

# BRITISH BIOMEDICINE CLINICAL TRIALS (BBMCT)

# STANDARD OPERATING PROCEDURE (SOP)



# **Standard Operating Procedure Clinical Trials**

**(Exclusive AIIMS Hospital,  
New Delhi)**



**British BioMedicine Clinical Trials (BBMCT)**  
**(2020)**

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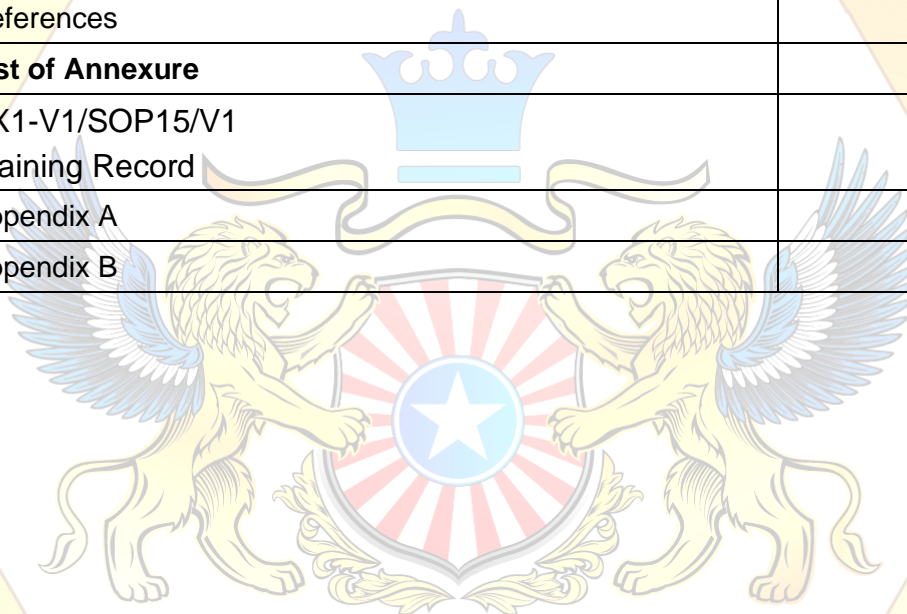
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# **Standard Operating Procedure Clinical Trials**

**(Exclusive AIIMS Hospital,  
New Delhi)**



**Title: Assessing Protocol Feasibility**

**SOP Code: SOP 01/V1**

**Date: 13/November/2020**

**Pages: 09 to 15**

**British BioMedicine Clinical Trials (BBMCT)  
(2020)**

## 1.1 Purpose

To describe the procedures for assessing the feasibility of conducting a study at AIIMS Hospital, New Delhi in compliance with standard protocol.

AIIMS Hospital, New Delhi is committed to maintain the highest scientific, clinical and ethical standards while conducting research. Further, BBMCT 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 AIIMS Hospital. This standard operating procedure (SOP) describes the steps for assessing the feasibility of conducting a research study at AIIMS Hospital.

Additionally, Institution and PI considers the potential benefits of proposed studies to disease control in AIIMS Hospital and development of the state's research portfolio.

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 AIIMS Hospital research network.

## 1.2 Scope

This SOP applies to the activities involved in assessing protocol feasibility for all research studies conducted at AIIMS Hospital involving human subjects.

This SOP applies to the assessment of protocols and funding for non-investigator-initiated studies.

## 1.3 Procedure

### 1.3.1 Protocol Assessment

When a Sponsor/CRO contacts the BBMCT about a potential study, the Director (BBMCT) will assess whether or not it would be feasible to conduct the protocol with the existing staff and facilities. Director (BBMCT) can use protocol checklist to ensure if protocol is feasible to conduct at AIIMS Hospital (AX1-V1/SOP 01/V1)

The Director (BBMCT) will discuss the protocol with the respective Head, AIIMS Hospital. The Investigator, Sub Investigator, and other appropriate site personnel will review the protocol to ensure the following:

#### **1.3.1.1 Clinical/Scientific/Ethical Feasibility**

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

#### **1.3.1.2 Operational Feasibility**

- Availability of personnel and other resources required to conduct the study.
- Availability of patients meeting the inclusion / exclusion criteria 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.

#### **1.3.1.3 Regulatory Feasibility**

- The PI/Director (BBMCT) reviews the protocol to determine whether there is anything required that may be problematic when submitting the project to the IEC. As part of the review the CTC can consult with IEC representatives.
- The Director (BBMCT) must check the following points before submitting the protocol to the IEC for approval, as IEC determines:
  - Research studies have the resources necessary to protect participants:
  - Adequate time for the researchers to conduct and complete the research.
  - Adequate number of qualified staff
  - Adequate facilities
  - Access to a population that will allow recruitment of the necessary number of participants.
  - Availability of medical or psychosocial resources that participants might need as a consequence of the research.

#### **1.3.1.4. Financial/ Legal Feasibility**

- A detailed review of the costs, including staff time needed to complete protocol activities and patient care visits are determined by the PI and the Director (BBMCT).
- The PI and Director (BBMCT) prepare the budget worksheet.
- The budget worksheet is compared with the sponsor's budget.
- The PI and Director (BBMCT) will negotiate with the sponsor to establish a feasible budget. Once an agreement is made, the budget will be signed by the PI and Director (BBMCT) sent to the sponsor.

- If an agreement cannot be reached with the study sponsor to cover all costs of the study, the PI and Director (BBMCT) will work together to determine whether the study will be conducted at AIIMS Hospital.
- The Legal expert will facilitate legal review of the contract.

### **1.3.2 Decision**

- All the above mentioned points (1.3.1.1, 1.3.1.2, 1.3.1.3 & 1.3.1.4) will be discussed in the respective meeting.
- The Director (BBMCT) will notify the sponsor of the site's decision. In the event that the protocol does not meet the abovementioned criteria, the Director (BBMCT) may, at his discretion, provide rationale for the decision to the PI and will inform the same to the sponsor, allowing the Sponsor the opportunity to make changes in the suggested part of the protocol and have it reassessed.
- In case of Investigator initiated studies, Sponsor will make the required changes in the protocol as suggested by the Principal Investigator or can provide rationale for the same.
- BBMCT Coordinator will submit the protocol to IEC for review and approval after incorporating all the changes suggested by Sponsor (if any) in the protocol.

### **1.4 Applicable Staff**

This SOP applies to all the personnels of the clinical research team (BBMCT) and PI with its members who may be responsible for making decisions regarding conduct of the research studies at AIIMS Hospital.

These include the following:

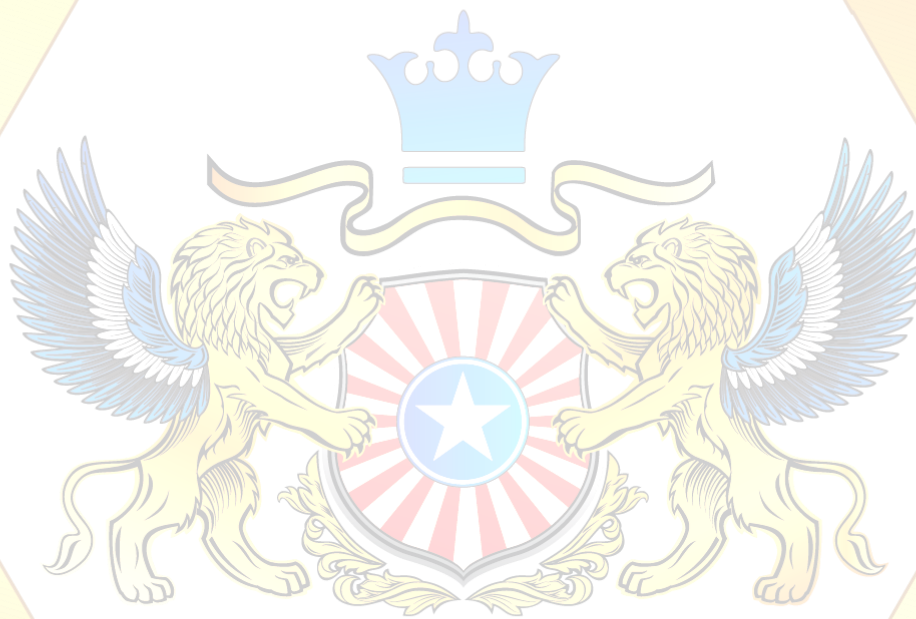
- Investigator
- Sub Investigator
- Legal Expert(s)
- Research Team (BBMCT)

### **1.5 Staff responsible for Implementation**

- Director (BBMCT) will ensure that the research team involved in the conduct of the study will comply with this site SOP.
- Director (BBMCT) and PI at his level will ensure that at the time of implementation of the SOP, the research team at AIIMS Hospital 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.

## References

1. 21 CFR 312.21 Phases of an investigation
2. 21 CFR 312.23 IND content and format
3. 21 CFR 312.60 General responsibilities of investigators
4. 21 CFR 56.109 IRB review of research
5. 21 CFR 56.111 Criteria for IRB approval of research
6. May 1997 International Conference on Harmonization (ICH) Good Clinical Practices
7. Schedule Y



## AX1-V1/SOP 01/V1

### PROTOCOL FEASIBILITY CHECKLIST

#### Factors to consider:

<b>1. Population</b>	
Do you have access to the right patient population?	
Will you need to recruit patients 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 patients?	
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?)	
<b>2. Protocol</b>	
Is the protocol well designed?	
Is the protocol ethical? Will the IRB have problems with it?	
Is the study question important?	
Will the subjects 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 patient compliance problems likely? If so, will it be necessary to monitor subjects' compliance with time-consuming phone calls or postcards?	
Are case report 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.)	
<b>3. Procedures</b>	
Are procedures frequent?	
Are procedures difficult, e.g., elderly patients asked to swallow pills?	

