, etc.
ix. Research should be conducted within the purview of existing relevant guidelines/regulations.

- **Ethics Committees**

i. During review, determine whether the prospective participants for a particular research is vulnerable.
ii. Examine whether inclusion/exclusion of the vulnerable population is justified.
iii. Ensure that COI do not increase harm or lessen benefits to the participants.
iv. Carefully determine the benefits and risks to the participants and advise risk minimization strategies wherever possible.
v. Suggest additional safeguards, such as more frequent review and

monitoring, including site visits.

vi. Only the full committee should do initial and continuing review of such proposals. It is desirable to have empowered representatives from the specific populations during deliberations.

vii. ECs have special responsibilities when research is conducted on participants who are suffering from mental illness and/or cognitive impairment. They should exercise caution and require researchers to justify cases for exceptions to the usual requirements of participation or essentiality of departure from the guidelines governing research. ECs should ensure that these exceptions are as minimal as possible and are clearly spelt out in the ICD.

viii. ECs should have SOPs for handling proposals involving vulnerable populations.

- **Sponsors**

i. The sponsor, whether a government, an institution or a pharmaceutical company, should justify the inclusion of vulnerable groups in the protocol and make provisions for protecting their safety.

ii. The sponsor must enable monitoring and ensure that procedures are in

iii. place for quality assurance (QA) and quality control (QC).

iv. The sponsor should ensure protection of the participants and research

v. team if the research is on sensitive topics.

- **Women in special situations**

Women have equal rights to participate in research and should not be deprived arbitrarily of the opportunity to benefit from research. Informed consent process for some women can be challenging because of cultural reasons. Hence, the women may consider consulting their husbands or family members, if necessary. Although autonomy of the woman is important, the researcher must follow the requirements of local cultural practices so as not to disturb the harmony in the household/family/community.

Risks for women participants in clinical trials/intervention studies

i. Researchers must provide the EC with proper justification for inclusion

of pregnant and nursing women in clinical trials designed to address the health needs of such women or their foetuses or nursing infants. Some examples of justifiable inclusion are trials designed to test the safety and efficacy of a drug for reducing perinatal transmission of HIV infection from mother to child, trial of a device for detecting foetal abnormalities or trials of therapies for conditions associated with or aggravated by pregnancy, such as nausea, vomiting, hypertension or diabetes

ii. If women in the reproductive age are to be recruited, they should be informed of the potential risk to the foetus if they become pregnant. They should be asked to use an effective contraceptive method and be told about the options available in case of failure of contraception

iii. A woman who becomes pregnant must not automatically be removed from the study when there is no evidence showing potential harm to the foetus. The matter should be carefully reviewed and she must be offered the option to withdraw or continue. In case the woman opts for continued participation, researchers and sponsors must adequately monitor and offer support to the woman for as long as necessary

iv. Prenatal diagnostic studies – research related to prenatal diagnostic techniques in pregnant women should be limited to detecting foetal abnormalities or genetic disorders as per the Pre-Conception and Pre-Natal Diagnostic Techniques (Regulation and Prevention of Misuse) Act, 1994, amended in 2003 and not for sex determination of the foetus.

v. Research on sensitive topics – when research is planned on sensitive topics, for instance, domestic violence, genetic disorders, rape, etc., confidentiality should be strictly maintained and privacy protected. In risk mitigation strategies, appropriate support systems such as counselling centres, police protection, etc. should be established. At no time should information acquired from a woman participant be unnecessary, hurtful or appear voyeuristic. The EC should be especially vigilant regarding these sensitive issues.

- **Children**

Children are individuals who have not attained the legal age of consent (up to 18 years). At younger ages, children are considered vulnerable because their autonomy is compromised as they do not have the cognitive ability to fully understand the minute details of the study and make decisions. At older ages, although they may attain the cognitive ability to understand the research, they still lack legal capacity to consent. Therefore, the decision regarding participation and withdrawal of a child in research must be taken by the parents/ LAR in the best interests of their child/ward

