Mahamana Pandit Madan Mohan Malaviya Cancer Centre (MPMMCC) & Homi Bhabha Cancer Hospital, (HBCH), Varanasi (Unit of Tata Memorial Centre, Mumbai)

Standard Operating Procedures

Clinical Research Secretariat

February 2024

Standard Operating Procedure

Clinical Research Secretariat (CRS)

Mahamana Pandit Madan Mohan Malaviya Cancer Centre
And
Homi Bhabha Cancer Hospital

Table of Contents

MPMMCC/HBCH, Varanasi - Clinical Research Secretariat (CRS)

SOP Codes: SOP 01/V1, SOP 02/V1, SOP 03/V1, SOP 04/V1, SOP 05/V1, SOP 06/V1, SOP 07/V1, SOP 08/V1, SOP 08A/V1, SOP 09/V1, SOP 10/V1, SOP 11/V1, SOP 12/V1, SOP 13/V1, SOP 14/V1, SOP 14/V1, SOP 15/V1, SOP 16/V1, SOP 17/V1, SOP 18/V1.

Effective Date: 02nd February 2024

Authors:

Name, Position CRS	Signature
Dr. Himanshu Pandey Professor, OIC, Surgical Oncology, MPMMCC & HBCH	02/02/2024
Dr. Anuj Gupta Associate Professor, Medical Oncology, MPMMCC & HBCH	02/02/2024
Dr. Jyotirmay Kirtania Professor, Anae. Crit. Care. & Pain, MPMMCC & HBCH	2/2/24
Dr. Pratibha Gavel Associate Professor, Biochemistry, MPMMCC & HBCH	2/2/24
Mr. Bhavesh P Bandekar Scientific Officer 'C', CRS	02.02.2024.

Approved by:

Name, Position CRS	Signature
Dr. Aseem Mishra OIC CRS	2/2/24

Accepted by:

Name & Position	Signature
Dr. Satyajit Pradhan Director, MPMMCC & HBCH	02.02.2024

Reviewed by:

Name, Position TRAC	Signature
Dr. Soumitra Saha Member Secretary, IEC, MPMMCC & HBCH	J. Saha 02.02.2024
Dr. Lincoln Pujari Ex-Secretary, DSMU, MPMMCC & HBCH	2.2.24
Dr. Shreyasi Ray, Secretary, DSMU, MPMMCC & HBCH	Shreyasi Ray 02.02.24
Dr. Akhil Kapoor, Associate Professor, OIC, Medical Oncology, MPMMCC & HBCH	2/2/24
Ms. Rohini Hawaldar CONSULTANT (TRAC)	Rhawaldar
Dr. Pankaj Chaturvedi Dy. Director, MPMMCC & HBCH, Project In-charge, Varanasi	

Acknowledgment:

We would like to thank all CRS Coordinators for their valuable assistance. We would also like to thank Mr. Pawan Kumar Pandey for his contribution towards CRS Research Pharmacy Management chapters updated in CRS SOP 2024. Also, Ms. Natasha Sisodia and Ms. Ankita Pal for their contribution towards the SOP formatting.

Content

Standard Operating Procedure

Clinical Research Secretariat (CRS)

Title: Preparing Standard Operating Procedures (SOPs): Writing, Reviewing, Distributing & Amending SOPs for the Clinical Research Secretariat (CRS), TMC

SOP Code: SOP 01/V1 Date: 02nd Feb 2024 Pages: 01-09

Tata Memorial Centre

MPMMCC: Sunder Bagiya, Near Nariya Gate, Banaras Hindu University Campus, Varanasi-221005, Uttar Pradesh, India

HBCH: Homi Bhabha Cancer Hospital, Ghanti Mill Road, Old Loco colony, Lahartara, Varanasi-221002, India

1.1 Purpose

This SOP describes the process for writing, reviewing, distributing, and amending SOPs within the CRS, MPMMCC/HBCH, Varanasi, and also provides a tool for training new personnel in the procedures by which specific activities will be performed at MPMMCC/HBCH, Varanasi.

This SOP will provide clear, unambiguous instruction to conduct activities of the CRS by the ICMR guidelines 2017, New Drugs and Clinical Trials Rules, 2019(NDCT Rules 2019), International Council on Harmonization (ICH) Good Clinical Practice (GCP) E6/R2, Indian GCP guidelines 2002, and all other regulatory guidelines as issued from time to time and Gazette notifications and its amendments as issued from time to time

1.2 Scope

This SOP covers the procedures of writing, reviewing, distributing, and amending SOPs within the CRS, MPMMCC/HBCH.

1.3 Procedure

OIC CRS will determine the activities which require SOPs and will appoint SOP team to formulate the SOPs. SOP team will consist of OIC CRS, CRS core team (comprising of former CRS OICs) and identified experienced CRS coordinator(s). SOP team will prepare the draft of the SOPs with description of the procedure (i.e., a detailed description of all tasks to be conducted under the SOP, including when they are to be accomplished, where, and by whom). Each step in the procedure will be numbered. All new or unusual terms will be defined. If an abbreviation is associated with a term, it will be placed in parentheses following the word. SOP team will also be responsible to amend the SOPs as and when required.

The draft SOPs will be reviewed by SOP review team (1-2 members of TRAC). The OIC CRS will approve the SOPs. The SOPs will then be signed by Director, MPMMCC/HBCH, Varanasi as these are for conduct of research studies at MPMMCC/HBCH, Varanasi.

The SOP team will-

- Assess the request(s) for SOP revision
- Propose a new SOP, or modification in existing SOPs as needed
- Select the format and coding system for the SOPs
- Draft the SOP
- Submit the draft for approval

OIC CRS

- Appoint SOP Teams
- Reviews and approves the SOPs
- Signs and dates the approved SOPs

Review Team

- Review and sign and date SOPs
  CRS Core team
- Assists in the formulation of SOP procedure

The Clinical Research Secretariat:

- Co-ordinates activities of writing, reviewing, distributing, and amending SOPs.
- Maintains a file of all previous SOPs of the CRS
- Maintains on file all current SOPs and the list of SOPs.
- Maintains a file of all SOP amendment requests.
- Maintains an up-to-date distribution list of each SOP circulated.
- Maintain a record of the investigators to whom SOPs are distributed
- Ensures that all members involved in conducting research at TMC have access to the SOPs

1.3.1. Identify the need for new SOP or amendment to the SOP

Any member of the CRS, SOP review team (1-2 members of TRAC), Investigator or other research team member, who notices an inconsistency or discrepancy / has any suggestions on how to improve the existing SOPs or requests to design an entirely new SOP, can make a request for revision by putting forth his / her request by using the Request Form for Formulation of new SOP/ Revision of an SOP Form (AX4-V1/SOP01/V1). This Formulation of new SOP/ Revision of an SOP Form (AX4-V1/SOP01/V1) is submitted to the OIC CRS. The OIC CRS will inform TRAC Committee.

If OIC CRS and TRAC committee agrees to the request, the OIC CRS will appoint an appropriate SOP team. This designated team will proceed with the task of revision / formulation process of the SOP.
If OIC CRS and TRAC Committee do not agree to the request, no further action will be taken.

The OIC CRS will inform the person who made the request for modification of the SOP in writing about the decision.

1.3.2 Appoint the SOP team

The OIC CRS will constitute SOP teams who have a thorough understanding of the ethical conduct of research studies. The SOP team will carry out the subsequent steps. (1.3.3-1.3.7)

1.3.3 List of relevant SOPs

- Write down step by step all the procedures for conduct of research
- Organize, devise and name each process
- Make a list of SOPs with coding format (e.g. AX1-V1/SOP01/V1)

1.3.4 Design a format and layout

Each SOP should be given a number and a title that is self-explanatory and is easily understood

A unique code number with the format SOP xx / Vy will be assigned to each SOP. xx is a two-digit number assigned to a specific SOP. “V” refers to version of the SOP and “y” is a number identifying the version e.g. SOP01/V1 is SOP number 01 with V=version no.02

Each Annexure (AX) is unique code with format AXn–Vp/SOP xx/Vy. e.g. AX1–V1/SOP01/V1 indicates AX is Annexure, 1 is Annexure no., V1 is version 2, belonging to the SOP 01/V1

Each Appendix will be given unique code with the format APPn/Vy e.g. APP1/V1 indicates APP is Appendix, 1 is Appendix no 1 and V1 is Version no.1

Each SOP will be prepared according to the template for Standard Operating Procedures (AX2-V1/SOP01/V1). Each page of the SOP will bear a header with the effective date which is the date of acceptance of the SOPs by the director, TMC.

1.3.5 Write, Review and Approve SOP

With reference to section 1.3.1 and 1.3.2 the draft SOP will be prepared by the SOP team

1.3.6 Review by Consultation

- The draft SOP will be reviewed by 1-2 members of TRAC committee and all Investigators.
- The SOP should be approved by all involved in that particular task.
- The final version will be forwarded to the OIC CRS for review and approval.

1.3.7 Preparation and submission of final draft

- SOP review team (1-2 members of TRAC) may review the draft / revised SOP
- During respective CRS meetings, members can put forth their suggestions / comments on the draft / revised SOP
- The suggestions agreed upon unanimously by CRS SOP team and SOP review team (1-2 members of TRAC) will be incorporated and the final SOP will be formulated
- The SOP team would stand automatically dissolved once the OIC CRS takes final decision regarding the SOP.
- Preparation and submission of final draft.

1.3.8 Final Approval of new/revised SOP

- The final version will be presented to the OIC CRS for review and approval. The OIC CRS will sign and date the SOP on the first page of the SOP document.
- This approved document will then be submitted to the MPMMCC/HBCH, Varanasi for acceptance. This date of acceptance is declared as the effective date for implementing the SOP.

1.3.9 Implementation, distribution and filing of SOPs

- Approved SOPs will be implemented from the effective date.
- The OIC CRS will inform the Investigators about the approved SOPs and instruct them to implement the SOP accordingly

- When a revised version is distributed, the old version will no longer be effective. A copy of the old version will be archived in a master file.
- One complete original set of current SOPs will be archived in the SOP master file, by the CRS and maintained in the CRS Office.
- Photocopies made from the paper versions of the SOP will be considered official (controlled version) only if stamped and signed by OIC CRS or an authorized individual. A distribution log should be maintained (AX5 –V1/SOP 01/V1)
- The uncontrolled copy of SOP will be readily available on MPMMCC & HBCH Website.(https://mpmmcc.tmc.gov.in/)

1.3.10 Review and request for revision of an existing SOP

- Any member of the CRS core team, TRAC committee or research team member who notices that current SOPs have some lacunae or have any suggestions to improve a procedure should make a written request, using a form (AX4-V1/SOP 01/V1)
- If the CRS and TRAC committee agree with the request, the OIC CRS will appoint an appropriate team for the revision process. If the committee does not agree, the OIC CRS will inform the concerned individual who made the request for revision.
- SOP will be reviewed yearly by the OIC CRS & CRS core team and will check if any important information or change needs to be included in the SOP. OIC CRS will decide to update/amend the SOP depending upon the need and requirement.
- Revised SOPs will be reviewed and approved as per Section 1.3
- The OIC CRS initializes the review of the SOP at least once every 3 years (all the updated guidelines will be incorporated) and records the dates of review in the SOP master file.

1.3.11 Manage and archive old SOPs

Old SOPs should be retained and clearly marked “superseded” and archived in a file by the secretariat. The process of evolution of previous SOPs of the IEC will be documented in secretariat. The process of evolution of previous SOPs of the CRS will be Documented in a defined format (AX3 –V1/SOP01/V1).

AX1-V1/SOP 01/V1

List of SOPs of Clinical Research Secretariat

Sr. No.	SOP TITLE	SOP CODE	Page Nos.

AX2-V1/SOP 01/V1

Template for Standard Operating Procedures

Clinical Research Secretariat	
Title: Title which is self-explanatory and easily understood	
SOP No: SOPxx/Vy	**Page:** a of b
SOP Code: SOP xx/Vy **Effective Date:** DD/MM/YYY **Authors:** xxxxxxxxxx **Reviewed by:** xxxxxxxx **Approved by:** xxxxxxx	

AX3-V1/SOP 01/V1

Document History of the SOP

Name of the author	Version	Effective date (dd-mm-yy)
NA	**NA**	**NA**

AX4-V1/SOP 01/V1

Request for Formulation of new SOP/ Revision of SOP

This form is to be completed by anyone who identifies a problem or a deficiency in an SOP until an authorized replacement is in place.

SOP No.	
Title:	
Details of problems or deficiency in the existing SOP: SOP Chapter No- Any specific point- Details-	
Identified by:	Sign and Date (DD/MM/YYYY):
FOR CRS OIC USE ONLY	
Need to formulate an entirely new SOP (i.e. SOP not existing previously) ☐ Yes ☐ No	
Discussed/ communicated with CRS core team on:	
SOP revision required: ☐ Yes ☐ No	
New SOP to be formulated: ☐ Yes ☐ No	
If yes, to be carried out by whom?	
If no, why not?	
Date SOP revised:	
Date SOP approved:	
Date SOP becomes effective:	

AX5-V1/SOP 01/V1

Log of SOP recipients

No.	Name of the Recipients	Designation	SOP code number	No. of copies	Date

Standard Operating Procedure

Clinical Research Secretariat (CRS)

Title: Assessing Protocol feasibility; for Investigator-initiated& Sponsored /Pharma Studies

SOP Code: SOP 02/V1 Date: 2nd Feb 2024 Pages: 10-17

Tata Memorial Centre

MPMMCC: Sunder Bagiya, Near Nariya Gate, Banaras Hindu University Campus, Varanasi-221005, Uttar Pradesh, India

HBCH: Homi Bhabha Cancer Hospital, Ghanti Mill Road, Old Loco colony, Lahartara, Varanasi-221002, India

2.1 Purpose

To describe the procedures for assessing the feasibility of conducting a study at MPMMCC/HBCH, Varanasi in compliance with the protocol, for Investigator-initiated studies & sponsored /Pharma studies.

MPMMCC/HBCH, Varanasi is committed to maintain the highest scientific, clinical and ethical standards while conducting research at MPMMCC/HBCH. Further, MPMMCC/HBCH is committed to comply with all applicable regulations and guidelines in this regard. In view of the same, before agreeing to participate in a clinical research study, the Principal Investigator (PI) and Institution must agree to the scientific, clinical, and ethical merits of the study; the financial impact to the hospital; compliance with regulations; and the operational feasibility of conducting the study at MPMMCC/HBCH. This standard operating procedure (SOP) describes the steps for assessing the feasibility of conducting a study at MPMMCC/HBCH.

Additionally, Institution and PI should consider, the potential benefits and relevance of the proposed studies to cancer care in MPMMCC/HBCH and evaluate the study in the context of our research priorities.

This standard operating procedure (SOP) describes the steps for fulfilling the regulatory, medical, and ethical requirements for assessing the appropriateness and feasibility of implementing a protocol within the MPMMCC/HBCH research network.

2.2 Scope

This SOP applies to the activities involved in assessing protocol feasibility for all research studies conducted at MPMMCC/HBCH involving human subjects/participants.

This SOP applies to the assessment of protocols for Investigator-initiated& sponsored /pharma studies.

2.3 Procedure

2.3.1 Protocol Assessment

The principal Investigator & DMG members will assess whether the proposed protocol is feasible to conduct with the existing staff and facilities. PI can use protocol checklist to ensure if it is feasible to conduct the study, as per the available protocol, at MPMMCC/HBCH (AX1-V1/SOP 02/V1)

In case of sponsored study, the sponsor can contact eligible PI for the potential study, for checking the study feasibility at site.

In case of sponsored study, the PI will give the feedback regarding the feasibility of the study,

The PI will discuss the new protocols in the respective Disease Management Group (DMG) meeting and seek DMG member’s feedback and approval for the conduct of the study before IEC submission.

2.3.1.1 Clinical/Scientific/Ethical Feasibility

- Clinical importance to MPMMCC/HBCH patients.
- Scientific merit.
- Benefits and risks associated with the protocol.
- Consistency with the priorities of the hospital and the clinical department.

2.3.1.2 Operational Feasibility

- Availability of personnel and other resources required to conduct the study.
- Availability of patients meeting the inclusion / exclusion requirements of the study.
- The level of interest expected from the physicians needed to recruit patients into the study.
- The operational complexity of the protocol.
- Whether there are any conflicting studies in progress.

2.3.1.3 Regulatory Feasibility

- The PI reviews the protocol to determine preliminary feasibility and identifies potential hurdles/ difficulties when submitting the project to the IEC. The PI/ CTC can consult with IEC administrator and refer IEC SOP for the same.

- The PI must check the following points before submitting the protocol to the IEC for approval:

o Research studies have the resources/procedures in place which would be necessary to protect subjects/participants:

o Adequate time for the researchers to conduct and complete the research.

o Adequate number of qualified staffs for the conduct of the study

o Adequate facilities

o Access to a population that will allow recruitment of the necessary number of subjects/participants.

o Availability of medical or psychosocial resources that subjects/participants might need as a consequence of the research.

2.3.1.4. Financial/ Legal Feasibility

- A detailed review of the costs, including time and resources needed to complete protocol activities and patient care visits are determined by the PI.
- The PI prepares the budget worksheet (for both Investigator-initiated& Pharma studies).
- The PI will discuss and negotiate with the sponsor to establish a feasible budget. Once an agreement is made, the budget will be signed by the PI and sent to the sponsor (for sponsored /pharma studies).

- If an agreement cannot be reached with the study sponsor to cover all costs of the study, the PI and CTC will work together to determine whether the study can still be conducted at MPMMCC/HBCH (for sponsor/pharma studies).
- The MPMMCC/HBCH Legal department will facilitate legal review of the contract.
- For all investigator-initiated studies the budget will be prepared as per IEC SOP with proper justification.

2.3.2 Decision

All the above-mentioned points (2.3.1.1, 2.3.1.2, 2.3.1.3 & 2.3.1.4) will be discussed in the respective DMG meeting.

Decision will be taken by consensus in the DMG meeting for the conduct of the protocol at MPMMCC/HBCH. DMG convener will minute the same in the respective DMG minutes of meeting.

The PI will notify the sponsor (in case of sponsored study) of the site's decision. In the event that the protocol does not meet the above-mentioned criteria the convener may, at his/her discretion, provide rationale for the decision to the PI and PI will inform the same to the sponsor, allowing the sponsor opportunity to make changes in the suggested part of the protocol and have it reassessed.

In case of Investigator-initiated studies, PI will make the required changes in the protocol as suggested by the DMG members or can provide rationale for the same.

PI will submit the protocol to IEC for review and approval after incorporating all the changes suggested by DMG members (if any) in the protocol.

Note: For all Investigator-initiated/Investigator-Sponsor/Collaborated studies, the above-mentioned procedure will be same for assessing the feasibility of the study, only the sponsor role will be performed by the Principal Investigator conducting the trials. The protocol feasibility should be checked by Principal investigator.

2.4 Applicable areas of the Hospital

- Applicable PIs Departments
- Disease Management group (DMG)
- MPMMCC/HBCH, Varanasi

2.5 Applicable Staff

This SOP applies to all the personnel of the clinical research team and DMG members and others who may be responsible for making decisions regarding conducting research studies at MPMMCC/HBCH.

These include the following:

- Investigator
- Disease Management Group members (DMG)
- Legal Expert
- Research Team

2.6 Staff Responsible for Implementation

OIC CRS will ensure that the SOP is updated and available on the MPMMCC/HBCH website for all the Investigators conducting studies and Investigators will ensure that the research team involved in the conduct of the study will comply with this site SOP.

PI at his/her level will ensure that at the time of implementation of the SOP, that the research team at MPMMCC/HBCH are trained and in the event that an SOP is modified, provide training regarding the change(s) and ensure their compliance with the changes.

Inform IEC that this site SOP will be implemented within the institution.

AX1-V1/SOP 02/V1

PROTOCOL FEASIBILITY CHECKLIST

Factors to consider:

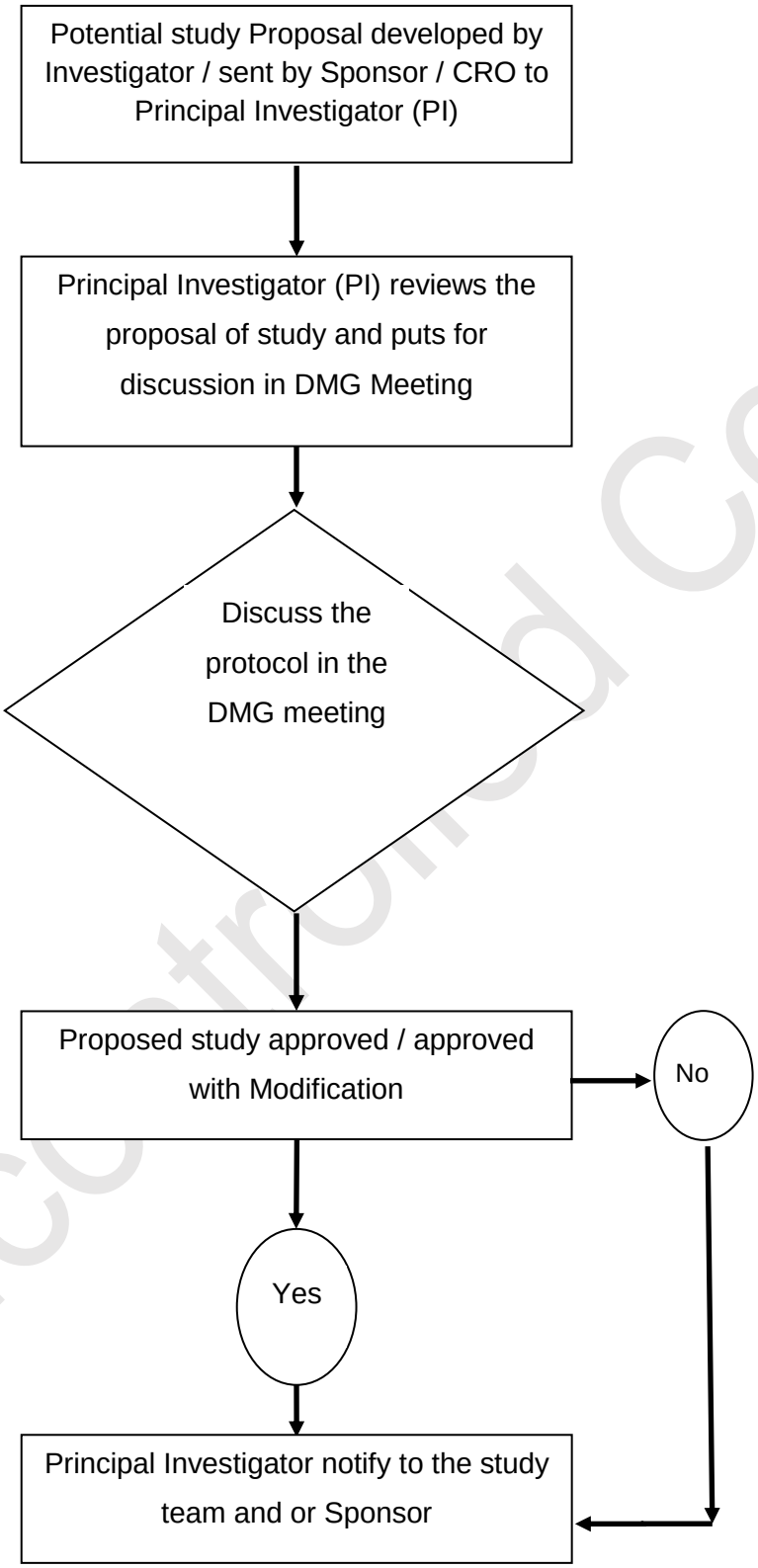
1. Population	
Do you have access to the right patient population?	
Will you need to recruit subjects/participants from external sources? If so, will sponsor provide funding?	
Is the proposed enrollment goal realistic?	
Is the proposed enrollment period realistic?	
Will enrollment compete with other studies seeking the same subjects/participants?	
Are inclusion/exclusion criteria overly restrictive? (Consider the likely screen failure ratio and the number of screen failures)	
Do you expect a significant number of adverse events? (How ill is this population?)	
2. Protocol	
Is the protocol well designed?	
Is the protocol ethical? Will the IEC have problems with it?	
Is the study question important?	
Will the subjects/participants benefit from participating in the study?	
Is the sponsor willing to consider suggestions or modifications if you do not think the protocol is feasible as written? (In case of sponsored study)	
Can other services (e.g., lab, radiology) meet the protocol requirements?	
Is necessary equipment available?	
Are participant's compliance problems likely? If so, will it be necessary to monitor subjects/participants' compliance with time-consuming phone calls or postcards?	
Are case record forms complex?	
Are drug or device storage/accountability requirements complicated?	
Will the drug be available for patients at the end of the study? (This can impact patient satisfaction.)	
3. Procedures	
Are procedures frequent? Are they over and above the standard of care?	
Are procedures difficult?	
Are procedures painful?	
Is the dosing schedule complex?	
4. Staff	
Are qualified staff available	
If needed, is training available?	
Does the PI have adequate time to devote to the protocol?	
Are additional specialists needed?	

AX1-V1/SOP 02/V1

PROTOCOL FEASIBILITY CHECKLIST

Factors to consider:

Are study visits complex, presenting possible scheduling difficulties, e.g., how many different study staff will participants have to meet in a given visit?	
5. Budgets	
Does preliminary budget appear adequate? (Sponsors or investigator generated)	
If the study is canceled prior to enrollment, will the sponsor pay for pre-study activities, e.g., IEC submission, meetings, chart reviews?	
Will sponsor pay for an adequate number of screen failures (especially important for difficult protocols)?	
Will the proposed payment schedule allow you to keep afloat, e.g., adequate up-front payment; payments paced according to work required by protocol?	
Any other protocol required equipments or procedure etc.	
6. Other	
Is adequate space available?	
Will electronic or remote data retrieval systems be used? If so, will sponsor provide training?	
Does the sponsor/PI expect this study to be audited by the regulatory bodies?	



Standard Operating Procedure

Clinical Research Secretariat (CRS)

Title: Clinical Trial Agreement (CTA)/Memorandum of Understanding (MoU)

SOP Code: SOP 03/V1 Date: 2nd Feb 2024 Pages: 18-24

Tata Memorial Centre

MPMMCC: Sunder Bagiya, Near Nariya Gate, Banaras Hindu University Campus, Varanasi-221005, Uttar Pradesh, India

HBCH: Homi Bhabha Cancer Hospital, Ghanti Mill Road, Old Loco colony, Lahartara, Varanasi-221002, India

3.1 Purpose

- This Standard Operating Procedure (SOP) describes the manner in which the Clinical Trial Agreement (CTA)&/or Memorandum of Understanding (MoU) between the Institution and/or principal investigator and another entity for the purpose of conducting research, are to be reviewed, processed and accepted. These other entities may include, but are not limited to; industry or commercial sponsors, contract research organizations (CROs), or other research collaborators.

- This SOP is in place to ensure that both, MPMMCC/HBCH and the Principal Investigator (PI), are legally protected in all necessary areas applicable to their specific project.

3.2 Scope

This SOP will apply to all industry-sponsored trials conducted at MPMMCC/HBCH (CTA) or Investigator-initiated studies which are multicentric or receive extramural funding (MOU).

3.3 Procedure

3.3.1. Review of draft CTA/MoU

Sponsor/CRO/Collaborating centre will provide draft CTA/MoU to Principal Investigator for finalization (for sponsor/pharma project). Investigator will draft a respective CTA/MoU for specific protocol to be conducted in MPMMCC/HBCH or for multicenter trial.

The Principal Investigator (PI) will send the draft CTA/MoU to the MPMMCC/HBCH legal department, and IEC (along with initial submission of project) for review.

The PI must check that the following elements, **when applicable** should be included in the contract to cover GCP and other responsibilities:

- Sponsor's name and address
- Institution name and address
- PI name and Address
- Protocol title with IP name
- A listing of the study, clinical, and legal responsibilities of Investigator site
- Effective date of CTA/MoU
- Estimated study starts and finish dates
- Terms of payment including terms for delays and termination of the study
- Number of study subjects/participants required to enter and complete the study and the criteria for a "completed" (fully paid) study subjects/participants
- Confidentiality agreement
- Information on personal data and biological material if any

- Dissemination of findings, and publication rights
- Data ownership rights
- Indemnification
- Research related injury responsibilities including the provision and payment and/or reimbursement of necessary medical care for research subjects/participants when appropriate
- Compensation guidelines
- Guidelines or requirements for promptly reporting findings that could affect the safety of subjects/participants or influence the conduct of the study
- Data and safety monitoring process and reporting requirements
- The notification to the PI/ study team by the Sponsor and/or CRO/collaborating centre of study results after the study has ended when participant safety could be directly affected by those study results, in order to consider informing subjects/participants
- Other legal issues as necessary per MPMMCC/HBCH Legal department(s).
- Clause on **25 % Institutional overhead** (15 % Professional service charges and 10 % TMC Service charges) on overall study budget
    - **15%** Professional charges of the actual expenditure incurred for the study will be charged at the end of every financial year
    - **10 %** TMC service charges of the total budget will be charged one time.

- Clause on sharing the invoices for the investigations/protocol procedures mentioned in the study protocol for the pharma sponsored studies. i.e. actual bills will not be shared to the sponsor for the payment made to the site.

- Archival fee is applicable as per the institutional policy. (Rs.10,000 / year per project)

PI/IEC/MPMMCC/HBCH Legal department must check for the availability of point in Contracts or other funding agreements that require the sponsor to promptly (no longer than within 30 days) report to the organization in case of any findings that could:

- Affect the safety of subjects/participants.
- Influence the conduct of the study or alter the IEC's approval to continue the study.

The MPMMCC/HBCH Legal department and IEC will correspond with the PI regarding any revisions that are required in the CTA.

MPMMCC/HBCH Legal department will approach Institutional head, in case of queries.

3.3.2 Revision of CTA/MoU

The MPMMCC/HBCH Legal department will correspond with the PI in case of suggestion/revision.

IEC will also correspond with the PI regarding any revisions that are required in the CTA/MoU.

In case of sponsored study PI will further correspond with the sponsor/CRO/collaborators for all the relevant suggestion/revision and changes if any put forward by MPMMCC/HBCH Legal department and IEC.

MPMMCC/HBCH Legal department, IEC may coordinate with respective PI with regards to suggestion/comments raised in the CTA/MoU, before finalization.

The PI will liaise with all the parties involved (IEC/Sponsor/Collaborators/MPMMCC/HBCH Legal dept) for all the correspondences with respect to CTA finalization.

Further PI or Sponsor (in case of sponsored study) will check the revision suggested and incorporate the suggested changes as applicable.

3.3.3 Finalization of CTA/MoU

Once the CTA/MoU is approved by the MPMMCC/HBCH Legal department and IEC, PI will further correspond with the sponsor/CRO/collaborators.

A minimum of three originals CTA should be prepared on stamp paper (Kindly refer IEC SOP for the value of stamp paper to be used for respective studies)/ as agreed by the sponsor/collaborators or as many originals as the Sponsor/CRO/collaborator specifies.

A minimum of three original finalized MoU can be printed on Stamp paper/Institutional Letter Head as agreed by both the parties involved and recommended by IEC. (Kindly refer IEC SOP for the stamp paper value to be used for respective studies CTA/MoU).

PI is responsible for assuring that all required signatures are obtained. All originals should be identical and have consistent signatures and dates.

Note: Institutional Head will sign the CTA /MoU only after IEC approval.

After signature of the Institution head (along with the institution stamp) and Principal investigator the originals will be sent to the Sponsor/CRO/Collaborator for signature.

A copy will be retained in the interim; this copy will be discarded when the signed original is returned from the sponsor/CRO/collaborator.

One copy of CTA will be submitted to Institution head, one will be retained by Principal Investigator and the other will be with the Sponsor/CRO/collaborator. The PI should keep the signed CTA/MoU in TMF/SMF.

One copy of the CTA/MoU will be submitted to the IEC for approval before the conduct of the

study at site.

3.3.4 Addendum/Amendment to CTA/MoU

During the course of the study, PI/Sponsor/collaborating centre can amend the CTA/MoU if required.
Any addendum/Amendment to the CTA also needs to be reviewed by MPMMCC/HBCH legal department and a copy will be submitted to IEC for review and opinion if any.
If any change is suggested by the PI, MPMMCC/HBCH legal department and/or IEC, the same will be discussed with the Sponsor (for sponsored study)/ Collaborating centre and finalized changes should be incorporated in the CTA/MoU.
Copy of the amended CTA/MoU will be submitted to IEC for review and approval if any.
One copy each of finalized (signed and dated) amended CTA will be retained by PI, one by the Institution head and one by the sponsor.
One copy of the finalized (signed and dated) amended CTA/MoU will be submitted to the IEC**.**

3.3.5 Memorandum of Understanding (MoU)

Site should have signed MoU for all Multicentric Investigator-initiated trials or Sponsor Investigator-initiated trials or Collaborative trials in which third party is involved expect other TMC institutes. Kindly follow IEC SOP for MoU templates and guidelines.

3.4 Applicable areas of the Hospital

- Legal Department
- IEC
- MPMMCC/HBCH, Varanasi
- Investigator (PI)

3.5 Applicable staff

This SOP applies to all members of the clinical research team involved in the process of finalizing the Clinical Trial Agreement at site. These include the following:

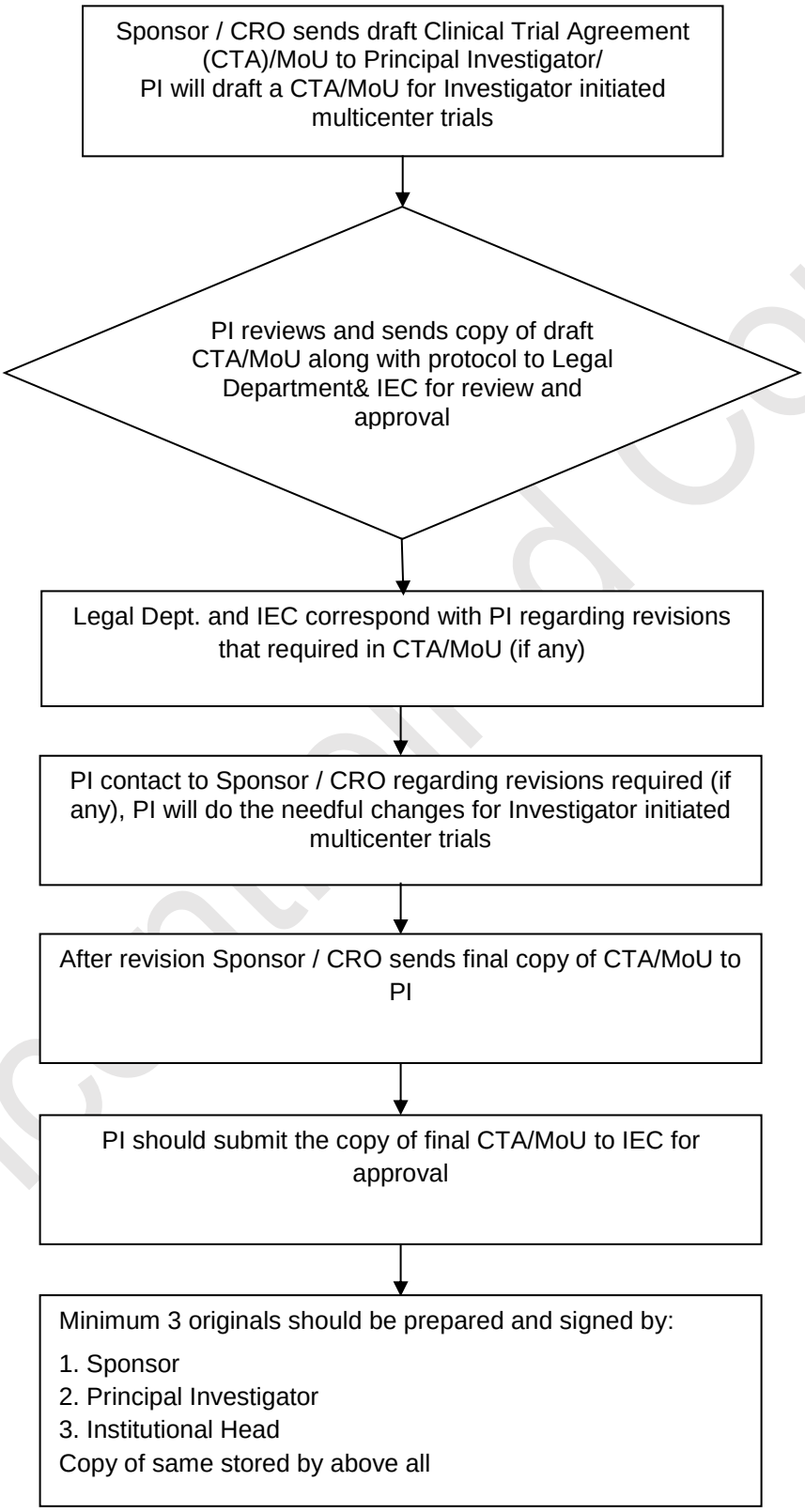
- Principal Investigator
- Legal Expert
- IEC
- Institution Head

3.6 Staff responsible for Implementation

OIC CRS will ensure that the SOP is updated and available on MPMMCC/HBCH website for all the Investigators conducting studies and Investigator will ensure that the research team involved in the conduct of the study will comply with this site SOP.

PI at his/her level will ensure that at the time of implementation of the SOP, that the research team at MPMMCC/HBCH are trained and in the event that an SOP is modified, provide training regarding the change(s) and ensure their compliance with the changes. Inform IEC that this site SOP will be implemented within the institution.

CTA Process



Standard Operating Procedure
Clinical Research Secretariat (CRS)

Title: Interaction with Institutional Ethics Committee (IEC)

SOP Code: SOP 04/V1 Date: 2nd Feb 2024 Pages: 25-45

Tata Memorial Centre

MPMMCC: Sunder Bagiya, Near Nariya Gate, Banaras Hindu University Campus, Varanasi-221005, Uttar Pradesh, India

HBCH: Homi Bhabha Cancer Hospital, Lahartara, Old Loco colony, Shivpurwa, Varanasi-221002, India

4.1 Purpose

To describe the procedures related to communication with the IEC during the entire study duration right from study initiation to completion, and to describe what documents should be retained to reflect interaction with the IEC.

4.2 Scope

This SOP will apply to all studies being conducted at MPMMCC/HBCH.