Are procedures painful?	
Is the dosing schedule complex?	
<b>4. Staff</b>	
Are qualified staffs available	
If needed, is training available?	
Does the PI have adequate time to devote to the protocol?	
Are additional specialists needed?	
Are study visits complex, presenting possible scheduling difficulties, e.g., how many different study staff will subject encounter in a given visit?	
<b>5. Budgets</b>	
Does preliminary budget appear adequate? (Sponsors or Director (BBMCT))	
If the study is canceled prior to enrollment, will the sponsor pay for pre-study activities, e.g., IRB 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	
<b>6. Other</b>	
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 Trials**

**(Exclusive AIIMS Hospital,  
New Delhi)**

The logo of All India Institute of Medical Sciences (AIIMS) is centered in the background. It features a blue crown at the top, a yellow banner with a red star in the center, and two yellow lions with blue wings on either side. The entire logo is set against a yellow hexagonal background.

**Title: Clinical Trial Agreement (CTA) with  
Sponsors or Contract Research Organizations  
(CRO)**

**SOP Code: SOP 02/V1**

**Date: 13/November/2020**

**Pages: 16 to 20**

**British BioMedicine Clinical Trials (BBMCT)  
(2020)**

## 2.1 Purpose

- This Standard Operating Procedure (SOP) describes the manner in which the Clinical Trial Agreement (CTA) are to be received, processed and accepted by the Institution and/or principal investigator to another entity for the purpose of conducting research. 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, BBMCT and the Principal Investigator (PI), are legally protected in all necessary areas applicable to their specific project.

## 2.2 Scope

This SOP will apply to all industry-sponsored trials conducted at BBMCT or trials initiated at AIIMS Hospital for multicenter purpose.

Any new trial which 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.

## 2.3 Procedure

### 2.3.1. Review of draft CTA

Sponsor/CRO will provide draft CTA to Director (BBMCT) for finalization.

The Director (BBMCT) will inform the same to the Institution head and send one copy each of the CTA along with the study protocol to the institution head, Legal department and IEC (along with initial submission of project) for review.

The Director (BBMCT) 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
- Estimated study start and finish dates
- Terms of payment including terms for delays and termination of the study
- Number of study subjects required to enter and complete the study and the criteria for a "completed" (fully paid) study subject
- 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 participants when appropriate
- Compensation guidelines
- Guidelines or requirements for promptly reporting of the findings that could affect the safety of participants or influence the conduct of the study
- Data and safety monitoring process and reporting requirements
- The notification of the research department by the Sponsor and/or CRO of study results after the study has ended when participant safety could be directly affected by those study results, in order to consider informing participants
- Other legal issues as necessary per BBMCT Legal expert(s).

[Note: While preparing budgets for Industry sponsor study, one should always, consider changes as per "D" category (Schedule of charges) or higher if offered by the Industry.]

PI/IEC/Legal expert must check for the availability of clause 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 participants.
- Influence the conduct of the study or alter the IEC's approval to continue the study.

The Legal department and IEC will correspond with the Director (BBMCT) regarding any revisions that are required in the CTA.

Legal expert will approach Institutional head, in case of queries.

### **2.3.2 Revision of CTA**

- The Legal expert(s) will correspond with the Director (BBMCT) in case of suggestion/revision including the revision suggested by Institutional head.
- IEC will also correspond with the Director (BBMCT) regarding any revisions that are required in the CTA.

- In case of sponsored study, Director (BBMCT) will further correspond with the Sponsor/CRO/collaborators for all the relevant suggestion/revision and changes if any put forward by Legal expert and IEC.
- The Institution head will be included in all correspondence between the Legal department, IEC and Sponsor/CRO/collaborator.
- Director (BBMCT) or Sponsor (in case of sponsored study) will study the revision suggested and incorporate the suggested changes as applicable.

### 2.3.3 Finalization of CTA

- Once the CTA is approved by the Legal expert and IEC, Director (BBMCT) will further correspond with the Sponsor/CRO/collaborators.
- A minimum of three originals should be prepared on stamp paper (INR100) or as many originals as the Sponsor/CRO/collaborator specifies.
- Director (BBMCT) 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 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 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.
- One copy will be retained by the Institution head, one by Director (BBMCT) and the other will be with the Sponsor/CRO. The PI should keep the signed CTA in TMF.
- One copy of the CTA will be submitted to the IEC for approval before the conduct of the study at site.

### 2.3.4 Addendum/Amendment to CTA

- During the course of the study, Director (BBMCT) /Sponsor can amend the CTA if required.
- Any addendum/amendment to the CTA also needs to be reviewed by legal experts and a copy will be submitted to IEC for review and opinion if any.
- If any changes suggested by the PI and IEC, the same will be discussed with the Sponsor (for sponsored study) and should be incorporated in the CTA.
- Copy of the amended CTA will be submitted to IEC for review and opinion 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.

## 2.4 Applicable staff

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

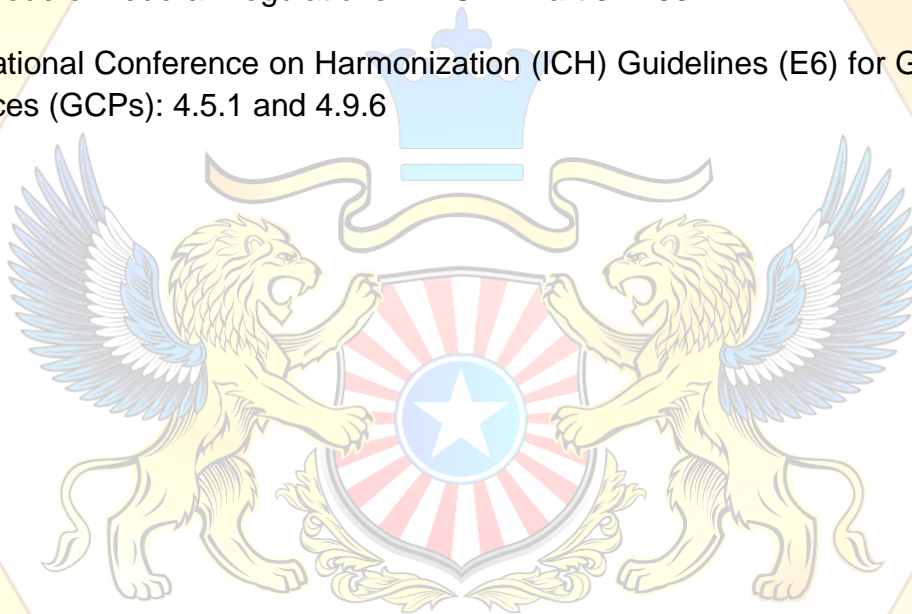
- Institution Head
- Principal Investigator
- Legal Expert
- IEC

## 2.5 Staff responsible for Implementation

- Director (BBMCT) will ensure that at the time of implementation of the SOP, that the research team at AIIMS Hospital 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 and Director (BBMCT) 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.

## References

1. FDA Code of Federal Regulations: 21 CFR Part 312.53
2. International Conference on Harmonization (ICH) Guidelines (E6) for Good Clinical Practices (GCPs): 4.5.1 and 4.9.6



# **Standard Operating Procedure Clinical Trials**

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New Delhi)**

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**Title: Interaction with Institutional Ethics  
Committee (IEC)**

**SOP Code: SOP 03/V1**

**Date:13/November/2020**

**Pages: 21 to 32**

**British BioMedicine Clinical Trials (BBMCT)  
(2020)**

### **3.1 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.

### **3.2 Scope**

This SOP will apply to all studies being conducted at AIIMS Hospital.

### **3.3 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 participant safety in addition to enhancing compliance with applicable SOPs, guidelines and regulations governing research studies.

Interaction with IEC required during the entire course of the research study, the phases could be:

#### **3.3.1 Initial Submission of project to IEC**

##### **a. Detailed description of project submission**

- The BBMCT Team should submit all study related documents to the IEC, no fewer than fourteen (14) days before the scheduled meeting.
- The BBMCT Team should complete the IEC submission form (Refer IEC SOP) and PI must sign and date in the form wherever required. CTC will obtain the PI signatures.
- BBMCT Team will check the submissions as per the IEC checklist (Refer IEC SOP) to ensure that all mandatory forms and documents are enclosed.
- The BBMCT Team 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, document enclosed relevant version number and date of all the documents (**AX1-V1/SOP 03/V1**).

- ◆ 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 investigator and study team.
  - ◆ Number of copies required for IEC submission will be as per IEC SOP Note: One additional copy for PI Acknowledgement
- The BBMCT Team should keep a copy of the acknowledged (IEC stamp with sign and date) submission letter of the above-mentioned documents in the Trial Master File (TMF) and send scan or copy to the sponsor (via mail or courier as required by the sponsor).
  - BBMCT Team will 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 in the Trial Master File (TMF).

#### **b. EC Response**

The BBMCT Team will 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 participants to be recruited in the study.
- Decision/opinion/approval of the clinical study, including required modifications, if any; (Note: Reply to the IEC in case of any suggested modifications)
- If conditional approval given, it is not valid for more than 6 months (Refer IEC SOP)
- Procedures for appealing the decision/opinion of the committee;
- 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.
- Following Schedule Y and GCP (ICH 3.2.1 et 3.2.2) a list of the members of the Ethics Committee and their qualifications, as well as the procedures of the said committee should be available.
- The BBMCT Team should keep an original copy of the IECs approval letter in the TMF and provide one copy to the sponsor/CRO (via email/fax).