- **Children can be included in research if the situation, condition, disorder or disease fulfils one of the following Condition**
    i. It is exclusively seen in childhood.
    ii. Both adults as well as children are involved, but the issues involved are likely to be significantly different in both these populations.
    iii. Both adults as well as children are involved in a similar manner and are of similar nature in terms of morbidity, severity and/or mortality, wherever relevant, and studies in adults have demonstrated the required degree of safety and efficacy.
    iv. Test interventions are likely to be at least as advantageous to the individual child participant as any available alternative intervention.
    v. Risk of test interventions that is not intended to benefit the individual child participant is low as compared to the importance of the knowledge expected to be gained (minor increase over minimal risk).
    vi. Research is generally permitted in children if safety has been established in the adult population or if the information likely to be generated cannot be obtained by other means.
    vii. The physiology of children is different from that of adults, and the pharmacokinetics of many drugs is age-dependent based on the maturation of the drug metabolism pathways. For example, children metabolize many drugs much more rapidly as compared to adults,

hence the dose of the drug per kg of body weight that needs to be given, is much higher in children as compared to adults. The absorption of drugs also varies with age. Pharmacokinetics and toxicity profile varies with growth and maturation from infancy to adulthood.

viii. The adverse effects of many drugs may also be different in children as compared to adults. For instance, tetracyclines cause teeth discoloration in young children, aspirin use is associated with Reye's syndrome in children.

ix. Age-appropriate delivery vehicles and formulations (e.g. syrups) are needed for accurate, safe, and palatable administration of medicines to infants and children.

x. The pathophysiology of many disorders is dependent on a child's growth, development and adaptive plasticity. Examples include adaptive changes in the motor system following a perinatal stroke.

- The EC should do the benefit–risk assessment to determine whether there is a need to put into place additional safeguards/protections for the conduct of research in children. For example, research should be conducted in child-friendly settings, in the presence of parent(s) and where child participants can obtain adequate medical and psychological support.
- The EC should take into consideration the circumstances of the children to be enrolled in the study including their age, health status, and other factors and potential benefits to other children with the same disease or condition, or to society as a whole.

- ECs must ensure that processes are in place to safeguard the quality of ethical review as well as compliance with national/international and applicable regulations.
- ECs should register with the relevant authority as per the regulatory requirements.
- Efforts should be made to seek recognition/certification/accreditation from recognized national/international bodies such as Strategic Initiative for Developing Capacity in Ethical Review (SIDCER), Association for the Accreditation of Human Research Protection Programmes (AAHRPP), CDSCO and Quality Council of India through National Accreditation Board for Hospitals and Healthcare Providers (NABH) or any other. Such certification/accreditation should be kept updated on a continuing basis.
- Certification/accreditation are voluntary exercises and help in quality assurance and quality improvement to ensure that ECs follow best practices in protecting the dignity, rights, safety, and well-being of their participants.
- Allow any officer authorised by the Central Licencing Authority to enter, with or without prior notice, to inspect the premises, any record, or any documents related to clinical trial, furnish information to any query raised by such authorised person, in relation to the conduct of clinical trial and to verify compliance with the requirements of these rules, Good Clinical Practices Guidelines and other applicable regulations for safeguarding the rights, safety and well-being of trial subjects.

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

- AV recording of the entire informed consent process is mandatory for all clinical trials approved by the DCGI, provided that they come under the following categories.
- An audio-video recording of the informed consent process in case of vulnerable subjects in clinical trials including procedure providing information to the subject and his understanding of such consent, shall be maintained by the investigator for record.

An audio-video recording of the informed consent process in case of vulnerable subjects in clinical trials of New Chemical Entity or New Molecular Entity including procedure of providing information to the subject and his understanding on such consent, shall be maintained by the investigator for record.

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 procedure of providing information to the subject and his understanding on such consent shall be maintained by the investigator for record.

Principal investigator, Co-Investigator or any other medically qualified member of staff in the team, as delegated by the Principal Investigator, who have the responsibility of obtaining an informed consent, will also be responsible for ensuring AV recording of the informed consent process, storing and archiving without violating the participant confidentiality

References

1. New Drugs and Clinical Trials Rules, 2019 – CDSCO. https://cdsco.gov.in/opencms/export/sites/CDSCO_WEB/Pdf-documents/NewDrugs_CTRules_2019.pdf
2. Kasturba Medical College, Manipal IEC SOPs.