4.3 Procedure

Interactions with the Institutional Ethics Committee (IEC) continue throughout the duration of a research study. Establishing effective ongoing IEC communication and reporting procedures are essential to the successful management of research studies. An effective working relationship with the IEC strengthens the team approach to the protection of subject/participant safety in addition to enhancing compliance with applicable SOPs, guidelines and regulations governing research studies.
All study team members should also refer to the current version of IEC SOP available on the MPMMCC/HBCH website.

Interaction with IEC required during the entire course of the research study, can be in the following phases:

4.3.1 Initial Submission of project to IEC

a. Detailed description of project submission

- The PI/ CoI/Study team member should submit all study related documents to the IEC, no fewer than Twenty-one (21) days before the scheduled meeting date.

- IEC has developed an IEC portal https://iecportal.org for online project submission. PI must submit the new proposal & other study documents through online portal. PI/CoI/study team member will have to create login ID and password on the IEC web portal by creating their profile on the online system.

- The PI/CoI/ Study team member should complete the online IEC submission form (Refer IEC SOP). After completion & uploading the required documents the PI/CoI/ Study team member shall submit the project. Further IEC administrator will check the submitted project for completeness.

- *In case of incorrect/incomplete (as per IEC SOP) submission PI/CoI will receive a notification **"error in submission"***. The investigator must login to the IEC portal to view the notifications from the IEC administrator, on the investigator dashboard. Additionally, an auto

email will also be sent to the investigator with document requests and other administrative findings and queries.

- PI/CoI should submit the final project after responding to the queries generated by the IEC administrator, and after receiving an email notification of satisfactory online submission, submit a hard copy of all the online submitted documents.

- PI must sign and date in the form wherever required. CTC will obtain the CoI and other team member's (e.g. DMG convenor/Senior member, HOD) signatures wherever required.

- PI/Co-I/ Study team member must check the submissions as per the IEC checklist (AX1-V3/SOP04/V3), Refer IEC SOP) to ensure that all mandatory forms and documents are enclosed.

- The Study team member will submit the signed forms and documents to the IEC. These include, but are not limited to:

  - Covering letter with brief description regarding the list of documents enclosed for IEC approval, including the no. of copies submitted, documents enclosed, relevant version number and date of all the documents (**AX1-V3/SOP 04/V3**).
  - Project submission Form as mentioned above
  - Study protocol
  - Other related documents necessary for initial review as mentioned in the IEC
  - Curriculum Vitae and updated GCP certificate of the investigators and study team.
  - **IEC fees of Rs. 40,000/- + applicable GST for initial review and Rs. 10,000/- + applicable GST** for review of protocol amendments for ongoing study should be levied in the favour of **"Homi Bhabha Cancer Hospital",** in case of sponsored/pharma studies. The fees may be paid online via NEFT transfers, as cheque or demand draft drawn in favor of "Homi Bhabha Cancer Hospital".
  - *Note: Kindly check the IEC SOP/Circular for any revision in IEC fees.*
  - Number of copies required for IEC submission will be as per IEC SOP

  Note: One additional copy needed for PI Acknowledgement

- The PI/Study ream member should keep a copy of the acknowledged (IEC stamp with sign and date) submission letter of the above-mentioned documents in the respective Trial Master File (TMF) and send scan or copy to the sponsor.

- PI/ Study team member must document the unique "Project no." given by the IEC after project submission for future communication and collect updated IEC membership roster and IEC registration number and should place it in the Trial Master File (TMF).

  Note: The IEC will accept new submissions from Principal Investigators only after ensuring that continuing review applications/status reports of the previously approved studies have

been submitted by the Principal investigator in a timely manner. The IEC will not accept a new research proposal from the PI unless the PI has submitted continuing review application/status reports for ongoing IEC approved studies.

b. IEC Response

All the submitted documents will be reviewed and discussed in the IEC meeting as per IEC SOP and IEC decision will be conveyed to PI through IEC response letter. The PI and Study team member should ensure that the letter of response from the IEC includes the following information:

- Clinical study identification, protocol number and title;
- Name and version date of all documents reviewed by the IEC.
- Date of review by the IEC
- Approval for the number of subjects/participants to be recruited in the study.
- Location of study conduct
- Information regarding the study register in the Clinical Trials Registry (if applicable)
- Decision/opinion/approval of the clinical study, including modifications required, if any (Note: PI needs to reply to the IEC in case of any modifications suggested, see below)
- If any other information, if applicable, as described in the IEC SOP
- Date of renewal of approval
- Signature of the IEC member secretary and date of the response.
- List of IEC members and their affiliation and role, that were present at the project discussion.
- The PI/ Study team member should keep an original copy of the IEC approval letter in the TMF and provide one copy to the sponsor/CRO (where applicable).
- Regulatory submission of DCGI (CDSCO)/ HMSC approval letter if applicable.

Immediately after receiving IEC approval, the PI should register the study on CTRI (Clinical Trial Registry of India) and if applicable on ClinicalTrials.gov (for investigator-initiated studies). For sponsored study, sponsor will register the study on CTRI and will provide the CTRI number to the PI.
PI shall notify the registration number(s) to IEC after receiving them.

After review of the submitted protocol in the IEC meeting, the IEC will issue a final approval letter or release a letter with a suggestion of minor or major modification. In such situation PI/CoI shall follow the following steps;

a. Minor revisions of study after initial review for approval;

As per IEC SOP, modifications done after initial review of the project that do not alter the risk-benefit assessment for the research and do not require substantial changes in protocol and informed consent document fall under the category of IEC decision **"revision with minor modifications/amendments**"

b. Major modifications/revisions of study after initial review for approval;

As per IEC SOP, modifications done after initial review of protocol that may alter the risk-benefit assessment for the research and require substantial changes in protocol and informed consent documents are categorised as **"revision with major modifications for resubmission"**

- Principal Investigator has to comply with the changes suggested by IEC and respond to the queries. The revised project will then be reviewed in the next meeting.
- The response of IEC could be in the following;
  - **Not approved**- The study is not approved in its current form. A negative decision on an application will be supported by clearly stated reasons. If the investigator wishes to appeal to the decision, he/she may do so by contacting the IEC Secretariat.
  - **Deferred-** The decision cannot be arrived at present and therefore is postponed to next meeting. Grounds for this may be: lack of quorum, lack of expertise etc.
  - **Noted-** Study documents that are notified to IEC.
  - **Query**- Further clarification/modification required
  - An IEC may decide to reverse its positive decision on a study if it receives information that may adversely affect the risk/benefit ratio/ safety of subjects/participants.
  - Any advice by the IEC that is non-binding will be appended to the decision.
  - The discontinuation of a trial will be recommended if the IEC finds that the goals of the trial have already been achieved midway, unequivocal results are obtained or if the IEC feels the continuation of the trial may potentially harm subjects/participants.
  - If necessary, the investigator may be invited to present the protocol or offer clarifications in the meeting. Representative of the patient groups or community can be invited during deliberations to offer their viewpoint.
  - Subject expert/s may be invited to offer their views or their review comments would be considered. The expert/s should not participate in the decision-making process. However, his / her opinion must be recorded.

- PI/CoI will submit a copy of the revised study related documents along with justification for modification, and clearly highlighted / demarcated sections with track changes for all the sections that have undergone changes.

- The IEC administrator will verify the completeness of the submitted documents as per IEC SOP and the PI will receive a project approval letter after satisfactory submission and approval in the IEC meeting.

4.3.2 Study Progress

PI can start project at site after receiving final approval letter from IEC and registering the study at CTRI. (Note: One must not start the recruitment before CTRI registration, as CTRI will not accept retrospective registration). During study progress at site, PI must communicate with IEC for all required notification and reporting such as:

4.3.2.1 Protocol Amendments

a. Major Amendments submission;

- Amendment is a revision, modification, addition to or deletion from an approved research protocol and respective documents. PI/CoI is responsible for IEC submission and approval of any such amendment in the study protocol before implementing them.

- PI/CoI/study team member shall notify the IEC of any such changes to the protocol and/or informed consent and/or of new information on the investigational product no fewer than Twenty-one (21) days before the next scheduled meeting.

- All amendments should bear amendment number and version number with date(s).

- Study team member must make sure that all changes or modifications in the amended version are underlined or highlighted with track changes along with detailed summary of changes.

- The amendment /documents along with the covering letter should be accompanied with post approval amendment reporting form (Refer IEC SOP)

- Number of copies required for IEC submission will be as per IEC SOP

  Note: One additional copy is needed for PI acknowledgement

- The PI/CoI/study team member should obtain a copy of the acknowledged (IEC stamp with sign and date) amendment submission letter of the above-mentioned documents, and file the same in relevant section of TMF and send Scan or a copy to sponsor/ CRO.

- The amendments in the protocol and/or informed consent and any new information on the IP will be valid only after IEC approval, and should immediately implement the documents at the site after approval.

- The PI/CoI/study team member should document the IEC approval letter in the relevant section of the TMF (Trial Master File) and send a copy to sponsor/CRO.

b. Minor amendments and notifications

- Minor amendments are those that do not increase the risk or decrease the potential benefit to subjects/participants and may be approved by the IEC (Refer IEC SOP).
- This may include but may not restrict to:
  - Renewed insurance policy
  - DCGI and DGFT approvals
  - Administrative notes
  - Documents of administrative nature
- The steps for submission of minor amendment to IEC is same as described for Major Amendment above, except while completing the amendment reporting form PI/CoI/study team member should check for minor protocol amendment.

4.3.2.2 Annual Status Report/ Continuing Review Application

- The purpose of Annual status report/ continuing review application report is to monitor the progress of the study which was previously approved; not only for the changes but to ensure continued protection of the rights, safety and welfare of research subjects/participants.

- PI/CoI/ Study team member must submit annual status report/continuing review application to the IEC (DSMU) annually, subsequent to the date of IEC approval to renew approval, before two months of expiry. IEC is responsible for determining the date of submission of continuing review application of the IEC approved projects including those that are reviewed more frequently in the year based on specific criteria. (e.g., an IEC may set a shorter approval period for high-risk protocols or protocols with a high risk: potential benefit ratio). This decision will be taken during the IEC meeting wherein the project is finally approved.

- The IEC will review the study progress, the rate of accrual of subjects/participants, the occurrence of unexpected events or problems along with protocol deviation/violation and non-compliance, any new information pertaining to the research and assess final reports of all research activities. The protocol, informed consent documents and assent documents will be examined to ensure that the information remains accurate.

The IEC has delegated this responsibility of initial detailed review of Continuing Review Application to DSMU.

- All information must be provided to IEC/DSMU, as requested in the continuing review application form (Refer IEC SOP)

- The Investigator/ Study team member should submit the continuing review application well in advance i.e. 10 months after IEC final approval.

- PI will receive a reminder emails from the IEC secretariat for submission of continuing review applications for projects, 3 months prior to the expiry of study approval/CRA approval validity date (as mentioned on the final approval letter/continuing review application approval letter).

- First reminder will be sent 3 months in advance to the lapse in validity/annual review. Failure to submit the CRA within the due date after the 1st reminder will result in issuance of warning letter and necessary action.

- IEC may close/suspend the study if PI fails to submit CRA on time and consider appropriate decision on publication and presentation of study data.

- Study team member should report the CRA on IEC portal and submit one hard copy of the report and keep one acknowledgement copy for record.

- Study team member should obtain a copy of the annual/continuing review application report acknowledged by IEC/DSMU, and file the same in TMF and send a copy to sponsor.

The submitted CRA will be reviewed by the IEC/DSMU members and any one of the following decisions may be taken:

1. Approval to continue the study
2. Revision with minor modifications-Studies for which modifications have been suggested by the IEC may not proceed until the conditions set by the IEC have been met. Studies should be amended and submitted to the IEC within one month for re-review.
3. Query – The IEC and/or DSMU has raised queries against the continuing review application submitted. PI should respond to the IEC/DSMU queries at the earliest to maintain the study approval validity.
4. Deferred/On-hold-The IEC has postponed the decision on approval of continuing the study due to reasons such as awaiting expert opinion, awaiting site monitoring reports from the DSMU etc.
5. Not approved-The IEC feels that there are major concerns in the conduct of the study.

The decision will also include any significant findings that have arisen during review process and this will be communicated to Principal Investigator. It is the responsibility of Principal Investigator to provide this information to the participants and once done submit the report to IEC.

- The IEC/DSMU, Secretariat will notify Principal Investigator in case committee recommended modifications, and PI will be requested to resubmit the relevant documents

within 1 month for the approval till then the project is suspended. Principal Investigator will be communicated about the decision within 14 working days after the minutes are finalized.

- The PI will receive a letter from IEC/DSMU, if the continuing review report/annual report is approved / accepted.

- The letter should be filed in the TMF and a copy should be provided to the sponsor.

Note: *If there is delay in approval of the continuing review report subsequently from the date of IEC approval, the PI cannot recruit any participant during that period, till IEC/DSMU, approve the continuing review report. Principal Investigator should ensure that data of participants recruited in the IEC approval lapse period of the study is removed from data analysis, as and when applicable.*

4.3.2.3 Deviations/Violation/Non-Compliance and Waivers

Deviation/ non-compliance/ violation/waiver may occur at site, when investigators/ trial sites, fail to-

- Follow the procedures written in the approved protocol;
- Comply with national / international guidelines / institutional guidelines or rules or procedures mandated by the IEC for the conduct of human research
- Respond to the IEC requests regarding statutory, ethical, scientific or administrative matters.

- PI/CoI/Study team member must submit the deviations /violations/waiver reports as per the IEC SOP and regulatory requirements.

As per IEC SOP the definition of Deviation/Violation/waiver/non-compliance are as follows:

a) Protocol Violation/s:

Divergence or departure from the expected conduct of an approved study not consistent with the current Institutional Ethics Committee approved version of the research protocol, consent document or addenda.

This usually

- Constitutes a change in the conduct of the research that should have received prospective IEC review and approval prior to implementing the change; or

- Has harmed or posed a significant risk of harm to a research subject/participant or others; or

- Has damaged the scientific integrity of the data collected or confounded the scientific analysis of the study results; or

- Has resulted from willful or voluntary misconduct on the part of a Principal Investigator or a member of the research team.

Examples:

- Subject / Participant was enrolled but did not meet the protocol's eligibility criteria.
- Subject / Participant received the wrong treatment or incorrect dose.
- Subject/Participant being consented after the screening procedures are completed
- Subject / Participant being consented after the first dose of the drug has been given
- Wrong version of the informed consent form being used.
- Consenting lapse e.g. LAR signing as impartial witness.

b) Protocol deviation/s

Definition: Divergence or departure from the expected conduct of an approved study not consistent with the current Institutional Ethics Committee approved version of the research protocol, consent document or addenda is a protocol deviation if it:

- Has no substantive effect on the risk posed to a research subject / participant or others;
- Will not affect the subjects/participants' willingness to participate in the study;
- Has no substantive effect on the value of the data collected;
- Does not confound the scientific analysis of the study results; and
- Did not result from willful or voluntary misconduct on the part of an Investigator or a member of the Investigator's study team.

Examples:

- Sample collections at different time points than specified in the protocol.
- Subject/Participant following up on days not specified in the protocol.

c) Protocol Waiver

It is a prospective deliberate decision to deviate from the protocol that has been approved by the sponsor. Such waivers must be notified to and approved by IEC Member Secretary/Chairperson.

e. g. Protocol Waiver means a prospective decision by a sponsor or investigator to permit accrual of a subject/participant who does not satisfy the approved inclusion/exclusion criteria for enrollment (age, concurrent medication).

When a deviation occurs, it should be reported to the sponsor as well as the IEC. In some instances, a sponsor will issue a waiver related to a specific subject/participant, to continue the participant in the study.

Examples of waivers are:

- It is in the subject's/participant's best medical interest to remain on study

- Exception to inclusion/exclusion criteria (age, concurrent medication)
- Visits out of sequence or out of protocol "window"
- Injection of study drug in left arm rather than right arm.

d) Non-compliance

Noncompliance is defined as failure to comply with national regulations, IEC policy or the determinations or requirements of the IEC.

i. Non-serious and Non-continuing non-compliance involves isolated incidents, e.g. an unintentional mistake, an oversight or a misunderstanding. The issue is not serious or continuing in nature.

ii. Serious Non-compliance: An action or omission, non-compliant with national regulations or IEC policy, taken by an investigator that any other reasonable investigator would have foreseen as increasing risks or compromising the rights and welfare of a subject/participant or other person.

iii. Continuing non-compliance: A pattern of repeated actions or omissions taken by an investigator that indicates a deficiency in the ability or willingness of an investigator to comply with national regulations, IEC policy or determinations or requirements of the IEC.

iv. Research Misconduct: Non-compliance that involves callous disregard for the protection of human subject/participants or for the integrity of research may meet the definition of research misconduct. This includes any fabrication, falsification, or plagiarism in proposing, performing, or reviewing research or reporting research results.

- Protocol deviation/ non-compliance/ violation/waiver can be detected during monitoring visit for the investigator-initiated study by IEC and for sponsored studies by the monitor/ CRA also. Sometimes it can be detected by PI /study team member.
- The IEC members and/or monitor/ CRA performing monitoring of the project at study site can detect protocol deviation/non-compliance / violation, if the project is –
  - not conducted as per protocol / national / international regulations
  - when scrutinizing annual / periodic reports / SAE reports
  - fail to respond to requests from IEC within reasonable time limit
  - fail to adhere to protocol required procedure.

Additionally, information regarding protocol deviation/ violation/noncompliance in studies that enroll human subjects/participants may come to the attention of the IEC through:

- Continuing reviews
- For cause monitoring
- Audit reports
- SAE reports
- DSMU minutes
- Any other sources

- The protocol deviation/non-compliance/ violation can be detected by Secretariat from failure to:
  - Comply with statutory requirements;
  - Respond to requests from the IEC within a reasonable time limit;
  - Respond to communication made by the IEC

- The PI/CoI and/or study team member may identify protocol deviation/non-compliance/ violation and the same should be submitted to IEC, preferably within 10 working days of knowledge (As per IEC SOP).
- The PI/CoI and/or study team member shall submit the protocol deviation/violation through online IEC portal. After online submission and acceptance by IEC, one signed and dated copy should be submitted to IEC and one copy should be filed in the Trial Master File (TMF).

- IEC will review the submitted documents and the action could include one or more of the following:
  - Determine that no further action is required, or take other actions as appropriate.
  - Inform the PI that the IEC has noted the violation/ noncompliance/ deviation, and instruct the PI to ensure that deviations/noncompliance/ violations do not occur in future and to follow IEC recommendations.
  - Enlist measures that the PI would undertake to ensure that such deviations/noncompliance/violations do not occur in future.
  - Observe the research or consent process, (depending on the nature and frequency of the deviation)
  - Suggest modifications to the protocol
  - Alter the interval for submission of the continuing review/annual project status
  - Require additional training of the investigator and study team
  - Reprimand the PI.
  - Seeking additional information from the Principal Investigator.
  - Audit of trial by the IEC.
  - Suspend the study till additional information is made available and is scrutinized.
  - Suspend the study till recommendations made by the IEC are implemented by the PI and found to be satisfactory by the IEC.
  - Suspend the study for a fixed duration of time.
  - Suspension or termination of the study
  - Revoke approval of the current study.
  - Inform DCGI/ other relevant regulatory authorities.
  - Keep other research proposals from the PI/ Co-PI under abeyance.
  - Review and/ or inspect other studies undertaken by PI/Co-PI.

- PI/CoI/study team member should response to the query letter (if any) to IEC in the given time with appropriate clarification and justification with respect to the query raised by the IEC.

- PI/CoI/study team member should file the final approval letter received from IEC in the Trial Master File and should share a copy with sponsor (if applicable)

4.3.2.4 Safety Information

- Safety information can be any information recently reported or obtained from sponsor/CRO particularly regarding risks associated with the research. Unanticipated risks are sometimes discovered during the course of studies. Information that may impact on the benefit /risk ratio should be promptly reported to the IEC to ensure adequate protection of the welfare of the study subjects/participants. The unanticipated risks may as well include any event that in the investigator's opinion, may adversely affect the rights, welfare and safety of study subjects/participants.

- Safety information is categorized as Serious Adverse event (SAEs) and unexpected event reports of both onsite and offsite.

- The Principal Investigator must review safety information received from the sponsor. It is recommended that the PI review of safety information must be documented.

- The Investigator must submit Serious Adverse Events (SAEs) and unexpected events reports, both onsite and offsite, including follow up reports for active study subjects/participants.

- Report all safety information to the IEC according to the IEC and regulatory requirements (e.g. Investigational New Drug [IND] submissions, Council for International Organizations of Medical Sciences [CIOMS] reports, Suspected Unexpected Serious Adverse Reaction (SUSAR), Periodic Safety Update Report (PSUR), Data Safety Monitoring Board [DSMB] reports).

- File the safety reports and any associated IEC correspondence, if any, in the TMF.

- Copies of the associated IEC correspondence should be provided to the sponsor according to sponsor requirements.

- Report any other information to the IEC that may adversely affect the safety of the subjects/participants or the conduct of the research study.

a. Off Site Safety Reports

- Off Site SAEs where adverse event reports that are serious, unexpected and related (definitely, probably and possibly) to the drug need prompt reporting to the IEC.

- The SAEs that are expected (if listed in the informed consent) or unexpected but unrelated to the drug (classified as per IEC SOP Off Site SAE Classification form) have to be logged by the PI and to be submitted timely. The following log has to be maintained continuously until the end of the study.

- The IEC Secretariat will in a timely manner accept the complete set of "Off-site SAE reports" and/ or the log.

- IEC/DSMU will will in a timely manner accept the log of the SAEs.

- Those off-site SAEs which qualify for prompt reporting, (classified as per the Offsite SAE Classification form – as per IEC SOP) will be reported to IEC /DSMU secretary.

- Sponsor/CRO will send two sets of the offsite SAE, Study team member will submit one to the IEC/DSMU (as per the IEC SOP) and file acknowledged (Stamped, signed and dated by the IEC /DSMU) copy in the TMF and send a copy to the sponsor/CRO.

- PI's must review the SAE listings in detail and report if a trend is observed and communicate the same to IEC/DSMU.

- PI/Co I may receive email or letter as applicable, if any queries are raised by the IEC/DSMU Secretary. PI/Co I must reply to the query immediately.

b. Onsite SAE reporting:

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

- IEC
- Sponsor or its representative
- CDSCO (in case of studies that require approval of the CDSCO)

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

1. IEC
2. Sponsor or its representative
3. CDSCO (in case of studies that require approval of the CDSCO)
4. Head of the Institution (in case of studies that require approval of the CDSCO)

In case the event is Death due to disease progression, the event should be notified in the SAE reporting format unless it is specified in the IEC approved protocol that such events will not be reported.

If the patient is out of trial and on survival follow up the event should be notified unless it is specified in the IEC approved protocol that such events will not be reported.

The SAE should be reported on the IEC portal and should be submitted to DSMU - 01 signed hard copy (original) and 01 acknowledgement copy for Investigators record.

PI/Delegated study team member should refer CTCAE Ver. 5.0 for SAE grading.

Follow-up reports on the SAEs should be submitted within 14 calendar days of the initial report or when any additional information regarding the event is available, whichever is earlier.

In case of research involving human subjects conducted, supported or otherwise subject to regulation by any United States government federal department or agency which takes appropriate administrative action (e.g. NIH, HHS), the PI must promptly communicate to the appropriate US Federal Department Agency head and the Office for Human Research Protection (OHRP) within 14 working days from the occurrence or knowledge of any of:

1. Any unanticipated problems involving risks to subjects or others
2. Any serious or continuing noncompliance with the United States HHS policy
3. Any serious or continuing noncompliance with the requirements or determinations of the IEC;
4. Any suspension or termination of IEC approval

4.3.2.5 Study Termination

a. Premature Termination / Suspension /Discontinuation of the study

- Research studies are usually terminated as per the recommendation of the IEC, PI, Sponsor or other authorized bodies wherein subject enrolment and subject follow-up are discontinued before the scheduled completion of the study.

- The IEC/Sponsor/PI/ other authorized bodies can prematurely terminate the study for the reasons, but not limited to, listed as follows:
  - When research is not conducted in accordance with IEC policies.
  - When research is associated with unexpected serious harm to subject/participant.
  - Failure to submit status report
  - Frequency of SAEs occurring at the institution or other sites in case of multicenter studies may require the study to be prematurely terminated for the safety of the participants.
  - If protocol non-compliance/violation is detected

b. Suspension/Termination/ Discontinuation by Investigator/Sponsor:

- PI/CoI may take a decision to suspend/terminate/discontinue a previously approved research in view to protect the rights or welfare of subjects/participants or when new safety information has appeared in the literature, or evolved from this or similar research.

- PI/Co I may decide to withdrawal study before site initiation due to reasons such as regulatory delays, logistic and budgetary infeasibility etc.

- Protocol non-compliance/violation due to any reason.

- Slow recruitment

- Frequency of SAEs occurring at trial site may require the study to be prematurely terminated for the safety of the participants.

- Sponsor finding treatment not to be effective as deemed in the protocol.

- Lack of funds, lack of adequate market potential, competing drugs have received marketing approval ahead of the test compound, etc.

- Overall trial enrolment was met, so all sites are being closed, even if some sites have not completed their enrolments.

- The IEC secretariat will receive the study protocol termination/suspension/discontinuation form prepared and submitted by the Principal Investigator and verify the contents of the report for inclusion of:

❖ Premature Termination Report / suspension / discontinuation / Withdrawal of IEC approved study before site initiation (Refer IEC SOP) signed and dated by the PI and/or other material (letter from Principal Investigator/sponsor etc.)

❖ The IEC secretariat will check the completeness of the information

❖ The IEC secretariat will receive and acknowledge the reports.

- Based on the above-mentioned reasons IEC secretary can send a notification letter for termination/suspension/discontinuation or query letter to request additional information to the PI.

- In case Sponsor is terminating the study, PI will receive a letter from Sponsor/CRO for the termination/suspension/discontinuation with the explanation for the same.

- PI and Study team member will report the protocol termination on the IEC portal in section premature termination/suspension/discontinuation form. Package along with covering letter (Refer IEC SOP) signed and dated by PI and other material (e.g. letter received from the Sponsor/PI/IEC)

- Study team member must obtain acknowledgment of the IEC member on the covering letter and file it in the TMF.

- PI/ Study team member must reply immediately in case of any query generated or any further information requested from the IEC.

- PI will receive acceptance letter from the IEC, study team member will keep the original letter of the Premature Termination/suspension/discontinuation report in the study file and send the file to archive (Refer SOP; Archival of Essential Documents). Inform the same to Sponsor/CRO.

- PI/CoI shall notify about the suspension/termination of the trial to the currently enrolled subjects/participants and ensure that procedures for withdrawal of enrolled subjects/participants take into account their rights and welfare (e.g., arranging for medical care of a research study subject/participant) and make sure that all the adverse events or outcomes has been reported to the IEC.

4.3.2.6 Study completion

- On the Study completion the PI/ Study team member will notify the IEC of the study completion on the IEC portal under section “Study completion form” (Refer IEC SOP)
- Additionally, PI and Study team member must submit letter provided by the sponsor/CRO to give adequate and sufficient information.
- Study team member must submit signed and dated hard copy of Study Completion Reports

Note: One additional copy needed for PI Acknowledgement.

- IEC may call PI and request for further information or take any other action. In case, further information / action is requested, the same should be followed by the PI and communicated to the IEC office within 30 days.
- After providing the information requested by the IEC, PI will receive acceptance letter from IEC.
- IEC acceptance letter should be filed and one copy must be send to Sponsor/CRO.

4.4 Applicable areas of the Hospital

- MPMMCC/HBCH, Varanasi
- Institutional Ethics Committee (IEC)
- PI Departments

4.5 Applicable Staff

This SOP applies to all the personnel of the clinical research team and others who may be responsible for the interaction with the IEC.

These include the following:

- Investigator
- Research Team (listed in the delegation log)

- IEC staff/members

4.6 Staff responsible for Implementation

OIC CRS will ensure that the SOP is updated and available on MPMMCC/HBCH website for all the Investigators conducting studies and Investigator will ensure that the research team involved in the conduct of the study will comply with this site SOP.

PI at his/her level will ensure that at the time of implementation of the SOP, that the research team at MPMMCC/HBCH are trained and in the event that an SOP is modified, provide training regarding the change(s) and ensure their compliance with the changes.

Inform IEC that this site SOP will be implemented within the institution.

AX1-V1/SOP 04/V1

Covering letter

To, Date:
Member Secretary,
Institutional Ethics Committee,
MPMMCC & HBCH,
Sundar Bagiya, Near Nariya Gate,
Sunderpur, BHU Campus, Varanasi-221005
Uttar Pradesh, India

Reference <Study Title/Study number>

Subject:

Dear Sir/Madam,

We are submitting following study documents to the Institutional Ethics Committee for the necessary review and approval as per IEC SOP and regulatory guidelines.
Please find enclosed the following study documents for your review and approval.

Sr.No.	Document Type
	Kindly list all documents enclosed for submission with version number and date

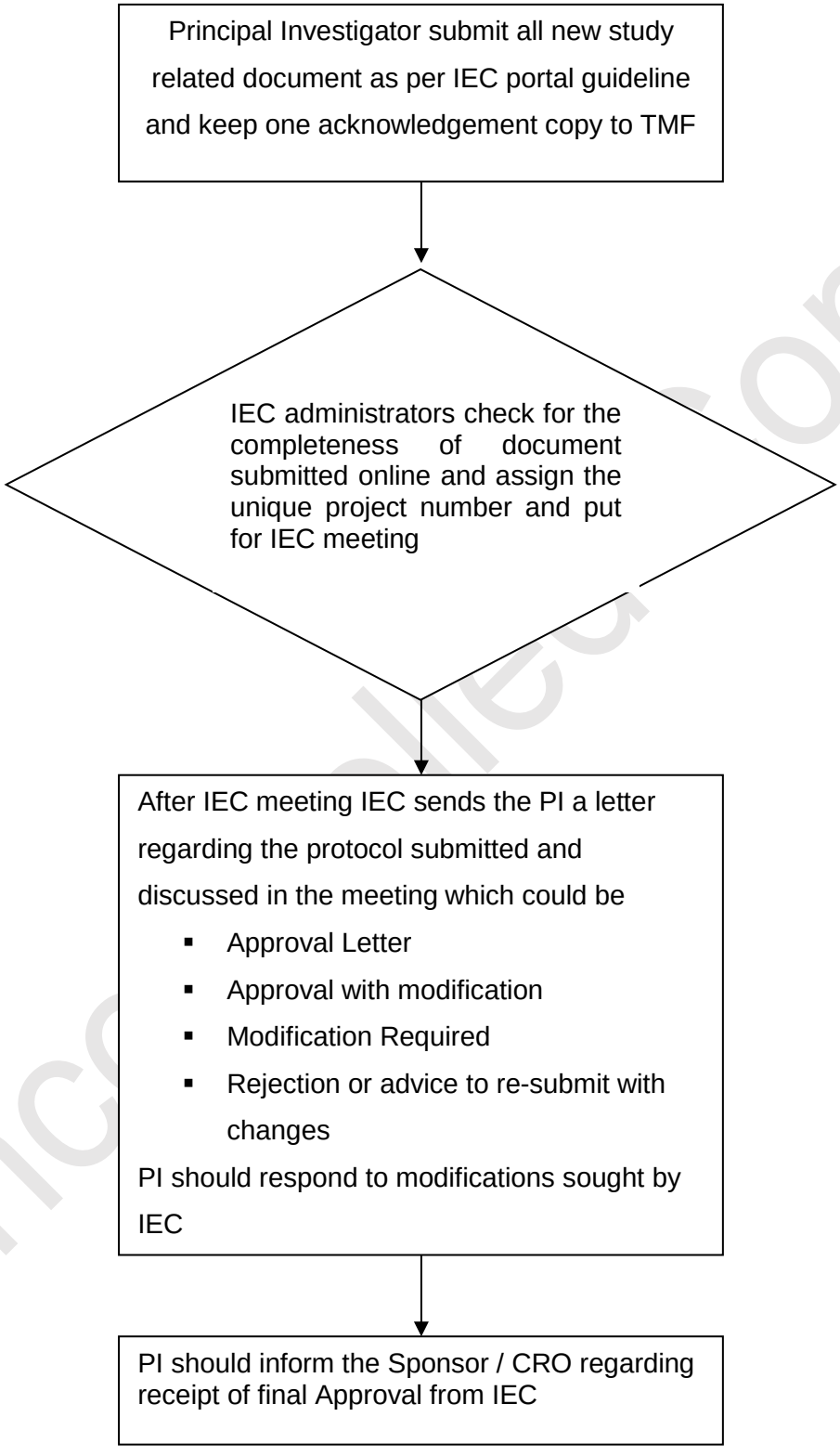
I would like to request you to review above-mentioned documents and provide the approval for the study.

Kindly revert back for any further clarification.

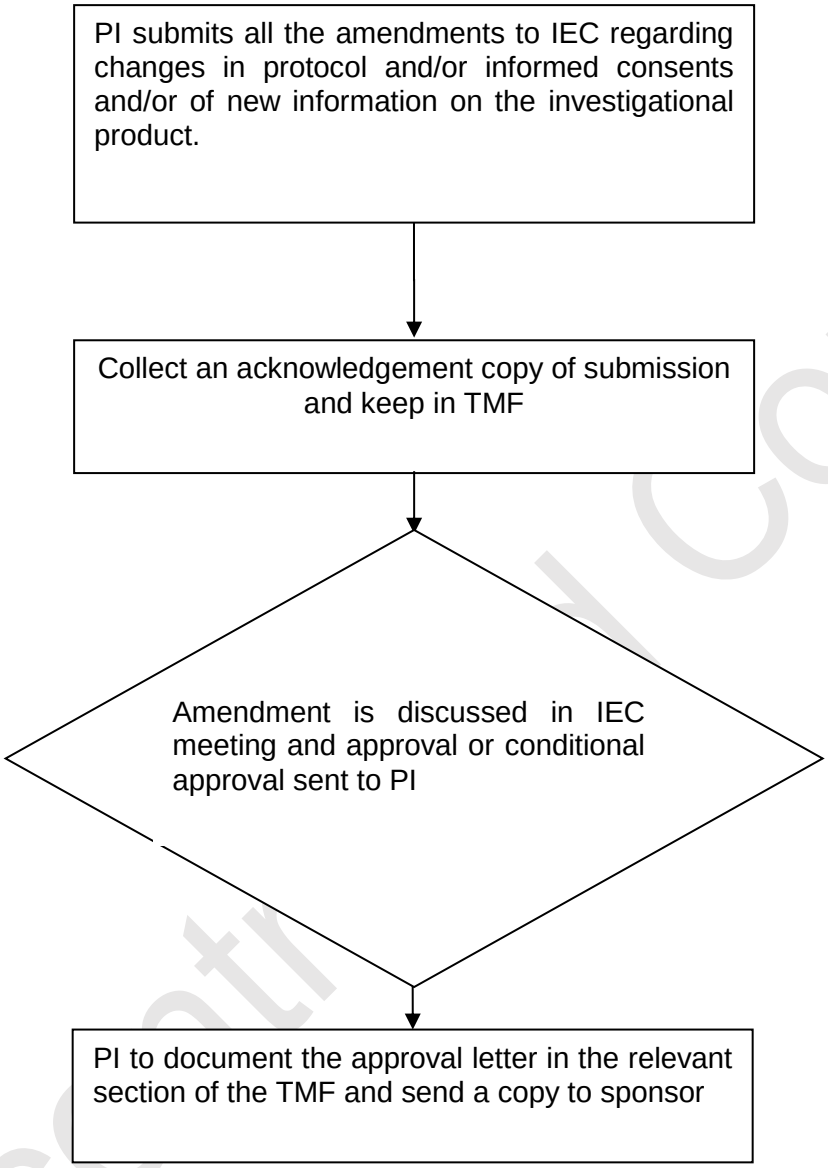
Thanks & regards,

<PI name>
<Designation>
MPMMCC & HBCH,
Sundar Bagiya, Near Nariya Gate,
Sunderpur, BHU Campus, Varanasi-221005
Uttar Pradesh, India

Study Submission:



Protocol Amendments:



Standard Operating Procedure
Clinical Research Secretariat (CRS)

Title: Study Team Responsibilities

SOP Code: SOP 05/V1 Date: 2nd Feb 2024 Pages: 46-53

Tata Memorial Centre

MPMMCC: Sunder Bagiya, Near Nariya Gate, Banaras Hindu University Campus, Varanasi-221005, Uttar Pradesh, India

HBCH: Homi Bhabha Cancer Hospital, Ghanti Mill Road, Old Loco colony, Lahartara, Varanasi-221002, India

5.1 Purpose

To describe the division and allocation of responsibilities and to clarify boundaries of responsibility within the study team, to ensure smooth running of the study under applicable regulatory requirements.

5.2 Scope

This SOP will apply to all study team members involved in the conduct of study at MPMMCC/HBCH.

5.3 Procedure

The Principal Investigator (PI) is the person ultimately responsible for the conduct of the research study at the site. However, all study team members are obligated to conduct research according to professional roles and responsibilities. According to the International Council for Harmonisation of Technical Requirements of Pharmaceuticals for Human Use (ICH) for Good Clinical Practice (GCP), “the investigator should have an adequate number of qualified staff and adequate facilities for the foreseen duration of the trial to conduct the trial properly and safely.” The qualifications and responsibilities of the research personnel should be clearly defined.

Study team involved in a study include, but are not limited to:

- Principal Investigator
- Co-Investigator
- Project Manager
- Clinical Trial Coordinator
- Research Nurse
- Bio-Statistician/Data Manager

There may also be other Study member that are associated with, but not directly involved in the research study, such as:

- Clinicians
- Specialist nurses
- Pharmacists
- Laboratory staff
- Support staff

5.4 Responsibilities of the Research Team

Good Clinical Practice (GCP) is a universal standard in clinical research that must be followed in every research protocol. GCP training and education are recommended for research team members, especially the Investigator and CTC. However, any member of the research team with a significant role in the conduct of a research study must be knowledgeable in GCP. All members of the clinical research team should GCP trained and certified.

5.4.1 Principal Investigator (PI)

Each research study will have a Principal Investigator (PI) who is the individual of record who assumes authority and accountability for the ethical conduct of a research study in accordance with all applicable federal and state laws and regulations and with institutional policy.