- Immediately after receiving IEC approval, register the study on CTRI and if applicable on ClinicalTrials.gov
- Notify IEC after receiving registration number.

### 3.3.2 Study Progress

PI can start project at site after receiving approval letter from IEC and as study progress at site BBMCT Team will communicate with IEC for all required notification and reporting such as:

#### 3.3.2.1 Protocol Amendments

##### a. Major Amendments

- Notify the IEC of any changes to the protocol and/or informed consent and/or of new information on the investigational product no fewer than fourteen (14) days before the next scheduled meeting.
- All amendments should bear amendment number and version number with date(s).
- CTC must make sure that all changes or modifications in the amended version are underlined or highlighted along with detailed summary of changes.
- The amendment /documents along with the covering letter should be accompanied by Amendment Reporting Form (Refer IEC SOP)
- Number of copies required for IEC submission will be as per IEC SOP  
Note: One additional copy for PI Acknowledgement
- The BBMCT Team 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 (via email/fax).
- The amendments in the protocol and/or informed consent and of new information on the IP will be valid only after IEC approval, and should immediately implement the documents at the site after approval.
- Document the approval letter in the relevant section of the TMF and send a copy to sponsor/CRO( via email/fax)

#### **b. Minor amendments and notifications**

- Minor amendments are those that do not increase the risk or decrease the potential benefit to subjects 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

#### **3.3.2.2 Deviations/Violation and Waivers**

- Submit protocol deviations/violations and waivers to the IEC for review and approval according to IEC and regulatory requirements
- Deviation/ non-compliance/ violation/waiver happens at site, when investigators/ trial sites, fail to -
  - follow the procedures written in the approved protocol
  - comply with national / international guidelines for the conduct of human research
  - fail to respond to the IEC requests
- BBMCT Team will submit the deviations /violations/waiver reports as per the IEC SOP.
- 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 procedures
- Protocol Waiver is analogous to a Protocol Deviation, except that prior IEC approval must be obtained before implementing the necessary departures from the protocol. Therefore, Protocol Waivers are anticipatory, while Protocol Deviations are not. E.g. Protocol Waiver means a prospective decision by a sponsor or investigator to

permit accrual of a subject who does not satisfy the approved inclusion /exclusion criteria for enrollment.

- IEC action could include one or more of the following:
  - IEC will inform the PI that IEC has noted the violation / noncompliance / deviation and inform the PI to ensure that deviations / noncompliance / violations do not occur in future and follow IEC recommendations.
  - IEC will enlist measures that the PI would undertake to ensure that deviations / noncompliance /violations do not occur in future.
  - call for additional information
  - Suspend the study till additional information is made available and is scrutinized
  - 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
  - Inform the Director, AIIMS Hospital
  - 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
- File the IEC acknowledged deviations/violations and waivers forms submitted in relevant file and send one copy to the sponsor/CRO.

### **3.3.2.3 Safety Information**

- Safety information can be any information recently reported or obtained from sponsor/CRO particularly regarding risks associated with the research.
- 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 participants.
- Report all safety information to the IEC according to the IEC and regulatory requirements (eg. 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 participants or the conduct of the research study.

**a. Off Site Safety Reports**

- Off Site SAEs are adverse event reports that are serious, expected, unexpected, related and unrelated (definitely, probably and possibly) to the drug and need prompt reporting to the IEC/DSMSC.
- The SAEs that are expected (if listed in the informed consent and IB) or unexpected but unrelated to the drug (classified as per the Offsite SAE Classification form – as per IEC SOP) have to be logged by the PI and to be submitted timely. The following log will be maintained continuously until the end of the study.
- IEC/DSMSC will accept the log of the SAEs every 3 months and/or at the time of continuing review/ annual status report.
- 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 /DSMSC secretary.
- Sponsor/CRO will send two sets of the offsite SAE, CTC will submit one to the IEC/DSMSC (as per the IEC SOP) and file acknowledged (Stamped, signed and dated by the IEC /DSMSC) 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/DSMSC.

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

**b. Onsite SAE reporting:**

Kindly Refer SOP for Safety Reporting

**3.3.2.4 Annual Report/ Continuing Review report**

- The purpose of Annual report/ continuing review 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 and welfare of research subjects.
- BBMCT Team will submit continuing review report/annual report to the IEC (DSMSC) annually, subsequent to the date of IEC approval to renew approval before two months of expiry.
- All information must be provided to IEC/DSMSC, as requested in the continuing review application form (Refer IEC SOP)
- BBMCT Team will should submit the continuing review application well in advance i.e. 10 months after IEC final approval.
- CTC should submit three hard copies of the report (1+2) and a soft copy.
- CTC should obtain a copy of the annual/continuing review report acknowledged by IEC/DSMSC, and file the same in TMF and send a copy to sponsor (via email/fax).
- The IEC/DSMSC, 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/DSMSC, if the continuing review report/annual report is approved / accepted.
- The letter should be file 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 patient during that phase, till IEC/DSMSC, approve the continuing review report.

### 3.3.2.5 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 enrollment 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 following reason but not limited to:
  - 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 patients.
  - Sponsor find treatment not effective
  - Lack of funds, lack of adequate market potential, competing drugs have received marketing approval ahead of the test compound, etc.
  - Overall trial enrollment was met, so all sites are being closed, even if some sites have not completed their enrollments.
- 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.
- BBMCT Team will prepare the protocol termination package along with covering letter, Premature Termination Report (Refer IEC SOP) signed and dated by PI and another material (e.g. letter received from the Sponsor/PI/IEC)
- BBMCT Team will must obtain acknowledgment of the IEC member on the covering letter and file it in the TMF.
- BBMCT Team will reply immediately in case of any query generated or any further information requested from the IEC.

- PI will receive acceptance letter from the IEC, CTC 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.

### 3.3.2.6 Study completion

- On the Study completion the BBMCT Team will notify the IEC of the study completion using study completion form (Refer IEC SOP)
- Additionally, BBMCT Team will submit letter provided by the sponsor/CRO to give adequate and sufficient information.
- BBMCT Team will submit one hard copy + soft copy of Study Completion Reports  
**Note:** *One additional copy for PI Acknowledgement*
- IEC may call PI and request for further information or take any other action. In case, further information / action are 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 may receive acceptance letter from IEC.
- IEC acceptance letter will be filed. One copy must be sent to Sponsor/CRO.

## 3.4 Applicable Staff

This SOP applies to all the personals 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)
- CTC
- IEC staff/members

## 3.5 Staff responsible for Implementation

- Director BBMCT and Investigator will ensure that the research team involved in the conduct of the study will comply with this site SOP.

- Director BBMCT will ensure that at the time of implementation of the SOP, that the research team at the clinical research unit in AIIMS Hospital are trained and in the event that an SOP is modified, provide training regarding the change(s) and ensure their compliance with the changes.

## References

1. 21 CFR 312.60 – General Responsibilities of Investigators
2. Guideline Good Clinical Practice
3. ICH Guidelines for Good Clinical Practice (E6)
4. ICH Guidelines for Good Clinical Practice (E6) section 3.1 – Responsibilities
5. ICH Guidelines for Good Clinical Practice (E6) section 4.10 – Progress Reports
6. ICH Guidelines for Good Clinical Practice (E6) section 4.11 – Safety Reporting
7. ICH Guidelines for Good Clinical Practice (E6) section 4.12 – Premature Termination or Suspension of a Trial
8. ICH Guidelines for Good Clinical Practice (E6) section 4.13 – Final Reports by Investigator / Institution
9. ICH Guidelines for Good Clinical Practice (E6) section 4.4 – Communication with IEC/IEC
10. ICH Guidelines for Good Clinical Practice (E6) section 5.21 – Premature Termination or Suspension of a Trial
11. IEC SOP: SOP 03/V1, SOP 06/V1, SOP 07/V1, SOP 08/V1, SOP 09/V1, SOP 12/V1, SOP 13/V1
12. Schedule Y : Responsibility of Investigator

## AX1-V1/SOP 03/V1

### Covering letter

To,  
Member Secretary,  
Institutional Ethics  
Committee, AIIMS Hospital,  
New Delhi

Date:

Reference <Study Title/Study

number> Subject:

Dear ,

We are submitting following study documents to the Ethics Committee for the necessary approval as per ICH/GCP guidelines and E6 chapters 3.2.1, 3.2.2 5.11/1b.

Please find enclosed 01 hard copy of dossiers and soft copies of the following study documents has already being submitted 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.