- The PI and Co PI are each fully responsible for:
  - Conduct of the study according to the protocol, applicable regulations and the GCP Guidelines (Indian and ICH as applicable) and also for compliance as per the undertaking given in NDCT Rule 2019 (Table 4).
  - The safety and welfare of subjects/participants in the trial.
  - Reading and understanding all the information in the essential documents, the investigator's brochure (IB), the informed consent, and the protocol.
  - Preparing and submitting Study documents for IEC review and approval.
  - Conducting study activities only after IEC approval and in accordance with the approved protocol, and assuring that IEC requirements are met.
  - The subjects/participants should be informed about the study as per the protocol and regulatory guidelines that the investigational agents are being used for investigational purposes (if applicable) and following all requirements relating to obtaining informed consent.
  - Reporting Adverse Events (AEs) to the Sponsor as per protocol.
  - Reporting Serious Adverse Events (SAEs) to the IEC, Sponsor (or Representative) and CDSCO (via Sugam portal)
  - Implementing modifications in approved research only after review and approval of the modification by the IEC, except where necessary to eliminate apparent immediate hazards to subjects/participants.
  - Providing progress reports/annual status report/continuing review application (CRA) to the IEC in a timely manner.
  - Assuring the disclosure of financial interest and arrangements to the sponsor and the IEC, and if required by the IEC, to subjects/participants, by any member of the research team that may present a conflict with the interests of subjects/participants in the study.
  - While retaining knowledge of and overall authority for the conduct of all research studies, supervise members of the research team qualified by appropriate education and experience to accept responsibility for study-related activities not directly performed by the PI. Assuring that delegation of responsibilities is appropriate and is documented (AX1-V1/SOP 05/V1) and

that individuals recruited as members of the research team are appropriately licensed and trained as per the GCP and applicable laws.

- Maintaining adequate and accurate records and making records available for inspection to external and internal monitors. Meeting with auditors and inspectors (DCGI, FDA, sponsor and internal), at the conclusion of their audits and/or monitoring visits to review findings and to implement changes to correct weaknesses or deficiencies.

- The PI/Co PI may delegate responsibility in the Site Delegation Log or Duty Delegation Log, to individual members of the research team; however, the PI/Co PI cannot delegate accountability for the ethical conduct of the study. The PI must sign the form that he/she delegates the responsibilities to each member of the research team. Each individual's name must be signed initialed and dated. The form must be updated, signed initialed and dated, each time there is a personnel change (AX1-V1/SOP 05/V1)

5.4.2 Responsibilities of Sub-Investigator (Sub I) /Co-Investigator (Co I)

- A Sub Investigator (Sub I)/ Co-Investigator (Co I) is a member of study team, qualified by education, experience, and with appropriate licensure or certification, and has been designated responsibilities by the PI at a trial site to perform critical trial-related procedures or to make important trial-related decisions.

- The Principal Investigator can assign some or all of his / her study related duties at the study site(s) to his subordinate who is under the supervision of the principal investigator.

- Sometimes the responsibilities designated by the PI could be the same as PI responsibilities. (Refer PI responsibilities)

5.4.3 Senior Clinical Trial Coordinator (CTC)/ Project Manager Responsibilities

The Senior Clinical Trial Coordinator/ Project Manager works in collaboration with the PI, the CTC/PM and the multidisciplinary research team to ensure that rigorous clinical research standards are maintained. Some examples of responsibilities of the Senior CTC/PM include:

- Provides guidance to the clinical research team from study start-up to closure, and manages all aspects of the research study (including timelines and reporting).

- Develops clinical research staff job descriptions.

- Evaluates staffing needs and hires qualified personnel as appropriate.

- Acts as liaison between the clinical research site and sponsor representatives.
- Prepares Investigator-initiated studies budget & prepare and negotiates sponsor studies budgets.
- Manages study contract negotiations.
- Supervises the training and education of staff, and manages work assignments.
- Tracks performance of clinical research studies.
- Conducts regular performance appraisals for direct reports.
- Design appropriate recruitment strategies and track study enrollment.
- Participating in audit/monitoring preparation activities of the sponsor, DCGI, FDA, other regulatory and accrediting agencies and Regulatory Affairs.

5.4.4 Clinical Trial Coordinator (CTC) Responsibilities

The Clinical Trial Coordinator (CTC) is a specially trained professional (nurse, health professional or other qualified clinical research team member) well versed with GCP and required regulatory guidelines, who manages most of the day-to-day responsibilities of a clinical research study.

The CTC works in collaboration with the PI and with a multidisciplinary research team to ensure that rigorous clinical research standards are maintained. The specific roles of the CTC are described in the procedures of each SOP. The responsibilities may be delegated to the position with the level of training and experience appropriate to the task and in accordance with the requirements of the trial. Some examples of responsibilities of the CTC include:

- Pre-screening and helping in enrolling subjects/participants in studies and managing their participation according to ethical, regulatory, Institution SOP and protocol-specific requirements.
- Documenting and assuring that the Consent process has been done before performing any study related procedures.
- Developing organizational aids and checklists to facilitate patient recruitment and the collection of complete and accurate study data.
- Maintaining the regulatory and study files for each research project.
- Communicating with the IEC as appropriate.

- Assuring proper handling and storage of the Investigational Product (IP).
- Reporting Serious Adverse Events (SAE) to the IEC, Sponsor, CDSCO, Institutional Head and concerned regulatory authorities.
- Meeting with sponsor representatives to discuss planned and ongoing studies.
- Overseeing study closure and reporting of results.
- Supervising other clinical research personnel, as appropriate.
- Participating as appropriate in the training of individuals recruited as members of the research team.
- Ensuring accurate and timely data entry.
- Proper handling and accurate processing of samples (such as blood and tissues).
- Other study related activities as per duty delegation log.

5.4.5 Other Study Team Member Responsibilities

- All members of the study team should adhere to GCP guidelines, applicable regulations, and standard operating procedures to ensure that the rights, safety, privacy and well-being of study subjects/participants are protected.
- Each staff member should fulfil the job responsibilities as outlined in the delegation log (AX1-V1/SOP 05/V1).
- Each staff member should also assess the skills required to conduct their delegated protocol-related duties and obtain any necessary training. The following are some responsibilities of the study team member
  - Conduct clinical studies according to applicable regulations and guidelines, Good Clinical Practices (GCP), New Drug and Clinical Trial Rules 2019, Good Laboratory Practices (GLP), Institutional research policies and applicable SOPs
  - Assure the safety and welfare of study subjects/participants by being knowledgeable about ongoing study protocols and investigational articles.
  - Comply with federal regulations governing disclosure of personal, professional or financial interests in a research study that may impact upon its conduct, evaluation or outcome.

- Maintain confidentiality of all clinical trial related information (including patient records).
- Fulfill job responsibilities specific to each job title according to applicable regulations and guidelines as well as the appropriate job descriptions maintained at the site.
- Assure that the PI is informed in a timely manner of all study-related activities.

5.5 Applicable areas of the Hospital

MPMMCC/HBCH, Varanasi

5.6 Applicable Staff

This SOP applies to all the personnel of the clinical research team and others who may be responsible for patient recruitment in the study. These include the following:

- Principal Investigator
- Research Team Members (listed in the delegation log)

5.7 Staff responsible for Implementation

OIC CRS will ensure that the SOP is updated and available on MPMMCC/HBCH website for all the Investigators conducting studies and Investigator will ensure that the research team involved in the conduct of the study will comply with this site SOP.

PI at his/her level will ensure that at the time of implementation of the SOP, that the research team at MPMMCC/HBCH are trained and in the event that an SOP is modified, provide training regarding the change(s) and ensure their compliance with the changes.

Inform IEC that this site SOP will be implemented within the institution.

AX1-V1/SOP 05/V1

Site Delegation Log or Duty Delegation Log

Note this form should only be used for trials where trial-specific forms are not supplied.

Study Title/Acronym:					**Protocol No./ MPMMCC project No:**				
Principal Investigator:					**Study Site:**				
Name	***Study Role**	****Key Delegated Study Task(s)**	**Start Date**	**Initials**	**Signature**	**Date of signature**	**Signature of (PI)**	**Date of signature**	**Stop Date**

List of Responsibilities:

***Identification of study role includes but is not limited to Co-Investigators, Clinical Trial Coordinator, study nurses, pharmacist (when appropriate) and others. List individuals delegated significant study-related tasks (ICH GCP 4.1.5). Signature/Initials required for all persons authorized to make entries and/or corrections to Case Report Forms (ICH GCP 8.3.24)**

**** Identify key study tasks when delegated by the investigator. Examples of key study tasks include:**

1	Informed Consent process	13	CRF Signature
2	Medical History review	14	IP administration
3	Con. Meds review	15	Data Query resolution
4	Measure of vital signs	16	Communications with IEC and sponsor
5	Collection of biological samples	17	Study conclusion signature
6	Handling of biological samples	18	Maintaining study records
7	Review of incl./exclusion criteria	19	Randomization
8	Safety assessments, reporting and reconciliation	20	Review & evaluation of reports
9	Authorization to randomize	21	Treatment decision
10	Investigational Product dispensing		
11	Investigational Product Accountability & maintenance	22	Archival activities
12	CRF Completion and data entry	23	Others:_____

Standard Operating Procedure
Clinical Research Secretariat (CRS)

Title: Communication with Sponsor or Contract Research Organization (CRO)

SOP Code: SOP 06/V1 Date: 2nd Feb 2024 Pages: 54-58

Tata Memorial Centre

MPMMCC: Sunder Bagiya, Near Nariya Gate, Banaras Hindu University Campus, Varanasi-221005, Uttar Pradesh, India

HBCH: Homi Bhabha Cancer Hospital, Ghanti Mill Road, Old Loco colony, Lahartara, Varanasi-221002, India

6.1 Purpose

This standard operating procedure (SOP) describes the communication between key research personnel at site and the sponsor/Contract Research Organization (CRO), including telephone and written interactions, during the entire course of a research study conducted at MPMMCC/HBCH, Varanasi and to ensure proper documentation of communications with the Sponsor/CRO concerning study activities.

6.2 Scope

This SOP applies to communications between the site and sponsors/CROs involved in the conduct of research study.

These communications serve to protect the safety and well-being of subjects/participants by assuring that studies are conducted in a compliant manner, sponsors/CROs are fully appraised of study site activities, and key research personnel are aware of new information about the study provided by the sponsor/CRO.

Any new study which is initiated during active period of the SOP will be covered under the SOPs, unless otherwise indicated. If necessary, a study specific SOP may be prepared.

6.3 Procedure

6.3.1 General communications

- Provide the sponsor/CRO a contact list of site personnel involved in study along with each individual's role and responsibilities.

- Communicate regularly, courteously and in accordance with MPMMCC/HBCH standards, with the sponsor/CRO about all the study related issues.

- Be familiar with the sponsor's SOPs pertaining to communications, including reporting timelines and preferred communication mode.

- Keep originals or photocopies of all study-related communications, including faxes with corresponding confirmations, e-mails, and written summaries of phone conversations. File all communication documents in the appropriate section of the TMF/SMF.

- Retain all sponsor-generated communications regarding conduct of the study in the correspondence section of the TMF/SMF. Budget, payment and other contractual or financial communications should be filed separately from the regulatory binder. Study team members will ensure that the information is communicated to the Principal Investigator (PI) and other key research personnel as applicable.

6.3.2 Pre-Study communication

- The Research Team Member is responsible for sending the Confidentiality Agreement to the sponsor/CRO once reviewed and signed by PI.
- The Research Team Member will notify the sponsor/CRO of the PI's decision to conduct the research study at MPMMCC/HBCH.
- Review the protocol and submit if any questions concerning interpretation of the protocol or conduct of the study to the sponsor/CRO in writing and file the copy in the TMF/SMF.
- Fill the questionnaires provided by the sponsor/CRO regarding the study related requirements.
- Prepare questions to clarify protocol procedures, subject/participant eligibility criteria, and other study-related issues in writing and file the reply in the Site Master File (SMF).
- The PI/CoI's will discuss logistics and feasibility of performing the study. This discussion will include a description of the potential subjects/participants available for the study and methods being considered for recruitment.

6.3.3 Communications while the study is ongoing

Investigator/CTC will:

- Submit the updated screening and/or enrollment logs to the sponsor/CRO by the preferred mode of communication
- Notify Sponsor/CRO about unanticipated issues, including adverse events (AEs) and Serious Adverse Events (SAEs), as per the sponsor's definitions and timelines, as defined in the protocol or SOP.
- Communicate protocol deviations, as they occur, according to the sponsor requirements.
- Submit completed CRFs (paper-based or e-CRF) to the sponsor/CRO in accordance with the Clinical Trial Agreement (CTA).
- Respond promptly to data queries as requested via fax, e-mail, and/or direct electronic data capture resolution, as per the sponsor's requirements and document the same in the specified TMF/SMF.
- Communicate significant regulatory changes as per the sponsor's requirements (e.g., IEC acknowledgement of an unanticipated issues or protocol deviation, IEC approval of a revised consent document, annual report etc.). Typically, these documents are reviewed during interim monitoring visits; however specific sponsors/CROs may require prompt notification in specific circumstances.
- PI will submit sponsor-generated protocol amendments to the IEC. Once approval is obtained, PI will train the study team regarding the changes prior to implementation and same will be documented and informed to Sponsor/CRO.
- Review safety reports received from the sponsor (e.g., off-site SAE/SUSAR) and report to the IEC as per IEC SOP. Notification of other key research personnel and/or enrolled

subjects/participants may be necessary (e.g., new risk identified related to investigational treatment).

6.3.4 Communication after study is completed

- Inform IEC regarding scheduled site close out visit.
- Communicate with sponsor and confirm the close out date.
- Provide the sponsor/CRO with any IEC required correspondence (e.g. information required in the IEC study closure letter) related to the study close out.
- Ensure that all close out activities are performed and all sponsor requirements are met.
- After receiving the final close out letter and study result from the sponsor, submit the same to the IEC in the required IEC format.
- File all the communication in the appropriate section of the TMF/SMF.

6.4 Sponsor Contact documentation:

1. All study personnel will document critical conversations with the Sponsor/CRO in the source notes, especially those pertaining to eligibility criteria, protocol deviations, and serious adverse experiences. Critical telephonic conversation should be transcribed and signed by study team member and filed in the TMF/SMF. (template can be used for the same)

2. Letters and Faxes – All study personnel will make copies of all correspondence written to the Sponsor/CRO. The CTC or delegate will file this correspondence in the TMF/SMF.

3. e-mails – All study personnel will print out copies of critical e-mails with the Sponsor/CRO. The CTC or delegate will file this correspondence in the TMF/SMF and if required in the source notes

At a minimum, the Sponsor/CRO should be notified:

- When the first subject/participant is enrolled in the study.
- When there is a question concerning a potential subject's/participant's eligibility.
- When recruitment issues occur.
- When a protocol violation occurs.
- When an SAE occurs.
- Responses to major monitoring findings.

6.5 Applicable Staff

This SOP applies to all the personnel of the clinical research team involved in communication with the Sponsor/CRO and responsible for the management of the data. These include the following:

- Principal Investigator
- Sub/Co-Investigator
- Research Team Members (as per duty delegation)

6.6 Staff responsible for Implementation

- PI and Senior CTC will ensure that the research team involved in the conduct of the study will comply with this site SOP and research members involved in the study are following this SOP while communicating with sponsor/CRO.

- Site staff will ensure that at the time of implementation of the SOP, that the research team at the Clinical Research Secretariat in MPMMCC/HBCH are trained and in the event that an SOP is modified, provide training regarding the change(s) and ensure their compliance with the changes. Training log should be maintained.

- Inform IEC that this site SOP will be implemented within the institution.

Standard Operating Procedure
Clinical Research Secretariat (CRS)

Title: Site Initiation, Site Initiation-Follow Up, Conduct and Close-out

SOP Code: SOP 07/V1 Date: 2nd Feb 2024 Pages: 59-68

Tata Memorial Centre

MPMMCC: Sunder Bagiya, Near Nariya Gate, Banaras Hindu University Campus, Varanasi-221005, Uttar Pradesh, India

HBCH: Homi Bhabha Cancer Hospital, Ghanti Mill Road, Old Loco colony, Lahartara, Varanasi-221002, India

7.1 Purpose

To describe the process that ensures that the site is organized and prepared for the proper conduct of the research study at MPMMCC/HBCH. This standard operating procedure (SOP) also describes the processes to be followed at site initiation, Site Initiation- follow up, conduct and closeout of research study at MPMMCC/HBCH.

7.2 Scope

This SOP will apply to all pharma sponsored research study initiation, Site Initiation- follow up, conduct and close-out at MPMMCC/HBCH as well as for investigator-initiated studies wherever applicable.

7.3 Procedure

A research study should be initiated at a site only after investigator and Sponsor/CRO involved in the study is satisfied that essential documents, agreements and IEC final approval are all in place. The site initiation process is designed to ensure that;

- Site has all essential documents in place for the site to conduct the study in compliance with the approved protocol and applicable guidelines and regulations.
- Site and the study team is aware of all the sponsor's procedures and SOPs for study conduct (such as safety recording and reporting, amendments, notification of any urgent safety measures/ violations or serious breaches) and has read and understood each.
- Site meets with all the required regulatory and sponsor requirements.

7.3.1 Preparing site for Site Initiation Visit

a. For preparing the site for initiation the investigator(s) or Clinical Trial Coordinator (CTC) should:

- Confirm the available date and time with the clinical research team that must attend the meeting and arrange the most suitable meeting date, time and place.
- Request an agenda for the visit; circulate the same to each team member.
- Confirm that investigator and team has reviewed the Protocol and Investigator's Brochure (IB) and any up-to-date information on investigational product (IP). The Investigator(s) must prepare a list of questions/concerns if any to be asked in the SIV.
- Ensure that the procedures stated in the study protocol are applicable at the site and fully understood by all the study team members.
- Confirm that all documents submitted to Institutional Ethics Committee (IEC) and approval received from IEC are available.

- Confirm that the clinical trial agreement (CTA), indemnification letter and budget are finalized and signed by all the involved parties.

- Notify appropriate departments regarding the sponsor/CRO visit (e.g., Laboratories, pharmacy, CT scan, bone scan and x-ray, etc).

- File all essential documents in TMF (or sponsor-supplied Investigator Study File), and compile any outstanding documents to provide to the Clinical Research Associate (CRA) at the initiation meeting.

Note: For all Investigator-initiated studies; Principal Investigator will ensure that the site is prepared as per the above-mentioned applicable points and documents.

7.3.2 During the Site Initiation Visit

a. During the initiation visit the investigator(s) or Clinical Trial Coordinator (CTC) should:

- Ensure that the Investigator's Trial Master File (TMF) contains the following mentioned applicable items and all the required regulatory documents:

o Protocol version [current approved version by the Institutional Ethics Committee (IEC)] and Investigator Statement

o Signed and executed Investigator contract

o CVs and licenses and valid GCP certificates of key site study staff

o Financial Disclosure forms

o Investigator Undertaking (IU)

o Form FDA 1572 for IND studies

o Duty Delegation Log

o IEC approval letter for the study

o IEC approved informed consent Documents (current version of all approved languages)

o Institutional and/or other regulatory authority approvals or valid clinical/other laboratory accreditation (if application)

o Valid clinical/another laboratory licensure

o Laboratory normal value ranges

o Notice that indicates the study has been submitted to the regulatory authorities (if applicable).

o Investigator Brochure, / Summary of Product Characteristics / Package insert. (If applicable).

- Case Report Forms (CRF), current, approved version
- Investigational product inventory management forms
- CTRI Registration details
- Any other essential documents submitted to IEC.
- IP (Investigational Product) is available in sufficient quantity.
- IEC Details including EC SOPs and EC composition etc.
- Site SOPs
- Vendors Manuals (e.g. IWRS/IVRS), (If applicable)

Note: For Investigator-initiated studies, PI & study team will ensure that whichever documents are applicable from above list will be available in the Trial Master File (TMF).

- Provide the study members name involved in the study and their responsibilities in the duty delegation and keep a copy in the TMF. Handover a copy to the monitor/CRA for sponsored/Pharma studies.
- Provide original and updated curriculum vitae of all study personnel / Investigators involved, as per sponsor requirements (if not provided earlier).
- Ensure that the names and contact numbers of the relevant medical and study personnel of the sponsor are available and documented clearly.
- Ensure that all relevant study site personnel fill out the Site Personnel/Signature Log and Training Log.
- Check that the procedures and plans for storage, dispensing and return of IP have been reviewed by the Principle Investigator and agreed and finalized with the Sponsor and CRS Research pharmacist (if applicable).
- In case of paper CRF's: Check that the quantity of CRFs that have been requested or shipped to the study site are sufficient for the number of subjects/participants that are likely to be recruited into the study also allowing for the archiving of one set of intact, unused CRFs. For Investigator-initiated studies, printout of the approved current version can be taken on the subject/participants visit or a set of blank forms can be kept in the file.
- Check that other related supplies are available or are to be shipped to the study site at a later date, and that they are available in sufficient quantities.
- Check that laboratory facilities and arrangements for the dispatch of samples to the central laboratory are organised and that any specialised equipment that may be required will be available throughout the period of the trial, e.g. collection kits, centrifuge machine, freezer, etc.
- Ensure that monitor/CRA gives sufficient time to CTC for CRF completion training

- Ensure and understand the requirements of the Sponsors/CRO regarding source documents and raw data, which will be required during monitoring visits to enable the monitor/CRA to perform source data verification at each monitoring visit.
- Ensure that the procedures relating to the archiving of study records at the end of the study is agreeable to the sponsor.
- During the initiation visit the Investigator or delegated team member (for investigator-initiated study) and monitor/CRA (for sponsor study) will provide a protocol-specific training session to all the members of the research team who will be involved in the research study. The investigator or monitor/CRA will ensure that the attendance sheets and other training documentation are completed.

b. The protocol-specific training session will include, but is not limited to, the following:
- Discuss the salient features of protocol on subject eligibility, study procedures, source documentation and Informed Consent process and its documentation.
- Subject recruitment
- Safety Reporting: Discuss in detail safety reporting procedures and timelines as per the protocol and applicable regulatory requirement.
- IP management (if applicable): Discuss in detail regarding inventory, dispensing record, destruction record etc. Also, discussion of randomization procedure, blinding & unblinding process if applicable.
- Protocol-specific forms and procedures
- Source documentation
- Additional information from the Investigator's Meeting (IM)
- Any other relevant information

c. The Investigator, monitor/CRA and CTC will:
- Develop a recruitment plan for subjects/participants
- Identify a back-up to the primary CTC

7.3.3 Follow-Up of site initiation visit-

Following should be checked before conduct of the study

- Confirm that the sponsor sends a written summary of key discussions and agreements made during the site initiation visit within 14 working days. Follow-up if necessary.
- Confirm readiness of the site to start the study.
- Confirm the receipt of all study-related materials (mentioned in point no. 7.3.2) such as CRFs, laboratory supplies, investigational product(s).

- Distribute protocol summaries and worksheets, if not done previously (the sponsor may provide study-related worksheets, however the site can prepare one).

- Notify all appropriate departments that the study is ready to enroll subjects/participants.

- Initiate study recruitment strategies and begin enrolling study subjects/participants.

7.3.4 Study conduct

a. Once the site is activated and starts recruiting subjects/participants, the Investigator and CTC will ensure the following

- All study activities are accomplished according to the protocol and applicable regulatory regulations.

- Subjects/Participants sign the IEC approved version of the consent form before any study-related procedures are carried out.

- Data collected in the Case Report Form (CRF) are supported by source documents (case file or certified copy of case file/EMR).

- Protocol deviations/noncompliance/violations/waivers if any should be notified to the IEC (Refer SOP for IEC communication) and the same must be documented in the source documents and appropriate CRF.

- Adverse events are reflected in the source documents and captured in the CRF. (With appropriate term, grade, causality, start and stop date and concomitant given if any.)

- Serious Adverse events (SAEs) are reported to the Sponsor/CRO and IEC within specified time frame (refer SOP for SAE reporting).

- SUSAR and CIOMS should be notified in the timely manner to the IEC.

- The IP is being dispensed correctly and IP accountability records are being maintained (Follow the SOP for IP management).

b. While the study is ongoing, the CTC will ensure the following

- The Sponsor/CRO is informed of all significant study events and staff members are documenting critical interactions with the Sponsor/CRO.

- Biological samples are being obtained, handled, stored, and shipped appropriately.

- Documents like CT scan, X ray, etc., CD’s are shipped properly in a timely manner.

- Prepare the site for monitoring and audits and take appropriate actions for any monitoring findings.
- Study supplies remain adequate.
- Study records remain confidential.
- All equipment is calibrated regularly and maintenance records are being kept.
- Track the follow up of expenses as per the budget agreed in CTA

7.3.5 Premature Termination or Suspension of a Study

a. If the research study is prematurely terminated or suspended for any reason, the investigator/institution should

- Immediately inform the IEC regarding the premature termination of the study in the format specified in the IEC SOP.
- Promptly inform (via phone/email) trial subjects/participants and include, where appropriate, the reason for suspension / early termination of the study. In case subjects/participants are not reachable by phone or email, inform them immediately on the next follow up visit.
- Assure appropriate ongoing therapy and follow-up for the subjects/participants, and, where required by the applicable regulatory requirement(s), to inform the regulatory authority(ies).
- In case the study is terminated for any reason other than safety, PI will ensure that the subjects/participants benefiting with the IP will continue to receive the same from sponsor until they are showing benefit or disease progression. (The same should be mentioned in the Protocol).
- The PI should maintain documents as specified in the TMF list and take measures to prevent accidental or premature destruction

In addition:

- If the PI terminates or suspends a research study without prior agreement of the sponsor, the PI should promptly inform the sponsor and the IEC regarding the termination. Provide the sponsor and the IEC with a detailed written explanation of the termination or suspension.

b. If the sponsor terminates or suspends a research study, the sponsor should notify the investigator(s), institution(s), the ethics committee and the regulatory authorities accordingly. The notification should document the reason(s) for the termination or suspension by the sponsor or by the investigator / institution.

7.3.6 Site close-out

a. Preparing the site for study close-out visits

- After the last subject/participant has completed all scheduled visits associated with the study, CRA will discuss with PI for convenient date and time to conduct the study close-out visit.

- Request the monitor/CRA for the visit agenda so key research personnel such as PI, Co I, CTC, research nurse and other team members will be available, as appropriate.

- Ensure all regulatory documentation and case report forms (CRFs) not previously monitored are complete and available for review.

- Ensure all data queries received to date have been resolved.

- Inventory IPs supply and complete final accountability records. If previously instructed to return or destroy IP, assure all required documentation is filed in the appropriate TMF for monitor/CRA review.

- Arrange monitor/CRA meeting with the PI and/or CoI and CTC to discuss any outstanding issues.

- PI will ensure that all outstanding payments are cleared as per CTA.

- For Investigator-initiated studies, PI and CTC will take care of all the above applicable points for study close-out visit.

b. Managing the study close-out visit

- Ensure all documentation (e.g., regulatory correspondence) is filed appropriately and ready for the monitor/CRA to review during the close-out visit.

- Discuss all open study-related issues and what steps will be taken to resolve them in order to satisfy the sponsor/CRO requirement(s).

- Review with the monitor/CRA the list of outstanding issues related to regulatory documents, source data verification, IP reconciliation, and any requirements for data retention and storage.

- Discuss any concerns regarding the possibility of a quality assurance audit and/or inspection by IEC or external regulatory bodies.

- If the study involved electronic data capture, determine when hard copies/CD of all CRFs will be provided to TMC, if applicable.

- The PI is responsible for ensuring the appropriate follow-up, as per the protocol, for any participant experiencing an ongoing unanticipated problem (e.g., serious adverse event) at the study end and providing this information to the sponsor/CRO, and assuring all requirements have been met.

- Arrange meeting of the PI and monitor/CRA to discuss any future considerations (e.g., publication of study data or future studies).

- File final site close out visit document in the Trial Master File (TMF).

c. *Follow-up after the study close-out visit*

- For any remaining IP(s), ensure the item(s) is returned to the sponsor/CRO per their requirements.

- If the randomization code for any IP was broken for any reason, ensure complete documentation has been filed.

- Ensure return or destruction of all other study-related materials, such as unused lab kits and CRFs.

- Ensure any equipment on loan from the sponsor is returned or if mutually agreed by both the parties can be retained at the site.

- After all data queries have been resolved, check TMF, subject files and other study files for completeness.

- Arrange for transfer of study documents to secure storage.

- Submit the Final Closure Report to the IEC, in accordance with IEC SOP for Study Completion or Closure.

- Provide the sponsor/CRO with a copy of the IEC closure letter.

- Verify participant reimbursement or compensation if any have been distributed per the study budget, as outlined in the Informed Consent and CTA.

- If the informed consent and CTA, protocol or contract state subjects/participants will be informed of their treatment arm, ascertain from the sponsor how and when this will be completed.

7.4 Applicable areas of the Hospital

MPMMCC/HBCH, Varanasi

7.5 Applicable Staff

This SOP applies to all the personnel of the clinical research team and others who may be responsible for site initiation, activation, conduct and close-out at MPMMCC/HBCH.

These include the following:

- Investigator
- Research Team
- CTC
- Research Nurse
- Support staff

7.6 Staff responsible for Implementation

OIC CRS will ensure that the SOP is updated and available on MPMMCC/HBCH website for all the Investigators conducting studies and Investigator will ensure that the research team involved in the conduct of the study will comply with this site SOP.

PI and Senior CTC will ensure that the research team involved in the conduct of the study will comply with this site SOP and research members involved in the study are following this SOP while communicating with sponsor/CRO.

PI will ensure that at the time of implementation of the SOP, that the research team at the Clinical Research Secretariat in MPMMCC/HBCH are trained and in the event that an SOP is modified, provide training regarding the change(s) and ensure their compliance with the changes.

Inform IEC that this site SOP will be implemented within the institution.

Standard Operating Procedure
Clinical Research Secretariat (CRS)

Title: Reviewing the Informed Consent form and Obtaining Informed Consent

SOP Code: SOP 08/V1 Date: 2nd Feb 2024 Pages: 69-82

Tata Memorial Centre

MPMMCC: Sunder Bagiya, Near Nariya Gate, Banaras Hindu University Campus, Varanasi-221005, Uttar Pradesh, India

HBCH: Homi Bhabha Cancer Hospital, Ghanti Mill Road, Old Loco colony, Lahartara, Varanasi-221002, India

8.1 Purpose

- To describe the information or essential elements required to be included in the informed consent documents associated with a research study.

- To describe the procedure for obtaining voluntary informed consent from a prospective subject/participant for a research study and also to ensure that a subject's/participant's consent is sought in such a way that the subject/participant or his/her representative has ample opportunity to consider whether to participate in the study and under conditions that minimize the possibility of coercion or undue influence.

- To ensure that freely & voluntarily given written Informed Consent is obtained from each subject/participant in accordance with applicable regulatory requirement, New Drugs and Clinical trial Rules 2019, Indian GCP, ICMR/CDSCO guidelines, ICH-GCP and Declaration of Helsinki.

8.2 Scope

This SOP will apply to all research studies conducted at MPMMCC/HBCH for informed consent procedure.

8.3 Procedure

Informed Consent must be obtained prior to performing any study related procedures.

8.3.1 Reviewing the Draft Informed Consent

Prior to submission of Informed Consent Form (ICF) to Institutional Ethics Committee (IEC) for approval, the PI must check the IEC SOP and NDCT Rules 2019 template and ICMR Guidelines for requirements for elements of ICF, to learn if specific formatting or wording requirements for informed consent / Assent in addition to those listed in the regulations is fulfilled.

In sponsored studies PI will review the ICD and If there is any discrepancy or missing element in the ICF, Investigator/CRC shall contact Sponsor/CRO for appropriate action and for Investigator-initiated studies PI will draft the ICF as per the applicable guidelines and will ensure that all the below mentioned points are included in the ICF.

- The informed consent process should be clearly described in the IEC submission. In addition to providing a description of the consent process including the person who would conduct the consent interview, and the information to be communicated to the prospective subject/participant or the Legally Authorized Representative/ Impartial witness, the following details should also be included in the ICF

- Study Title:
- Project/Study Number:

- Subjects/Participants Initials:
- Date of Birth/Age:
- Subjects/Participants Name/Thumb impression and date:
- Address& Contact No:
- Qualification:
- Occupation: Student / Self Employed / Service / House wife, other (please specify), If any (if Applicable)
- Annual Income: INR, (If Applicable)
- Name and Address of the Nominee (s) and relation to subject: (If Applicable)
- Relation to subject: (If Applicable)
- Name of Legal and acceptable representative: (if applicable)
- Sign and date of LAR
- Address & Contact No.: (If Applicable)
- Name, Address and contact number of the Impartial witness (if applicable)
- Sign and date of Impartial witness (if applicable)
- Name of PI/Co-PI/Co-I
- Sign and date of PI/Co-PI/Co-I

Before the consent form is submitted to the IEC, the PI will review the document to ensure that, it is in compliance with the IEC's requirements and with applicable regulations, NDCT Rules 2019 and Indian GCP, ICH GCP, ICMR guidelines.

If there is any discrepancy or missing element in the ICF, Investigator/CRC shall contact Sponsor/CRO for changes or make appropriate changes (in case of Investigator-initiated study).

In order to assess the informed consent process, the submission to the IEC should be detailed enough to allow the IEC to determine that an appropriate process will be followed. In addition to providing a description of the consent process including the person who would conduct the consent interview, and the information to be communicated to the prospective subject/participant or the Legally Authorized Representative/ Impartial witness, the Research Plan should include:

- the person who would provide consent or permission;
- any waiting period between informing the prospective subject/participant and obtaining consent;
- steps taken to minimize the possibility of coercion or undue influence;
- the language used by those obtaining consent; and,
- the language understood by the prospective subject/participant or the legally authorized representative.

The language used in the written informed consent form, should be nontechnical and should be understandable to the subject/participants or the subject's/participant's Legally Acceptable Representative (LAR) and or to the Impartial Witness (IW), wherever applicable.

The Informed Consent document must be available in the appropriate required local languages with the translation certificate(s). For ICDs other than in local language (Hindi & Marathi), considering the expected patient pool, back translations will be required with respective translation certificate. Sponsor/CRO may submit back translations for Hindi & Marathi and the same can be submitted to IEC (Not mandatory).

For Investigator-initiated studies, it's not mandatory to submit translation certificate, and back translation for Hindi & Marathi are not mandated by IEC. Back translation for other than local languages (Hindi & Marathi) shall be considered by PI depending upon the expected patient pool.

The informed consent process may be periodically audited by the IEC or appropriate compliance or designated personnel to assess conduct. Information presented in order for the IEC to approve research will be reviewed and must include, but is not limited to the following:

- The investigator obtained the legally effective informed consent of the subject/participant and Impartial Witness and or subjects/participants legally authorized representative, where applicable.

- The circumstances of the consent process provided the prospective subject/participant or the legally authorized representative sufficient opportunity to consider whether to participate.

- The circumstances of the consent process minimized the possibility of coercion or undue influence.

- The information communicated to the subject/participant or the legally authorized representative during the consent process was in anon-technical language & understandable to the subject/participant or the representative.

- The information being communicated to the subject/participant or the representative during the consent process did not include exculpatory language through which the subject/participant or the legally authorized representative was made to waive or appear to waive any of the subject's/participant's legal rights.

- The IEC will determine that the required disclosures (mentioned in 4a.5.5) provided to each subject/participant or a legally authorized representative are in accordance with legal and

regulatory requirements as required elements of informed consent. The IEC will also consider whether additional disclosures are required for inclusion in the consent process.

8.3.2 General procedure for obtaining Informed Consent from Subjects / Participants:

a. The Investigator and CTC are responsible for ensuring that the informed consent and its translated version and assent, if applicable, have been approved by the IEC before they are used in a study and that the correct version of the documents are used when the study is ongoing.

b. The process of Informed Consent should begin after identification of a prospective subject/participant. Subject/Participant must be asked regarding the literacy and the language he/she would prefer for communication, reading and writing.

c. No investigator may involve subject/participant in research, unless the investigator has obtained the legally effective informed consent of the subject/participant.

d. PI / Co-I (delegated in the duty delegation log) should conduct the consent procedure and obtain freely & voluntarily given consent from a subject/participant before any study related procedure or examination is undertaken.

e. Before requesting an individual's consent to participate in research, the investigator must provide the below mentioned required disclosures to each subjects/participants and Impartial witness and or legally authorized representative (if applicable) in accordance with legal and regulatory requirements.

The disclosure should be in the language he or she is able to understand which should not only be scientifically accurate but should also be sensitive to their social and cultural context.

- Statement that the study involves research and explanation of the purpose of the research.
- Expected duration of the participation of the subject/participant.
- Description of the procedures to be followed, including all invasive procedures.
- Description of any reasonably foreseeable risks or discomforts to the Subject/Participant.
- Description of any benefits to the Subject/Participant or others reasonably expected from research. If no benefit is expected Subject/Participant should be made aware of this.
- Disclosure of specific appropriate alternative procedures or therapies available to the Subject/participants.
- Statement describing the extent to which confidentiality of records identifying the Subject/Participant will be maintained and who will have access to

Subject's/Participant's medical records.

- Trial treatment schedule and the probability for random assignment to each treatment (for randomized trials).
- 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.
- An explanation about whom to contact for trial related queries, rights of Subjects/Participants and in the event of any injury.
- The anticipated prorated payment, if any, to the subject/participant for participating in the trial.
- Responsibilities of subject/participant on participation in the trial.
- Statement that participation is voluntary, that the subject/participant 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/participant is otherwise entitled.
- Statement that there is a possibility of failure of investigational product to provide intended therapeutic effect.
- Statement that in the case of placebo-controlled trial, the placebo administered to the subjects/participants shall not have any therapeutic effect.
- Any other pertinent information

Additional elements, which may be required:

• Statement of foreseeable circumstances under which the participation of the subject/participant may be terminated by the Investigator without his or her consent.

• Additional costs to the subject/participant that may result from participation in the study.

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

• Statement that the Subject/Participant or Subject's/Participant'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/Participant's willingness to continue participation will be provided.

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

• Approximate number of Subjects/Participants enrolled in the study.

The person (PI/CoI) who explains the study will allow enough time for the potential subject/participant to read the consent form and will answer any questions that are raised.

The PI/CoI obtaining the consent will ensure the following**:**

- Adequate time is provided to subject/participant before participation (at least 24 hours)
- Details of all questions asked by participant and answers given by PI/Co-I will be documented.
- The subject/participant understands the study requirements.
- The subject/participant signed and dated the consent freely & voluntarily.
- The consent form is signed and dated by the subject/participant and the PI/Co I who obtained the consent, and Impartial Witness and or LAR, if applicable.
- The subject/participant is given a copy of the signed & dated consent form.
- All these aspects will be documented in a narrative in the source file of the patient or in EMR.

PI / CTC should ensure that prior to a subject's/participant's participation in the research study; the written consent document should be personally signed and dated by the subject/participant and by the PI/Co I who conducts the informed consent discussion.

The PI/CTC will ensure that the original, signed copy of the consent is stored in a separate ICF file and a copy is given to subject/participant.

After initial consent process or participating in the study, if a participant is not willing to consent or wants to prematurely withdraw consent for the study, PI should respect the participant's decision and should document the same in the source notes.

Although a participant is not obliged to give his or her reasons for not consenting or prematurely withdrawing from the study, the PI/Co I can make a reasonable effort to ascertain the reason, while fully respecting the subjects/participants rights. In case the participant indicated that reason for withdrawal is because of adverse events, all efforts will be made to follow-up the patient till the adverse event resolves.

8.3.3 Obtaining Informed Consent from literate subjects / participants:

a. PI/ Co I/ must explain the study to the potential subject verbally (in the preferred language of the subject/participant), providing all pertinent information (mentioned in 4.5.5), and must allow the potential subject/participant ample opportunity to ask questions.

b. Following this verbal explanation, the potential subject/participant should be provided with an IEC approved written Informed Consent Document and should be given sufficient time to consider whether or not to participate in the research study.

c. After giving brief details about the study and allowing the potential subject/participant time to read the consent form, an Investigator will meet with the potential participant and answer any additional questions he/she may have.

d. Once an individual has all his/her questions answered and has agreed to voluntarily participate in the study, the participant will sign and date the consent form.

e. The PI/ Co I/ who has explained and taken consent from the subject/participant must also sign and date the consent form.

f. The PI's/Co-I's Investigator's signature and date means that the informed consent process has taken place with the subject/participant and that the subject/participant:

- meets all eligibility criteria as per protocol
- was appropriately consented (as described above) and voluntarily agreed to

participate in the study.

- understands the requirements of the study

g. The entire consent process including the questions asked by the subject/participant and answers given by the PI/ Co I/Designee must be documented in detail in the source notes or EMR, additionally the documentation should include:

- Subject/participant name
- Trial Short name or short title
- Enrollment number/ Trial ID number
- Date of birth and completed age
- Language, version number and date of Informed Consent Form
- Date on which the subject/participant & Investigator signed the Consent Form
- Statement that a copy of Signed consent given to subject/participants.

h. The Investigator obtaining the consent (delegated by the PI) will document the process in the subjects/participants source notes. The CTC present at the time of consent process may transcribe the consent process in the source notes and will sign and date the consent process. The PI/Co I will sign and date the same consent process and confirm the process written by CTC is appropriate.

8.3.4 Obtaining Informed Consent from non-English speaking subjects/participants:

a. If the patient population contains numerous non-English speaking people who may qualify for the study, the PI/Co I will ensure that the informed consent is translated into the local languages and that the translated consent form is also approved by the IEC.

b. The CTC will file the certificate of translation in the TMF with the translated consent (for sponsored study).

c. PI/Co I who speaks the same language as the potential subject/participant will explain the study to the subject/participant and will also be available at subsequent study visits to ensure that the subjects/participants questions' can be answered as the study progresses. In case the PI/CoI is not familiar with the language the patient speaks and understands and reads, he/she may take the help of an interpreter. This should be documented in the narrative.

d. Before obtaining the consent from the potential patient kindly follow the above-mentioned points 8.3.2.a, b, and c.

e. The subject must sign and date the consent in the preferred language. The Investigator obtaining the consent will document the process in the subject's source notes as mentioned in 8.3.3.g

f. The CTC present at the time of consent process can transcribe and document the consent process in the source notes and will sign and date the consent process. The PI/Co I will sign and date the same consent process to confirm that the process written by CTC is appropriate.

8.3.5 Obtaining Informed Consent from illiterate subjects / participants:

If an adult person identified for the study speaks and understands any other local language, but cannot read and write, he/she can be enrolled in a study as illiterate subject/participant, consistent with applicable regulations. However, here we need an Impartial Witness.

a. The PI must ensure (1) the person retains the ability to understand the concepts of the study and evaluate the risks and benefits of being in the study when it is explained verbally (still competent) and (2) is able to indicate voluntary approval or disapproval to participate in the research study.

The information should be given (as mentioned in point 8.3.2.a) to the subject/participant and / or their relative(s) in a language and at a level of complexity that is understandable to the subject/participant and or his/ her relative(s) in both written and oral form, whenever possible.

a. The consent form should document the method used for communication with the prospective subject/participant and the specific means by which the prospective subject/participant communicated agreement to participate in the study.

b. An impartial witness should witness the entire consent process and sign the consent document. An Impartial Witness (IW), should be someone, who is independent of the study and study team, who cannot be unfairly influenced by people involved with the study, who attends the informed consent process if the subject/participant or the subjects/participants

legally acceptable representative cannot read and write, and who reads out to the participant the informed consent document and any other written information supplied to the subject/participant. The IW must be able to read, write and speak the language of the participant. The participant must give consent by putting his / her thumb impression on the consent form. By convention subject/participant should give left thumb impression.

c. Alternatively, the subject/participant (if capable) can sign the consent form. In such case it has to be documented in the narrative in the source notes that though the subject/participant is illiterate he/she can sign.

d. IW should be present during the entire consent process and must sign the consent form with date in presence of investigator obtaining consent. An IW sign and date attests that the participant gave voluntary consent to participate in the study.

e. After obtaining consent, follow the above-mentioned points 8.3.2.b, c & d

f. For documenting the process in source notes, follow the points 8.3.3.g & h

8.3.6 Obtaining Assent from Children

- PI/Co I must obtain simple oral assent for children between 7 (84 months and above) and 11 years of age, and this oral assent must be obtained in the presence of parent/LAR.

For children between 12 and 18 years of age, written assent must be obtained. If a child becomes 13 years old during the course of the study, then written assent must be obtained in addition to parent/LAR consent. This is a joint decision-making process between the child and the concerned adult. In cases of verbal assent, the parent /LAR's counter-signature must be obtained confirming that the child's verbal assent has been taken. Re-assent must be taken in all the same situations as re-consent as mentioned above.

For children less than 7 years of age, parental consent is sufficient. As assent is part of the informed consent process, the regulations as per the CDSCO guidelines for regulatory clinical trials apply for assent as well.

- The type and amount of information given needs to be simplified as per the child's cognitive and developmental level. The information should be simple, and age-appropriate. Content of the assent form has to be in accordance with the developmental level and understanding capacity of the child. For example, a child aged 8 years should be told what exactly she/he is going to undergo, although they may not understand the concept of research. Younger children are better able to grasp the more practical aspects of research (e.g., what they are expected to do or what will happen) than they are to understand the abstract concepts such as randomization. For a 15-year-old, however, the assent process should be more similar to the informed consent process. If the study is of a long duration study, the researchers may have to repeat the assent process with more information, as the child grows older.

- PI/Co I will explain the study in language appropriate to the child's age before any study procedures, including screening evaluations, will be accomplished. This explanation will include a discussion of the discomforts or inconveniences the child may experience if he/she agrees to participate.

- An assent form is required for the study will be determined by the IEC. If it is required and the minor is reasonably able to understand the study purpose and requirements, then in addition to having consent form signed by the parent, the minor must sign the assent form. (Child in between 12-18 year of age are eligible for assent)

- If recommended by IEC both parents (Father & Mother) should sign assent as well as consent for child.

- The PI/Co I who explains the study will allow enough time for the minor to read the assent form and will answer any questions that are raised.

- **Consent process for illiterate parents /LARs**

  - When a participant is willing to participate but not willing to sign or give thumb impression or cannot do so, then verbal/oral consent may be taken on approval of the EC, in the presence of an impartial witness who should sign and date the document. This can be documented through audio or video recording of the participant, the PI and the impartial witness, all of whom should be captured in the frame. However, verbal consent should be an exception for specific reasons carried out with the approval of EC and not to be followed routinely.

  - In non-regulatory, observational studies, sometimes literate or illiterate, parents /LARs may verbally agree to participate but refuse to give their thumb impression. In such cases, again, the documentation of the consent process needs to be done by a literate impartial witness.

- **PI/CoI should ensure that the following will be required when children are enrolled in research**:

As per the National Commission for Protection of Child Rights, a child is defined as a person from 0 to 18 years of age.

  - Research proposals should be scientifically sound.

  - Risk or harm is a very important consideration in research involving children. Risk refers to a potential harm that can occur to the child as a direct or indirect consequence of the research procedure. The risks entailed in research procedures need to be considered when they are over and above the routine care of the participant.

  - Research may include any procedure the participant undergoes for research including questionnaires, investigations such as blood sampling, bone marrow aspiration, liver biopsy etc., or therapeutic interventions such as medication or surgery, over and above the routine standard of care for the patient. Harm occurring from participating in research may be physical (such as pain from a needle prick for blood sampling), psychological (such as fear of separation from parents) or social (such as missing school and friends etc.). Risks must be assessed in relation to benefits.

  - A benefit is a good outcome. The benefit is usually potential, which means positive but uncertain outcome. The benefit may be direct, as in a direct benefit to the participant; or indirect.

- Examples of direct benefits include the possibility of recovery, reduction in pain, improvement in disease severity, etc. Indirect benefits include the opportunity to understand more about the disease, develop social relationship with other patients, etc. Payments for participation should not be considered in the benefit-risk- ratio. Also, patients and participants may consider other benefits such as better access to doctors, access to investigations which are not otherwise freely available, being special patients as part of research, etc. These indirect benefits may be more misunderstood by illiterate patients from poor socioeconomic strata.

- **The PI/Co I obtaining the assent will ensure the following**

- All of the parent's and minor's questions were answered.
- The parent and minor understand the study requirements.
- The parent or LAR /Impartial Witness signed the assent and consent freely & voluntarily.
- The minor signed the assent voluntarily.
- The assent was signed and dated by the subject/participant, parent or LAR/Impartial Witness and the PI/Co I who obtained the consent.
- The consent form was signed and dated by the parent or LAR and the PI/Co I who obtained the consent.
- The parent and minor are given copies of the signed consent and assent.

- The CTC will ensure that the original, signed copies of the assent and consent are stored in the separate file and one copy should be given to parent and minor.

- After obtaining consent from parent and assent from children, follow the above-mentioned points 8.3.2.a, b, c & d.

- PI/CoI can request for Waiver of assent and IEC may provide waiver in the following situations:

- If the research has the potential of directly benefiting the child and this benefit is available only in the research context. In such situations, the child's dissent may be overruled.

- Waiver of assent may also be considered if the research involves children with mental retardation and other developmental disabilities, where the children may not have the developmental level and intellectual capability of giving assent.

- Assent may also be waived under the same conditions in which adult's informed consent maybe waived.
- Dissent or refusal of a child to participate must always be respected. Explanation must be given to ensure that the child understands that she/he may withdraw her/his assent at any time during the study.

8.3.7 Re-consenting the subjects/participants

- Many times, new information becomes available which would necessitate amendment of protocol (excluding any new safety related information which can harm the participant if not

immediately implemented by the investigator). **At such times, investigator / CTC should also review the informed consent to determine if it should be revised to reflect the new information.** This new information may be:

- Long term follow-up or study extension is planned at a later stage.
- There is change in treatment modality, procedures, site visits.
- In case minor, attains 18 years of age, or the legally acceptable representative has changed.
- There is possibility of disclosure of identity through data presentation or photographs (which should be camouflaged adequately) in an upcoming publication.
- **Future research may be carried out on stored biological samples if not anonymized**

o No changes to the study procedures that are a result of the protocol amendment will be implemented until the IEC approval of the amendment is received.

o If the consent form is changed as a result of a protocol amendment, the PI/CTC will ensure that the revised consent is approved by the IEC.

o The PI/ Co I will explain the changes to the subject/participant and will provide the subject/participant with the revised consent form for review and signature.

If the subject/participant decides to continue in the study and signs the consent form and the PI/Co-I also sign and dates the revised ICD, the CTC/delegated member will provide the subject/participant with a copy of the revised consent and will place the original in the separate file. Narrative for the reconsenting should be documented in source file/EMR (Refer Source Documentation SOP).

8.3.8 If Incorrect version of ICF used

If the Investigator/CTC discovers that an outdated version of the consent form was used for a subject/participant whose participation in the trial has not been completed, he/she will:

- Contact the subject and explain the reason for re-consenting the subject on the correct version.
- Instruct the subject to sign the consent with current date while signing and dating the correct version (i.e., do not back-date the consent form).
- Maintain both signed versions of the consent in the separate file.
- **Report Protocol Deviation/Violation to the IEC as per the IEC SOP format and mention the corrective action taken by the PI.**

- Write an explanatory memo in the file so that future auditors will understand why two signed informed consent documents for the same subject are present in the file. If the CTC is unable to contact the subject, the explanatory memo should also document the dates and methods by which the attempts to reach the subject were made.

Note: Please refer IEC SOPs from time to time for any new information/update and comply with the same

8.4 Applicable staff

This SOP applies to all the personnel of the clinical research team and others who may be responsible for making decisions about participation in clinical research at MPMMCC/HBCH. These include the following:

- Investigator
- Research Team Members (as per duty delegation log)

8.4 Staff responsible for Implementation

OIC CRS will ensure that the SOP is updated and available on MPMMCC/HBCH website for all the Investigators conducting studies and Investigator will ensure that the research team involved in the conduct of the study will comply with this site SOP.

PI at his/her level will ensure that at the time of implementation of the SOP, that the research team at MPMMCC/HBCH are trained and in the event that an SOP is modified, provide training regarding the change(s) and ensure their compliance with the changes.

Inform IEC that this site SOP will be implemented within the institution.

Standard Operating Procedure
Clinical Research Secretariat (CRS)

Title: Audio Visual (AV) Recording of Informed Consent Procedure.

SOP Code: SOP 08A/V1 Date: 2nd Feb 2024 Pages: 83-90

Tata Memorial Centre

MPMMCC: Sunder Bagiya, Near Nariya Gate, Banaras Hindu University Campus, Varanasi-221005, Uttar Pradesh, India

HBCH: Homi Bhabha Cancer Hospital, Ghanti Mill Road, Old Loco colony, Lahartara, Varanasi-221002, India

8A.1. Intent / Purpose:

- To describe the detailed procedure for recording, documenting, storage and archival of Audio-Visual (AV) Informed consent and assent process for regulated studies conducted in MPMMCC/HBCH.

- To ensure that Audio-Visual (AV) Informed consent is obtained from potential subject/participant identified under regulated studies (wherever applicable), as per the DCGI office order dated 25-Aug-2015, G.S.R. 611. (E) dated 31st July 2015 and New Drugs and Clinical Trial Rules, 2019.

8A.2. Scope:

a. This SOP will apply to all regulated studies (approved for AV consenting) being conducted in MPMMCC/HBCH, which requires informed consents and assents procedures for participating in the studies.

b. This SOP will be applicable to 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, which shall be maintained by the investigator for record.

This SOP will not be applicable to studies which are not falling under the purview of DCGI office order dated 25-Aug-2015, G.S.R. 611. (E) dated31st July 2015 and New Drugs and Clinical Trial Rules, 2019

8A.3. Conduct of the Policy / Protocol / Procedure:

As per the gazette notification dated July 31, 2015, it has been mandated that 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.

8A.3.1. Procedures for Audio-Visual (AV) recording of Informed Consent process:

A) Requirement/Infrastructure for AV consent process recording

- For recording the Audio-Visual consent process, rooms have been identified in MPMMCC/HBCH. Investigator/Coordinator should conduct the AV consenting in the identified locations or PI can allocate a place considering all the requirements for AV consenting.

- The identified rooms are free from disturbances, and ideal to ensure that subjects/participants are comfortable and privacy & confidentiality is maintained. PI will have to coordinate with the CRS department for availability & booking of the room prior to scheduled AV consenting.

- The camera should have following features to record the AV consenting;

  - Camera having video facility with non-editable date
  - Sufficient battery backup (at least 2 hours)
  - Sufficient memory (at least 4 GB)
  - Good resolution

Recording should be done at a distance where it can capture all the members involved in the consenting procedure.

- Investigator should ensure that faces of investigators, subject/ LAR/Impartial Witness and study team members involved in the consenting procedures are clearly visible in the recording frame.

- The voice recording device for recording the AV consenting procedures is rested on the hard platform which is free from vibration/any other disturbances.

- Before starting the actual consent procedure, Investigator should ensure that the devices are working properly.

- Investigator/Coordinator must ensure that there is enough memory/space before starting the recording process.

Note: In case of Pharma sponsored study, Investigator can use the handy camera if provided by the sponsor & the camera should meet all the specification mentioned in the guidelines and if the member recording the procedure is not from the study team then he/she should be delegated in the duty delegation log as photographer.

B) Before AV Consent recording (Pre AV-recording)

- Investigator/Coordinator/delegated study team member should ensure that the necessary infrastructure or requirements are in place and functional.

- Investigator should explain/inform the potential identified participant& relatives that the audio-visual recording of informed consent process is mandatory by law (Government of India notification) and meant for their safety and to ensure that the patients & relatives understood the elements mentioned in the consent form and voluntarily consent to participate after understanding the consent process. Consent for AV recording should be taken before starting the AV process.

- The entire process of Informed consent will be documented on audio visual consent procedure.

- Principal Investigator/ Co Investigator should assure patient about patient's confidentiality and how the site will maintain and store the data at site (refer point F below for Confidentiality & Privacy).

- Investigator should also inform the subject/participant that the AV recording can be reviewed by only study team members, ethics committee members, regulatory authority inspectors and/or judicial authority where there is a reasonable suspicious of serious non-compliance with the informed consent process and if a legal case is filed.

- Verbal consent and or assent (if applicable) for AV recording of informed consent process must be taken from subject/participant and LAR/IW (if applicable). The same should be documented in the source notes/EMR with subject/participant and LAR/IW signature.

- The approval confirmed by subject /participant and LAR/IW must be recorded at the starting of audio-visual recording by asking subjects/participant and LAR/IW if it was explained to them that the consenting process will be audio visually recorded and whether they agree for the same. The same should be documented in the patient source notes and should be signed by the Investigator conducting the consent process.

- While taking assent, including children a parent or LAR must orally consent to audio/visual recording. The same should be documented in the patient source notes and should be signed by the Investigator conducting the consent process.

Note: Subject/participant *cannot participate in the study, if he/she refuses or is not willing to consent for audio visual recording of consent process (If applicable)*.

C) During AV Consent recording

- Subjects/Participant should be made comfortable first before starting Audio-Visual consent process.

- PI/Co Investigator/delegated study team member should ensure that the team involved in the consenting process and the subject/participants/LAR and or IW are sitting in such a manner that the camera can capture everybody in the frame and the facial expressions and voice are recorded clearly.

- PI/Co Investigator/delegated study team member must mention current date and time and should identify the study protocol and introduce the study team present for the consenting procedure by name and designation and role in the study.

- PI/Co Investigator/delegated study team member should request subject/participant to give their introduction and mention his/her name, age and address and also mention the literacy status of the subject/participant.

- In order to identify the subject/participant, his / her photo ID/hospital case file cover page must be recorded.

- Incase patient is illiterate, Impartial Witness (IW) will be present during the consent process and the IW should be requested to give his/her introduction and mention his/her name, address and contact details and also mention the language he/she understands and speaks.

- In case of presence of LAR, the subject/participant /LAR should mention the relation, his/her name, contact details, as well as the reason why subject/participant cannot give consent.

- In case Investigator does not know the language of the subject/participant/LAR/IW, a study team member who understands the language, would become the interpreter.

- Before requesting an individual's consent to participate in clinical trial the Investigator must provide the individual with the information mentioned in the SOP 08/V1 (*point 8.3.2.*) in a language that is non-technical and understandable by the potential subject/participant and relatives and the same shall be recorded through audio-visual means.

- PI/CoI/study team member will also explain the potential subject/participant about the compensation guideline as explained in the study and shall ask the him/her to mention the nominee name, relationship and contact details (address and contact number) and the same will be documented in the ICF.

- All the questions asked by subject/participant /LAR/IW and answers provided by the PI/CoI or delegated study team member should be recorded clearly.

- After explaining the Informed Consent Form, PI/CoI or delegated study team member must give time to subject/participant to read and understand the consent form. If subject/participant wants to discuss the consent form with family/ relatives or consult family physician, the investigator should respect the decision and allow subject/participant to take the ICF home. The recording will stop and Investigator must mention date and time, which should be recorded appropriately. Also, the investigator will mention that the subject/participant wants time to read and discuss the consent form with family and relatives.

- On the next visit, when the potential subject/participant inform their willingness for participation in the mentioned/explained study to them, PI/CoI/delegated study team member

should resume the recording from where it was stopped last time and again mention the date and time of the recording.

- PI/Co-I/delegated study team member will ask the potential subject/participant /LAR/IW (wherever applicable) to voluntarily sign/ give thumb impression (incase he/she is illiterate) on the consent form, only after patient and LAR are satisfied with the answers given by the Investigator. (All the questioned asked and answers given should be recorded clearly).

Note: In case patient is literate/Non-English Speaking/ Illiterate, kindly follow the procedures mentioned in the SOP08/V1;8.3.3/8.3.4/8.3.6 respectively.

- The signing process should be recorded clearly, and the same should be viewed in future as the actual signature done in the real time, both by the subject/participant and/or LAR/IW and the Investigator.

- In case the patient is illiterate, Impartial Witness will write the address, contact number and other details of the patients in the ICF columns and he/she will sign in the mentioned place and date the same. IW name, address and contact number should be recorded clearly. (Note: *IW/cannot write in the subject/participant column i.e. cannot mention subject/participant name and date*)

- In case the subject/participant is minor, follow the procedure mention the SOP 08/V1 (point 8.3.6) and both the process of assent and consent should be recorded and documented clearly. In addition to that, guardian shall mention the child's name, age and the requested details while AV consenting process.

- PI/CoI/delegated study team member conducting the consent process will also sign and date the same consent form at the end of the consent process.

D) After AV consent recording

- After consenting procedure Investigator/study coordinator should save the recording and then transfer the recorded data by using pen drive to PI's computer/hard drive and must delete the information from the recording room computer.

- The AV file should be patient specific and should have standardized nomenclature for identification. The same file will also be stored in the separate DVDs for respective patients and should contain the same nomenclature on the DVD.

E.g. the file can contain;
- Patient screening no
- MPMMCC project no
- Study protocol number (If any)
- Date of consent
- PI Name

- Subject/participant Initial

- To maintain the confidentiality of the subjects/participants, The PI's PC should be encrypted using password protection.

- The DVDs should be stored in the TMF (Separate file can be maintained).

After the AV recording, the entire process must be documented in a detailed narrative in the source file or EMR.

E) Archival

Audio visual recording of informed consent process and other related documents should be preserved safely after the completion / termination of the study for at least a period of 5 years (or as per prevailing guidelines) if it is not possible to maintain the same permanently. The AV recording should be stored in a safe and secure place with access only to the PI.

F) Principle of Privacy and Confidentiality

The identity and records of the trial subjects/participant should be kept confidential during the audio-visual recording of informed consent process, as far as possible, and identity details of said subjects/participant are not disclosed unless following circumstances exist:

- There are essential valid legal reasons for the purposes of therapeutics or other interventions
- Specific consent in writing of the subject/participant concerned, or someone authorized on their behalf is obtained, and
- It has been ensured that the said subject/participant does not suffer from any form of hardship, discrimination or stigmatization as a consequence of having participated in the trial.
- Investigator will be responsible for safeguarding the confidentiality of trial data, which might lead to the identification of the individual subjects/participant.
- Data of individual subjects/participant can be disclosed only in a court of law under the orders of the presiding judge or in some cases may be required to be communicated to Drug regulatory/ Health authority.

8A.4.Applicable areas of the Hospital

- Clinical Research Secretariat
- Disease Management group (DMG)
- MPMMCC/HBCH, Varanasi

8A.5. Applicable staff

This SOP applies to all the personnel of the clinical research team and others who may be responsible for obtaining Audio Visual Informed Consent Form in the clinical research studies at MPMMCC/HBCH.

These include the following:

- Investigators
- Research Team Members (as per duty delegation log)
- Photographer (If applicable)

8A.6. Staff responsible for Implementation

OIC CRS will ensure that the SOP is updated and available on MPMMCC/HBCH website for all the Investigators conducting studies and Investigator will ensure that the research team involved in the conduct of the study will comply with this site SOP.

PI at his/her level will ensure that at the time of implementation of the SOP, that the research team at MPMMCC/HBCH are trained and in the event that an SOP is modified, provide training regarding the change(s) and ensure their compliance with the changes.

Inform IEC that this site SOP will be implemented within the institution.

Standard Operating Procedure
Clinical Research Secretariat (CRS)

Title: Recruiting study Subjects/Participants

SOP Code: SOP 09/V1 Date: 2nd Feb 2024 Pages: 91-97

Tata Memorial Centre

MPMMCC: Sunder Bagiya, Near Nariya Gate, Banaras Hindu University Campus, Varanasi-221005, Uttar Pradesh, India

HBCH: Homi Bhabha Cancer Hospital, Ghanti Mill Road, Old Loco colony, Lahartara, Varanasi-221002, India

9.1 Purpose

This SOP describes the procedures the study team will use for recruiting eligible subjects/participants into a study while following the protocol and fulfilling ethical responsibilities for protecting the rights, safety and welfare of subjects/participants and maintenance of a screening log.

9.2 Scope

This SOP will apply to all clinical studies being conducted at MPMMCC/HBCH.

9.3 Procedure

There are several steps involved in subjects/participant recruitment. These can be summarized into developing a recruitment plan or strategies and activities covering the entire recruitment period, including pre-screening and screening the subjects/participant to ensure that they meet the inclusion and exclusion criteria; and the enrolment in the study.

ICH GCP requires that records are kept of every subjects/participant that undergoes pre-trial screening (ICH GCP 8.3.20) i.e. details of all subjects/participants approached for a study should be maintained. For the purposes of this SOP, this shall be referred to as a screening log.

9.3.1 Recruitment strategies

Investigator must schedule a meeting prior to enrolment, in order to secure the co-operation of study team to obtain a sufficient number of subjects/participants. PI will give the protocol training and training log should be maintained in the TMF/SMF.

During the meeting the study protocol will be reviewed/ re-discussed and the inclusion and exclusion criteria and study related procedures and tests will be discussed in detail.

Investigator can provide the detailed inclusion and exclusion pamphlet to the entire study team members for their reference.

Using the eligibility criteria for the study, the Investigator/study team or CTC will review records from the Investigator's patient population OPD & inter departmental referrals to determine the suitability and availability of candidates for the protocol.

Study team should inform the Investigator/ CTC, if they identify any potential subject/participant for the study.

Any queries regarding subject/participant eligibility must be referred to the Principal

Investigator.

The investigator is responsible for ensuring the unbiased selection of an adequate number of suitable subjects/participants according to the protocol.

Investigator should check whether the subject(s)/participant(s) so identified could be included in the study according to the protocol.

PI will make sure that the study team is being made aware of all the current information of the study and the eligibility criteria to increase the screening number and to avoid loss of subjects/participants.

The investigator should keep a confidential list (e.g. Screening log AX1-V1/SOP 09/V1, and enrolment log (AX2-V1/SOP 09/V1). This list facilitates the investigator / institution to reveal identity of the subjects/participants in case of need and also serve as a proof of subjects/participants existence. The investigator / institution shall also maintain a subjects/participant screening log to document identification of subjects/participants who enter pre-study screening.

9.3.2 Participants Identification/Pre-screening

Appropriate patients assessed in the OPDs (general and private) by the investigators.

The study team/investigator/CTC must study the patient's past and current history and investigations to evaluate if subject meets the eligibility criteria.

If the subject/participant meets the eligibility criteria, the study team must inform the investigator/CTC and CTC must document the following details in screening log (AX1-V1/SOP 09/V1)

- Case number
- Subjects/Participants name
- Contact number
- Disease stage/other information required as per protocol
- Date screened

CTC must store the case file in the relevant department till the eligibility is confirmed.

9.3.3 Subjects/Participants screening

All potentialparticipants must be sent to the respective investigator or CTC for further counselling and to obtain Informed consent.

Investigator should begin the informed consent process and obtain informed consent prior to screening (refer to the applicable SOP) and also document the date that the ICF was signed

(or the reason if it was not signed) in the source notes and the enrolment log.

CTC should schedulesubjects/participants visit for performing the study-specific screening procedures.

CTC must review the screening check list to ensure that all the protocol specific screening procedures are performed and facilitate the same.

Investigator and CTC will review the screening reports and will confirm subject's/participant's eligibility.

If investigator finds the prospective subjects/participants eligible, investigator must inform the same to the subjects/participants and the sponsor/CRO, if applicable.

If a prospective study subject/participant is found to be ineligible, inform the same to subjects/participants and or LAR and document the reasons for screening failures in the enrolment log and in the source documents. Store the enrolment log (AX2-V1/SOP 09/V1) in the study files.

9.3.4 Subjects/Participants enrolment/ randomization:

Once the subjects/participant is found suitable for the study, based on available information as per standard of care, informed consent must be obtained prior to initiating any trial specific procedures. Document recruitment activities on the source notes, & EMR and/or enrolment log as appropriate while maintaining subject/participant confidentiality.

Once a patient has consented, enrol the eligible subject/participant into the study and follow the trial randomization procedures, if any.

When a subject/participant is enrolled in a study, the following information will be entered on the source notes and EMR:

- Study short title
- Subject/participant randomization number
- Date of randomization
- Randomization group/arm
- Place a study sticker containing study ID and study name on the patients file.

If the trial is blinded, the investigator should promptly document and explain to the sponsor in case of premature unblinding (e.g., accidental unblinding, unblinding due to a serious adverse event) of the investigational product(s) and should ensure that the code is broken only in accordance with the protocol.

9.4 Applicable staff

This SOP applies to all the personnel of the clinical research team and others who may be responsible for subjects/participants recruitment in the study.

These include the following:

- Investigator
- Research Team (listed in the delegation log)
- CTC

9.5 Staff responsible for Implementation

OIC CRS will ensure that the SOP is updated and available on MPMMCC/HBCH website for all the Investigators conducting studies and Investigator will ensure that the research team involved in the conduct of the study will comply with this site SOP.

PI at his/her level will ensure that at the time of implementation of the SOP, that the research team at MPMMCC/HBCH are trained and in the event that an SOP is modified, provide training regarding the change(s) and ensure their compliance with the changes.

PI & study team member will ensure that the study team is following the SOP during the recruitment of the subjects/participants in the IEC approved protocol. Inform IEC that this site SOP will be implemented within the institution.

AX1-V1/SOP 09/V1
Screening Log*

Study Title:
IEC project No:
Principal Investigator:

Sr. no.	Date	Case No	Patient Initials	Eligible for enrollment (Y/N)	Ineligibility Reason	Remark

Subject to change as per protocol requirements

AX2-V1/SOP 09/V1

Enrolment Log/Randomization Log*

Study Title:
IEC project No:
Principal Investigator:

Screening No.	Trial ID/ Enrolment No	Date	Case No.	Patient Initial	Trial Arm (if applicable)	Randomized by

Subject to change as per protocol requirements

Standard Operating Procedure
Clinical Research Secretariat (CRS)

Title: Source Documentation

SOP Code: SOP 10/V1 Date: 2nd Feb 2024 Pages: 98-103

Tata Memorial Centre

MPMMCC: Sunder Bagiya, Near Nariya Gate, Banaras Hindu University Campus, Varanasi-221005, Uttar Pradesh, India

HBCH: Homi Bhabha Cancer Hospital, Ghanti Mill Road, Old Loco colony, Lahartara, Varanasi-221002, India

10.1 Purpose

This SOP defines the process and requirements related to the creation, maintenance and retention of all source documentation for the research studies conducted at MPMCC/HBCH.

10.2 Scope

This SOP will apply to all clinical trials conducted at MPMCC/HBCH.

10.3 Procedure

10.3.1 Information regarding source documents

Source documents are records, independent of the Case Report Form (CRF), which document the subject's/participant's eligibility for participation in the study, all study-related treatments and procedures, observations that constitute the data for the research study, and any other data pertinent to the study.

Examples of source documents include, but are not limited to, the following:

- EMR and Patient's hospital case file
- Signed and dated Informed Consent Forms.
- Subjects/Participants medical record or office charts.
- All treatment charts/chemotherapy protocol sheets/RT sheets/ admission sheets
- Patient-specific correspondence which is retained in the medical record or office chart.
- Laboratory test results, requisition forms, and maintenance records.
- Films of x-rays, MRIs, CTs, and other diagnostic tests along with their interpretation.
- ECG tracings and interpretations
- Subjects / Participants' diaries
- Data recorded directly onto the CRF e.g. QOL CRF (if identified in the protocol)
- Study worksheets signed and dated by delegated team member (if data is recorded that is not otherwise available in the EMR.) Such worksheets should preferably be on MPMMCC & HBCH Continuation Sheets and should be signed and dated by the PI/Co-I.

Proper data collection is essential to the outcome of research study. All research related information should be recorded in a way that ensures the integrity of the data. Maintaining the confidentiality of research subject's /participant's personal information is an integral part of their protection, and is the focus of numerous guidelines and laws.

All entries in the CRF must be supported by data recorded in the source document. Since the source documents are the primary source for all study-related data, proper completion and retention of source documents is of paramount importance. If an event or outcome is not properly documented in the source document, it is assumed to have not occurred.

PI and study team must apply ALCOAC to achieve data quality.

- **A**ttributable: is it obvious who wrote it?
- **L**egible: can it be read?
- **C**ontemporaneous: is the information current and in the correct time frame?
- **O**riginal: is it a copy; has it been altered?
- **A**ccurate: are conflicting data recorded elsewhere?
- **C**omplete

MPMCC/HBCH has also adopted the computerized system to generate and maintain patient records and enable the authorized individual to create, modify, maintain, archive, retrieve, or transmit data. CIS and EMR are the two systems. CIS is used for data entries and EMR is used to view data and all relevant patient reports, procedures, etc.

EMR and CIS are interlinked, one can make changes in CIS but EMR can only be use to view data and does not allow any changes.

The following information will be available on the EMR, but not limited to:

- **Patient Registration details**
- **General Hospital consent form**
- **Clinical evaluations:** History, Examination, Remarks and Addendum, Clinical notes, Clinical diagnosis, JC and Treatment Plan in the EMR all.
- **Investigation report:** This link categorizes the reports as Outside Scanned Reports, Radiology, Nuclear Medicine (PET / Bone Scan etc.), All Lab Reports and Surgical Pathology or others.
- **Treatment details:** This link will give the treatment details related to Surgery Record: PAC, Major / All surgeries (Major & Minor), Anesthesia Records, chemotherapy and radiation details. Inpatient admission and discharge date etc.
- **Follow Up records.**

10.3.2 Documentation of source data

The documentation of source data should primarily be done in the EMR. PI and study team members should ensure all study specific entries on EMR should contain some study identifiers such as Protocol number, Short study title etc.

PI should keep a signed and dated copy of all relevant data/ information which is not available on EMR e.g., admission notes, participants medical record or office charts, all treatment charts, chemotherapy protocol sheets, Radiotherapy sheets etc.

If required, PI/ Study team member can take the printout of EMR to make a paper copy of the source documents. All such printout copies should be signed and dated by the PI/Co-I/

delegated study team members.

Investigator and research team members must start documentation of source data as soon as the subject/ participant is identified for the study.

The source documentation must contain adequate information to verify that the participant satisfies the study eligibility criteria as defined in the protocol.

Once each subject/participant has signed the approved informed consent form, the following medical information should be documented preferably on EMR by Investigator/ study team members. The information may include but not limited to:

A) Screening Visit

- Demographic data of the subject/participant (Name, Date of birth and Sex)
- Patient's medical history, diagnosis, and medical follow up if any
- Concomitant medication, current and previous if any (with start and stop date)

B) After enrolment and randomisation

- Detailed informed consent process
- Date of screening and randomization details
- Subjects/Participants screening and randomization number
- Randomization arm if applicable
- In case of screen failure, investigator must document the reason for the same
- Also mention if subjects/participants consented for the biological or genetic study (if any).

C) During study conduct

- Protocol specific procedures and visits
- Details of Study specific visits, assessments, investigations, interventions and/or treatments including IP, adverse events, follow up visits and any other events/ occurrences as defined in the respective protocol

All medical decisions must be taken by a medically qualified study team member listed in the duty delegation log.

In case of AE or SAE, Investigator or CTC should document details of the available information related to the event including possible etiology, relevant test results, treatment received, and the subsequent and final outcome with appropriate start and stop date.

All diagnostic testing results including laboratory reports, CT scan, MRI, ECGs, etc. are to be properly maintained and retained as source documents. If these reports require review by the PI/ Co I, this review must be completed within a stipulated time period of the report being

received and must be signed and dated by the investigator to document that this review was completed.

Reports of objective tests (e.g. laboratory reports, X-rays, ECG, scans, etc.) must be signed by the investigator and interpretation should be done (where applicable) for each report categorizing as “Clinically significant (CS)” or “Non-Clinically Significant (NCS)”

Note: PI/ CoI will mention NCS/CS on each report as per their individual interpretation with respect to protocol.

Source document should be updated at each subsequent visit. Documentation, outlining any issues associated with a specific subject’s/participant’s involvement in the research study, should be updated as necessary at each subsequent study visit with any new medical conditions or with any past medical history that becomes known to the research team.

Case Report Forms and source documents are maintained separately, but source documents should be available along with the case report form for source data verification.

All communications between the various parties (PI, CoI, CTC, subject/participant or subject’s/participant’s relative, monitor, sponsor/CRO) and communication method should be documented with sign and date.

All data must be entered in a sequential manner, without leaving any empty spaces. If any missed data is observed related to subject/participant, it should be documented promptly on the current date with appropriate justification.

Use preferably black ink in study files and source documents.

Note: Any document in which research study data is recorded for the first time, will considered to be a source document (e.g. notes, appointment book, subject/ *participant reports or medical file, diaries, etc.)*

10.3.3 Correction of Source Document

Any corrections in the paper source documents, if any, must be crossed out with a single line (original entry should be visible) and the correction written next to the original must be dated and initialled.