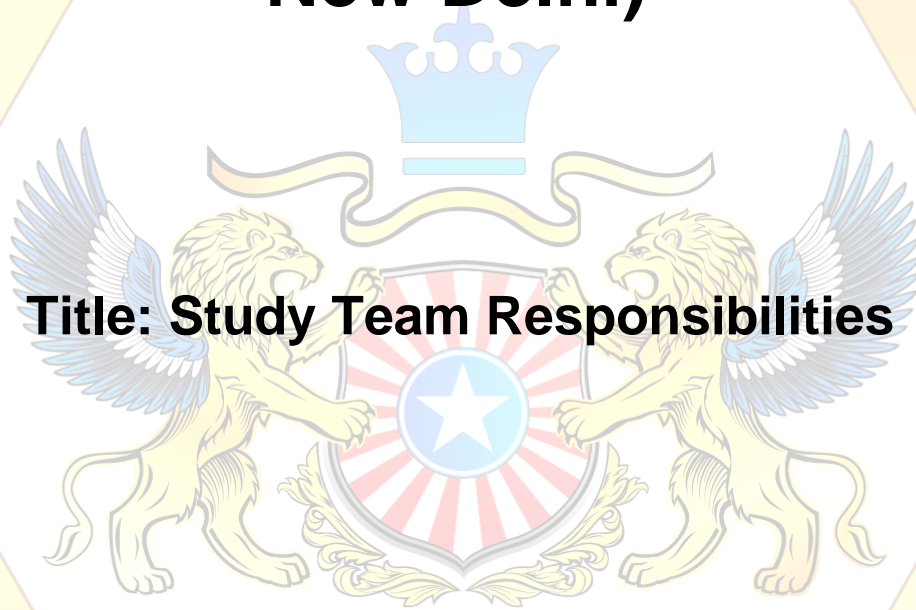
Kindly revert back for any further clarification. Thanks & regards,

<PI name>  
<Designation>  
AIIMS Hospital,  
New Delhi

# **Standard Operating Procedure Clinical Trials**

**(Exclusive AIIMS Hospital,  
New Delhi)**

**Title: Study Team Responsibilities**



**SOP Code: SOP 04/V1**

**Date:13/November/2020**

**Pages: 33 to 41**

**British BioMedicine Clinical Trials (BBMCT)  
(2020)**

## 4.1 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.

## 4.2 Scope

This SOP will apply to all study team members involved in the conduct of study at AIIMS Hospital.

## 4.3 Procedure

The Principal Investigator (PI) is the person ultimately responsible for the conduct of the research study at site. However, all study team members are obligated to conduct research according to professional roles and responsibilities. According to the International Conference on Harmonisation Guidelines (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
- Clinical Trial Coordinator
- Research Nurse

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

## 4.4 Responsibilities of the Research Team

### 4.4.1 Principal Investigator (PI) /Co Principal Investigator (Co PI)

- Each research study will have a Principal Investigator (PI) (and may have a Co 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:
  - The Investigator(s) shall be responsible for the conduct of the study according to the protocol and the GCP Guidelines and also for compliance as per the undertaking given in Appendix VII.

- The safety and welfare of 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.
  - Informing all participants, including participants used as controls, that the investigational agents are being used for investigational purposes and following all requirements relating to obtaining informed consent.
  - Preparing and submitting protocol documents for initial 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.
  - Reporting Adverse Events (AEs) to the Sponsor as per protocol.
  - 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 participants.
  - Appropriate control, inventory, distribution, storage, record keeping and destruction or return of Investigational Product (IP).
  - Prompt reporting to the IEC of all events that require prompt reporting.
  - Providing progress reports/annual report 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 participants, by any member of the research team that may present a conflict with the interests of 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 04/V1) and that individuals recruited as members of the research team are appropriately licensed and trained.
  - Maintaining adequate and accurate records and making records available for inspection to external and internal monitors. Meeting with auditors (DCGI, FDA, sponsor and internal), at the conclusion of their audits, to review findings and to implement changes to correct weaknesses or deficiencies.
- The PI/Co PI may delegate responsibility 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 04/V1)

#### **4.4.2 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, 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)

#### **4.4.3 Senior Clinical Trial Coordinator (CTC) Responsibilities**

- The Senior Clinical Trial Coordinator works in collaboration with the PI, the CTC and the multidisciplinary research team to ensure that rigorous clinical research standards are maintained. Some examples of responsibilities of the Senior CTC 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 and negotiates study 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.

#### **4.4.4 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:

- Screening and enrolling subjects 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.
- Participating in audit preparation activities of the sponsor, DCGI, FDA, other regulatory and accrediting agencies and Regulatory Affairs.
- Supervising other clinical research personnel, as appropriate.
- Participating as appropriate in the training of individuals recruited as members of the research team.
- Design appropriate recruitment strategies and track study enrollment.
- Accurate and timely data entry.
- Proper handling and accurate processing of samples (such as blood and tissues).
- Other study related activities as per delegation log.

#### **4.4.5 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 participants are protected.
- Each staff member should fulfil the job responsibilities as outlined in the delegation log (AX1-V1/SOP 04/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), Schedule Y, Good Laboratory Practices (GLP), Institutional research policies and applicable SOPs
  - Assure the safety and welfare of study subjects 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.

#### **4.5 Applicable areas of the Hospital**

All India Institute of Medical Sciences (AIIMS Hospital, New Delhi)

#### **4.6 Applicable Staff**

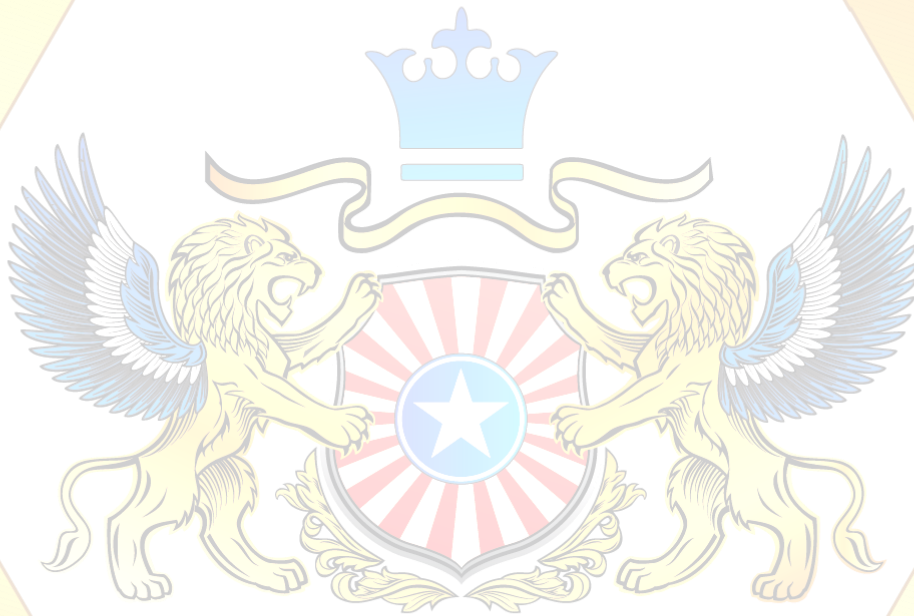
- This SOP applies to all the personals of the clinical research team and others who may be responsible for patient recruitment in the study. These include the following:
  - Principal Investigator
  - Research Team (listed in the delegation log)
  - CTC
  - Other support staff

#### **4.7 Staff responsible for Implementation**

- Director BBMCT and Investigators will ensure that the research team involved in the conduct of the study will comply with this site SOP.
- Director BBMCT will ensure that at the time of implementation of the SOP, that the research team are trained and in the event that an SOP is modified, provide training regarding the change(s) and ensure their compliance with the changes.

## References

- 21 CFR 312.60 – General Responsibilities of Investigators
- Guideline Good Clinical Practice
- ICH Guidelines for Good Clinical Practice (E6)
- ICH Guidelines for Good Clinical Practice (E6) section 3.1 – Responsibilities
- OCRN SOP AD102.002 “Responsibilities of Clinical Research Personnel
- Schedule Y : Responsibility of Investigator



## AX1-V1/SOP 04/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. :				
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

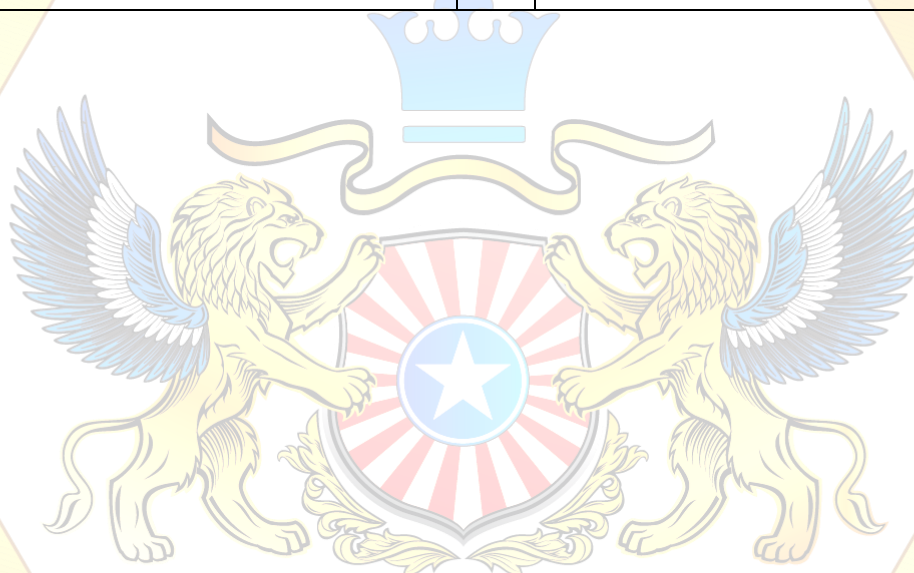
#### List of Responsibilities:

\*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	20	Review & evaluation of reports
9	Authorization to randomize	21	Treatment decision
10	Investigational Product dispensing	22	
11	Investigational Product Accountability & maintenance	23	Archival activities
12	CRF Completion		Others: 22 a _____ 22 b _____ 22 c _____



# **Standard Operating Procedure Clinical Trials**

**(Exclusive AIIMS Hospital,  
New Delhi)**

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

**SOP Code: SOP 05/V1**

**Date:13/November/2020**

**Pages: 42 to 46**

**British BioMedicine Clinical Trials (BBMCT)  
(2020)**

## 5.1 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 AIIMS Hospital and to ensure proper documentation of communications with the Sponsor/CRO concerning study activities.