No revisions or corrections to the source document can be backdated; all corrections must be dated on the date the correction is made. A note of explanation is needed to clarify source documentation, this note is to be dated with the date that the explanation is written, signed by the individual that made the original source document entry or delegated study team members.

Never obscure the original entry, erase or delete the original entry or cover the original entry in a paper document with correction fluid.

Any source data corrections in the EMR should be done on current date with respective clarification for the same. The following details should also be mentioned in this note

- Reference to the original note which needs correction including the date
- Reason for correction
- Name of the person making the correction

10.3.4 Maintenance of Source Document

After completion of the study, source documents should be retained by the PI for the period of 3 years (or as per prevailing guidelines).

10.4 Applicable Staff

This SOP applies to all the personnel of the clinical research team who may be responsible for data entries as per the delegation log. These include the following:

- PI/Co I
- Research Team (listed in the delegation log)

10.5 Staff responsible for Implementation

OIC CRS will ensure that the SOP is updated and available on MPMCC/HBCH website for all the Investigators conducting studies and Investigator will ensure that the research team involved in the conduct of the study will comply with this site SOP.

PI at his level will ensure that at the time of implementation of the SOP, that the research team at MPMCC/HBCH are trained and in the event that an SOP is modified, provide training regarding the change(s) and ensure their compliance with the changes.

Inform IEC that this site SOP will be implemented within the institution.

Standard Operating Procedure
Clinical Research Secretariat (CRS)

Title: CRS Research Pharmacy Management

SOP Code: SOP 11/V1 Date: 2nd Feb 2024 Pages: 104-139

Tata Memorial Centre

MPMMCC: Sunder Bagiya, Near Nariya Gate, Banaras Hindu University Campus, Varanasi-221005, Uttar Pradesh, India

HBCH: Homi Bhabha Cancer Hospital, Ghanti Mill Road, Old Loco colony, Lahartara, Varanasi-221002, India

11.1. Purpose

- To provide detailed procedures and requirements related to the receipt, appropriate handling, storage and dispensing of Investigational Products (IPs) and supplies in compliance with applicable national and state regulations, international standards, and institutional policies and procedures.

- This document will provide details on operational activities to be performed by the delegated staff with respect to IPs handling. This SOP will provide detailed information on the following sub topics under pharmacy management. Each subtopic will be defined separately with appropriate information;

  - Receipt of IP
  - Inventory Management of Investigational Product (IP)
  - Management of IP storage Temperature
  - IP Return and Destructions
  - Regulatory Instructions
  - Sponsors responsibility
  - Study Closeout

- Additional instructions shall be followed, if any described in the study protocol, Manual of Procedures (MoP) and any other study specific standard operating procedures (SOPs) provided by the sponsor and or any of the collaborating centers.

- All investigators should also refer to the current version of the IEC SOP available on the MPMMCC/HBCH website.

11.2 Scope

This SOP applies to all clinical trial IP supplies stored in CRS research pharmacy and for all the future IP supplies planned to be stored in the CRS pharmacy.

To educate all the Principle Investigators, Co Investigators and study team, involved in the indent, receipt, storage, maintenance and handling of study IP supplies about the operating procedures of the CRS pharmacy and the roles and responsibilities of the CRS research pharmacist.

This SOP will not be applicable to the products that are not supplied under any trial and those which do not qualify the criteria to store the product in the CRS pharmacy.

In circumstances where a PI/Co-I cannot comply with the general standards outlined in this document, he/she must coordinate with the CRS research pharmacist and inform the CRS OIC.

11.3 Procedure

The CRS has been given the responsibility for maintaining the research pharmacy and ensuring that the study IP is being handled in compliance with NDCT Rules 2019, ICH GCP, Indian GCP, national, international quality standards and as specified in the respective study protocol. The research pharmacy has been developed to maintain and handle the trial IP as per the applicable guidelines and laws and to support the PI and Co I to store and handle the products in the requested conditions with secure and limited access.

11.3.1. Inventory Management of IP

The objective of this is to ensure that all the team members involved in the Inventory management process are aware of their responsibilities as per GCP, NDCT Rules 2019 and CDSCO guidelines, applicable guidelines and institutional policies.

This will describe the inventory management of IP for clinical research conduct at MPMMCC/HBCH and will ensure compliance.

11.3.1.1. IP Indent:

- **IP Indent for investigator-initiated studies:**
  IP can be indented / procured through our institute online Material Management Systems by Study PI and or team member. The PI/CoI will need to log into the MPMMCC/HBCH Intranet (link: http://intranet.tmc.gov.in) and then click on the On-Line Indent and enter the unique Username and Password. Required IP and quantity can be indented in the system.

- **IP Indent for Sponsored/Pharma studies*:***
  The procedure for study drug request will be discussed immediately after study final approval or during the SIV. Initial supply is always sent automatically from sponsor either before or on the day of SIV. PI/ study team member should notify CRS pharmacy (written communication) in advance about the arrival of study drug at site for permission to store the IP at CRS pharmacy (AX3– V1/SOP11/V1) after study initiation; the PI will intimate CRO or sponsor regarding drug inventory procedures followed in the CRS research pharmacy. During the conduct of the study, study team member will keep accountability for IP indent to place an order in advance to ensure the availability of study drug at site. The indent mechanism will be a preferred method either by web (IWRS) or by telephone (IVRS) as agreed by the PI and sponsor.

11.3.1.2. IP Receipt

Upon receipt, CRS Research pharmacist and/or delegated study team member will check if the IP received is in the required/mentioned condition with respect to temperature and will verify the following things against the protocol and shipment invoice;

- Study name and number
- Study drug name/Lot number

- Study drug dose and formulation
- Check the template if provided with the consignment or the temperature record upon receipt of IP.
- Expiry date/Retest date
- Quantity of drug against the invoice received
- Signatory/Prescription Roaster (Attached)
- Statement: “CAUTION: New investigational Test Article-Limited to investigational use.”

- After ensuring that the IP is intact and received in safe condition, the study team member will acknowledge the received IP in the respective IWRS/IVRS system for sponsored study and the confirmation from the system will be documented in the TMF. The inventory receipt of the IP will be done by the CRS research pharmacist in the CRS pharmacy Inventory system. Copy of the same can be maintained in the Trial Master File. The updated record of the system can be shared with the PI only after the request email from PI/delegated study team member.

- For investigator-initiated studies the inventory receipt of the IP will be done by the CRS Research pharmacist and or study team member in the CRS pharmacy Inventory system. Copy of the same can be maintained in the Trial Master File/Site Master File. The updated record of the system can be shared with the PI only after the request email from PI/delegated study team member.

- In case CRS Research pharmacist and or study team member witness any discrepancies upon receipt of IP, wherein the temperature is not maintained or the quantity is not matching with the invoice received, or found any damaged products, CRS Research pharmacist /study team member will immediately inform the respective PI. PI/study team member/ CRS Research pharmacist will communicate with the sponsor for further action. An appropriate action will be taken according to specific instruction provided by the sponsor and/or as described in the protocol /IB in accordance with the applicable guidelines and regulations.
  Unless clarified from the sponsor the drug cannot be used and must be kept separately with proper labeling as “Quarantine”.

Note: The CRS research pharmacy inventory log is specific for CRS research pharmacy recording and maintenance use only, study team member should maintain their own logs and if requested (via mail/letter) a copy of their respective study records will be shared.

11.3.1.3. IP Dispensing

- CRS Research pharmacist (if delegated) will dispense the IP to the study team member after completion of prescription form duly signed by the PI/Co-I or delegated study team. Further the study team member will be responsible to dispense the IP to the respective research subject scheduled for the protocol study visit.

- CRS Research pharmacist (if delegated) and or delegated study team member will follow the respective protocol for drug dispensing procedure. The IP dispensing could be done via IVRS/IWRS or as specified in the protocol.

- Before dispensing the IP upon receipt of authorized prescription (AX1– V1/SOP01/V1) CRS Research pharmacist (if delegated) and /or delegated study team member shall check & ensure that the following details are mentioned on the IP package;
  - Participant ID
  - Study number
  - Protocol number
  - Name of investigator
  - Dispensing Date
- The IP label should be rechecked before dispensing and should clearly show the above details and the 'CAUTION - New Investigational Test Article-Limited to investigational use only' (for sponsored studies only). For Investigator-initiated studies IP stored in CRS pharmacy, CRS Research pharmacist will put IP labels (Format Attached) (AX2– V1/SOP11/V1) and the same will be informed to respective PI.

- For injectable IP, CRS Research pharmacist will hand over the IP to the research nurse (delegated) and research nurse will be responsible for dose calculation, drug preparation and administration (as per study protocol).

- For oral IP, CRS Research pharmacist /study team member shall ensure that the bottles/ strips dispensed are intact and the quantity is sufficient (as mentioned in the prescription form) for use until next scheduled visit. In case the quantity to be dispensed is not outlined in the protocol, the CRS Research pharmacist or the study team member will calculate the number of IPs to be dispensed which will be sufficient until next scheduled visit and shall dispense accordingly.

- In case of 6 month follow up or more, wherein the intact bottles are required to be dispensed as per the protocol, study team member/ CRS Research pharmacist may dispense the IP as long as the following conditions are fulfilled;
  - The patients are scheduled to visit prior to the IPs expiration date.
  - The study team should be aware of the IP expiry date and the same should be informed to the subject and relatives.

    A sticker says 'Do not use after "mention expiration date"' is mentioned on each bottle or container.

11.3.1.4. IP Accountability

CRS pharmacy has its own pharmacy inventory system to maintain study drug accountability, which will document IP receipt, storage, dispensing of IP stored under purview of CRS pharmacy. This log is designed for CRS documentation only.

Every time IP received, dispensed, returned or destroyed, every action must be documented in the CRS pharmacy accountability log and in the system. The inventory balance should match the actual IP inventory available at pharmacy.

- CRS Research pharmacist (if delegated) and or delegated study team member will make sure that the accountability log/system is updated with respect to the amount of drug dispensed to the subject and also ensure the records updated includes the following, if applicable:

- Name of the institution
- Name of investigational product, dose form and strength
- Protocol title and number
- Name of principal investigator
- Name of manufacturer or product source
- Lot number or other control/identification number
- Study subject initials/unique identification number
- Dose received/dispensed
- Quantity received/dispensed
- Date received/dispensed
- Remaining balance
- Initials of recorder

- CRS Research pharmacist and or study team member should document all the requested details in the CRS drug accountability log and or system, whenever they access the pharmacy for drug storage, dispensing and accounting.

11.3.1.5 Inventory of drug supply maintenance

Study team member will ensure that the sponsor will supply sufficient IP to the site as per the institutional target accrual. In case of Investigator-initiated studies PI will ensure sufficient availability of IP at site and reordering of drug on regular interval for availability of adequate IP at site.

Sponsor will be responsible for IP re-resupply and will ensure that the site has sufficient IP for study continuation and future enrolment. For IPs stored at CRS pharmacy, inventory will be maintained till study closeout or as per prevailing guidelines.

11.3.1.6 Storage and Security

- **Procedure for IP Storage: Requirement for Storage and handling of IP during the conduct of the study:**

- The research pharmacy will provide required secure storage conditions for IP. PI shall take permission for storing IP in CRS research pharmacy; the letter seeking permission (AX3–V1/SOP11/V1) should include the project number, PI name, drug name, strength, quantity and the required temperature for drug maintenance. PI/Co-I should identify and mention the name of the responsible Coordinator/research nurse/study team member who will be coordinating with the CRS Research pharmacist (AX8-V1/SOP11/V1). No IPs will be stored without permission in the CRS research pharmacy. During the conduct of the study, PI must intimate OIC CRS &CRS Research pharmacist regarding the IP resupply, prior to the IP arrival.
- PI can request OIC, CRS for access to visit CRS research pharmacy, to check the IP storage and to ensure if the IP is stored as per the protocol requirement.

  Note: IP that are not stored in the CRS research pharmacy *(e.g. stored in the respective PI department) will not be the responsibility of the CRS and this SOP will not be applicable for such storage, additional guidelines can be followed for this.*

- After inventory confirmation of the study products in the IVRS/IWRS system, CRS Research pharmacist/ study team member shall store the IP in the CRS research pharmacy, in the required storage condition as directed in the study protocol, IB or package insert.
- CRS Research pharmacist will ensure that the proper storage conditions are maintained for the IPs. This should include but not limited to;

- Suitable security (controlled and limited access)
- Appropriate temperature controls and temperature monitoring measures to prevent exposure to extreme temperature, light and humidity.
- Adequate ventilation and sanitation
- Separation of quarantined and expired IPs from active stock.

For blinded studies active IP must be stored separately from placebo agents.

- Drugs can be stored under following conditions;

- **Storage at room Temperature (15 to 25 °C):**
- CRS research pharmacy is equipped with cupboards having separate cabinets for respective DMGs and an identifier has been placed on each shelf (e.g. Breast DMG, Head & Neck DMG, GI DMG, etc.)

- .A separate drug storage box should be used for each study. CRS Research pharmacist will store the study product in the respective study boxes in their respective allotted cabinets

- CRS Research pharmacist and or study team member should enter all the requested details in the CRS drug accountability log, whenever they access the CRS research pharmacy for IP storage, dispensing and accounting visits. Study team member will hand over the study IPs to CRS Research pharmacist for IP storage and CRS Research pharmacist will hand over the IPs to delegated study team member at the time IP dispensing and accountability visits

- Calibrated thermometer has been installed in the CRS research pharmacy to record the temperature. Temperature for the day should be recorded in the temperature log (AX5-V1/SOP11/V1).

- **Storage in Walk-in Cooler/Refrigerator (2-8 °C):**

- **Walk-in Cooler/Refrigerator** has separate area for storage of respective DMG drug and an identifier has been placed on each compartment (e.g. Breast DMG, Head & Neck DMG, GI DMG, etc.)

- Separate storage boxes for each study should be kept in the respective compartment to store the products.

- Limited access to PI/Co-I/research nurse/study coordinator, in the CRS research pharmacy. The access to visit CRS research pharmacy can only be allowed with prior permission from OIC CRS with valid justification.

- Separate drug accountability log is kept in the CRS department to document individual DMG IP details and their accountability under individual PI names with box numbers and study details (AX4– V1/SOP11/V1). The records will be updated in the CRS research pharmacy data management system.

- CRS Research pharmacist and or study team member should enter all the requested details in the CRS drug accountability log, whenever they access the CRS research pharmacy for IP storage, dispensing and accounting visits. Study team member will hand over the study IPs to CRS Research pharmacist for IP storage and CRS Research pharmacist will hand over the IPs to delegated study team member at the time IP dispensing and accountability visits.

- **Walk-in Cooler/Refrigerator** is installed in the CRS research pharmacy to store the IP requiring temperature between 2-8°C.

- Special precautions have been taken to prevent temperature fluctuations by incorporating alarm system which will give alert to the CRS department and the security in case the temperature fluctuates beyond the predetermined limits.

- To record the actual temperature reading, temperature logger has been installed, which will record actual temperature twice a day (i.e. morning and evening).

- **IP Security:**
- The IP stored in the CRS research pharmacy is under close observation of CRS Research pharmacist and kept in secured lock & key facility.

- Limited access only to the authorized personnel, in special situations in presence of CRS Research pharmacist after OIC-CRS approval.

- The CRS research pharmacy is under surveillance to ensure secure conditions.

- IPs requiring special storage and/or handling must be identified and availability of space and equipment for storage will be determined by the CRS department and or CRS Research pharmacist before receipt of the study product.

- In the case of a power outage, an identified backup power source has been put in place to supplement the primary source, if needed.

- In case of an equipment malfunction, the CRS research pharmacy has a policy in place wherein the IP can be transferred to Hospital pharmacy to maintain investigational products within appropriate conditions.

11.3.2 Management of IP Temperature

11.3.2.1. Temperature monitoring

- CRS research pharmacy uses Calibrated temperature logger, having the facility of continuous temperature monitoring system with a display of minimum, maximum and average temperature of the pharmacy drug storage area.

- A temperature log (AX5–V1/SOP11/V1) has been maintained by the department of CRS. CRS research pharmacist is responsible for documenting the actual average temperature twice a day. (Except Sunday and Hospital holidays)

- The record will be verified by the CRS in charge by signing the log

- temperature logger has been installed to record and display the Refrigerator temperature. Electronic readings will be recorded in the temp logger, at the interval of 1 hours, at maximum. In case the electronic logger not working, the temperature must be recorded manually, then daily temperature readings must be maintained, at minimum twice daily. (Except Sunday and Hospital holidays)
- If, for any reason, temperature conditions have not been preserved, the occurrence must be documented as well.

- The cold storage is wired with the hospital security system department which provides continuous 24-hours surveillance. In situations where in temperature exceeds the acceptable range an alarm will ring near the security area which will alert the respective departments for further appropriate action.
- In such situation, if required, IP will be transferred to a similar space having all the required conditions.
- The temperature and condition of the unit will be observed prior to return of the inventory to the unit.
- In the event of a temperature deviation, any IP inventory in question will be quarantined in the appropriate storage condition until the IP is deemed appropriate for use.
- The quarantined inventory will be segregated from the other IP and should be clearly marked as not for dispensing.
- Temperature monitoring device provided by Sponsor will not be used by CRS research pharmacy in addition or in place of CRS research pharmacy device.

11.3.2.2 Temperature Excursions

Temperature excursion can occur anytime when there is a deviation from the storage conditions described in each specific protocol storage requirement. However before documenting any temperature excursion, rounding rules will be taken into account. e.g. room temperature 14.5 will round up to 15 and cannot be considered as excursion. Alternatively, a temperature of 14.4 would be rounded down to 14 and this would be considered as temperature excursion.

- For standard controlled room temperature, reportable excursions are defined as a temperature deviation of >±5˚C from the acceptable temperature range as defined, sustained for a continuous time period of up to 2 hours.
- For cold storage, reportable excursions are defined as a temperature deviation of >±2 ˚C from the acceptable temperature range as defined above, sustained for a continuous time period of up to 2 hours.
- In case of temperature excursion, PI will be notified of such event via email and official letter from CRS research pharmacy outlining all the details regarding the deviation. PI will be responsible for notifying such events to sponsor and Ethics.

Affected IPs during excursion should be kept separately as quarantine until further guidance and written information from sponsor or PI.

11.3.3 IP Return and Destructions

11.3.3.1 Empty containers

- In order to maintain cleanliness and avoid confusion, all the empty containers of IPs should be immediately disposed after inventory and IP storage. This will include all the empty boxes of IP shipment and additional thermocol boxes. Study team member and CRS Research pharmacist will be responsible to ensure that there no empty boxes lying in the CRS research pharmacy after IP inventory.

- Used or partially used IP vials and supplies: Partially used IP vials should be kept separately and should not be mixed with the intact IPs to avoid confusion. Partially used IPs should be returned to sponsor on the immediate monitoring visit, after proper accountability and documentation. CRS research pharmacy will not accommodate partially used IP for more than 90 days.

- PI will be responsible for accountability of partially used IPs and IP accountability visit and CRS research pharmacy should be informed in advance about such visit and requirement of IPs for accountability.

11.3.3.2 Oral subject/participants returns

- Subject/participants on their scheduled visit shall return the package of used IPs /partly used or unused IPs to the study coordinator/research nurse.
- The person collecting the used IPs package shall check the package for number of drugs consumed and number of drugs remaining in the packet. Accountability for the same has to be documented in the source notes and accountability log shared by the sponsor or maintained by the investigator in case of investigator-initiated studies.
- In case, study coordinator/research nurse notices extra or less pills than accounted as per the scheduled visit, they must ask the patient for the reason and document the same in the source notes. In case the CRS Research pharmacist notice about any such instances, he/she will inform the study team and they ensure the aforementioned justification for the same.
- After reconciliation the returned IP container will be retain for further reconciliation by the monitor during monitoring visit and the used IPs shall be returned on the same monitoring visit or no longer than 90 days.
- Returned IP containers cannot be stored in the CRS research pharmacy, for more than 90 days.

11.3.3.4 Expired/Unused IP

- All expired IPs will be retained at CRS research pharmacy separately with proper instruction. These IP will be stored for no longer than 90 days from the date of expiry.
- All unused IPs will be retained at CRS research pharmacy for no longer than 90 days after enrolment completion date.
- At the end of 90 days or agreed extension any remaining expired IP will be returned to respective PI. A note for the same will be documented in the respective accountability log.

11.3.3.5 Return, Transfer, and Destruction

- Study team member will be responsible for IP return, transfer or destruction. CRS Research pharmacist can guide study team member for drug destruction process.
- IP packages will be returned to the sponsor after confirmation and documentation by the monitor at monitoring visit or as agreed by the PI.
- Study team member will maintain the return receipt in the TMF.
- For investigator-initiated studies; IP destruction will be done in accordance with the institutional policies.
- For sponsored trial IP will not be destroyed at site, it will be sponsors responsibility to transfer the IP from site for destruction. In case sponsor request site to destroy the used drugs at site it has to be a written communication and for such destruction, hospital destruction guidelines will be followed.
  - Information regarding the policy for IP return, transfer or on-site destruction should be discussed and informed to OIC CRS at the time of permission to store the drug at CRS.
  - Any time IP is returned to the product supplier, destroyed on site, or is transferred from one protocol to another, this occurrence must be informed to CRS department and shall be documented in the accountability log(s)
  - The following information should be included for record keeping:
  - Study MPMMCC project no.
  - DMG name, PI name & department
  - Information specific to the IP including but not limited to the IP name, strength, dosage form, quantity of IP per container, number of containers, lot/control number, etc.
  - Date of return/destruction/transfer
  - Name and signature of personnel responsible for destruction.
- Destruction certificate should be stored in the TMF/SMF.
- Records of IP accountability are kept as long as required by Sponsor or for the period of 5 years (or as per prevailing guidelines).

11.3.4 Regulatory Instructions

11.3.4.1 Duty Delegation

- Identified qualified and trained personnel after completing the respective and applicable SOP/ protocol training should be listed in the duty delegation log. These study team members will be responsible for the duties delegated to them by the PI.
- CRS Research pharmacist and delegated team members listed in CRS research pharmacy Signature & Delegation Log (AX6– V1/SOP11/V1) appointed under CRS will manage the IPs stored in the CRS research pharmacy as per the task delegated in delegation log. PI can allocate the entire IP responsibility from drug receipt, storage & maintenance, dispensing, return to sponsor and inventory in the CRS research pharmacy inventory systems (subject to approval from OIC CRS) or PI can request to only maintain the IP in the CRS research pharmacy.
- In case PI decides to allocate the entire IP management responsibilities to CRS Research pharmacist, PI will have to include the CRS Research pharmacist in the study team and delegate the responsibilities according to the IEC SOP.

11.3.4.2 Team Member responsibility

Following will be the responsibilities of the study team members;

A) Study Product Accountability/Dispensing Logs

- CRS Research pharmacist and or study team member will ensure that all drugs dispensed under research protocol should be accounted for in the inventory system.
- The study product accountability log or dispensing log may take the form of a continuous computerized record or a paper document. If a computerized log is used, it will have an audit trail
- Information included in the accountability log:
  - Study MPMMCC project no.
  - DMG name, PI name & department.
  - Name, dosage form, strength of the study product.
  - Date of receipt of the study product
  - Quantity received
  - Quantity dispensed
  - Balance of drug currently available

Note: CRS research pharmacy record will be maintained by research • CRS Research pharmacist under the supervision and control of OIC CRS.

B) Record Retention

- CRS research pharmacy record will be maintained by the CRS Research pharmacist under the department of CRS for all the IPs stored in the CRS research pharmacy.
- All records will be retained as per prevailing regulatory requirements.
- Records must not be destroyed until written approval given by the Sponsor/PI and IEC has been granted.

11.3.4.3. Training

Study team member must be trained on GCP, CRS research pharmacy SOP, and respective study protocol and Investigator Brochures (IB). The training records have to be documented and maintained appropriately in the trial master file.

CRS Research pharmacist should be trained (brief training) in GCP and also by the study team member on the respective protocol if delegated for complete IP management and the same shall be documented (AX7– V1/SOP11/V1).

11.3.4.4. Study Specific documentation

CRS Research pharmacist and or study team member will document the study details including continuous receipt and dispensing of the study products in the CRS research pharmacy accountability log and pharmacy software.

- PI/study team member will be responsible to follow the current IEC-approved version for each protocol for IP management and also to update the CRS OIC for the same. A soft copy of the IEC approved protocol and respective amendments should be notified to CRS Research pharmacist for record and updates.
- PI & the study team will be responsible for submitting the investigator Brochure (IB) or most recent product package insert to CRS for reference and record.
- Depending on the responsibilities defined in the protocol, a treatment assignment list may be developed and maintained by the CRS Research pharmacist. Access to this information must be limited to only appropriate personnel, especially if blinding is a concern in the trial.
- The names of the investigator, coordinator, and product supplier, along with an authorized prescriber signature list (AX8– V1/SOP11/V1) must be maintained by the PI and study team for each protocol, as applicable. This list should be updated whenever there is a change in delegated duties.
- Any relevant correspondence between the CRS research pharmacy and the investigator, or any other involved authorities that is important to a study must be saved. Some examples of

important correspondence include monitoring temperature fluctuation, IP destruction, drug withdrawal from CRS research pharmacy, study termination, IP expiry notification etc.

- PI/team must inform the CRS In-charge in case of study closeout and early termination, for taking further decision for IP management.

11.3.4.5. Inventory logs

- CRS Research pharmacist and or study team member will ensure that all IPs dispensed under research protocol should be accounted for in the inventory system.
- The IP accountability log or dispensing log may take the form of a continuous computerized record or a paper document. If a computerized log is used, it must have an audit trail;
- Information included in the accountability log:
  - Study MPMMCC project no.
  - DMG name, PI name & department.
  - Name, dosage form, strength of the study product.
  - Date of receipt of the study product
  - Quantity received
  - Quantity dispensed
  - Balance of drug currently available

CRS Research pharmacist handling the IP must document the IP accountability and all other required details in the respective forms.

Note: CRS research pharmacy record will be maintained by CRS Research pharmacist *under the purview of OIC CRS.*

11.3.4.6. Record requirements

All study-related records will be maintained for period of 5 years (or as per prevailing regulations) after completion/ discontinuation or withdrawal/Termination of the study.
Records will be maintained by the CRS research pharmacy while the study is ongoing and records may be transferred to CRS storage after closeout, which is readily retrievable.

11.3.4.7 CRS research pharmacy access to protocol

For studies where, CRS Research pharmacist delegated to manage the study IP, the study protocol shall be maintained in a shared folder, accessible only to CRS Research pharmacist and study team member.

11.3.5 Sponsors responsibility

11.3.5.1 Prior to study initiation

- CRS OIC and CRS Research pharmacist should be informed regarding the protocol approval and SIV training where applicable. A softcopy of protocol approval letter, protocol and IP related documents should be shared with CRS for documentation.
- CRS Research pharmacist should be informed and called for IP management training at the time of SIV, in case the PI wants CRS research pharmacist to manage the IP related responsibilities during the entire conduct of the study. Roles and responsibilities of the research CRS Research pharmacist should be explained in detail and the same shall be documented.
- In case the PI delegates the responsibility of drug receipt, inventory, accountability, dispensing, return, destruction and other drug related responsibility, then the CRS Research pharmacist can be given access to IWRS/IVRS of the respective protocol.
- OIC CRS and CRS Research pharmacist should be kept in all the email correspondence with respect to subject randomization, scheduled visit for IP dispensing, IP dispensed from warehouse, IP return to sponsor, etc. where applicable.
- Amendment or update related to IP should be communicated to CRS research pharmacist.
- At the time of site feasibility visit/ SIV (if requested prior) and also at Inspections or Audits, the CRS research pharmacist will give a CRS research pharmacy tour and explain pharmacy operating procedures and management system. Such tours will be documented (Format attached).
- OIC CRS should be copied in every communication with respect to IP management.

11.3.5.2 Monitoring Visit

- The PI/ CoI must inform the CRS OIC in advance regarding the scheduled monitoring visits for IP accountability and their requirements and help from CRS research pharmacy.
- IP accountability during routine monitoring visit will be done at the CRS research pharmacy counter or in the adjacent monitoring room.
- CRS Research pharmacist will hand over the required IPs for the respective protocols for accountability visit after signing the necessary accountability logs that have all details of IPs handed over for monitoring. It will be the responsibility of the study team member to return the IPs back to the CRS research pharmacy.
- Investigator/coordinator/research nurse should provide all protocol records related to study products for inspection.

- The CRS research pharmacist can show the physical storage area via a Video call to the monitor at request during a monitoring visit after approval of the OIC-CRS on a case by case basis.

11.3.5.3 Protocol Deviations

Protocol deviations may include any action or inaction that is noncompliant with the protocol, GCP, the protocol-specific MOP, or any other information relating to a clinical trial. Investigator/team will be responsible for continuous vigilance to identify and report deviations related to such events to IEC in coordination with CRS department. Deviations can be notified in the following conditions but not limited to;

- Improper storage of study products including any significant excursions in temperature, moisture, light, etc.
- Unresolved or unreconciled accountability discrepancies.
- Failure of dispensing.

Kindly refer the IEC SOP for notifying the deviation/violation.

- SOP 08/V5 Review of Protocol Deviation / Violation / Waiver/ Non-Compliance

11.3.5.4. Quality assurance:

The CRS research pharmacist will work under the purview of CRS OIC and is expected to follow and maintain the quality assurance system by taking the following steps to ensure quality assurance.

- The CRS research pharmacist/ delegated CRS team members should conduct a quarterly audit to ensure compliance with applicable regulations, policies and standards. Quarterly audit format is attached (AX11– V1/SOP11/V1)
- Aspects of IP review may include study product storage, control, accountability, dispensing, and disposal.
- When problems are identified, CRS Research pharmacist / delegate must inform CRS OIC and action should be taken to resolve the problems and it should be appropriately documented.

11.3.5.5. Additional Considerations/Responsibilities

- The CRS Research pharmacist should be available at all times during working hours for IP dispensing to study team members
- If the CRS Research pharmacist, an equally qualified individual, a backup, must be available who can perform the functions. The same shall be documented.

- The backup must be trained for handling of IPs by the CRS research pharmacist/ delegated CRS team member to perform activities including, but not limited to, the following: study product dispensing, receipt and inventory, storage, accountability, and record keeping
- The backup individual should be knowledgeable about specific aspects of the protocol(s) that they are covering and should be delegated in the duty delegation log.

11.3.6 Study Closeout

11.3.6.1 Study completion /Closeout visit:

After study completion or termination, the study team member should schedule a closeout visit in coordination with the study monitor. All remaining IP supplies will be returned or destroyed at site based on the agreed terms between both the parties.

- Remaining IPs will be retained for a maximum period of 3 months after study completion/termination. After completion of 3 months the IP will be returned to the respective PI for return/ destruction as per the hospital destruction policy.
- PI and study team (and CRS Research pharmacist where delegated) shall ensure that all the following IP related documentation has been done:
  - Investigational drug product shipment invoices documentation
  - Completed Drug accountability records
  - Temperature logs
  - Documentation of investigational drug product destruction
  - Participant enrollment log
  - Participant identification code list
  - Participant-specific preparation records (batch control records for compounded items) and worksheet
  - Instructions for handling investigational drug product
  - Site-specific dispensing guidelines
  - Signature sheet and CRS research pharmacy delegation log
  - Sponsor investigational drug product and pharmacy-related correspondence
  - Other pharmacy related documents (e.g., protocols and amendments, investigator's brochure, IRB correspondence) the CRS research pharmacy shall maintain soft copy of the aforementioned documents.
  - The records can be maintained for the period of5 years or as specified in the protocol.

11.3.6.2 Record Keeping Responsibilities

The records required for documentation of details of the IP will have restricted accessibility. They will be kept separately from other pharmacy documents and records and will be available for monitoring and inspection if requested in writing. Such records will contain documents needed for protocol-specific storage, dispensing, inventory and accountability records. CRS

Research pharmacist will be responsible for maintain the pharmacy records.

Note: CRS research pharmacy record will be maintained by CRS Research pharmacist *under the purview of OIC CRS.*

11.3.7 Maintenance& Cleaning of CRS research pharmacy:

The following procedures must be followed for cleaning the area and equipment stored in CRS pharmacy:

11.3.7.1 Cleaning of Equipment

Walk- in Cooler/Refrigerator:

- The person responsible for cleaning the Walk-in Cooler/Refrigerator should wear the gloves (available outside the Walk-in Cooler/Refrigerator door) before opening the refrigerator.
- The equipment shelves should be mopped with clean moist lint free cloths (with disinfectant water).

  Note: Disinfectant are always available as concentrates, dilution should always be made correctly with freshly collected water, before use.
- After cleaning with wet cloth, clean with dry lint free cloth.
- The outer part of the main door should be cleaned with wet followed by dry lint free cloth. Never use dripping nylon mop for cleaning.
- During the entire procedure, the temperature should be checked for maintenance.
- Precaution should be taken for the drugs stored in the Walk-in Cooler/Refrigerator, and should not be misplaced.
- After cleaning the Refrigerator, the attendant closes the Walk-in Cooler/Refrigerator door and the same should be recorded.
- The Walk-in Cooler/Refrigerator shall be cleaned once quarterly and the outside door shall be cleaned once weekly.
- The record of cleaning shall be maintained in a muster with the following details ;(Format attached AX9– V1/SOP11/V1)

  - Cleaning date & time
  - Specify cleaning Area
  - Name & Signature of the attendant.

Cleaning of Cabinets &CRS research pharmacy Area;

- Vacuum the CRS research pharmacy area starting from ceiling, cabinets and floor to remove all the dust present on the ceiling, shelves of all the cabinets and floor.
- Before cleaning the cabinet shelves, kindly empty the cabinet and place the IPs in another empty shelf with proper recording of IPs that has been shifted. After cleaning replace the IP at the same place. This procedure should be repeated for all the cabinets containing drugs.
- After removing the dust clean the cabinets with wet lint free disinfectant cloth followed by dry cloth.
- The shelves of the cabinets should be cleaned every 3-6 monthly.
- The floor will be cleaned by wet disinfectant mop followed by dry mop. The floor of the CRS research pharmacy must be cleaned daily; outer door of cabinets shall be cleaned weekly.
- The record of cleaning shall be maintained in a muster with the following details;(Format attached AX10– V1/SOP11/V1)

  - Cleaning date & time
  - Specify cleaning Area
  - Name & Signature of the attendant.

11.3.8 Instrument Calibration:

CRS research pharmacy Instruments (Walk-in cooler & thermo hygrometer) will be calibrated by the Hospital management system (Department of Biomedical Engineering). It will be the responsibility of the CRS Research pharmacist to keep a check on the calibration and renewal date. Renewal request shall be sent to (Department of Biomedical Engineering), at least 1 month prior to expiry date. Calibration certificate shall be documented in the pharmacy record and can be shared with PI on request.

11.4 Applicable areas of the Hospital

- Clinical Research Secretariat (CRS)
- CRS research pharmacy
- MPMMCC/HBCH, Varanasi

11.5 Applicable staff

This SOP applies to all the personnel of the clinical research team and others who may be delegated to handle the research IP of their respective DMG at MPMMCC/HBCH.

These include the following:

- Investigators
- CRS Research pharmacist
- Clinical Trial Coordinator (CTC)and other delegated study team members

11.5.1 Staff responsible for Implementation

- OIC CRS will ensure that the research team involved in the conduct of the study will comply with this site SOP.
- PI will ensure that at the time of implementation of the SOP, that the research team at MPMMCC/HBCH are trained and in the event that an SOP is modified, provide training regarding the change(s) and ensure their compliance with the changes.
- CRS will Inform IEC that this site SOP will be implemented within the institution.

11.5.2 Specific Staff education requirements

All delegated project staff should be ICH-GCP and NDCT Rules 2019 trained and familiar with the protocol.

AX1– V1/SOP11/V1

STUDY PRESCRIPTION FORMAT

Prescription No:-*(For CRS research pharmacy Use only)* _____

Prescription Form

Protocol Number_____

Project No.: _____ **Date:** ____/____/____
DD / MM / YYYY

PI Name: _____

DMG: _____

Rx (Only for Study Drugs)	**For Pharmacy Use Only**	
Drug	Batch Number	Quantity
Dispensed Date and Time:		
Authorized Prescriber's CC No. & Signature:	**CRS Research pharmacist's CC No. & Signature:**	

AX2– V1/SOP11/V1

STUDY DRUG LABEL

"New Investigational Test Article-Limited to Investigational Use Only"	
STUDY NO.:	PI NAME:
PATIENT ID:	PROTOCOL NO.:
INVESTIGATOR NAME:	
DISPENSING DATE:	

AX3– V1/SOP11/V1

Date

To
Officer In-Charge
Clinical Research Secretariat
MPMMCC/HBCH
Varanasi-221005

Subject- Permission to store study drugs in CRS research pharmacy
Protocol No: -

Protocol Title: -

Principal Investigator: -
Respected Sir
This is for your kind information that we have received the IEC approval for above-mentioned study. As a part of this study we will be receiving the study medications and this medication needs to be stored in a secure and temperature control environment as per protocol specifications.
Study product details and storage conditions are as follows

Sr. No.	Drug Name	Quantity to be stored	Temperature requirement
1			
2			
3			

Please find the study IEC approval letter attached herewith for your kind perusal. Other essential documents softcopies as enlisted were sent to CRS research pharmacy email. We will also submit the subsequent study amendments (if any).