## 5.2 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 by assuring that studies are conducted compliantly, sponsors/CROs are fully appraised of study site activities, and key research personnel are informed of new information about the study provided by the sponsor/CRO.

Any new study which 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.

## 5.3 Procedure

### 5.3.1 General communications

- Provide the sponsor/CRO a contact list of site personnel involved in study start up, along with each individual's role and responsibilities.
- Communicate regularly, courteously and in accordance with AIIMS Hospital standards, with the sponsor/CRO about all 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.
- Retain all sponsor-generated communications regarding conduct of the study (e.g., teleconference announcement) in the correspondence section of the TMF. Budget, payment and other contractual or financial communications should be filed separately from the regulatory binder. Ensure information is communicated to the Principal Investigator (PI) and other key research personnel as applicable.

### 5.3.2 Pre-Study communication

- The CTC is responsible for sending the Confidentiality Agreement to the sponsor/CRO once reviewed and signed by PI.
- Notify the sponsor/CRO of the PI's decision to conduct the research study.
- 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.
- Fill the questionnaires provided by the sponsor/CRO regarding the study related requirements.
- Prepare questions to clarify protocol procedures, subject eligibility criteria, and other study-related issues in writing and file the reply in the TMF.
- The PI/Co I will discuss how the site is equipped to perform the study. This discussion will include a description of the potential subjects available for the study and methods being considered for recruitment.

### 5.3.3 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), 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, per the sponsor's requirements and document the same in the specified TMF.
- Communicate significant regulatory changes per the sponsor's requirements (e.g., IEC acknowledgement of an unanticipated issues or protocol deviation, IEC approval of a revised consent document, etc.). Typically these documents are reviewed during interim monitoring visits; however specific sponsors/CROs may require prompt notification in specific circumstances.
- 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

- Forward safety reports received from the sponsor (e.g., off-site SAE/SUSAR) to the PI who will review the event and report to the IEC as per IEC SOP. Notification of other key research personnel and/or enrolled subjects may be necessary (e.g., new risk identified related to investigational treatment).

#### **5.3.4 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 requires in the IEC study closure letter) related to the study close out.
- Ensure that all close out activities are performed and all sponsors 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.

### **5.4 Sponsor Contact**

1. Telephone Contacts – 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. If requires the CTC or delegate will file the Telephone Contact copy in the TMF.
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.
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 and if required in the source notes.

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

- When the first subject is enrolled in the study.
- When there is a question concerning a potential subject's eligibility.
- When recruitment issues occur.
- When a protocol violation occurs.
- When an SAE occurs.

### **5.5 Applicable Staff**

This SOP applies to all the personals 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 Investigator
- CTC
- Pharmacist
- Support Staff

## 5.6 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 unit 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.

## References

1. 21 CFR 312.32 IND safety reports
2. 21 CFR 312.33 Annual reports
3. 21 CFR 312.44 Termination
4. 21 CFR 50 Protection of Human Subjects
5. 21 CFR 56 Institutional Review Boards
6. Beaumont SOP Site-Sponsor/CRO communications dated 21/9/2010
7. FDA Information Sheet, October 1998: Sponsor-Investigator-
8. IEC Interrelationship
9. May 1997 International Conference on Harmonization (ICH) Good Clinical Practices



# **Standard Operating Procedure Clinical Trials**

**(Exclusive AIIMS Hospital,  
New Delhi)**

The logo of All India Institute of Medical Sciences (AIIMS) is centered in the background. It features a blue crown at the top, a yellow ribbon with a blue border, and two golden lions with blue wings flanking a shield. The shield has a red and white sunburst design. The entire logo is set against a large, light yellow hexagonal background.

**Title: Site Initiation, Activation, Conduct and  
Close-out**

**SOP Code: SOP 06/V1**

**Date:13/November/2020**

**Pages: 47 to 54**

**British BioMedicine Clinical Trials (BBMCT)  
(2020)**

## 6.1 Purpose

To describe the process which ensures that the site is organized and prepare for the proper conduct of the research study at AIIMS Hospital. This standard operating procedure (SOP) also describes the processes to be followed at site initiation, activation, conduct and closeout of research study at AIIMS Hospital. Sponsor/CRO are requested to pay the Admin Startup fee of Rs 1,00,000 (One Lakh) as distributed. And Rs 80,000 (Eighty Thousand Rupees) during study close out (Record Archival).

S.No.	When	Comments	Amount
1	Before	Up-front, non-refundable payment to defray the cost of start-up work such as preparing regulatory documents, attending investigator meetings, site initiation training, enrollment efforts, etc	Rs 50,000.00
2	After	Completion of : (1) execution of the Agreement, (2) submission of all regulatory documents to CRO, and (3) IRB approval.	Rs 50,000.00

## 6.2 Scope

This SOP will apply to all pharma sponsored research study initiation, activation, conduct and close-out at AIIMS Hospital.

## 6.3 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 approvals 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 regulatory guidelines.
- Site 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 is met with all the required regulatory and sponsor requirements.

### 6.3.1 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 from the sponsor; 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 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.
- Confirm that all documents required by Institutional Ethics Committee (IEC) are available.
- Confirm that the clinical trial agreement (CTA), indemnification letter and budget are finalized and signed.
- 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.

### **6.3.2 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:
  - Signed protocol and Investigator Statement
  - Signed and executed Investigator contract
  - CVs and licenses of key site study staff
  - Financial Disclosure forms
  - Investigator Undertaking (IU)
  - Form FDA 1572 for IND studies
  - IEC approval letter for the protocol
  - IEC membership roster (updated)
  - IEC approved informed consent form
  - Institutional and/or other regulatory authority approvals
  - Valid clinical/other laboratory licensure
  - Laboratory normal value ranges
  - Notice that indicates the study has been submitted to the regulatory authorities (if applicable).
  - Investigator Brochure, if applicable.

- Case Report Forms (CRF)
  - Investigational product inventory management forms
  - Any other essential documents.
- 
- Provide the study members name involved in the study and their responsibilities in the duty delegation to the monitor/CRA.
  - 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 agreed and finalized with the Sponsor and 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 Participants/patients that are likely to be recruited into the study also allowing for the archiving of one set of intact, unused CRFs
  - 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 delegate (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:
- Aim and Objective of the protocol
  - Time and events schedule for the protocol
  - Subject recruitment
  - Obtaining informed consent

- Procedure for dispensing the IP
  - IP storage and records
  - Protocol-specific forms and procedures
  - Source documentation
  - Adverse event reporting
  - 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
  - Identify a back-up to the primary CTC

### **6.3.3 Study Activation and Initiation Visit Follow-Up**

- a. In preparation for study activation
- Confirm that the sponsor sends a written summary of key discussions and agreements made during the site initiation visit. Follow-up if necessary.
  - Confirm readiness of the site to start the study.
  - Confirm the receipt of all study-related materials 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 participants.
  - Initiate study recruitment strategies and begin enrolling study patients/participants.

### **6.3.4 Study conduct**

- a. Once the site is activated and starts recruiting patients, the Investigator and CTC will ensure the following
- All study activities are accomplished according to the protocol and applicable regulatory regulations.
  - Subjects sign the correct version of the consent form before any study-related procedures are accomplished.
  - Data collected in the Case Report Form (CRF) are supported by source documents.
  - Protocol deviations/non compliance/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 CCM 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.

- 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.
  - Study supplies remain adequate.
  - Study records remain confidential.
  - All equipment is calibrated regularly and maintenance records are being kept.

### **6.3.5 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 the trial participants and include, where appropriate, the reason for suspension / early termination of the study.
  - Assure appropriate therapy and follow-up for the participants, and, where required by the applicable regulatory requirement(s), should inform the regulatory authority (ies).
  - The PI should maintain documents as specified in the TMF list and take measures to prevent accidental or premature destruction

#### **In addition:**

- b. 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.
- c. If the sponsor terminates or suspends a research study, the PI should
- In case the sponsor chooses to or is required to terminate prematurely or suspend the research study, then 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.

### **6.3.6 Site close-out**

- a. Preparing the site for study close-out visits
- After the last patient has completed all scheduled visits associated with the study, arrange a mutually convenient date and time with the monitor/CRA 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 Co I and CTC to discuss any outstanding issues.
  - PI will ensure that all outstanding payments are cleared as per CTA.
- 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. Include the CTC as appropriate.
  - If the study involved electronic data capture, determine when hard copies/CD of all CRFs will be provided to AIIMS HOSPITAL, if applicable.
  - The PI is responsible for ensuring the appropriate follow-up, per the protocol, for any participant experiencing an ongoing unanticipated problem (e.g., serious adverse event) at study end and providing this information to the sponsor/CRO, 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).
- 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 will be informed of their treatment arm, ascertain from the sponsor how and when this will be completed.

## 6.4 Applicable Staff

This SOP applies to all the personals of the clinical research team and others who may be responsible for site initiation, activation, conduct and close-out at AIIMS HOSPITAL.

These include the following:

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

## 6.5 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.
- PI will ensure that at the time of implementation of the SOP, that the research team at the clinical research unit in AIIMS HOSPITAL 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.