Documents Enclosed
- ☐ IEC Approval Letter
- ☐ Prescriber Log

Following documents emailed to CRS Pharmacy
- ☐ IEC Approved Protocol
- ☐ Investigator Brochure
- ☐ Package Inserts

Kindly grant us the permission to store the drug in CRS research pharmacy

Thanks and Regards,
Authorized Signature and Date

AX4– V1/SOP11/V1
DRUG ACCOUNTABILITY LOG

PROJECT NO: PI NAME: DRUG NAME:

		DRUG ACCOUNTABILITY			DETAILS OF PERSON HANDLING THE DRUGS		
SR. NO.	DATE	INWARD	DISPENESED	STOCK AVAILABLE	NAME	DESIGNATION	SIGNATURE

AX5– V1/SOP11/V1
TEMPERATURE RECORD

Site: CRS research pharmacy
Temperature: Upto 25 Degree
Drug Stored: Study/Trial Drugs of studies under DMGs
Month:

		Temperature (Degree Celsius)						
Sr. No.	Date		Morning (°C)			Evening (°C)		Initials
		Time	Min	Max	Time	Min	Max	

Signature and Date of OIC, CRS: _____ Page _____ of _____

AX6– V1/SOP11/V1
CRS research pharmacy Signature & Delegation Log

Site Name: - CRS research pharmacy, MPMMCC, 1st Floor D&T Building, Sunderpur, Varanasi-221005

OIC, DAE-CTC Name	OIC Signature	OIC Initials	Date From	Date To

Print name (CC Number)	Role*	Signature	Initials	**Tasks Delegated	From Date (dd-mmm-yyyy)	To Date (dd-mmm-yyyy)	OIC Signature and Date

*Study roles can include but not limited to: **CRS Research pharmacist, Back-Up pharmacist, Delegated Team members**

PI Signature: (Sign once site closed): _____ Date: _____

1.Study Drug Receipt
2. Pharmacy Audit
3. Pharmacy Inventory software data entry
4.Study Drug Order
5. Record deviations/violations
6. Pharmacy Inventory software data quality check
7.Study Drug accountability
8. Communication with PI
9. Pharmacy Inventory software management and Troubleshoot
10.Study drug dispensing
11. Communication with Other concern Department
12. Pharmacy record maintenance
13.Pharmacy Temperature recording
14. Pharmacy Periodic Inventory and stock check

AX7– V1/SOP11/V1
Training Log

Protocol Title: _____ Date:_____

Name of The Pharmacist:_____ CC No:_____

Department: _____

Training Subject	Date	Comments

I have received and understood the safety and health training listed above and acknowledge that it has been given to me.

Pharmacist's Signature	Date	Supervisor's Signature	Date

AX8– V1/SOP11/V1 (Authorized delegate for Prescription Signature Log)

Protocol Title:			
Short Title:		**IEC Protocol No:**	
Principal Investigator:		**DMG:**	
Sponsor/ Investigator-initiated Study:		**CONTACT/EXTN. NO.:**	

Name & CC No.	Role	Signature	Initials	Start date (dd-mm-yyyy)	End date (dd-mm-yyyy)	Authorization by PI Sign& Date	Authorization by OIC-CRS Sign& Date
	PI						

Confirm all information above is correct and sign at the end of the study:

Principal Investigator | **Signature of Principal Investigator** | **Date (dd/mm/yyyy)**

AX9– V1/SOP11/V1
CLEANING REPORT
(FOR WALK-IN COOLER)

QUARTER	DATE	TIME	NAME OF ATTENDANT	SIGN OF ATTENDANT	SIGN OF PHARMACIST
1					
2					
3					
4					

Signature and Date of OIC, CRS_____

AX10– V1/SOP11/V1

CLEANING REPORT
CABINETS & PHARMACY AREA

WEEK	DATE	TIME	NAME OF ATTENDANT	SIGN OF ATTENDANT	SIGN OF PHARMACIST
1					
2					
3					
4					
5					
6					
7					
8					
9					
10					
11					
12					
13					
14					
15					
16					
17					
11					
19					
20					
21					
22					
23					
24					
25					
26					

Signature and Date of OIC, CRS_____

AX11– V1/SOP11/V1

CRS research pharmacy Audit Tool

Instructions: List the protocol number, the date range that is being reviewed and the date of the review. Once the review begins, check √ the appropriate boxes for each question listed in the criteria section. When the review is completed for all applicable documents, the reviewer will sign and date the form. Use the comments section for clarification and action on any "no" entries checked.

Reviewed from (date)_____Through (date)_____

Document	*Criteria*	Yes	No	N/A
I.MAINTENANCE OF RECORDS				
A. Are the following documents present?	1. Drug Storage request letter with all necessary documents			
	2. Prescriber signature list and Pharmacy Duty Delegation log			
	3. Drug Accountability/ Inventory records			
	4. Drug shipment receipts/ Receipt emails			
	5. Temperature Log			
	6. Pharmacy Equipment calibration and Maintenance records			
	7. Pharmacist License and certificate, training records, GCP certificate			
	8. Drug Destruction records			
	9. Previous Internal Audit reports			
	10. Pharmacy Access / Visit tour records			
Comments/Problems				
C. Study Product Specific Documents	*1.* Most recent version of the protocol for which the drugs are stored in pharmacy (Soft Copy)			
	2. . Most recent version of Investigators Brochure(s) ***(For pharma studies only)***			
	3. Most recent version of Package Insert(s) ***(For pharma studies only)***			

Document	*Criteria*	Yes	No	N/A
Comments/Problems				
III. SECURITY AND STORAGE OF THE INVESTIGATIONAL DRUGS				
A. Inspect the investigational drug storage area.	1. Are the investigational drugs stored according to the IEC approved protocol/ Manufacturer's specification?			
	2. Are expired stored / Used drug stored separately?			
	3. Is study drug stored in a secure, limited access area?			
	4. Does Expired drug/Used drug stored for more than 90 days?			
Comments/Problems				
IV. DRUG ACCOUNTABILITY, PREPARATION AND DISPENSATION				
A. Accountability	1. Does entries made in Inventory log corresponds precisely with shipment receipts and prescription form?			
	2. Are the accountability records legible and complete with each entry signed by the authorized personnel?			
	3. Does drug accountability log present and completed?			
	4. Does the inventory balance documented on the accountability record correspond precisely with the actual physical inventory?			
	a. If No, provide actual numbers of the agent counted as well as the amount recorded on the accountability record for each discrepancy noted			

Drug	Accountability on Record	Inventory Amount	Remark

Comments/Problems				
C. Prescription Review	1.Were any prescription reviewed during this assessment? If yes then Details:			

Project No	Visit Code	From Date	Through date

Document	*Criteria*		Yes	No	N/A
Comments/Problems					
	1. Are the prescriptions signed by an authorized prescriber whose name appears on the study prescriber log?				
	2. If the dispensed study product and the quantity dispensed, has a corresponding entry been made in the Accountability Log?				
	3. Are the prescriptions and/or Accountability Records legible and complete with each entry initialed by authorized personnel?				
Comments/Problems					
V. Inventory Management Software					
	1. Does timely entries were done in Pharmacy Inventory management software?				
	2.Does entries made in software correspond with hard copies of Inventory and dispensing logs?				
	3. Does pharmacy software data is secure and available to only authorize personal.				
	4. Does pharmacy software has valid audit trails for corrections made in entries?				
	5. Does software data backup is available? Please specify how often the data backup took place.				
	6. Does any updates of modification done in software since last visit. If yes Does Software update/ Change report is available?				
Comments/Problems					

Comments/Corrective action to follow up on any "no" entries:

Problem	Corrected by/date

Reviewer
Sign and Date

OIC, CRS MPMMCC
Sign and Date

AX12– V1/SOP11/V1
CRS RESEARCH PHARMACY VISIT RECORD

Date: _____

DMG: _____ PI Name:

_____ Project No.: _____

Study Short Name: _____

Visitor's Name: _____

Designation: _____

Name of Organization: _____

Purpose of Tour:
- □ Site Initiation Visit
- □ Site Monitoring
- □ Site Audit
- □ Site Inspection
- □ Study Closed-Out Visit
- □ Other,

Suggestion (If Any):
_____

_____

Is Information/Intimation Done A Day Before the Tour? (Y/N):
(Note: The CRS research pharmacy Tour Will Be Forbidden If Not Inform Prior)

_____ _____
Signature of Visitor Signature of Study Team Member

_____
Signature of CRS Research pharmacist

Standard Operating Procedure
Clinical Research Secretariat (CRS)

Title: Managing Investigational Products (IP)

SOP Code: SOP 12/V1 Date: 2nd Feb 2024 Pages: 140-147

Tata Memorial Centre

MPMMCC: Sunder Bagiya, Near Nariya Gate, Banaras Hindu University Campus, Varanasi-221005, Uttar Pradesh, India

HBCH: Homi Bhabha Cancer Hospital, Ghanti Mill Road, Old Loco colony, Lahartara, Varanasi-221002, India

12.1 Purpose

To describe process and requirements for the receipt, storage, dispensing, and return or destruction of Investigational Product (IP) at site

12.2 Scope

This Standard Operating Procedure (SOP) will apply to all studies being conducted at MPMMCC/HBCH.

Any new trial which is initiated during active period of the SOP will be covered under the SOPs, unless otherwise indicated. If necessary, a study specific SOP may be prepared.

12.3 Procedure

12.3.1 Prior to receipt of Investigational Product (IP)/ Study Drug

PI must identify an area with restricted access and appropriate temperature control for IP storage. One option is the CRS research pharmacy, which has dedicated secure space, to store and manage study IPs under protocol required conditions. PI can approach OIC CRS for permission for study drug storage and management (for details refer SOP chapter 11).

PI should identify team members who would be responsible for IP receipt, storage, dispensing, accountability and recording the temperature for the storage area and returning or destruction of the IP/ study drug.

If the Investigator decides to store the study drug in the CRS research pharmacy, CRS Research pharmacist / delegated member will be responsible for temperature recording and if delegated by investigator, CRS Research pharmacist will be responsible for IP receipt, storage, dispensing & accountability (Investigator may delegate some of the responsibility to CRS Research pharmacist and the others can be shared by delegated study team member)

The above persons must be identified on the study delegation log.

12.3.2 Receipt of Investigational Product (IP)/ Study Drug

Upon receipt of the IP shipment at the site, the CTC/ CRS Research pharmacist /delegated member (as per delegation log) will unpack the IP box and check the IP inventory against the shipping form.

Checking the inventory will include the following:

- Checking the packaging numbers
- Unique Kit numbers/IP number

- Lot/batch numbers
- Number of IPs in the container (s)
- IP expiry date

Any discrepancies (e.g. tampering/ breakage of the IP kit, mismatch in the number of kits, temperature excursions etc.) identified must be documented and informed to the sponsor/CRO/ point of contact immediately and seek advice for the next steps.

Such IP must be stored separately and must be dispensed only after confirmation from the sponsor/CRO/designee. This must be done by the person designated for IP management.

If the inventory matches the drug received, the CTC/ CRS Research pharmacist /delegated person will sign and date (note: mention logger temperature present in the IP container on the receipt form) on the shipping receipt or Investigational Product Receipt Form, return a copy to the sponsor, and file the original in the Trial Master File (TMF)/Site Master File (SMF).

Shipment inventory must be done as per the study specific procedure (e.g. IVRS or IWRS, accountability log etc.)

The IP must be immediately transferred to the designated storage area at conditions as mentioned in the protocol.

The temperature of the storage area must be recorded with a calibrated thermometer for the temperature range once daily or as mentioned in the protocol. It is strongly recommended that accurate temperature must be recorded.

If available maintain the hard copy of auto generated temperature logger.

12.3.3 IP / Study Drug Storage

Temperature of the IP storage area must be maintained on a 24-hour basis for recording temperature. The temperature will be recorded once daily or as mentioned in the protocol, except on holidays and Sundays.

In case a temperature excursion is noted, the CRS Research pharmacist /CTC/designated study team member must inform Investigator telephonically followed by email at the earliest:

- Inform the PI for Investigator-initiated studies & document the same
- Inform the sponsor / CRO for pharma studies & document the same
- Try to identify the cause of temperature excursion
- Quarantine the IP till response from sponsor
- Take remedial actions in consultation with sponsor/CRO

IP that has undergone a temperature excursion must be kept separately and must not be dispensed till a confirmation from sponsor/CRO is obtained i.e. the IP is **“fit for use”.**

12.3.4 IP / Study Drug Dispensing

IP must be dispensed by the CTC/delegated member/CRS Research pharmacist (if delegated) to subjects/participants randomized on the study after fulfilling the eligibility criteria in accordance with the protocol.

Upon dispensing the IP, the CTC/delegated member/ CRS Research pharmacist (if delegated) must note following in the source note and IP package:

- Trial/Study ID number (both source notes and IP package)
- Initial of the subject/participant (both source notes and IP package)
- Date of IP dispensing (both source notes and IP package)
- Batch number and quantity of IP dispensed (in the source note)
- Expiry date (in the source note)

This information must be captured in Real time basis on the IP stickers available on IP containers (AX2-V1/SOP11/V1), in the subject/participant source notes as well as in the Drug Accountability Logs (AX1-V1/SOP 12/V1)

The CTC/delegated member/ CRS Research pharmacist (if delegated) will maintain a record of drug dispensed to and retrieved from each subject/participant. To accomplish this, the CTC/delegated member/ CRS Research pharmacist (if delegated) will use the CRF or drug accountability diary, if any and only if provided by the Investigator/sponsor/CRO.

The CTC/delegated member/CRS Research pharmacist (if delegated) will explain to each subject/participant the drug accountability needs for the study (e.g., the need for the subject/participant to return unused, partially used, and empty packages).

Requests for IP resupply must be done as per the study specific procedures.

12.3.5 IP/ Study Drug Return

The study subject/participant will return all used/partially used/unused IP and study-related supplies to CTC/delegated member on the specified visit mentioned in the protocol.
The CTC/delegated member will count the returned IP and compare this with the amount of IP expected to have been used since the previous study visit or with the start date of the use of IP.

CTC/delegated member must document IP returned by the subject/participant in the subjects/participants source file as well as in the drug accountability logs (AX1-V1/SOP 12/V1) as per the study requirement.

In case of missing IP or extra IP, the CTC/delegated member must obtain the information from the subject/participant and document the clarification provided in the source notes, IP dispensing log and CRF. This documentation should be done in real time basis.

The CTC/delegated member will keep the Drug Dispensing Log and the drug accountability CRF pages updated, regardless of when the monitor will perform final accountability.

The CTC/delegated member/CRS Research pharmacist (if delegated) will store the returned IP separately in a secure area until it is verified by the CRA/Monitor.

Whether the IP is to be returned to the sponsor or destroyed on-site will be determined by the instructions in the protocol/agreement.

The documentation of the destruction/ return must be maintained in the TMF/SMF.

12.3.6 Return of IP to Sponsor

As specified in the protocol, the IP will be returned to the sponsor at intervals or at the end of the study. The CTC/delegated member will follow the protocol or other instructions from the Sponsor or CRO to decide whether empty containers must be returned or can be destroyed at site.

The CRA/Monitor will perform the independent drug accountability review and will seal the IP that need to be shipped back to the Sponsor/CRO.
The CRA/Monitor will arrange the preferred carrier for the shipment of used and or unused IP back to the sponsor/CRO.

The CTC will arrange for a gate pass for the shipment that needs to send back to sponsor/CRO.

Unless instructed otherwise by the CRA/Monitor, the CTC/delegated member will:

- Perform an inventory of the drug supplies.
- Compare inventory with the study medication records.
- Document discrepancies in the CRF or in a memo to file.
- Complete the Drug Return/Destruction Form (in presence of monitor) or similar form provided by the sponsor or CRO.

Include a copy of the signed and completed Drug Return Form with the drug shipment and place the original in the study file.

12.3.7 On-Site Destruction of IP

If the Investigator/sponsor/CRO request for on-site destruction of the IP, the CTC/delegated member should:

- Investigator can request CRS Research pharmacist (letter from PI) with prior permission from OIC CRS, to help for onsite IP destruction process. The letter should include the study title, IEC project no. Drug name, batch number, number of vials/boxes required to be destructed. For sponsored study PI should request sponsor IP return and destruction at sponsors' site.

  Note: PI can request CRS Research pharmacist *for IP destruction, only for IPs stored in CRS research pharmacy.* CRS Research pharmacist *will guide the respective team for onsite IP destruction procedure.*

- CRS Research pharmacist shall communicate with the drug destruction team from department of Microbiology for IP destruction/disposition and obtain a copy of the site's SOP of Waste Management from department of Microbiology for IP destruction/disposition, provide a copy to the Investigator and CTC will share the copy with monitor, and file a copy in the TMF/SMF.
- Obtain written confirmation from the CRA/Monitor identifying the specific IP that can be destroyed.
- Obtain appropriate paperwork concerning destruction of the drug that is required in the site's Waste Management SOPs and place a copy in the TMF/SMF.
- Provide the Investigator/CRA/Monitor with written proof of IP destruction at site.
- Complete the Drug Return/Destruction Form or similar form provided by the sponsor/CRO. Provide a signed copy of the form to the CRA/Monitor and retain the original in the TMF/SMF.

12.3.8 IP Record Retention

At study completion, the CTC will file all drug records with other regulatory documents in accordance with the record retention policy mentioned in the protocol.

12.4 Applicable areas of Hospital

- CRS research pharmacy
- MPMMCC/HBCH, Varanasi
- PIs Department

12.5Applicable staff

This SOP applies to all members of the study team involved in the process receipt, storage, dispensing, and return or destruction of Investigational Product (IP). These include the following:

- Principal Investigator (PI)
- Clinical Research Team (as per delegation log)

12.6 Staff responsible for implementation

OIC CRS will ensure that the SOP is updated and available on MPMMCC/HBCH website for all the Investigators conducting studies and Investigator will ensure that the research team involved in the conduct of the study will comply with this site SOP.

PI at his/her level will ensure that at the time of implementation of the SOP, that the research team at MPMMCC/HBCH are trained and in the event that an SOP is modified, provide training regarding the change(s) and ensure their compliance with the changes.

PI will ensure that the research team involved in the conduct of the study will comply with this site SOP.

Inform IEC that this site SOP will be implemented within the institution.

AX1-V1/ SOP 12/V1

Drug Accountability Log

Project Title & Project No.:
Principal Investigator:
Drug /IP Name:

	Patient ID	Kit no./ Batch no	Date of Expiry	Quantity	Date	Dispensed by (Initial & sign)	Return Date	Quantity Returned	Received by (Initial & sign)	Remarks

AX2-V1/SOP 12/V1

Drug accountability diary (for Patient)

Sr. No.	Date	Number/ Quantity of IP taken	Comments/ Symptoms	Remark (if IP missed)

Standard Operating Procedure
Clinical Research Secretariat (CRS)

Title: Storage & Archival of Essential Documents

SOP Code: SOP 13/V1 Date: 2nd Feb 2024 Pages: 148-167

Tata Memorial Centre

MPMMCC: Sunder Bagiya, Near Nariya Gate, Banaras Hindu University Campus, Varanasi-221005, Uttar Pradesh, India

HBCH: Homi Bhabha Cancer Hospital, Ghanti Mill Road, Old Loco colony, Lahartara, Varanasi-221002, India

13.1 Purpose

To describe the procedure of storage &archiving of essential documents during the entire course of the study and also to document the method to archive the essential documents at MPMMC/HBCH for the required period of time

13.2 Scope

This SOP will apply to all clinical trials conducted at MPMMCC/HBCH.

13.3 Procedure

Essential Documents are those documents which individually and collectively allow the evaluation of the conduct of a study and the quality of the data generated. These documents demonstrate the compliance of the Investigator, Sponsor and Monitor with the Good Clinical Practice, protocol, SOPs and with all applicable regulatory requirements.

Essential Documents are needed for IEC monitoring, Sponsor's monitoring visits, independent audits and inspection by the Regulatory Authorities if applicable.

The Principal Investigator (or CI if appropriate) is responsible for storage during the study & archiving after completion of the study, of the essential documents at the respective study site in accordance with the requirements of the Sponsor, the institution and local requirements.

The Investigator should maintain documents as specified in the essential documents' list (AX1-V1/SOP 13/V1) and take measures to prevent accidental or premature destruction.
Filing space should be available for the storage of Trial Master File (TMF)/Site Master File (SMF) during the conduct of the clinical trial. Investigator site files will normally be stored at PIs office or local secure filing area. At the end of the trial the files must be transferred to PI specified site archiving facility.

The various Essential Documents needed for different stages of the study are classified under three groups:

13.3.1 Filing of essential documents before the clinical phase of the study commences

Before the study initiation visit, the CTC will create, or will be given by the Sponsor/Contract Research Organization (CRO), a binder in which all required regulatory documents, forms and correspondence should be filed. If the Sponsor/CRO requires additional forms, or documents, these will be maintained in addition to the documents listed in AX2-V1/SOP12/V1. If there is more than 1 study file, the files can be labeled as study file no e.g. (1 of_, 2of_, 3of_)

The CTC will ensure that the appropriate documents are placed in the TMF/SMF on a regular basis. The CTC will make the file available for review by the Monitor at each site visit.

13.3.2 Storage of essential documents during the clinical conduct of the study

Signed informed consents must be stored in a separate file/binder which should be named "Signed Informed Consent Forms" and mention PI name, study number and title on the binder. If the Sponsor/CRO has given any specific directions concerning storage of informed consents in the TMF/SMF, then they must be stored as specified by the Sponsor/CRO.

Original source documents (case file) will be kept in the PI's department during the conduct of the study. A copy of the source documents (case file) will be created once the study is completed and the original source documents (case file) will be stored in the hospital medical records.
Contracts such as the Confidentiality Agreement, Clinical Trial Agreement, Memorandum of understanding and Publication Policy Agreement can be stored separately in the investigator's offices (i.e., not with the study records).

All communications with IRB, Sponsor/CRO and the documents received from the sponsor/CRO (e.g. News Letters, Central Lab information's, etc.) will be stored in a timely manner in the file/binder.
Subject/Participant reimbursements document will be stored in separate file/binder.

A separate file/binder for each subject/participant can be prepared, if required, by the investigator for filing any extra documents like printout of the screen shot of the web screening and randomization confirmation, drug dispensing record, etc.

The CTC or delegate will transcribe the appropriate data from the source documents into each subjects/participants Case Report Form (CRF).

The CTC will ensure that the CRFs are stored in a secure location.

All site-related materials should be made available for review by the sponsor's representatives (monitors and auditors) or regulatory authority(s).

13.3.3 Archival of essential documents after completion or termination of the study

Essential documents need to be archived once the trial is completed e.g. the trial has undergone a final closeout visit (refer SOPs of close out visit in IEC communication: Interaction with sponsor.)

During the final closeout visit monitor along with the PI and the CTC must identify the study specific documents that require to be archived.

The documents identified must be inventoried, packed in archival boxes, sealed and boxes must be labeled appropriately to indicate the tenure of archival, the content of the box and the study reference number (AX3-V1/SOP 13/V1).
(*Note: Xerox copy of the subject/participant source will be stored in the archiving boxes.*)

The PI must assign an area to store the sealed archival boxes with restricted access.

The documents should be archived in an appropriate room or locked cupboard (consider fire protection without water sprinkler systems, water protection, protection for humid conditions, pest and termite proof etc.). The room or cupboard must be secure with access only by authorized personnel.

Documents must be stored in a way that preserves their integrity and readability and restricts access to appropriate individuals only.

Upon request of the Sponsor, Monitor, Auditor, IEC, or Regulatory Authority, the Investigator should make available all requested trial-related records.

PI/CTC must record and retain the inventory AX4-V1/SOP 13/V1– Archive Inventory) record for future reference.

The study documents must be archived for 3 years (or as per prevailing guidelines) post the study close out (for investigator-initiated and sponsor initiated) and in case of pharma studies until the sponsor confirms that the records are no longer required; whichever is earlier. However; prior to destroying the records, a confirmation for destruction of records must be sought by the PI from sponsor.

If the Principal Investigator leaves MPMMCC/HBCH, he/she will provide the Sponsor/CRO with written notice of the location of the study records and the name and phone number of an alternate contact in the event of an audit.

In case PI/Co-PI requires post archival access to the archived documents, PI/Co PI must send a request email/letter to OIC, CRS with details regarding the study documents required to be accessed. Following details must be mentioned in the mail/letter;

- Project No:
- Study Title:
- PI Name:
- Name of documents
- Reason to access the documents:
- Any supporting letter (if available):

The person accessing the documents must fill the attached log (AX5-V1/SOP 13/V1) available at the archival area.

All the accessed documents must be placed at the original location as mentioned in the point 13.3.3

13.4 Applicable Staff

This SOP applies to all the personnel of the clinical research team who may be responsible for archival of essential documents at MPMMCC/HBCH.

These include the following:

- Investigator
- Research Team including CRC (listed in the delegation log)

13.5 Staff responsible for Implementation

OIC CRS will ensure that the SOP is updated and available on MPMMCC/HBCH website for all the Investigators conducting studies and Investigator will ensure that the research team involved in the conduct of the study will comply with this site SOP.

PI at his level will ensure that at the time of implementation of the SOP, that the research team at MPMMCC/HBCH are trained and in the event that an SOP is modified, provide training regarding the change(s) and ensure their compliance with the changes.

Inform IEC that this site SOP will be implemented within the institution.

AX1-V1/SOP 13/V1

Essential Documents for Conduct of Clinical Trial (Adapted fromE6(R2) Good Clinical Practice: Integrated Addendum to ICH E6(R1), Kindly refer for more details)

A) Before the Clinical Phase of the Trial Commences

During this planning stage the following documents should be generated and should be on file before the trial formally starts.

	Title of Document	Purpose	Located in Files of	
			Investigator/Institution	Sponsor
1	**INVESTIGATOR'S BROCHURE (IB)**	To document that relevant and current scientific information about the investigational product has been provided to the investigator.	X	X
2	**SIGNED PROTOCOL AND AMENDMENTS, IFANY, AND SAMPLE CASE REPORT FORM(CRF)**	To document investigator and sponsor agreement to the protocol/amendment(s) and CRF.	X	X
3	**INFORMATION GIVEN TO TRIAL SUBJECT** -**INFORMED CONSENT FORM** (including all applicable translations)	To document the informed consent.	X	X
	ANY OTHERWRITTENINFORMATION	To document that subjects will begiven appropriate written information (content and wording) to support their ability to give fully informed consent.	X	X
	ADVERTISEMENT FOR SUBJECT RECRUITMENT (if used)	To document that recruitment measures are appropriate and not coercive.	X	

4	**FINANCIAL ASPECTS OF THE TRIAL**	To document the financial agreement between the investigator/institution and the sponsor for the trial.	X	X
5	**INSURANCE STATEMENT** (where required)	To document that compensation to subject(s) for trial-related injury will be available.	X	X
6	**SIGNED AGREEMENT BETWEEN INVOLVED PARTIES,** e.g.: – Investigator/institution and sponsor – Investigator/institution and CRO – Sponsor and CRO – Investigator/institution and authority(ies) (where required)	To document agreements.	 X X X	 XX (where required) XX
7	**DATED, DOCUMENTED APPROVAL/FAVORABLE OPINION OF INSTITUTIONAL REVIEW BOARD(IRB)/INDEPENDENT ETHICS COMMITTEE(IEC) OF THE FOLLOWING:** • Protocol and any amendments • CRF (if applicable) • Informed consent form(s) • Any other written information to be provided to the subject(s) • Advertisement for subject recruitment (if used) • Subject compensation (if any) • Any other documents given approval/favorable opinion	To document that the trial has been subject to IRB/IEC review and given approval/favorable opinion. To identify the version number and date of the document(s).	X	X

8	**INSTITUTIONAL REVIEWBOARD/INDEPENDENT ETHICS COMMITTEECOMPOSITION**	To document that the IRB/IEC is constituted in agreement with GCP.	X	X (where required)
9	**REGULATORY AUTHORITY(IES) AUTHORIZATION/APPROVAL/NOTIFICATION OF PROTOCOL** (where required)	To document appropriate authorization/approval/notification by the regulatory authority(ies) has been obtained prior to initiation of the trial in compliance with the applicable regulatory requirement(s).	X (where required)	X (where required)
10	**CURRICULUM VITAE AND/OR OTHERRELEVANT DOCUMENTS EVIDENCING QUALIFICATIONS OF INVESTIGATOR(S) AND SUBINVESTIGATOR(S)**	To document qualifications and eligibility to conduct trial and/or provide medical supervision of subjects.	X	X
11	**NORMAL VALUE(S)/RANGE(S) FOR MEDICAL/LABORATORY/TECHNICAL PROCEDURES(S) AND/OR TEST(S) INCLUDED IN THE PROTOCOL**	To document normal values and/or ranges of the tests.	X	X
12	**MEDICAL/LABORATORY/TECHNICAL PROCEDURES/TESTS** – Certification or – Accreditation or – Established quality control and/or external quality assessment or – Other validation (where required)	To document competence of facility to perform required test(s), and support reliability of results.	X (where required)	X
13	**SAMPLE OF LABEL(S) ATTACHED TO INVESTIGATIONAL PRODUCT CONTAINER(S)**	To document compliance with applicable labelling regulations and appropriateness of instructions provided to the subjects.		X

14	**INSTRUCTIONS FOR HANDLING OF INVESTIGATIONAL PRODUCT(S) AND TRIAL-RELATED MATERIALS (if not included in protocol Investigator's Brochure)**	To document instructions needed to ensure proper storage, packaging, dispensing, and disposition of investigational product(s) and trial-related materials.	X	X
15	**SHIPPING RECORDS FOR INVESTIGATIONAL PRODUCT(S) AND TRIAL-RELATED MATERIALS**	To document shipment dates, batch numbers and method of shipment of investigational product(s) and trial-related materials. Allows tracking of product batch, review of shipping conditions, and accountability.	X	X
16	**CERTIFICATE(S) OF ANALYSIS OFINVESTIGATIONAL PRODUCT(S) SHIPPED**	To document identity, purity, and strength of investigational product(s)to be used in the trial.		X
17	**DECODING PROCEDURES FOR BLINDEDTRIALS**	To document how, in case of an emergency, identity of blinded investigational product can be revealed without breaking the blind for the remaining subject's treatment.	X	X (third party if applicable)
18	**MASTER RANDOMIZATION LIST**	To document method for randomization of trial population.		X (third party if applicable)
19	**PRE-TRIALMONITORINGREPORT**	To document that the site is suitable for the trial (may be combined withA.20).		X
20	**TRIAL INITIATION MONITORING REPORT**	To document that trial procedures were reviewed with the investigator and the investigator's trial staff (maybe combined with A.19).	X	X

Contains Non-binding Recommendation

B. During the Clinical Conduct of the Trial

In addition to having on file the above documents, the following should be added to the files during the trial as evidence that all new relevant information is documented as it becomes available.

	Title of Document	Purpose	Located in Files of	
			Investigator /Institution	Sponsor
1	**INVESTIGATOR'S BROCHURE (IB) UPDATES**	To document that investigator is informed in a timely manner of relevant information as it becomes available.	X	X
2	**ANY REVISION TO:** -Protocol/amendment(s) and CRF -Informed consent form -Any----other written information provided to subjects -Advertisement for subject recruitment (if used)	To document revisions of these trial related documents that take effect during trial.	X	X
3	**DATED, DOCUMENTED APPROVAL/FAVORABLE OPINION OF INSTITUTIONAL REVIEW BOARDIRB)/INDEPENDENT ETHICS COMMITTEE (IEC) OF THE FOLLOWING:** • Protocol amendment(s) • Revision(s)of: — Informed consent form — Any other written information to be provided to the subject — Advertisement for subject recruitment (if used) • Any other documents given approval/favorable opinion • Continuing review of trial (where required)	To document that the amendment(s) and/or revision(s) have been subject to IRB/IEC review and were given approval/favorable opinion. To identify the version number and date of the document(s).	X	X

4	**REGULATORY AUTHORITY(IES) AUTHORIZATIONS/APPROVALS/NOTIFICATIONS WHERE REQUIRED FOR:** • Protocol amendment(s) and other documents	To document compliance with applicable regulatory requirements.	X (where required)	X
5	**CURRICULUM VITAE FOR NEW INVESTIGATOR(S) AND/OR SUBINVESTIGATOR(S)**	(SeeA.1).	X	X
6	**UPDATES TO NORMAL VALUE(S)/RANGE(S) FOR MEDICAL/LABORATORY/TECHNICAL PROCEDURE(S)/TEST(S) INCLUDED IN THE PROTOCOL**	To document normal values and ranges that are revised during the trial(seeA.11).	X	X
7	**UPDATES OF MEDICAL/LABORATORY/TECHNICAL PROCEDURES/TESTS** – Certification or – Accreditation or – Established quality control and/or external quality assessment or – Other validation (where required)	To document that tests, remain adequate throughout the trial period(seeA.12).	X (where required)	X
8	**DOCUMENTATION OF INVESTIGATIONAL PRODUCT(S) AND TRIAL-RELATED MATERIALS SHIPMENT**	(SeeA.15).	X	X
9	**CERTIFICATE(S) OF ANALYSIS FOR NEW BATCHES OF INVESTIGATIONAL PRODUCTS**	(SeeA.16).		X
10	**MONITORING VISIT REPORTS**	To document site visits by, and findings of, the monitor.		X

11	**RELEVANT COMMUNICATIONS OTHER THAN SITE VISITS** – Letters – Meeting notes – Notes of telephone calls	To document any agreements or significant discussions regarding trial administration, protocol violations, trial conduct, adverse event (AE)reporting.	X	X
12	**SIGNED INFORMED CONSENT FORMS**	To document that consent is obtained in accordance with GCP and protocol and dated prior to participation of each subject in trial. Also, to document direct access permission (see A.3)	X	
13	**SOURCE DOCUMENTS**	To document the existence of the subject and substantiate integrity of trial data collected. To include original documents related to the trial, to medical treatment, and history of subject.	X	
14	**SIGNED, DATED, AND COMPLETED CASE REPORT FORMS (CRF)**	To document that the investigator or authorized member of the investigator's staff confirms the observations recorded.	X (copy)	X (original)
15	**DOCUMENTATION OF CRF CORRECTIONS**	To document all changes/additions or corrections made to CRF after initial data were recorded.	X (copy)	X (original)
16	**NOTIFICATION BY ORIGINATING INVESTIGATOR TO SPONSOR OF SERIOUS ADVERSE EVENTS AND RELATED REPORTS**	Notification by originating investigator to sponsor of serious adverse events and Related reports.	X	X

17	**NOTIFICATION BY SPONSOR AND/ORINVESTIGATOR, WHERE APPLICABLE, TOREGULATORY AUTHORITY(IES) AND IRB(S)/IEC(S) OF UNEXPECTED SERIOUS ADVERSE DRUG REACTIONS AND OF OTHER SAFETY INFORMATION**	Notification by sponsor and/or investigator, where applicable, to regulatory authorities and IRB(s)/IEC(s) of unexpected serious adverse drug reactions and of other safety information in accordance.	X (where required)	X
18	**NOTIFICATION BY SPONSOR TO INVESTIGATORS OF SAFETY INFORMATION**	Notification by sponsor to investigators of safety information.	X	X
19	**INTERIM OR ANNUAL REPORTS TO IRB/IEC AND AUTHORITY(IES)**	Interim or annual reports provided to IRB/IEC and to authority(ies).	X	X (where required)
20	**SUBJECT SCREENING LOG**	To document identification of subjects who entered pre-trial screening.	X	X (where required)
21	**SUBJECT IDENTIFICATION CODE LIST**	To document that investigator/institution keeps a confidential list of names of all subjects allocated to trial numbers on enrolling in the trial. Allows investigator/institution to reveal identity of any subject.	X	
22	**SUBJECT ENROLMENT LOG**	To document chronological Enrolment of subjects by trial number.	X	

23	**INVESTIGATION PRODUCTS ACCOUNTABILITY AT THE SITE**	To document that investigational product(s) have been used according to the protocol.	X	X
24	**SIGNATURE SHEET**	To document signatures and initials of all persons authorized to make entries and/or corrections on CRFs.	X	X
25	**RECORD OF RETAINED BODY FLUIDS/TISSUE SAMPLES (IFANY)**	To document location and identification of retained samples if assays need to be Repeated.	X	X

Contains Non-binding Recommendation

C. After Completion or Termination of the Trial

After completion or termination of the trial, all of the documents identified in Sections 8.2 and 8.3 should be in the file together with the following

	Title of Document	Purpose	Located in Files of	
			Investigator /Institution	Sponsor
1	**INVESTIGATIONAL PRODUCT(S) ACCOUNTABILITY AT SITE**	To document that the investigational product(s) have been used according to the protocol. To document the final accounting of investigational product(s) received at the site, dispensed to subjects, returned by the subjects, and returned to sponsor.	X	X
2	**DOCUMENTATION OF INVESTIGATIONAL PRODUCT DESTRUCTION**	To document destruction of unused investigational products by sponsor or at site.	X (if destroyed at site)	X
3	**COMPLETED SUBJECT IDENTIFICATION CODELIST**	To permit identification of all subjects enrolled in the trial incase follow-up is required. List should be kept in a confidential manner and for agreed upon time.	X	
4	**AUDIT CERTIFICATE** (if available)	To document that audit was performed.		X
5	**FINAL TRIAL CLOSE-OUT MONITORING REPORT**	To document that all activities required for trial close-out are completed, and copies of essential documents are held in the appropriate files.		X

6	**TREATMENT ALLOCATION AND DECODING DOCUMENTATION**	Returned to sponsor to document any decoding that may have occurred.		X
7	**FINAL REPORT BY INVESTIGATORTO IRB/IEC WHERE REQUIRED, AND WHERE APPLICABLE, TO THE REGULATORY AUTHORITY(IES)**	To document completion of the trial.	X	
8	**CLINICAL STUDY REPORT**	To document results and interpretation of trial	X (if applicable)	X

AX2-V1/SOP 13/V1
Contents of Trial Master File (TMF)

1. Study Protocol [all versions with amendments (if any)]
2. Informed consent forms (all required languages), Translation and back translations with certificate
3. Case Report Forms (CRFs)
4. Investigator's Brochure (if any)
5. Investigational Product Information (if any)
6. IP Accountability Logs
7. Duty Delegation Log/Drug Inventory Logs, per patient
8. CV, Medical registration (as applicable) and current valid GCP certificates of all study team members
9. Investigator's Undertaking
10. DCGI/CDSCO submission Acknowledgement (if applicable)
11. CTRI Registration Details
12. IEC approval letters
13. Continue Review Applications (CRAs)
14. SAE reporting forms and other details
15. IEC communication
16. Contracts and Agreements (if any)
17. Laboratory details (if any)
18. Others

Title: Storage & Archival of Essential Documents

AX3-V1/SOP 13/V1

Archiving box labels

Study Reference Number OR MPMMCC project no:	
Study Title	
Name of Sponsor	
Name of Principal Investigator	
Archival Date	
Archive Until	
Contents of BOX 1: 1. 2 3 4 5 6 7 8 9 10	

Title: Storage & Archival of Essential Documents

AX4-V1/SOP 13/V1

Archive Inventory

Study Reference Number OR MPMMCC Project Number	
Study Title	
Name of Sponsor	
Name of Principal Investigator	
Archival Date	
Archive Location	On-site/Off-site/Storage area
Archive Until	

BOX Number 1	Content
Box Number 2	

Title: Storage & Archival of Essential Documents

AX5-V1/SOP 13/V1

Archival Data Access log

Sr. No	Date	Project No.	PI Name	Study Title	Archival Location	Name of achieved documents, required	Reason to access the archived documents	Name & CC no. of person accessing the document	Signature & Date

Title: Storage & Archival of Essential Documents

Standard Operating Procedure
Clinical Research Secretariat (CRS)

Title: Safety Reporting

SOP Code: SOP 14/V1 Date: 2nd Feb 2024 Pages: 168-177

Tata Memorial Centre

MPMMCC: Sunder Bagiya, Near Nariya Gate, Banaras Hindu University Campus, Varanasi-221005, Uttar Pradesh, India

HBCH: Homi Bhabha Cancer Hospital, Ghanti Mill Road, Old Loco colony, Lahartara, Varanasi-221002, India

14.1 Purpose

To describe the procedure for reporting safety reports (Serious Adverse Events 'SAE') occurring in research studies to IEC, Sponsor/CRO, CDSCO and Institutional head

14.2 Scope

This SOP will apply to all clinical trials approved by IEC and conducted at MPMMCC/HBCH.

14.3 Procedure

14.3.1. Managing AEs and SAEs during study

PI must educate and train the study team about adverse events, SAEs, causality assessments, NCI CTCAE criteria (expected and un-expected) and the importance of documenting in the source notes and reporting to the IEC, Sponsor/CRO, CDSCO and Institutional head.

At the start of the study, the PI/ study team members should ensure that all subjects/participants will be provided with a copy of the ICD, with the contact information of PI/designee, who will be the point of contact in case of any medical event.

PI and the study team must review the IEC, Sponsor/CRO and CDSCO requirements and specific protocol requirements for SAE reporting, as well as the timelines associated with them.

For sponsored studies, the sponsor will outline the procedures for reporting and recording AEs and SAEs in the protocol. All AEs and SAEs should be recorded on the Case Report Forms (CRFs), the SAE Form, (the template as per NDCT Rules 2019), should be reported on Sugam portal and in the source documents at the site.

When a subject/participant reports an adverse event (at each clinical visit/telephonic contact), study team member should inform PI/CoI who must provide the necessary and appropriate medical care to the subject/participant.

In the event that the PI/study team member learns about the adverse event/SAE from the subject/relative over telephone; then the PI/Study team member must collect all the information about the event from the subject/relative and document it in the subject/participant file and include details such as;

- Date and time of the event discussion
- Date and time of the event occurred (start and stop date).
- Any medicine or advice taken or offered.
- Details of the person who provided the information.
- Prescription of investigations and medication/treatment received if any.
- In the event of death, the cause leads to the fatal event. Death certificate if possible.

The study team must make all attempts to contact the treating doctor if any to obtain additional information and these attempts should be documented. Any additional information/documentation obtained from the treating doctor/institute should be maintained with the subjects/participants file.

In events where, original records are not available an attested copy must be obtained and maintained. The subject/participant on recovery may be invited for an unscheduled visit if deemed necessary by the PI/ Co I.

PI/ study team member must document the adverse events using the protocol-defined terminology [e.g. CTCAE guideline, applicable version as per IEC SOP, Sponsor requirement] and Grade the severity of the AE using the protocol-defined criteria (i.e. Grade I/II/III/IV or V).

PI must assess and assign causality/attribution for any AEs. The attribution or causality is the determination of whether an AE is related to the Investigational Product (IP) or procedure.

PI/Co I/Study team member must document the event start and stop date and whether study medication prescribed was continued/interrupted/discontinued, any concomitant medication started to manage the event.

The final assessment of the severity and causality must be made and signed-off by the PI/Co I (As per delegation log)

If the event qualifies any of the below mentioned criteria, it should be considered as Serious Adverse Event (SAE):

- Results in death
- Is life-threatening
- Requires inpatient hospitalization or prolongation of existing hospitalization
- Results in persistent or significant disability/incapacity (as per reporter’s opinion)
- Is a congenital anomaly/birth defect?
- Other medically important condition

For reporting SAE or expedited reporting, PI must complete the necessary documentation (e.g. SAE Reporting Form available on the IEC portal, SUGAM portal and respective forms provided by sponsor if any) and submit the same to the IEC, CDSCO andto the sponsor/designee and Institutional Head within the required time frame from the study team getting to know of the event.

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

1. IEC
2. Sponsor or its representative
3. CDSCO (in case of studies that require approval of the CDSCO)

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

1. IEC
2. Sponsor or its representative
3. CDSCO (in case of studies that require approval of the CDSCO)
4. Head of the Institution (in case of studies that require approval of the CDSCO)

14.3.2. Reporting SAE to Institutional Ethics Committee (*IEC(DSMU))*

PI/CoI shall report all SAE to the IEC /DSMU that accorded approval to the study protocol within 24 hours of their occurrence in the format required by the IEC/DSMU (as per IEC SOP).

If the outcome of an SAE is 'Death' the IEC/DSMU should be notified within 24hrs of the knowledge of the PI. If complete information is not available and delay is expected, then the initial report can be submitted with the available information.

In case the event is Death due to disease progression, the event should be notified in the SAE reporting format unless it is specified in the IEC approved protocol that such events will not to be reported.

If the patient is out of trial and on Survival follow up and has an SAE, it should be reported unless specified in the protocol.

PI must complete the required information in the SAE reporting Form (available on IEC portal) and sign and date the same after final review and confirmation of IEC administrator/DSMU coordinator and submit the signed copy to the DSMU department.

Serious Adverse Event should be graded as per CTCAE guidelines and the SAE causality and relatedness must be marked carefully by the investigator

Investigator/study team member must submit one copy of the SAE report form. One acknowledged copy (stamped signed and dated by IEC representative) of the form will be filed in the TMF and the same must be send to the Sponsor/CRO.

Investigator will keep a track on the progress report of the patient and must ensure the process for management of adverse event is robust and the subject/participant gets timely and appropriate medical attention/intervention as required.
IEC/DSMU will discuss the submitted SAEs in the IEC meeting and will take a decision regarding compensation, if applicable.

Follow-up reports on the SAEs should be submitted within 14 days of the initial report or when any additional information regarding the event is available, whichever is earlier.

IEC/DSMU can send back the report to PI in case the report is not complete.

In case of query PI will receive a mail or formal letter with instructions for specific actions from the IEC/DSMU and PI/Co I must respond to the query letter immediately.

14.3.3 Reporting SAE to Sponsor/CRO

PI/Co I/ Study team member must inform the sponsor/CRO regarding the SAE within 24 hours of occurrence or within the timeframe stated in the protocol. If the SAE is life-threatening or a death, the sponsor/CRO must be notified immediately. (In addition to IEC/DSMU SAE reporting form, PI has to fill protocol specific SAE reporting form as required by the Sponsor/CRO).

The PI/Co I/CTC should use the SAE reporting form provided by the Sponsor/CRO and will follow the SAE reporting instruction mentioned in the protocol.

The PI/Co I/ Study team member should collect as much of the information as possible for completing the SAE reporting form.

PI/Co I must document the following SAE related information in the source notes:

- Date of the report
- Description of event, including relationship to study drug
- Determination of seriousness
- Possible cause of SAE other than trial medication
- Relevant medical conditions
- Concomitant medications

The completed and signed (by PI or CoI as per delegation log) SAE reporting form will be sent to sponsor/CRO via fax or e-mail as agreed by the sponsor/CRO.

The details of the communication and the confirmation of this reporting (for example fax

confirmation receipt) must be maintained in the TMF.

Sponsor can contact Investigator in case of any query or further information required. PI/Co I will keep a track on the progress report of the patient and must ensure the process for management of adverse event is robust and the subject/participants gets timely and appropriate medical attention/intervention as required.

PI must inform the Sponsor/CRO regarding the progress report of the subject/participant till the subject/participant has recovered or is discharged from the hospital or till death.

The Study team member will ensure that the SAE is properly documented in the subject's/participant's chart and CRF, and that the appropriate forms are retained in the TMF.

*(Note: In addition to CDSCO, IEC and Sponsor, PI must send a SAE copy to Institution head (follow up SAE). ***** (in case of studies that require approval of the CDSCO)*

14.3.4 Reporting SAE to CDSCO

The Investigator shall report all serious and unexpected adverse events to the CDSCO, the Sponsor or his representative whosoever had obtained permission from the CDSCO for conduct of the clinical trial and the Institutional Ethics Committee, within twenty-four hours of their occurrence.

(Note: For Investigator-initiated trial, it is the responsibility of the investigator to report the event to IEC, CDSCO and Institutional Head for regulated studies.)

The sponsor or his representative conducting clinical trials in India are requested to prepare the SAE reports for submission to CDSCO as per CDSCO guideline mentioned on the website.

PI/Co I must report the SAE to Central Licensing Authority and make sure it contains all the required clinical, administrative as well as technical information in proper manner as per the information requested on the CDSCO- SUGAM website (https://cdscoonline.gov.in/CDSCO/homepage).

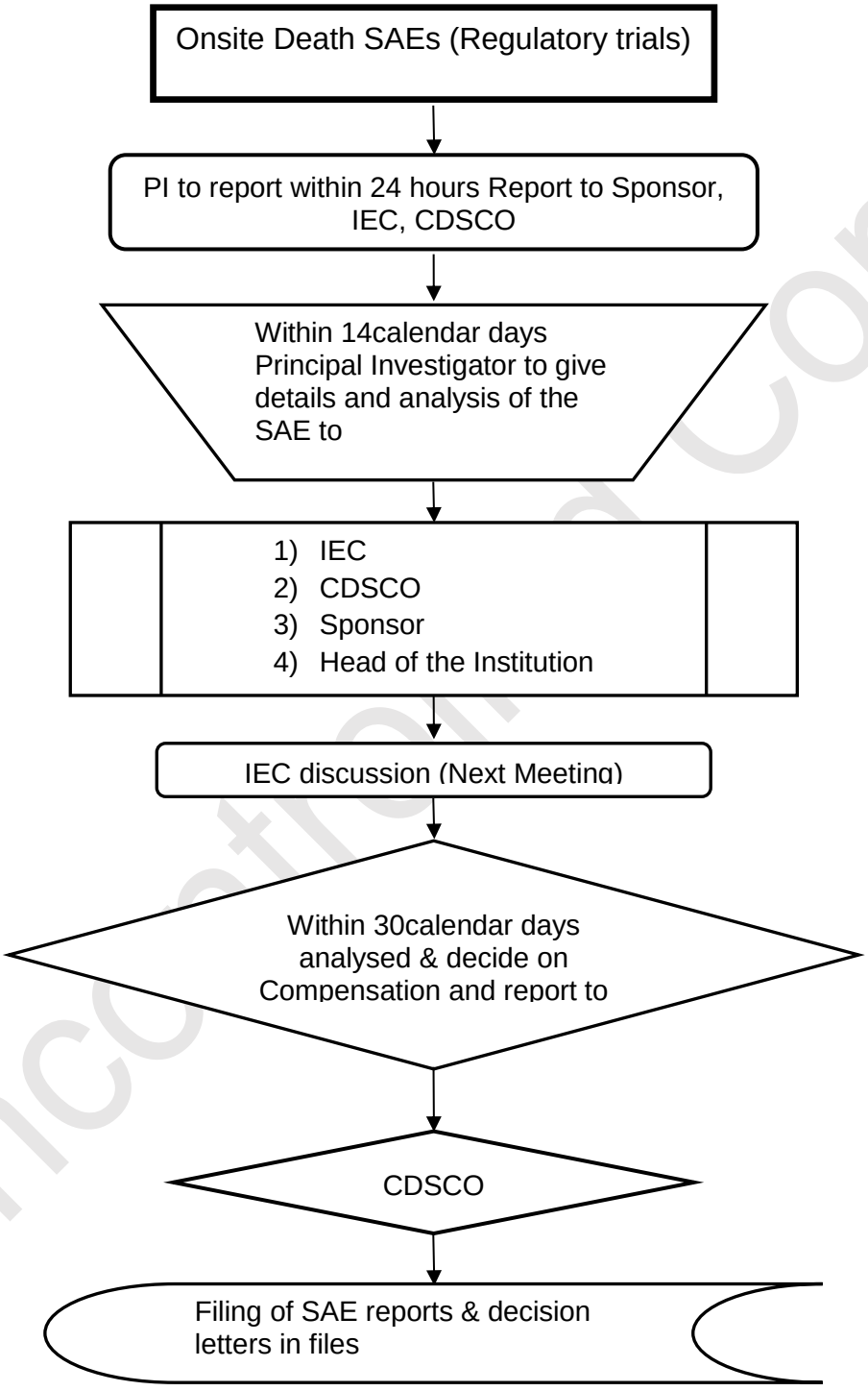
14.3.5. Compensation:

In case of injury/ SAE during clinical trial to the subject of such trial, complete medical management and compensation shall be provided in accordance with Chapter VI of NDCT Rule 2019.

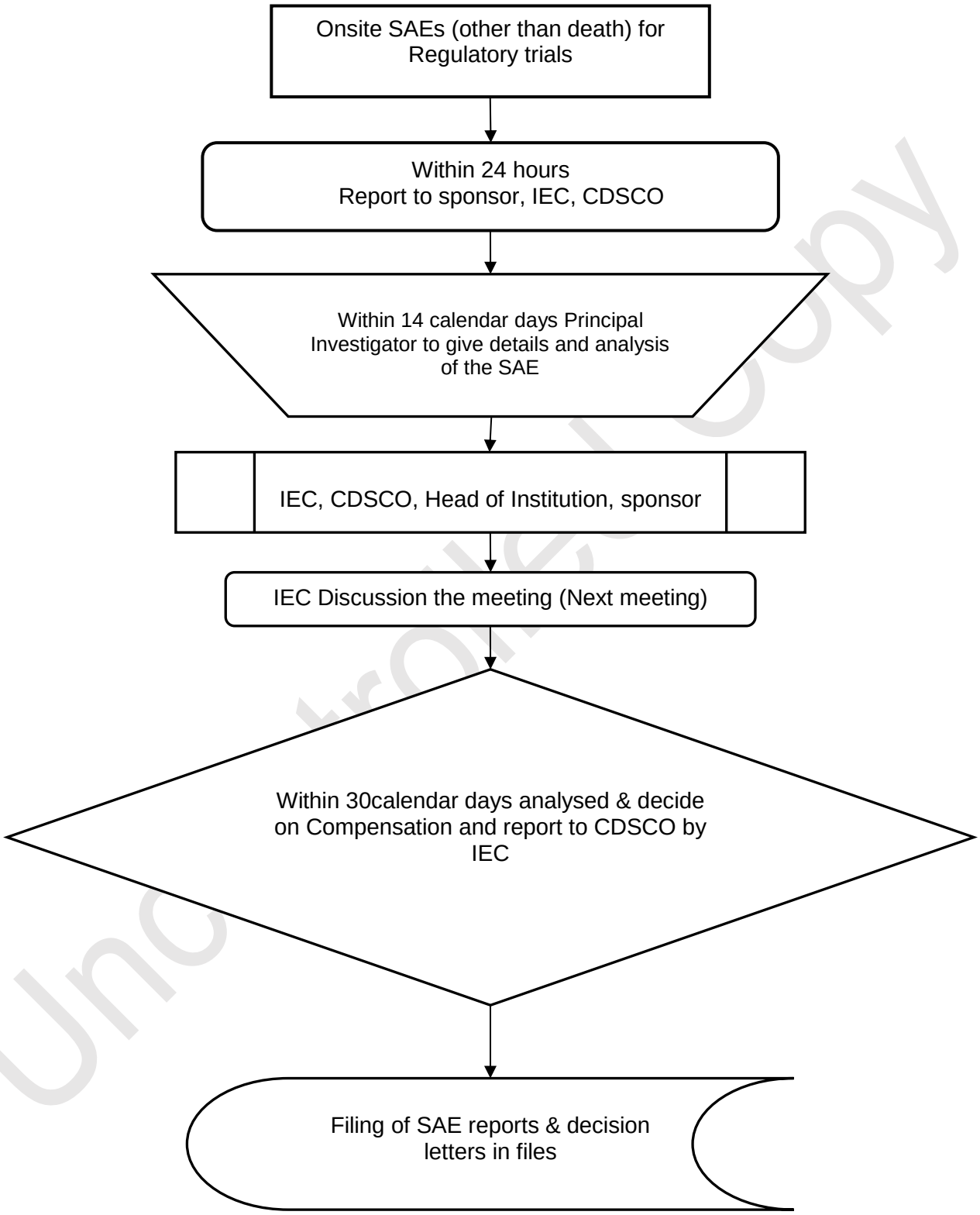
The ethics committee shall forward its report or order on the event, after due analysis, along with its opinion on the financial compensation, if any, determined in accordance with the formula specified in the Seventh Schedule, to be paid by the said sponsor or its representative, who has obtained permission from the Central Licensing Authority for conduct of clinical trial or bioavailability or bioequivalence study, as the case may be, to the Central Licensing

Authority; in accordance with Chapter VI of these rules. (Kindly refer NDCT Rules Chapter VI for details) & IEC SOP for details.

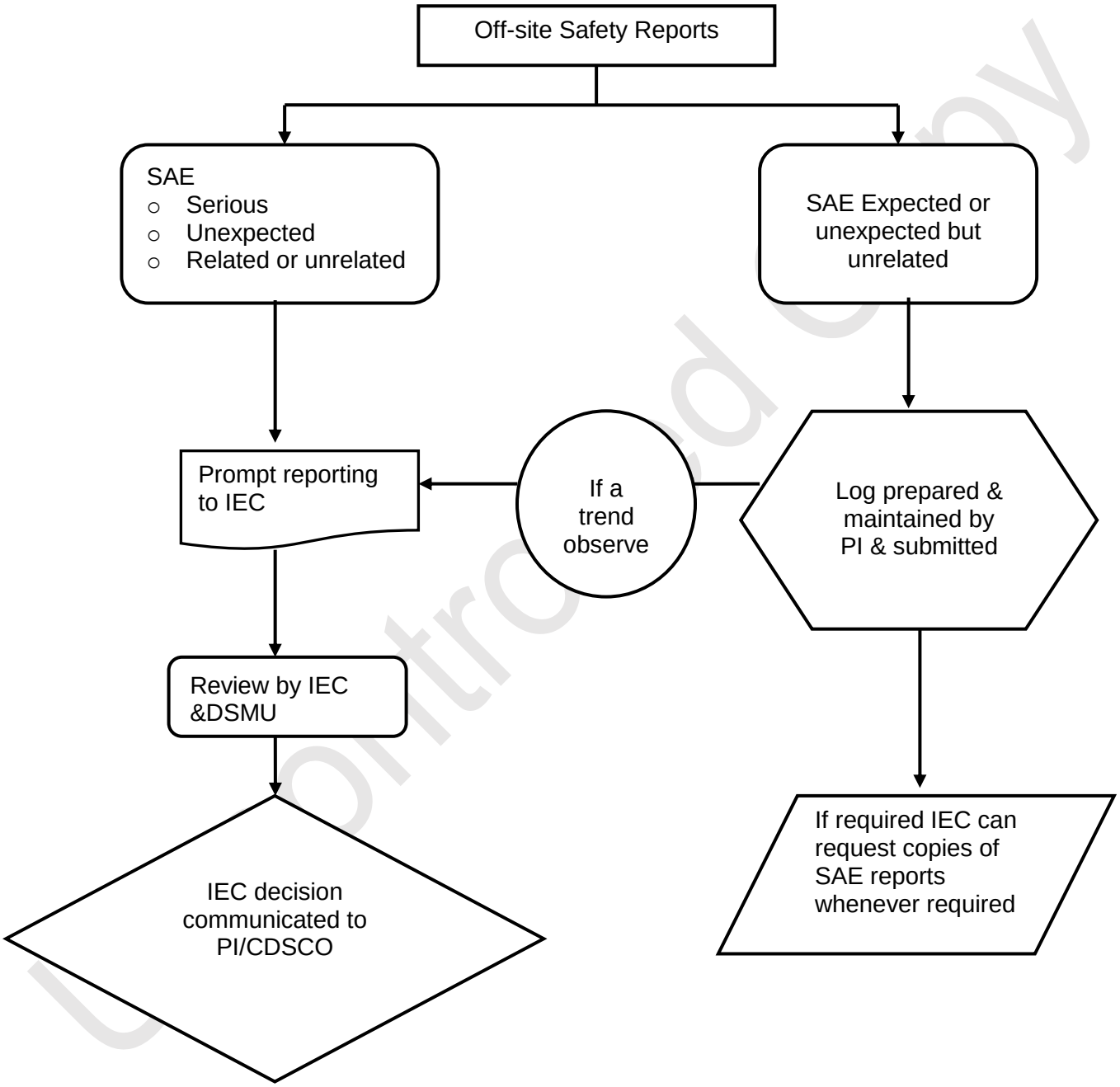
Flow Chart (Onsite SAE-Regulatory Trial)



Flow Chart (Onsite SAE for Regulatory trial)



Flow Chart (Off site Safety Reporting)



14.4 Applicable areas of the Hospital

- MPMMCC/HBCH, Varanasi
- IEC/DSMU

14.5 Applicable Staff

This SOP applies to all the personnel of the clinical research team who may be responsible for reporting SAE.

These include the following:

- Investigator
- Research Team (listed in the delegation log)

14.6 Staff responsible for Implementation

OIC CRS will ensure that the SOP is updated and available on MPMMCC/HBCH website for all the Investigators conducting studies and Investigator will ensure that the research team involved in the conduct of the study will comply with this site SOP.

PI at his level will ensure that at the time of implementation of the SOP, that the research team at MPMMCC/HBCH are trained and in the event that an SOP is modified, provide training regarding the change(s) and ensure their compliance with the changes.

Inform IEC that this site SOP will be implemented within the institution.

Standard Operating Procedure
Clinical Research Secretariat (CRS)

Title: Managing Biological Samples

SOP Code: SOP 15/V1 Date: 2nd Feb 2024 Pages: 178-181

Tata Memorial Centre

MPMMCC: Sunder Bagiya, Near Nariya Gate, Banaras Hindu University Campus, Varanasi-221005, Uttar Pradesh, India

HBCH: Homi Bhabha Cancer Hospital, Ghanti Mill Road, Old Loco colony, Lahartara, Varanasi-221002, India

15.1 Purpose

This SOP describes the procedures for collection, preparation, storage and shipment of biological sample.

15.2 Scope

This SOP will apply to all biological samples collected, processed, stored and shipped by MPMMCC/HBCH, unless alternate directions are provided by the sponsor or Contract Research Organization (CRO).

15.3 Procedure

15.3.1. Collection of Samples

Study Nurse or the person delegated in the duty delegation log will collect the biological samples on scheduled visit as described in the protocol.

After collecting the sample, the study nurse or delegated person will record the details in the biological sample collection form (AX1-V1/SOP 15/V1)

15.3.2. Preparation of Samples

The sample either is stored as collected and/or processed as mentioned in the protocol or laboratory manual provided by the sponsor/CRO.

Using a permanent marker, study nurse or CTC will record the patient initials, patient ID and the date and time when the sample was obtained on each sample labels.

In case of any damage to sample or if samples are unusable immediately inform to Investigator & Sponsor/ CRO (in case of sponsored study) and report deviation to IEC and document the same in the source note, if required.

15.3.3. Storage of Samples

Before shipments, site personnel will store all biological samples at a temperature mentioned in the protocol

15.3.4. Shipment of Samples

Site personnel will

- Call the courier person as agreed by the sponsor/as mentioned in the protocol and schedule the date and time for shipping the sample.
- Inform the courier person to bring the required materials for shipment as mentioned in the protocol.

- Complete all the biological sample inventory form available in the collection kit listing all the samples in the shipment.
- Arrange a gate pass as per MPMMCC/HBCH policy.
- Keep a photocopy of the Biological Sample Inventory page in the TMF.
- Return of samples.

15.4 Applicable Staff

This SOP applies to all the existing personnel of the clinical research team and any new member appointed who may be responsible for study related activities as mentioned in this SOP (per the delegation log).

These include following

- Investigators
- Research Team member (listed in the delegation log)

15.5 Staff responsible for Implementation

OIC CRS will ensure that the SOP is updated and available on MPMMCC & HBCH website for all the Investigators conducting studies and Investigator will ensure that the research team involved in the conduct of the study will comply with this site SOP.

PI at his level will ensure that at the time of implementation of the SOP, that the research team at MPMMCC & HBCH are trained and in the event that an SOP is modified, provide training regarding the change(s) and ensure their compliance with the changes.

Inform IEC that this site SOP will be implemented within the institution.

AX1-V1/SOP 15/V1

(Note: Template for investigator-initiated studies. For sponsored studies, refer the sponsor template.)

Protocol no:

Protocol Title:

PI name:

Trial ID no	Subject/Participant Initial	Sample ID	Type of Sample	Date	Time	Collected by

Standard Operating Procedure
Clinical Research Secretariat (CRS)

Title: Reimbursement

SOP Code: SOP 16/V1 Date: 2nd Feb 2024 Pages: 182-186

Tata Memorial Centre

MPMMCC: Sunder Bagiya, Near Nariya Gate, Banaras Hindu University Campus, Varanasi-221005, Uttar Pradesh, India

HBCH: Homi Bhabha Cancer Hospital, Ghanti Mill Road, Old Loco colony, Lahartara, Varanasi-221002, India

16.1 Intent / Purpose

This SOP describes the procedures involved in reimbursement to the study subjects/participants for their involvement in the research and research related activities as agreed in Clinical Trial Agreement (CTA) and or Memorandum of Understanding (MoU) and mentioned in ICF and as per CDSCO Rules and ICMR guidelines.

16.2 Scope

This SOP applies to all study team members who are engaged in study related activities and delegated in the delegation log for research related reimbursement (if applicable) to all the subjects/participants involved in the studies being conducted in MPMMCC/HBCH.

16.3 Procedure

16.3.1. Information regarding reimbursement

Subjects/Participants may be paid for the inconvenience and time given, and should be reimbursed for expenses incurred, in connection with their participation in research. They may also receive free medical services in case of SAE or AE as mentioned in the protocol/CTA/MOU. However, payments should not be so large or the medical services so extensive as to induce prospective subjects/participants to consent in research against their better judgement (inducement). All payments, reimbursement and medical services to be provided to research participant should be approved by the IEC. Care should be taken:

When a LAR is asked to give consent on behalf of an incompetent person, no remuneration should be offered except a refund of out of pocket expenses;

When a participant is withdrawn from research for medical reasons related to the study the subjects/participant should get the benefit for full participation;

When a subjects/participant withdraws his/her consent for any other reasons he/she should be paid in proportion to the amount of participation.

Reimbursement must be done as agreed by the investigator and sponsor/CRO in the Clinical Trial Agreement (CTA) and or Memorandum of Understanding (MoU) and as defined in the Informed consent document.

16.3.1. Procedure for reimbursement

CTC as designated will reimburse the amount to the subjects/participants as mentioned below:

- PI will open a respective study account in the MPMMCC/HBCH accounts department by submitting the following documents to account department;

  - Final IEC approval letter

- Final approved Budget from IEC
- Request letter

- Accounts department will open the account for the request project and will allot a unique “project account no” to PI. PI shall maintain the account number for further communication with respect to amount deposition and reimbursement.

- In case of Investigator-initiated trial supported by Intramural funding the amount will be transferred to the respective accounts number by TRAC. TRAC will send a letter of intimation for the same to PI. For studies supported by extramural grants, PI will submit the above-mentioned documents and the extramural funding approval letter. PI can directly deposit the cheque received from the extramural funding or and provide the accounts details for fund transfer to the respective account.

- Keep a track of subjects/participants visits as mentioned in the protocol, travel, concomitant medication prescribed for adverse event (if any), and if any unscheduled visit scheduled during the study period for reimbursement.

- Must reimburse travel cost, upon presentation of receipt of a valid ticket (if available or as agreed in the CTA/MoU) or bills for the protocol specified visits or unscheduled visits if any.

- Must collect the original bills from the subjects/participants for above listed things for reimbursement

- Payment voucher must be prepared for the same; it will include subject/participant hospital case number, name, amount to be paid, study account number and reason for reimbursement.

- Investigator or designee will approve and sign the voucher. Subjects/ Participants will sign or put his/her thumb impression in case subjects/ participants is illiterate on the copy of the voucher (subjects/participant will sign/thumb while submitting the voucher to the accounts department).

- Copy of signed voucher (by investigator/designee and subject/participant) and bills should be filed in a separate file.

- Original voucher and bills will be forwarded to the concerned authority as per the hospital policy for approval.

- The voucher and bills will be forwarded to the accounts department of the MPMMCC/HBCH.

- The competent authority from accounts department will sanction and release the amount.

  Note: Kindly maintain a ledger book/ excel sheet of all the invoice.

16.3.1. Process for Online cashless Reimbursement procedure

IEC/DSMU has developed an online process to reimburse the study related expenses born by the subjects/participants for respective protocol related procedure. PI/study team member can follow the below mentioned process for online reimbursement;

1. PI/study team member can contact DSMU officer or can login to IEC portal and download the form for online linking of cashless payments for subjects/participants.

2. Complete the requested details inclusive of name of Principal Investigator, Protocol Number and Study Title, IEC Project Number, Account Number, Number of Co-investigators, Name of 2 co-ordinators) to allow access.

3. The completed signed and dated by the Principal Investigator should be submitted to DSMU office. DSMU will further forward the email to IT department to provide access and link study for the online reimbursement.

4. Once access and linking is confirmed

Open **Project Employee Management System**→ Enter CC No. of the delegated user (Principal Investigator/ delegated member)and password→ Select Project name →enter Case Number → Add subject/participant name and then Save.

5. Once the subject/participant is added

Open **Project Employee Management System**

Enter User ID & Password→Login→Enter Case No.→Select Requisition Option→

Select Test/procedure name→ Save → Click on Memo Tab → Select Prepare →Memo → Click on Deduct Checkbox→ Select all the tests/procedure done under respective protocol by selecting on checkboxes→ Save→ Once a memo is generated→ Print the Memo

Note: The above-mentioned process has been drafted with concordance with IEC/DSMU procedure, kindly check IEC SOP/DSMU circular for any update or changes.

In case of Serious Adverse Event (SAE) which found to be related to the IP or protocol specified procedure, PI/ Co-I will make sure that subject/participant should get reimbursed for every expense occurred during the management of the adverse event.

CTC will always keep a copy of the updated account statement to make sure the account has sufficient balance for reimbursement.

CTC should send the expense invoices to sponsor on regular intervals, to receive the amount on time.

16.4 Applicable Staff

This SOP applies to all the existing personals of the clinical research team and any new member appointed who may be responsible reimbursing the study subject/participant as mentioned in this SOP (as per the delegation log).

These include the following:

- Investigator
- Research Team member (listed in the delegation log)

16.5 Staff responsible for Implementation

OIC CRS and Investigator will ensure that the research team involved in the conduct of the study will comply with this site SOP.

PI will ensure that at the time of implementation of the SOP, that the research team at the clinical research Secretariat in MPMMCC/HBCH are trained and in the event that an SOP is modified, provide training regarding the change(s) and ensure their compliance with the changes.

Inform IEC that the site SOP will be implemented within the institution.

Standard Operating Procedure
Clinical Research Secretariat (CRS)

Title: Study Team Training and Study Handover

SOP Code: SOP 17/V1 Date: 2nd Feb 2024 Pages: 187-193

Tata Memorial Centre

MPMMCC: Sunder Bagiya, Near Nariya Gate, Banaras Hindu University Campus, Varanasi-221005, Uttar Pradesh, India

HBCH: Homi Bhabha Cancer Hospital, Ghanti Mill Road, Old Loco colony, Lahartara, Varanasi-221002, India

17.1 Purpose

This SOP defines the procedure and recommendation of training of study team members and adequate handover to new PI, Co-I or any other study team member, to ensure that the patient safety, protocol compliance, data integrity and overall quality assurance at the investigational site is protected and integrated as per the applicable regulations and guidelines.

Study team member must understand the responsibilities of the trials conducted at site and be appropriately qualified by education, training and/or experience to perform his or her research-related task(s). Some training may be obtained through internal hospital accepted training and certification program(s) or through external hospital accepted training and certification program(s).

The purpose of a handover is to ensure continuity of operations when the study team member, usually responsible, is not available due to temporary or permanent absence. A handover can be supported by a discussion between responsible person planning for temporary or permanent absence and the person identified for taking the handover and to explain the status of the tasks, a summary of the work status in an email/ memorandum or, a more detailed file.

17.2 Scope

This SOP will apply to all study team members conducting studies in MPMMCC/HBCH.

17.3 Procedure

17.3.1 Study Team Training

On appointment, all study team members will be given an appropriate study depending on the job specification to possess the right experience and qualifications and further training may be provided to bring them up to the required level for specific tasks. Duty delegation / job responsibility document will be given to every Clinical Trial Coordinator (CTC)/ team member. Training may include but not limited to (as per the role & responsibility);

- Protocol including background, purpose of the study, including study objectives and design
- Study procedures
- Investigator's Brochure (IB)
- Investigational product(s): Pharmacological and/or technical aspects of the product(s); management and accountability utilizing an investigational product accountability log
- Subject recruitment and screening, including criteria for inclusion and exclusion
- Obtaining informed consent
- All essential documents such as case report forms (CRFs), informed consent forms, etc.

- Adverse Event/Serious Adverse Event Reporting
- Data collection and record keeping

GCP requires that all Investigators, other study team members must undergo training which will enable them to understand their responsibilities, applicable regulations, guidelines and research studies and training should be documented in the training log. Protocol related specific and GCP regulation related training should be given. PI should give the protocol training for Investigator-initiated studies and Sponsor for pharma studies at the time of SIV.

Each Investigator, CTC and study team members will review and understand the site's SOPs. It is recommended that SOP training must be included in the orientation of new clinical research personnel. All applicable clinical research personnel should be knowledgeable of new or revised SOPs.

Good Clinical Practice (GCP) is a universal standard in clinical research that must be followed in every research protocol. GCP training and education are recommended for research team members, especially the Investigator and CTC. However, any member of the research team with a significant role in the conduct of a research study must be knowledgeable in GCP. All members of the clinical research team should GCP trained and certified.

Before study initiation Investigator/Sponsor/CRO will organize SIV meeting at site to train all study team members and all study team members should attend the meeting for thorough understanding of the study.

PI and study team member(s) should be prepared to demonstrate all training received. CVs, GCP and other training certificates should be updated as required. It is recommended that an assessment of the employee’s knowledge of the regulations and guidelines can be conducted upon recruiting and on a regular basis. It is recommended that an assessment of any additional protocol-specific skill requirements be conducted prior to activation of each new study. Respective PI will be responsible for his/her study team training.

Clinical Research Secretariat (CRS) Department conducts two training programs namely Clinical Research Methodology (CRM) and GCP once in a two year. Study team member should attend the course to acquire training or to update themselves.

Updated CRS SOP will be available on MPMMCC/HBCH website; PI can arrange a training program for a study team member on updated SOPs. Additionally, PI should maintain the training log (AX1-V1/SOP17/V1) to document the training record.

It is recommended that the PI and study team must maintain the Site SOP training Record (AX1-V1/SOP17/V1) at their respective unit and should make available whenever asked by the OIC, CRS.

17.3.2 Study Handover

If any study team member is leaving the organization, he/she must ensure that the proper handover is given to the next delegated person identified by the PI, the identified person should be briefed in time before the person goes on leave to allow for any follow up questions.

Prior to leaving the study, the existing study team member should complete the following training for the person taking over the study:

- Training on protocol and procedures e.g. SOPs and explanation of relevant documents
- Information regarding study subjects/participants, study documents and all study related activities
- Outstanding data entry and/or data queries
- Training to complete source documents
- Explanation on the objectives & priorities
- Notification to the sponsor of the study team changes
- Notification to the active subjects/participants of the study team changes if the research team contact information will change for the subjects/participants.
- Provide a list of study-specific contacts (e.g., sponsor, monitor, vendors involved etc.)
- ISF, all logs and IP inventory should be handed over to new person and same documented in a log.
- Provide a list of outstanding issues
- The leaving person has to make sure that the documentations concerned for the tasks is up to date and easily available, and if needed, revise it when preparing the hand over.

If there is a change in PI, the following documents need to be revised and completed:

- Inform Sponsor and IEC regarding the change in PI in the Study team.
- Consider revising the protocol and informed consent form, as appropriate. Also consider notifying current subjects/participants; correspondence sent to all subjects/participants must be approved by the IEC, if applicable.
- Update the Form FDA 1572 or the Investigator Agreements, Investigator Undertaking and other required forms
- Update the Duty Delegation log
- Ensure that the new PI has completed the SOP required training and study-specific training

Written hand over should be given in order to ensure the continuity of work. The format can be a briefing note, a check list, or a schedule prepared to give all information.

When the study member returns from leave a hand over should be prepared to give updates on the status of the tasks.

The existing and new study team member should document the study handover in a note to file or other documentation in the TMF/SMF. The note should contain some of the items above and the date of the handover. The new study team member should obtain documented study-specific training and any required approvals prior to being added to the duty delegation log.

17.4 Applicable Staff

This SOP applies to all the existing personals of the clinical research team and any new member appointed who may be responsible for training and study handover as mentioned in this SOP (as per the delegation log).

These include the following:

- Investigator
- Research Team members (listed in the delegation log)

17.5 Staff responsible for Implementation

OIC CRS will ensure that the SOP is updated and available on MPMMCC/HBCH website for all the Investigators conducting studies and Investigator will ensure that the research team involved in the conduct of the study will comply with this site SOP.

PI at his level will ensure that at the time of implementation of the SOP, that the research team at MPMMCC/HBCH are trained and in the event that an SOP is modified, provide training regarding the change(s) and ensure their compliance with the changes.

Inform IEC that this site SOP will be implemented within the institution.

It is the responsibility of each individual who are about to go on short / long term absences or leave their current position / the Agency to prepare a hand over file.