## References

1. 21 CFR 312.50 General responsibilities of sponsors
2. 21 CFR 312.56 Review of ongoing investigations
3. 21 CFR 312.59 Disposition of unused supply of investigational drug
4. 21 CFR 312.60 General responsibilities of investigators
5. 21 CFR 312.62 Investigator recordkeeping and record retention
6. 21 CFR 312.64 Investigator reports
7. 21 CFR 312.66 Assurance of IRB review
8. 21 CFR 312.68 Inspection of investigator's records and reports

9. 21 CFR 54.6 – Record Keeping and Record Retention
10. CDSCO guidelines: Appendix V
11. Good Clinical Practices
12. ICH Guidelines for Good Clinical Practice (E6)
13. May 1997 International Conference on Harmonization (ICH)
14. Schedule Y



# **Standard Operating Procedure Clinical Trials**

**(Exclusive AIIMS Hospital,  
New Delhi)**

The logo of All India Institute of Medical Sciences (AIIMS) is centered in the background. It features a blue crown at the top, a yellow ribbon, and two yellow lions with blue wings flanking a shield. The shield has a red and white sunburst design with a blue star in the center.

**Title: Reviewing and Obtaining Informed  
Consent Form**

**SOP Code: SOP 07/V1**

**Date:13/November/2020**

**Pages: 55 to 65**

**British BioMedicine Clinical Trials (BBMCT)  
(2020)**

## 7.1 Purpose

- To describe the information or essential element required to be included in the informed consent documents associated with research study.
- To describe the procedure for obtaining voluntary informed consent from a prospective subject for a research study and also to ensure that a subject's consent is sought in such a way that the subject 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 participant in accordance with applicable regulatory requirement, Schedule Y, ICH-GCP and Declaration of Helsinki.

## 7.2 Scope

This SOP will apply to all research studies conducted at AIIMS Hospital for informed consent procedure.

## 7.3 Procedure

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

### 7.3.1 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 requirements for element of ICF, to learn if specific formatting or wording requirements for informed consent / Assent in addition to those listed in the regulations are fulfilled.

In addition, PI must ensure that the as per the guideline (Gazette dated 30.01.2013), following should be inserted namely (Refer IEC SOP) for regulated studies

- Subject Initials:
- Date of Birth:      Age:
- Subject Name:
- Add & Contact No:
- Qualification: Occupation: Student / Self Employed / Service / House wife ,other (please specify), If any \_\_\_\_\_
- Annual Income: INR,
- Name and Address of the Nominee (s) and relation to subject:
- Name:
- Relation to subject:
- Address & Contact No.:

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, Schedule Y and ICH GCP guidelines.

If there is any discrepancy or missing element in the ICF, contact Sponsor/CRO or PI (in case of Investigator initiated study) for appropriate action.

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 counselling, and the information to be communicated to the prospective participant or the Legally Authorized Representative, the Research Plan should include:

- the person who would provide consent or permission;
- any waiting period between informing the prospective 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 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 or the subject's Legally Acceptable Representative (LAR) and or to the Impartial Witness (IW), wherever applicable.

The Informed Consent must be available in the appropriate required local languages with the translation certificate.

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 participant and Impartial Witness and or participant's legally authorized representative, where applicable.
- The circumstances of the consent process provided the prospective 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 individuals communicating information to the participant or the legally authorized representative during the consent process provided was in the language understandable to the participant or the representative.
- The information being communicated to the participant or the representative during the consent process did not include exculpatory language through which the participant or the legally authorized representative was made to waive or appear to waive any of the participant's legal rights.

- The IEC will determine that the required disclosures (mentioned in 8.3.2.a) provided to each subject or a legally authorized representative 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.

### **7.3.2 General procedure for obtaining Informed Consent from Subjects / patients:**

The Investigator and CTC are responsible for ensuring that the informed consent 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.

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

No investigator may involve a human being as a subject in research, unless the investigator has obtained the legally effective informed consent of the subject

PI / Co I should conduct the consent procedure and obtain freely & voluntarily given consent from a subject.

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

- a. 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.
  - The aims and methods of the research.
  - The expected duration of the subject's participation.
  - Description of the procedures to be followed, including all invasive procedures.
  - Any foreseeable risk or discomfort to the subject resulting from participation in the study.
  - The benefits that might reasonably be expected as an outcome of research to the subject or to others. If no benefit is expected subject should be made aware of this.
  - Any alternative procedures or courses of treatment that might be as advantageous to the subject as the procedure or treatment to which she/he is being subjected.

- The extent to which confidentiality of records could be able to safeguard, confidentiality and the anticipated consequences of breach of confidentiality.
- Information regarding direct access to the participants original medical records for verification of clinical trial procedures or data to the monitor, the auditor, the IEC, and the regulatory authority will be granted, without violating the confidentiality of the participant, to the extent permitted by the applicable laws and regulations and that, by signing a written consent form, the participant or the participants legally acceptable representative is authorizing such access.
- Trial treatment schedule(s) and the probability for random assignment to each treatment (for randomized trials).
- Compensation and/or controlled available to the Subject in the event of a trial-related injury.
- An explanation about whom to contact for trial related queries, rights of Subjects and in the event of any injury, with appropriate address and contact numbers.
- The anticipated prorated payment, if any, to the Subject for participating in the trial.
- Subject's responsibilities on participation in the trial.
- Freedom of individual / family to participate and to withdraw from research any time without penalty or loss of benefits which the subject would otherwise be entitled to.
- Right to prevent use of his/her biological sample (DNA, cell-line, etc.) at any time during the conduct of the research.
- Foreseeable extent of information on possible current and future uses of the biological material and of the data to be generated from the research and if the material is likely to be used for secondary purposes or would be shared with others, clear mention of the same.
- Publication, if any, including photographs and pedigree charts.
- Any other pertinent information.

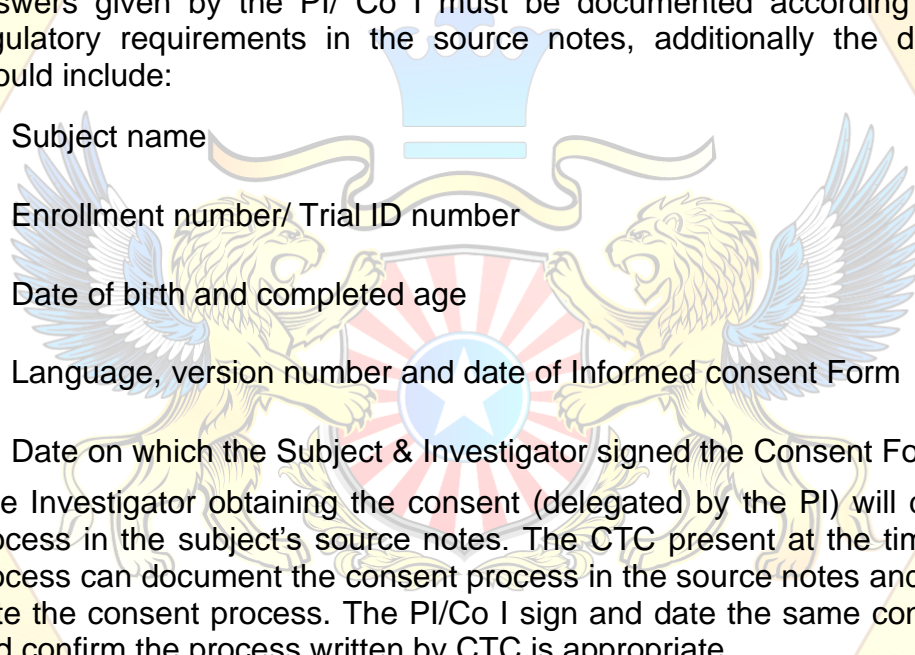
#### **Additional elements, which may be required**

- Statement of foreseeable circumstances under which the Subject's participation may be terminated by the Investigator without the Subject's consent.
- Additional costs to the Subject that may result from participation in the study.
- The consequences of a Subject's decision to withdraw from the research and procedures for orderly termination of participation by Subject.
- Statement that the Subject or Subject's representative will be notified in a timely manner if significant new findings develop during the course of the research which may affect the Subject's willingness to continue participation will be provided.

- A statement that the particular treatment or procedure may involve risks to the Subject (or to the embryo or fetus, if the Subject is or may become pregnant), which are currently unforeseeable
  - Approximate number of Subjects to be enrolled in the study
- b. The person (PI/Co I) who explains the study will allow enough time for the potential subject to read the consent form and will answer any questions that are raised.
- c. The PI/Co I obtaining the consent will ensure the following:
- Adequate time provided to subject before participation
  - All of the subject's questions were answered.
  - The subject understands the study requirements.
  - The subject signed the consent freely & voluntarily.
  - The consent form is signed and dated by the subject and the PI/Co I who obtained the consent, and Impartial Witness and or LAR, if applicable.
  - The subject is given a copy of the signed & dated consent form.
- d. PI / CTC should ensure that prior to a participant's participation in the research study; the written consent document should be personally signed and dated by the subject and by the PI/Co I who conducts the informed consent discussion.
- e. The PI/CTC will ensure that the original, signed copy of the consent is stored in the separate file and a copy is given to subject.
- f. After initial consent process or participating in the study, if participant is not willing to consent or want to prematurely withdraw consent for the study, PI should respect the participant 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 participant's rights.

### **7.3.3 Obtaining Informed Consent from literate subjects / patients:**

- a. PI/ Co I must explain the study to the potential subject verbally (in the preferred language of the subject), providing all pertinent information (mentioned in 7.3.2.a), and must allow the potential subject ample opportunity to ask questions.
- b. Following this verbal explanation, the potential subject should be provided with a written consent form/ Patient Information Sheet (PIS) and should give sufficient time to consider whether or not to participate in the research study.
- c. After allowing the potential subject time to read the consent form, an Investigator should meet with the potential subject and answer any additional questions he/she may have.

- 
- d. Once an individual had all his/her questions answered and has agreed to voluntarily participate in the study, the subject should sign and date the consent form.
  - e. The PI/ Co I who has explained and taken consent from the subject must also sign and date the consent form.
  - f. The Investigator's signature means that the informed consent process has taken place with the subject and that the subject:
    - meets all eligibility criteria as per protocol
    - was appropriately consented (as described above)
    - understands the requirements of the study
  - g. The entire consent process including the questions asked by the subject and answers given by the PI/ Co I must be documented according to legal and regulatory requirements in the source notes, additionally the documentation should include:
    - Subject name
    - 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 & Investigator signed the Consent Form
  - h. The Investigator obtaining the consent (delegated by the PI) will document the process in the subject's source notes. The CTC present at the time of consent process can document the consent process in the source notes and will sign and date the consent process. The PI/Co I sign and date the same consent process and confirm the process written by CTC is appropriate.

#### **7.3.4 Obtaining Informed Consent from non English speaking subjects / patients:**

- 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.
- c. PI/Co I who speaks the same language as the potential subject will explain the study to the subject and will also be available at subsequent study visits to ensure that the subject's questions can be answered as the study progresses.

- d. Before obtaining the consent from the potential patient kindly follow the above mentioned points 7.3.2.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 7.3.3.g
- f. The CTC present at the time of consent process can document the consent process in the source notes and will sign and date the consent process. The PI/Co I sign and date the same consent process and confirm the process written by CTC is appropriate

### **7.3.5 Obtaining Informed Consent from illiterate subjects / patients:**

- a. If a person identified for the study who speaks and understand English and or any other local language, but cannot read and write, can be enrolled in a study as illiterate subject, consistent with applicable regulations.
- b. The PI must ensure (1) the person retains the ability to understand the concepts of the study and evaluate the risk and benefit of being in the study when it is explained verbally (still competent) and (2) is able to indicate approval or disapproval to participate in the research study.
- a. The information should be given (as mentioned in point 7.3.2.a) to the Subjects and / or their legal representatives in a language and at a level of complexity that is understandable to the Subject(s) and or his/ her LAR in both written and oral form, whenever possible.
- b. The consent form should document the method used for communication with the prospective subject and the specific means by which the prospective subject communicated agreement to participate in the study.
- c. An impartial third party should witness the entire consent process and sign the consent document. The witness may be a family member or friend. The witness may not be a person involved in the design, conduct, or reporting of the research study.
- d. The subject must give consent by putting his / her thumb impression on the consent form. By convention subject should give left thumb impression.
- e. Alternatively the subject (if capable) can sign the consent form. In such case it has to be documented in the source notes that though the subject is illiterate but is capable to sign.
- f. Impartial Witness and or LAR present during the entire consent process must sign the consent form with date in presence of investigator obtaining consent.
- g. After obtaining consent, follow the above mentioned points 7.3.2.b, c & d
- h. For documenting the process in source notes, follow the points 7.3.3.g & h

### 7.3.6 Obtaining Informed Consent from Children

- a. PI/Co I must obtain assent form from a subject and consent form from a parent in case of children between 7-17 years of age.
- b. If recommended by IEC both parents should sign assent as well as consent for child.
- c. 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 7 – 17 year of age are eligible for assent)
- d. The 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.
- e. The PI/Co I who explains the study will ensure that a parent or legal guardian for the child is present during the explanation and observes the assent procedure.
- f. 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.
- g. 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 legal guardian signed the assent and consent freely & voluntarily.
  - The minor signed the assent voluntarily.
  - The assent signed and dated by the subject, parent or legal guardian and the PI/Co I who obtained the consent.
  - The consent form was signed and dated by the parent or legal guardian and the PI/Co I who obtained the consent.
  - The parent and minor are given copies of the signed consent and assent.
- h. 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.
- i. After obtaining consent from parent and assent from children, follow the above mentioned points 7.3.2.a, b, c & d.

### **7.3.7 Revised Informed Consent Form**

When the Investigator / CTC receive updates to the Investigator's Brochure, IND Safety Reports, or protocol amendments, he/she should also review the informed consent to determine if it should be revised to reflect the new information.

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.

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.

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

If the subject decides to continue in the study and signs the consent form, the CTC/delegated member will provide the subject with a copy of the revised consent and will place the original in the separate file.

### **7.3.8 If Incorrect version of ICF used**

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

Contact the subject and explain the reason for re-consenting the subject 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.

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.

## **7.4 Applicable staff**

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

- Investigator
- Legal Expert
- CTC
- Support staff if required

## 7.5 Staff responsible for Implementation

Director BBMCT 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 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.

## References

1. 21 CFR 312.60 – General Responsibilities of Investigators
2. 21 CFR 50.20 – General Requirements for Informed Consent
3. 21 CFR 50.25 – Elements of Consent
4. 21 CFR 50.27 – Documentation of Informed Consent
5. 45 CFR 46.116 – General Requirements for Informed Consent
6. 45 CFR 46.117 – Documentation of Informed Consent
7. GCP Informed Consent Process
8. ICH Guidelines for Good Clinical Practice (E6) section 1.28 – Informed Consent
9. ICH Guidelines for Good Clinical Practice (E6) section 1.37 – Legally Authorized Representative
10. Schedule Y – Appendix V

# **Standard Operating Procedure Clinical Trials**

**(Exclusive AIIMS Hospital,  
New Delhi)**

**Title: Recruiting Study Subjects**

**SOP Code: SOP 08/V1**

**Date:13/November/2020**

**Pages: 66 to 71**

**British BioMedicine Clinical Trials (BBMCT)  
(2020)**

## **8.1 Purpose**

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

## **8.2 Scope**

This SOP will apply to all clinical studies being conducted at AIIMS Hospital.

## **8.3 Procedure**

There are several steps involved in subject 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 subject to ensure that they meet the inclusion and exclusion criteria; and the enrollment in the study.

ICH GCP requires that records are kept of every subject that undergoes pre-trial screening (ICH GCP 7.3.20) i.e. details of all subjects approached for a study should be maintained. For the purposes of this SOP, this shall be referred to as a screening log.

### **8.3.1 Recruitment strategies**

Investigator must schedule a meeting prior to enrollment, in order to secure the co- operation of study team to obtain a sufficient number of subjects.

During the meeting the study protocol will be revised/ re discussed and the inclusion and exclusion criteria will be discussed in detail.

Investigator will provide the detailed inclusion and exclusion pamphlet to the entire study team member to place in their respective OPDs.

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

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

Any queries regarding subject eligibility must be referred to the Principal Investigator.

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

Investigator should check whether the subject(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.

The investigator should keep a confidential list of names of all Study Subjects allocated to each study. This list facilitates the investigator / institution to reveal identity of the subject(s) in case of need and also serve as a proof of Subject's existence. The investigator / institution shall also maintain a Subjects' screening log to document identification of Subjects who enter pre-study screening.

### **8.3.2 Subject Identification/Pre screening**

Subject with proven or suspected diagnosis of cancer assessed in the OPDs (general and private) by the investigators.

The study team/Investigator/CTC must study the subject past and current history to evaluate if subject meets the eligibility criteria.

If the subject meets the eligibility criteria the study team must inform the investigator/CTC and CTC must document the following details in screening log (AX1-V1/SOP08/V1)

- Case number
- Subject 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 confirms.

### **8.3.3 Subject screening**

All eligible subjects must be send to the respective investigator or CTC for further counselling and to obtain Informed consent form.

Investigator should begin the informed consent process and obtain informed consent prior to screening (refer to the applicable SOP). Document the date that the informed consent form was signed (or the reason if it was not signed) in the source notes and the enrollment log.

CTC should schedule subject 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.

Investigator and CTC will review the screening reports and will confirm subject eligibility.

If investigator finds the prospective subject eligible, investigator must inform the same to the subject and the sponsor/CRO.

If a prospective study participant found to be ineligible, inform the same to subject and or LAR and document the reasons for screening failures in the enrollment log and in the source documents. Store the enrollment log in the study files.

#### **8.3.4 Subject randomization/enrollment**

Enroll eligible participants into the study and follow the trial's randomization procedures, if any.

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

- Subject randomization number/enrollment number
- Date of randomization/enrollment
- Randomization group/arm

Document recruitment activities on the source notes and/or enrollment log as appropriate while maintaining subject/participant confidentiality.

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.

#### **8.4 Applicable staff**

This SOP applies to all the personals of the clinical research team and others who may be responsible for subject recruitment in the study.