AX1-V1/SOP17/V1

Training Record

Department Name/Clinical Research Secretariat_____

Name of Trainer:_____

Sr. No.	Date	Standard Operating Procedure Code	Trainee Initials	Trainee signature & Date

Reviewed by: _____ Date _____/_____/_____

AX2-V1/SOP17/V1

Project/ Study handover Log

Project Title & Project No: _____

Sr. No	Date	Handover given by	Handover given to	Handover details with respect to study	Sign & Dt. of person giving the handover	Sign & Dt. of person taking the handover	Sign & Dt. of PI

Appendix A

List of Abbreviations

Sr. No.	Acronym	Full Title/Description
1	ACTREC	Advance Centre for Treatment, Research and Education in Cancer
2	AE	Adverse Event
3	CA	Confidentiality agreement
4	CD	Compact Disc
5	CDA	Confidential Disclosure Agreement
6	CDSCO	Central Drug Standard Control Organization
7	CFR	Code of Federal Regulation
8	CIOMS	Council for International Organizations of Medical Sciences
9	CIS	Clinical Services- Information System
10	Co I	Co-Investigator
11	CTC	Clinical Trial Coordinator
12	CRF	Case Report Form
13	CRM	Clinical Research Methodology
14	CRO	Contract Research Organisation
15	CRS	Clinical Research Secretariat
16	CS	Clinically significant
17	CT scan	Computerized Tomography Scan
18	CTA	Clinical Trial Agreement
19	CTCAE	Common Terminology Criteria for Adverse Events
20	CTRI	Clinical Trial Registry India
21	CV	Curriculum Vitae
22	DCGI	Drugs Controller General of India
23	DGFT	Directorate General of Foreign Trade
24	DMG	Disease Management Group

Sr. No.	Acronym	Full Title/Description
25	DNA	Deoxyribonucleic Acid
26	DSMU	Data Safety Monitoring Unit
27	EC	Ethics Committee
28	ECG	Electrocardiogram
29	EDC	Electronic Data Capture
30	EMR	Electronic Medical Record
31	FDA	Food and Drug Administration
32	FDF	Financial Disclosure Form
33	GCP	Good Clinical Practices
34	GLP	Good Laboratory Practices
35	HOD	Head of Department
36	IB	Investigator's Brochure
37	ICF	Inform Consent Form
38	ICH GCP	International Conference on Harmonization Good Clinical Practices
39	IEC	Institutional Ethics Committee
40	IM	Investigator Meeting
41	IND	Investigation New Drug
42	INR	Indian National Rupees
43	IP	Investigational Product
44	ISF	Investigational Site File
45	IU	Investigator Undertaking
46	IVRS	Interactive Voice Response System
47	IW	Impartial Witness
48	IWRS	Interactive Web Response System
49	JC	Joint Clinic
50	LAR	Legally Authorized Representative
51	MRI	Magnetic Resonance Imaging

Sr. No.	Acronym	Full Title/Description
52	MoP	Manual of Procedure
53	M & V cell	Maintenance & Verification cell
54	NCS	Non-Clinically Significant
55	NDA	New Drug Application
56	OIC CRS	Office In Charge Clinical Research Secretariat
57	OPD	Out Patient Department
58	PET	Positron Emission Tomography
59	PI	Principle Investigator
60	PIS	Patient Information Sheet
61	PM	Project Manager
62	PSF	Patient Source File
63	PSUR	Periodic Safety Update Report
64	QA	Quality Assurance
65	SAE	Serious Adverse Event
66	SDV	Source Data Verification
67	SIV	Site Initiation Visit
68	SMF	Site Master File
69	SOP	Standard Operating Procedure
70	STD	Subscriber Trunk Dialling
71	Sub I	Sub Investigator
72	SUSAR	Suspected Unexpected Serious Adverse Reactions
73	TMC	Tata Memorial Centre
74	TMF	Trial Master File
75	TMH	Tata Memorial Hospital
76	TRAC	TMC-Research Administration Council

Appendix B
Glossary

Accountability: Refers to the process, documents and records to demonstrate that investigational products(s) have been used in compliance with protocol and an audit trail is available for all the transactions (receipts, dispensing and return) at any given time point.

Addendum: A written formal clarification in an essential trial document (such as protocol, informed consent form, investigator's brochure etc.)

Adverse events (AE): Any untoward medical occurrence in a patient or clinical investigation participant administered an investigational product and which does not necessarily have a causal relationship with this treatment. The adverse event can therefore be any unfavorable or unintended sign or experience associated with the use of the investigational product, whether or not related to the product.

Adverse Drug Reaction: In the pre-clinical experience with a new medicinal product or its new usages, particularly as the therapeutic dose(s) may not established all noxious or unintended responses to the product related to any dose should be considered adverse drug reactions. The phrase "responses to a medicinal product" means that a causal relationship between the product and the adverse event is at least a reasonable possibility, i.e., the relationship cannot be ruled out. Regarding marketed products, a response to a product which is noxious and unintended and which occurs at doses normally used in man for prophylaxis, diagnosis or therapy of diseases or for modification of physiological function.

Agenda: Refers to a list of topics to be discussed in a meeting.

Agreement: Refers to a document signed between two or more parties describing the terms of agreement.

Amendment: Change(s) made to essential trial documents (such as protocol, ICD, IB, etc) that have an impact on the overall conduct of the study.

Annual Reports: Yearly summary reports submitted to IEC or regulatory agency on the progress of the trial.

Approval Letter: Refer to the action letter from the regulatory agency after the review of a new application, which states that the drug is approved.

Approval: The affirmative decision of the IEC that the clinical trial has been reviewed and may be conducted at the institution site within the constraints set forth by the IEC, the institution, Good Clinical Practice (GCP), and the applicable regulatory requirements.

Archival: Refer to the storage of data/ records at the end of a clinical trial for the stipulated timeframes.

Archiving: Refers to the place or store (something) in an archive.

Arm: Refer to a treatment group in a randomized trial.

Assent: A process by which a child voluntarily confirms his or her willingness to participate in a clinical trial after having been informed of all the aspects of the trial that is relevant to his/her decision to participate.

Audit: A systematic and independent examination of trial-related activities and documents to determine whether the evaluated trial-related activities were conducted and the data were recorded, analyzed, and accurately reported according to the protocol, sponsor's standard operating procedures (SOPs), good clinical practice (GCP), and the applicable regulatory requirement(s).

Auditor: A person appointed by the sponsor who is independent of the study and is qualified by training and experience to conduct an audit of the research study.

Authorized person: A personnel who has the authority to access and review the trial related documents and activities.

Back Translation: Refer to process by which vernacular language translation of a trial documents id back translated into English.

Baseline Assessment: Refer to the pre-treatment evaluations on study subjects as they enter a clinical trial and before any investigational products or interventions are given.

Baseline: Refer to the pre-treatment time point of a clinical trial.

Benefit Risk Assessment: Refer to the evaluation of risks that a clinical trial poses to the study subject's vis-a-vis-its benefits.

Benefit: Refers to the achievement of a desired outcome in a clinical trial.

Bias: Refers to a systematic tendency built into the design or conduct of the study, which skews the results. Bias can occur systematically across all treatment groups leading to an under or over estimation of the results.

Bill: A printed or written statement of the money owed for goods or services

Biological Sample: A biological specimen including, for example, blood, tissue, urine, etc.

Budget: It is a quantitative expression of a plan for a defined period of time. It may include planned sales volumes and revenues, resource quantities, costs and expenses, assets, liabilities and cash flows.

Budgeting: An estimate of the total cost involved for a particular activity or for the conduct of entire clinical trial.

Calibrated: Mark (a gauge or instrument) with a standard scale of readings.

Calibration: A quantity control process of standardizing the equipments, machine, apparatus etc. used in clinical trials.

Carrier: Refers to a person or thing that carries, holds, or conveys something to desired place/person.

Case Report Form (CRF): A case report form is a paper or electronic questionnaire specifically used in research study. The Case Report Form is the tool used by the sponsor/ Investigator of the research study to collect data from each participating site.

Causality: Determination of the relatedness of an adverse event to the study drug or procedure.

Central Drugs Standard Control Organization (CDSCO): CDSCO is a national regulatory body for Indian pharmaceuticals and medical devices.

Central Laboratory: A laboratory having a centralized function of evaluating the protocol required lab parameters for all the sites involved in a trial.

Centrifuge Machine: Refer to a piece of equipment, generally driven by an electric motor, used to separate the components of blood in blood banks.

Clinical Diagnosis: Refers to both the process of attempting to determine or identify a possible disease or disorder, and to the opinion reached by this process.

Clinical Information System (CIS): It is a part of Hospital Information System. The entries are made at the time of Clinical Assessments and information entered get reflected in the Electronic Medical Record (EMR)

Clinical notes: Records which relate to the physical or mental health of an individual which have been made by or on the advice of a health professional in connection with the care and treatment of that person.

Clinical Research Associate (CRA): A person appointed by the Sponsor or Contract Research Organization (CRO) for monitoring and reporting the progress of the trial and for verification of data. The monitor ensures that the trial is conducted, recorded and reported in accordance with the Protocol, Standard Operating Procedures (SOPs), Good Clinical Practice (GCP) and the applicable regulatory requirements.

Clinical Significance: Changes in a subject's clinical condition considered as important and which may not be related to the study drugs(s).

Clinical Study Report: Written description of the trial enumerating the clinical and statistical interpretation.

Clinical Trial: A systematic study of new drug(s) in human subject(s) to generate data for discovering and / or verifying the clinical, pharmacological (including pharmacodynamic and pharmacokinetic) and /or adverse effects with the objective of determining safety and / or efficacy of the new drug.

Clinical Trail Agreement: A document signed and dated by the investigator, Institution head and the sponsor of a trial that describes the responsibility, timelines, payment schedule and other relevant terms of agreement between the involved parties.

Clinical Trial Coordinator (CTC): Clinical trial Coordinators are the primary point of contact for communication with sponsor, investigator, IEC, other departments, hospital staff, patients and patient's relatives, and can be appoint by a CRO/ Site Management Organization or investigator usually. CTC is responsible for supervision, coordination and successful management of a clinical trial at a particular research site.

Clinical Trial Coordinator (CTC): The Clinical Research Coordinator (CRC) is a specialized research professional working with and under the direction of the clinical Principal Investigator (PI). While the Principal Investigator is primarily responsible for the overall design, conduct, and management of the clinical trial, the CRC supports, facilitates and coordinates the daily clinical trial activities and plays a critical role in the conduct of the study. By performing these duties, the CRC works with the PI, department, sponsor, and institution to support and provide guidance on the administration of the compliance, financial, personnel and other related aspects of the clinical study.

Clinical Trial Registry India: It is a free and online system for registration of all clinical trials being conducted in India (www.ctri.nic.in). Registration of clinical trials in the CTRI is now mandatory, as per notification of the Drugs Controller General (India).

Clinical Trial/Study: A systematic study of pharmaceutical products on human subjects – (whether patients or non-patient volunteers) – in order to discover or verify the clinical, pharmacological (including pharmacodynamics, pharmacokinetics), and / or adverse effects, with the object of determining their safety and / or efficacy.

Clinical/Contract Research Organization (CRO): An organization to which the sponsor may transfer or delegate some or all of the tasks, duties and / or obligations regarding a Clinical Study. All such contractual transfers of obligations should be defined in writing. A CRO is a scientific body – commercial, academic or other.

Clinical: Related to human participants.

Co-Investigator (Co-I): A person legally qualified to be an investigator, to whom the Investigator delegates a part of his responsibilities.

Co- Principal Investigator (Co-PI): An individual who shares the clinical trial responsibility with principal investigator.

Coercion: Refers to unacceptable subject recruitment procedures, which involves under inducement, duress or indirect pressure to participate in a clinical trial.

Collaborators: Refers to a person who works jointly on an activity or project.

Common Terminology Criteria for Adverse Events (CTCAE) Guideline: Is designed as an instrument to be used to document AEs identified through a combination of clinical and laboratory evaluation. CTCAE is NOT a tool to assist with data extraction from source documents without the direct participation and supervision of clinical investigators.

Common Terminology Criteria for Adverse Events (CTCAE): Common Toxicity Criteria also referred to as the Common Terminology Criteria for Adverse Events, is a standardized classification of side effects used in assessing drugs for cancer therapy.

Communications: Documents narrating the conversation or discussion between two or more patients for e.g. letters, e-mails, fax, telephonic log, etc.

Comparator: A marketed product (i.e., active control), or placebo, used as a reference in a clinical trial.

Compensation: Refer to medical care or payment provided to a subject for a trial related injury.

Compliance: Adherence to trial-related requirements, good clinical practice (GCP) requirements, and the applicable regulatory requirements.

Concomitant Medication: Medication taken by a study subject for diseases/medical conditions other than the study disease.

Confidentiality Disclosure Agreement (CDA): A document used between the Institution and an outside party that defines the terms and basic criteria used to assure that the party (or parties) receiving confidential information (i.e. data, methods, procedures) will maintain the information in confidentiality and will not use the confidential information for any purpose other than that described in the CDA.

Confidentiality: Maintenance of privacy of study subjects including their personal identity and all medical information, from individuals other than those prescribed in the Protocol. Confidentiality also covers the prevention of disclosure of sponsor's proprietary information to unauthorized persons.

Congenital anomaly: Refers to a defect that is present at birth.

Consent Form: Documents used to obtain the written, signed and dated consent form a subject for the voluntary participation in a trial.

Consent: A process by which a subject voluntarily confirms his or her willingness to participate in a particular trial, after having being informed of all aspects of the trial that are relevant to the subject's decision to participate. Informed consent is documented by means of a written, signed, and dated informed consent form.

Contract Research Organization (CRO): An organization to which the sponsor may transfer or delegate some or all of the tasks, duties and / or obligations regarding a Clinical Study. All such contractual transfers of obligations should be defined in writing. A CRO is a scientific body – commercial, academic or other.

Contract: A written, dated and signed agreement between two or more involved parties that sets out arrangements on delegation and distribution of tasks and obligations and, if appropriate, on financial matters. The protocol may serve as the basis of a contract. It may also be called as Letter of Agreement (LOA) or Professional Service Agreement (PSA).

Convenience: Refer to the state of being able to proceed with something without difficulty.

Correlation: A measure of the strength of the relationship between two variables e.g. the positive correlation between cigarette smoking's and the incidence of lung cancer; the negative correlation between age and normal visions.

Council of International Organization of medical Sciences (CIOMS): It is an international, nongovernmental, not-for-profit organization established jointly by WHO and UNESCO in 1949. CIOMS serves the scientific interests of the international biomedical community in general and has been active in giving idea of guidelines for the ethical conduct of research, among other activities.

Counseling: The provision of professional assistance and guidance in resolving personal or psychological problems.

CRS Core committee Member: Individual serving as member of Clinical Research Secretariat, MPMMCC/HBCH. The Committee has been constituted by Institutional head for CRS support.

Data Archival: The storage of data under proper environmental and access control after the completion of trial.

Data integrity: Refers to maintaining and assuring the accuracy and consistency of data over its entire life-cycle, and is a critical aspect to the design, implementation and usage of any system which stores, processes or retrieves data.

Data queries: A request for clarification on a data item collected for a clinical trial; specifically, a request from a sponsor or sponsor's representative to an investigator to resolve an error or inconsistency discovered during data review.

Data Safety Monitoring Board: A Data Monitoring Committee — sometimes called a Data and Safety Monitoring Board — is an independent group of experts who monitor patient safety and treatment efficacy data while a clinical trial is ongoing.

Data Safety and Monitoring Unit (DSMU): The DSMU is the unit of IEC which is charged with the mission of developing and enacting quality assurance procedures to monitor the

overall progress of institutional clinical trials and ensuring adherence to procedural requirements.

Data: Refer to recorded information regardless of form (manual or electronic)

Delegation Log: A document enlisting the roles and responsibilities of each member of the study Team.

Delegation: Allocation of specific trial related duties to the individual study team members in a clinical trial.

Demographic Data: Refer to a Characteristics of subjects or study populations, which include such information as age, sex, family history of the disease or condition for which they are being treated, and other characteristics relevant to the study in which they are participating.

Destruction: Clinical trial material (used or unused) destroyed either during or at the end of the trial.

Deviations: A variation from processes or procedures defined in a protocol. Deviations usually do not preclude the overall evaluability of subject data for either efficacy or safety, and are often acknowledged and accepted in advance by the sponsor.

Diagnosis: The determination of the nature of disease.

Diary: Forms containing study specific information (safely, efficacy, drug compliance etc.) required to be filled in by the study subjects.

Direct Access: An environment in which the access to trial related information is not controlled.

Disability: A substantial disruption of a person's ability to conduct normal life functions.

Disclosure: Refer to release of protected health information of a study subject by one entity to another entity.

Discrepancy: The failure of a data point to pass a validation check

Disease: A condition that impairs the normal functioning of an organism or body.

DMG members: Individuals serving as a member of the respective Disease Management Group (DMG). The group has been constituted in accordance with the disease management requirements at MPMMCC/HBCH.

Documentation: Refer to records that describes or document study method, conduct and results.

Dose: The amount of drug to be used for a medical condition.

Dosing schedule: Refer to the amount of a drug product to be given at each specific dosing time.

Drop Out: Refer to a study subject who does not complete the protocol specified visits in a clinical trial.

Drug Accountability Log: Logs designed to capture all the transactions (such as receipt, dispensing, return, destruction etc.) of an investigational product in order to ascertain 100% accountability at any time point.

Drug Accountability: A process by which accountability of each unit of an investigational product is established.

Drug: As defined by the Food Drug and Cosmetic Act, drugs are articles (other than food) intended for the use in the diagnosis, cure, mitigation, treatment, or prevention of disease in human or animal or to affect the structure of any function of the body of human or animals.

Drugs Controller General India (DCGI): The office of Drug Controller General of India under Central Drug Standard Control Organization (CDSCO) having the prime responsibility for regulating clinical trials in India.

Duration: Refers to time scale.

Duty Delegation Log: Am document that enlist the specific trial related duties performed by individual study team members along with their signature, date and/or initials.

e-CRF: Auditable electronic record designed to capture information required by the clinical trial protocol to be reported to the sponsor on each trial subject.

Effective date: The date of approval of the SOPs signed and dated by the OIC CRS and by Director, TMC, and subsequently the SOP is implemented from that date.

Effective date (CTA): The date of finalization of the CTA signed and dated by the respective persons and subsequently the CTA is implemented from that date

Efficacy: A test products ability to produce beneficial effect on the duration or course of the study.

Eligibility Criteria: Refer to the inclusion/exclusion criteria that make a subject eligible for a clinical trial.

E-mails: Messages distributed by electronic means from one computer user to one or more recipients via a network.

Electronic Medical Record (EMR): It is a digital version of the traditional paper-based medical record for an individual. It is an official health record for an individual that is shared

among multiple facilities.

Endpoint: An outcome or event to answer the primary hypothesis of a clinical trial.

Enrollment number: Refers to a unique number allotted to research participants after randomization process.

Enrolment Log: Refer to a log that captures the dates of enrolment and other protocol required information of a clinical trial subject.

Essential Documents: Essential documents are those documents that individually and collectively permit evaluation of the conduct of a trial and the quality of the data produced. Essential documents include the Trial Master File, source documents and Case Report Forms (CRFs).

Etiology: Refers to the cause, set of causes, or manner of causation of a disease or condition.

Exclusion criteria: Refer to the criteria that make a subject ineligible for a clinical trial.

Expected event: Refers to the event that has been addressed or described in one or more of the following: Informed consent document(s) for this study, IRB application for this study, grant application or study agreement, protocol or procedures for this study, investigators' brochure or equivalent.

Facility: Refers to place or site where clinical trials are conducted.

Fax: It is a scanned copy of both text and image printed on a paper, sent from one party to another through a telephone line.

Final Report: Refers to the clinical study report prepared at the end (completion or termination) of a clinical trial.

Financial Disclosure Form: A form signed by Investigators and Sub-Investigators t disclose their financial interest in the sponsor company for whom they intent to participate in the clinical trial.

Follow-up Report: A report/response to provide additional information, clarification, or corrections to a previous report.

Good Clinical Practice (GCP): It is a standard for clinical studies or trials that encompasses the design, conduct, monitoring, termination, audit, analyses, reporting and documentation of the studies. It ensures that the studies are implemented and reported in such a manner that there is public assurance that the data are credible, accurate and that the rights, integrity and confidentiality of the subjects are protected. GCP aims to ensure that the studies are scientifically authentic and that the clinical properties of the “Investigational Product” are properly documented.

Good Laboratory Practices (GLP): A standard for the conduct and reporting of non-clinical laboratory studies intended to assure the quality and integrity of safety data submitted to regulatory authorities.

Grants: Refer to the financial assistance provided by the funding agency/sponsors to carry out a research project.

Guidelines: Refers to a document that aims to streamline process according to a set routine.

Handover: an act or instance of handing something over to another delegated person.

Hospitalization: Refer to a condition that requires admission to a hospital for its management.

IEC members: Individuals serving as regular members of the Institutional Ethics Committee, TMC. The Committee has been constituted in accordance with the EC membership requirements set forth in Schedule Y

IEC membership roster: A form in which names of IEC members are enlisted.

Illiterate subjects: Patient who is unable to read or write

Impartial Witness (IW): Impartial Witness is a person, who is independent of the trial, who cannot be unfairly influenced by people involved with the trial, who attends the informed consent process if the subject or the subject's legally acceptable representative cannot read, and who reads the informed consent form and any other written information supplied to the subject."

Inclusion and Exclusion Criteria: The characteristic that must be present (inclusion) or absent (exclusion) in order for a subject to qualify for a clinical trial, as per the protocol for the trial.

Inclusion Criteria: Specifications of the subjects (patients / healthy volunteers) including age, gender, ethnic groups, prognostic factors, diagnostic admission criteria etc. for participation in a research study.

Inconveniences: The state or fact of being troublesome or difficult with regard to one's personal requirements or comfort.

Investigational New Drug (IND): Investigational New Drugs means substances with potential therapeutic actions during the process of scientific studies in human in order to verify their potential effects and safety for human use and to get approval for marketing.

Indemnification: A legal statement or document indicating protection or exemption from liability for compensation or damages from a third party.

Informed Consent Form (ICF): A document that describes the rights of the study participants and includes details about the study such as its purpose, education, required procedures, risk,

potential benefits and key contacts.

Informed Consent: A process by which a subject voluntarily confirms his or her willingness to participate in a particular trial, after having been informed of all aspects of trial that are relevant to the subject's decision to participate. Informed Consent is documented by means of a written, signed and dated informed document (ICD)

Injury: An instance of being injured

Institution: Any public or private medical facility where a clinical study is conducted.

Institutional Ethics Committee (IEC): It is an independent body formally designated to review, approve, and monitor biomedical and behavioral research involving humans with the aim to protect the rights and welfare of the participants. It is an independent body whose responsibility is to ensure the protection of the rights, safety and well-being of human participants involved in a clinical trial and to provide public assurance of that protection.

Integrity: The quality of being honest and having strong moral principles.

Interactive Voice Response System (IVRS): IVRS is a System or a phone technology that allows a computer to automatically detect voice and touch tones using a normal voice phone. It helps in clinical trial and Pharmaceutical industry for efficient Clinical trials data management, error-free study of clinical trials, reduction of monotony and cumbersome work, thereby meeting the challenges and requirements of rapidly growing Clinical research and pharmaceutical industry.

Interactive Web Response System (IWRS): Interactive Web Response System is service to facilitate the logistical issues surrounding the conduct of clinical trials. This system works using a standard web browser and email service, allows study administrators and investigators to security interact with the study database, making study development fast and easy.

International Conference on Harmonization-Good Clinical Practice (ICH-GCP): Good clinical practice (GCP) is an international ethical and scientific quality standard for designing, conducting, recording, and reporting trials that involve the participation of human subjects. Compliance with this standard provides public assurance that the rights, safety, and wellbeing of trial subjects are protected; consistent with the principles that have their origin in the Declaration of Helsinki, and that the clinical trial data are credible.

Investigational Product (IP): A pharmaceutical product (including the Comparator Product) being tested or used as reference in a clinical study. An Investigational Product may be an active chemical entity or a formulated dosage form.

Investigator Meeting (IM): A meeting conducted before initiating a clinical trial for the uniform understanding of the protocol, processes and trial logistics among all the participating trial sites.

Investigator Statement: Refers to agreement signed by the investigator to provide certain

information to the sponsor and assure that he/she will comply with FDA regulations related to the conduct of a clinical investigation of an investigational drug or biologic.

Investigator Training: Refers to imparting training on study protocol, trial procedures and processes to the investigator.

Investigator Undertaking (IU): A formal written, commitment (submitted to regulatory authorities) by trial investigator(s) assuring their compliance with the study protocol and all the applicable regulatory requirements.

Investigator: A person responsible for the conduct of the study at the trial site. Investigator is responsible for the rights, health and welfare of the study subjects. In case the study is conducted by a team of investigators at the study site then the designated leader of the team should be the Principal Investigator. Also see Principal Investigator, Sub-investigator.

Investigator-initiated studies: Academic institutions routinely carry out investigator-initiated clinical trials. In such trials, the investigator has the dual responsibility of being an investigator as well as the sponsor.

Investigator's Brochures (IB): A compilation of the clinical and nonclinical data on the investigational drug(s) that is relevant to the study of the investigational drug(s) in human subjects.

IP number: Refers to the unique number given on the investigational product.

Laboratory Normal Ranges: Refer to the normal value ranges for standardized laboratory tests.

Laboratory Report: Refer to a document that contains results of the laboratory test for a specific subject.

Legal Expert: A legal scholar versed in civil law or the law of nations to protect the peoples involved in the clinical research

Legally Acceptable Representative (LAR): A LAR is an individual or judicial or other body authorized under applicable law to consent on behalf of a prospective participant to participate in research or to undergo a diagnostic, therapeutic, or preventive procedure as per research protocol.

Less than minimal risk: Probability of harm or discomfort anticipated in the research is nil or not expected. For example, research on anonymous or non-identified data/samples, data available in the public domain, meta-analysis, etc.

Lost to follow up: Refer to a trial subject who is not traceable by any means before completion of his/her participation in the trial.

Lot/batch number: Refers to a unique number provided on the investigational product for

identification.

Maintenance: The process of preserving a condition or situation or the state of being preserved.

Material Transfer Agreement (MTA): A contract that governs the transfer of tangible research materials between two organizations when the recipient intends to use them for their own research purposes.

Master SOP files: An official collection of the Standard Operating Procedures (SOP) of CRS, TMC accessible to all staff, Investigators, Researchers, auditors and government inspectors as a paper copy with approval signatures

Medical History: The information on overall general health, past illnesses and current medical problems of a subject.

Medical record: The case history of a medical patient as recalled by the patient. Original documents, data, and records (e.g. hospital records, clinical and office charts, laboratory notes, memoranda, subjects diaries or evaluation checklist, pharmacy dispensing records, recorded data from automated instruments, copies or transcriptions certified aft6er verification as being accurate and complete, microfiches, photographic negatives, microfilms or magnetic media, X-rays, subjects files, and record kept at the pharmacy, at the laboratories, and at medico-technical departments involved in the clinical trial).

Minimal risk: Probability of harm or discomfort anticipated in the research is not greater than that ordinarily encountered in routine daily life activities of an average healthy individual or general population or during the performance of routine tests where occurrence of serious harm or an adverse event (AE) is unlikely. Examples include research involving routine questioning or history taking, observing, physical examination, chest X-ray, obtaining body fluids without invasive intervention, such as hair, saliva or urine samples, etc.

Minor Protocol deviation: Changes or alterations in the conduct of the trial which do not have a major impact on the subject's rights, safety or well-being, or the completeness, accuracy and reliability of the study data.

Minor: An individual who has not attained the legal age of consenting to a trial as per the applicable regulations.

Modification: The act of making changes or amendment to an information, document or process.

Memorandum of Understanding (MoU): A document intended to describe a bilateral or multilateral agreement between parties. It is often a preliminary document and is generally not intended to create a legal commitment between the parties but to set out the working principles of the relationship.

Monitor: A person appointed by the Sponsor or Contract Research Organisation (CRO) for

monitoring and reporting the progress of the trial and for verification of data. The monitor ensures that the trial is conducted, recorded and reported in accordance with the Protocol, Standard Operating Procedures (SOPs), Good Clinical Practice (GCP) and the applicable regulatory requirements.

Monitoring Visit report: A written report prepared by the monitor after each site visit to document the progress and conduct of clinical trial at site

Monitoring: The act of overseeing the progress of a clinical trial and of ensuring that it is conducted, recorded, and reported in accordance with the protocol, standard operating procedures (SOPs), good clinical practice (GCP), and the applicable regulatory requirement(s).

Non-compliance: Non-performance of the study in compliance with the approved protocol, national regulations, ICH GCP, and other applicable regulations and/or failure to respond to the IEC request for information/action.

Non-expected event: Refers to the nature or severity of which is not consistent with the applicable product information (e.g., Investigator's Brochures for an unapproved investigational product or package insert/summary of product characteristics for an approved product).

Non-Investigator-initiated Studies: Studies not initiated by Investigator and supported by sponsor or initiated by the Sponsor or collaborators.

Normal value ranges: Refers to the normal value ranges for standardized laboratory tests of any laboratory.

Notes to File: Refers to the notes to explain the deviation/violation of a particular activity/process.

Offsite: Event occurring at other centers/sites

Onsite: Event occurring at site

Out patients Department (OPD): OPD is a department in which patient are seen on daily basis.

Outdated version: When revised version of protocol/ICF/IB etc. published, the old version is no longer effective and it is called as outdated version.

Pamphlet: Refer to a small booklet or leaflet containing information or arguments about a single subject.

Participants: Refer to a subject who takes part in a clinical trial.

Patient Case Files: Refer to the hospital/clinic file that contains complete medical information of a patient/subject.

Patient Diaries: Refer to a document given to the subjects for recording certain observations/readings on the condition of their health either at home or at trial site.

Patient ID: A unique identifier assigned by the investigator to each trial subject to protect the subject's identity and used in lieu of the subject's name when the investigator reports adverse events and/or other trial related data.

Patient: Refer to an individual who required medical care or treatment.

Payment: The action or process of paying someone or something or of being paid.

Pharmacist: Refer to a person qualified to prepare and dispense drugs and certified by concerned authority to do so.

Pharmacy: Refer to a place where drugs are prepared and dispensed.

Photocopies: Refers to a photographic copy of printed or written material produced by a process involving the action of light on a specially prepared surface.

Premature Termination: Early termination of a trial before data is sufficiently strong to be convincing.

Previous SOPs of the CRS: A collection of previous official versions of a SOPs and relevant information regarding changes and all preplanned deviations

Principal Investigator (PI): The investigator who has the responsibility to co-ordinate between the different Investigators involved in a study at one site or different sites in case of a multi-center study.
Privacy: Refer to a state of being private.

Procedure: A particular method of performing a task.

Protocol Amendments: Any changes or formal clarifications appended to the protocol.

Protocol compliance: Adherence to trial-related requirements, good clinical practice (GCP) requirements, and the applicable regulatory requirements given in protocol.

Protocol deviation: Changes or alterations in the conduct of the trial which do not have a major impact on the participant's rights, safety or well-being, or the completeness, accuracy and reliability of the study data.

Protocol Feasibility: An analysis of the ability to complete a project successfully, considering legal, economic, technological, scheduling and other factors. Rather than just diving into a project and hoping for the best, a feasibility study allows project managers to investigate the

possible negative and positive outcomes of a project before investing too much time and money.

Protocol violation: A protocol deviation that may affect the participant's rights, safety, or wellbeing or alter the risk benefit ratio, and/or affect the participants' willingness to participate in the study, and/or impact the completeness, accuracy and reliability of the study data.

Protocol Waiver: Protocol Waiver is analogous to a Protocol Deviation, except that prior IEC approval must be obtained before implementing the necessary departures from the protocol.

Protocol: A document that states the background, objectives, rationale, design, methodology (including the methods for dealing with AEs, withdrawals etc.) and statistical considerations of the study. It also states the conditions under which the study shall be performed and managed.

Publication: Refer to publishing the results of a clinical trial in a peer-reviewed journal.

Quality: Refer to preset standard for measuring the outcome.

Queries: A request for clarification on a data item collected for a clinical trial; specifically, a request from a sponsor or sponsor's representative to an investigator to resolve an error or inconsistency discovered during data review.

Random: Refer to an element of chance or having no specific pattern.

Randomization: Refer to the process of assigning trial subjects to treatment or control groups using an element of chance in order to reduce bias.

Recipients: Individual who would receive a copy of SOP

Re-consenting: Refer to a process of again consenting a subject in the same protocol.

Recruitment: Refer to the act of enrolling subjects with the proper inclusion criteria.
References: Refer to a list relevant published literature on a topic along with complete citation.

Reimbursement: Is an act of compensating someone for an expense often; a person is reimbursed for out-of-pocket expenses when the person incurs those expenses through employment or in an account of carrying out the duties for another party or member

Related Event: Refer to an adverse event that is related to the administration of investigational products.

Relatedness: Refer to the extent of relationship between occurrence of an adverse event and administration of investigational of a drug/ placebo.

Requestors: Investigators, Sponsors, Contract Research Organizations, Regulatory authorities, Hospital administrators, and such others.

Requisition forms: An official form on which a request in made.

Research Nurse: Refer to the qualified nurse who assists the investigator in the conduct of a research project.

Research Team: Investigator, Co-Investigator, Clinical Trail coordinator and research nurse involved with the study.

Revision date: Date/year by which the SOP may be revised or reviewed.

Rights: that which is morally correct, just, or honorable.

Risk: The probability of harm or injury (physical, psychological, social, or economic) occurring as a result of participation in a research study. Both the probability and magnitude of possible harm may vary from minimal to significant.

Safety assessment: Refer to the assessment of adverse event and serious adverse events experienced by the participants in a clinical trial.

Safety Recording: Refer to the process of proper recording of the safety events information arising in clinical trials after administration of IP.

Safety: Refer to the condition of being protected from or unlikely to cause danger, risk, or injury.

Schedule Y: Requirements and guidelines on clinical trials for import and manufacture of new drug

Scheduled visit: A clinical encounter that encompasses planned trial interventions, procedures, and assessments that may be performed on a subject

Screening and/or enrollment logs: The form includes a log of subjects who were screened, screen failures, enrolled, withdrawn, and completed the study.

Screening Log: Refer to a log captures the details of all the subjects screened for a clinical trial.

Screening number: A number is given when a potential subject for enrollment in a trial is entered in screening log.

Screening Reports: Various reports which are being perform to check that the patient is eligible for enrolment in the trial or not.

Serious Adverse Event (SAE): Any untoward medical occurrence (due to the participation in the concerned trial) that at any dose that results in death, is life-threatening, requires

inpatient hospitalization or prolongation of existing hospitalization, persistent or significant disability/incapability.

Shipment: Refers to the action of shipping goods.

Site Activation: After site selection, it takes several steps to bring a site to the point where it is ready to recruit patients. This process is called site activation, and it consists of a variety of tasks including: Negotiate a financial contract, gain approval from Institutional Review Board (IRB) or, EC, provide clinical supplies, obtain other documents from site (CV, financial disclosure, etc.

Site Closeout: Refer to closing a clinical study after the same has been completed or prematurely terminated/suspended.

Site Initiation: Refers to the activation of a site for initiation a clinical trial after the ethics committee and regulatory approval has been obtained and other trial specific requirements have been fulfilled.

SOP Team: A team of members selected from the CRS including the CRS Core Committee, TRAC members and Clinical Trail Coordinators as identified by the OIC CRS who oversee the creation, preparation, review and periodic revision of the CRS, TMC SOPs

Source data verification: Refer to the verification of source documents and other trial records for accuracy, completion and compliance with protocol, GCP and applicable regulatory guidelines.

Source documents: All information in original records and certified copies of original records of clinical findings, observations, or other activities in a clinical trial necessary for the reconstruction and evaluation of the trial. Source data are contained in source documents (original records or certified copies).

Sponsor: An individual or a company or an institution that takes the responsibility for initiation management and/or financing of clinical study. An Investigator who independently initiates and takes full responsibility for trial automatically assumes the role of sponsor. Here sponsor refers to individuals or organization that pays for or contributes to the costs involved in conducting clinical trials. e.g.: Pharma companies, collaborators, Device Company, biological material.

Sponsor-Investigator: An individual who both initiates and investigates, and under whose immediate direction the investigational drug is administered or dispensed. The term does not include any person other than an individual. The requirements applicable to a sponsor-investigator under this part include both those applicable to an investigator and a sponsor.

Standard Operating Procedures (SOP): Standard elaborate written instructions to achieve uniformity of performance in the management of clinical studies. SOPs provide a general framework for the efficient implementation and performance of all the functions and activities related to a particular study.

Study Subject (Subject): An individual participating in a clinical trial as a recipient of the Investigational Product. A Study Subject may be a healthy person volunteering in a trial or a person with a medical condition that is unrelated to the use of the Investigational Product or a person whose medical condition is relevant to the use of the Investigational Product.

Study Team: Refer to a group of individuals including investigators, research fellows, resident, research nurses etc. to perform clinical trial-related procedures and/or to make important trial-related decisions.

Study Termination: The clinical study has stopped recruiting or enrolling participants early and will not start again. Participants are no longer being examined or treated.

Suspected Unexpected Serious Adverse Reaction (SUSAR): An adverse reaction that is both unexpected (not consistent with the applicable product information) and also meets the definition of a Serious Adverse Event/Reaction.

Suspension: The clinical study has stopped recruiting or enrolling participants early, but it may start again.

Temperature Log: A log that captures the storage temperature (minimum/maximum) of investigational products on a daily basis.

Termination: The act of concluding participation, prior to completion of all protocol-required elements, in a trial by an enrolled subject.

Toxicity: An adverse effect produced by a drug that is detrimental to the participant's health.

Training Log: A documented trail of all the trainings undertaken by clinical research personnel. It generally includes the topic of the training, training modality, completion date and signature of the personnel.

Transfers of Patients: Refer to the process of transfer of subjects to another place/hospital for investigation/any other study related procedure.

Trial Master File (TMF): A trial master file contains essential documents for a clinical trial that may be subject to regulatory agency oversight. The trial master file should consist of essential documents, which enable both the conduct of a clinical trial and the quality of the data produced to be evaluated. Those documents shall show whether the investigator and the sponsor have complied with the principles and guidelines of good clinical practice and with the applicable requirements. The Trial Master file should be created and maintained in accordance with ICH-GCP guidelines.

Unanticipated issues: Issues that occur during the conduct of research; may increase the level of risk to participants or have other ethical implications that may affect participants' welfare; and were not anticipated by the researcher in the research proposal submitted for research ethics review.

Vendor: Refer to a supplier of goods or services.

Version: Refer to the number assigned to an essential document in use. Version number is important to provide an audit trial.

Voluntary: The act of giving one's own free will without any coercion or undue inducement.