These include the following:

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

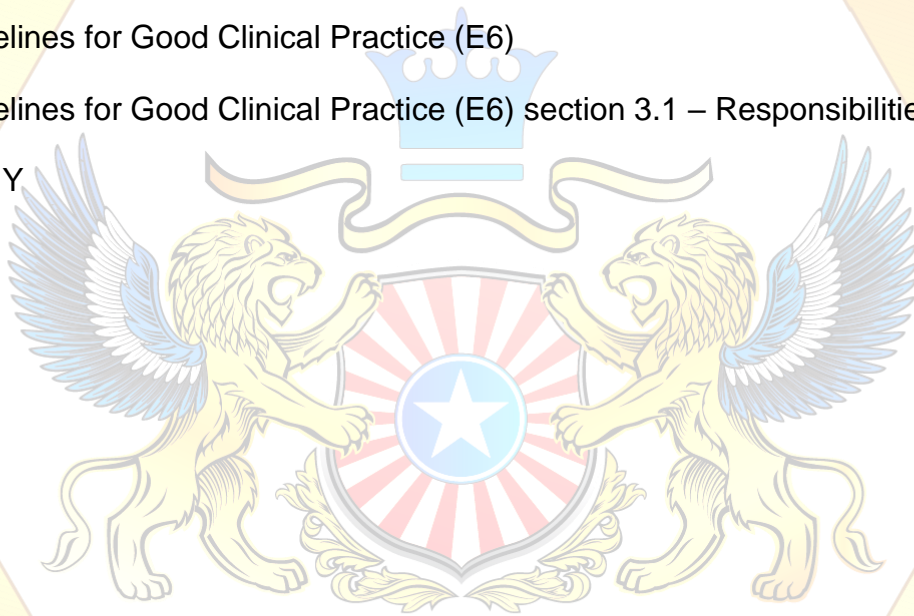
#### **8.5 Staff responsible for Implementation**

Director BBMCT 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 unit are trained and in the event that an SOP is modified, provide training regarding the change(s) and ensure their compliance with the changes.

## References

1. 21 CFR 312.60 – General Responsibilities of Investigators
2. 21 CFR 50.20 – General Requirements for Informed Consent
3. 21 CFR 50.25 – Elements of Informed Consent
4. Guideline Good Clinical Practice
5. ICH Guidelines for Good Clinical Practice (E6)
6. ICH Guidelines for Good Clinical Practice (E6) section 3.1 – Responsibilities
7. Schedule Y



## AX1-V1/SOP 08/V1

Study Title:  
Study No:  
Principal Investigator:

### Screening Log\*

Sr. no.	Date	Case No	Patient Initials	Age	Diagnosis	Remark

\*Subject to change as per protocol requirements

# **Standard Operating Procedure Clinical Trials**

**(Exclusive AIIMS Hospital,  
New Delhi)**



**Title: Source Documentation**

**SOP Code: SOP 09/V1**

**Date:15/November/2020**

**Pages: 72 to 77**

**British BioMedicine Clinical Trials (BBMCT)  
(2020)**

## 09.1 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 AIIMS Hospital.

## 09.2 Scope

This SOP will apply to all clinical trials conducted at AIIMS Hospital.

## 09.3 Procedure

### 09.3.1 Information regarding source documents

Source documents are records, independent of the Case Report Form (CRF), which document the subject'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:

- Copy of Informed Consent Forms.
- Subject's medical record or office charts.
- 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
- Patient diaries
- Data recorded directly onto the CRF if identified in the protocol or pre-study report as source data.
- Study worksheets if data is recorded that is not otherwise available in the medical record

Proper data collection is essential to the outcome of research study. All of the information from a research study should be recorded in a way that ensures the integrity of the data. Maintaining the confidentiality of research subjects' personal information is an integral part of subject 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 ALCOA\* to achieve data quality.

- **Attributable:** is it obvious who wrote it?
- **Legible:** can it be read?
- **Contemporaneous:** is the information current and in the correct time frame?
- **Original:** is it a copy; has it been altered?
- **Accurate:** are conflicting data recorded elsewhere?

AIIMS Hospital has also adopted the computerized system to generate and maintain patient's record 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 report, procedures, etc.

EMR and CIS are interlinked, one can do changes in CIS but EMR can only be use to view data and do 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 ENR all.
- **Investigation report:** This link categorize 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 (Major / All surgeries (Major & Minor), Anesthesia Records, PAC. In patient admission and discharge date.
- **Follow Up record.**

### 09.3.2 Documentation of source data

Investigator and CTC must start documenting the source since the subject is identified for the study.

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

Once each participant has signed the approved informed consent form, medical record information may be obtained from the subject, treating doctors, relative and other providers, as necessary. The information should include but not limited to:

- Demographic data of the subject (Name, Date of birth and Sex)
- Patient medical history, diagnosis, and medical follow up if any
- Concomitant medication, current and previous if any (with start and stop date)
- Detailed informed consent and randomization process
- Date of screening and randomization
- Subject screening and randomization number
- Randomization arm if applicable
- Protocol specific procedures
- Also mention if subject consented for the biological or genetic study (if any).
- In case of screen failure patients, investigator must document the reason for the same with sign and date.

Investigator and study team member (as per delegation log) are authorized to document the above mentioned information. Person documenting (as per delegation log) the information must sign and date the source note.

CTC can put a study specific sticker on the source file for quick identification. Sticker can include details like: Patient ID, Patient Initials, Study Arm, Consent and randomization date and if required date of birth.

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

All diagnostic testing results including laboratory reports, CT scan, MRI, ECGs, etc. are to be properly filed and retained as source documents. If these reports require review by the PI/ Co I, this review must be completed within a reasonable time period of the report being received and must be signed and dated by the investigator to document that this review was completed.

This file should be updated at each subsequent visit. Documentation, outlining any issues associated with a specific 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.

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

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

Case Report Forms and source data are maintained separately, but source documents should accompany the case report form for sponsor verification.

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

All data must be entered in a sequential manner, without leaving any empty spaces. If any missed data observed related to subject, should be documented promptly on 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 be considered to be a source document (e.g. notes, appointment book, subject reports or medical file, diaries, etc)*

#### **09.3.3 Correction of Source Data**

Any corrections in the source documents must be crossed out with a single line (original entry should be visible) 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. If 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.

Never obscure the original entry, erase the original entry or cover the original entry with correction fluid.

#### **09.3.4 Maintenance of Source Data**

Source document (hospital case file) will be available in the PIs department after patient given his/her consent.

Patient or patient relative will not be allowed to take source document outside the hospital, if required they can take a photocopy of the required document.

Patient will submit the source document to the respective CTC after completion of all the required procedure.

In case of screen failure patient, CTC will maintain photocopy of the file and the original file will be returned to the respective parent unit.

After completion of the study, copy of source document will be retained and original will be returned to the hospital medical record or parent unit.

## 09.4 Applicable Staff

This SOP applies to all the personals 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)
- CTC

## 09.5 Staff responsible for Implementation

DIRECTOR BBMCT 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 unit in AIIMS HOSPITAL are trained and in the event that an SOP is modified, provide training regarding the change(s) and ensure their compliance with the changes.

## References

1. FDA Guidance: E6 Good Clinical Practice (GCP), Sections 4.9 and 5.18.4
2. 21CFR11
3. Schedule Y

# **Standard Operating Procedure Clinical Trials**

**(Exclusive AIIMS Hospital,  
New Delhi)**



**Title: Managing Investigational Products (IP)**

**SOP Code: SOP 10/V1**

**Date:15/November/2020**

**Pages: 78 to 86**

**British BioMedicine Clinical Trials (BBMCT)  
(2020)**

## 10.1 Purpose

To describe process and requirements for the receipt, storage, dispensing, and return or destruction of Investigational Product (IP) at site.

## 10.2 Scope

This Standard Operating Procedure (SOP) will apply to all studies being conducted at AIIMS Hospital.

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.

## 10.3 Procedure

### 10.3.1 Prior to receipt of Investigational Product (IP)/ Study Drug

PI must identify an area with restricted access and appropriate temperature control for IP storage.

Assign 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.

The person must be identified on the study delegation log.

### 10.3.2 Receipt of Investigational Product (IP)/ Study Drug

Upon receipt of the IP shipment at the site, the CTC/delegated member 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 accountability.

If the inventory matches the drug received, the 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).

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.

### **10.3.3 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. The capture of minimum and maximum values of temperature will be recorded if only specified by the sponsor/CRO.

In case a temperature excursion is noted, the CTC/designated study team member must inform Investigator and the following telephonically followed by email at the earliest:

- Inform the sponsor / CRO and document the same
- Try to identify the cause of temperature excursion
- 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”**.

#### **10.3.4 IP / Study Drug Dispensing**

IP must be dispensed by the CTC/delegated member to subjects randomized on the study after fulfilling the eligibility criteria in accordance with the protocol.

Upon dispensing the IP the CTC/delegated member must note following in the source note and IP package:

- Trial/Study ID number (both source notes and IP package)
- Initial of the subject (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, in the subject source notes as well as in the Drug Accountability Logs (AX1-V1/SOP10/V1).

The CTC/delegated member will maintain a record of drug dispensed to and retrieved from each subject. To accomplish this, the CTC/delegated member will use the CRF or drug accountability diary (AX2 V1/SOP10/V1), if any and only if provided by the sponsor/CRO.

The CTC/delegated member will explain to each subject the drug accountability needs for the study (e.g., the need for the subject to return unused, partially used, and empty packages).

Requests for IP resupply must be done as per the study specific procedures.

#### **10.3.5 IP/ Study Drug Return**

The study subject will return all drug and study-related supplies to CTC/delegated member on the specified visit mentioned in the protocol.

The CTC/delegated member will count the returned drug and compare this with the amount of drug expected to have been used since the previous study visit.

CTC/delegated member must document IP returned by the subject in the subject's source file as well as in the drug accountability logs (Attachment A) as per the study requirement.

In case of missing IP or extra IP, the CTC/delegated member must obtain the information from the Subject and document the clarification provided in the source notes, drug 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 will store the returned drug separately in a secure area until it is verified by the CRA/Monitor.

Whether the drug is to be returned to the sponsor or destroyed on-site will be determined by the instructions in the protocol.

The documentation of the destruction/ return must be maintained in the TMF.

### **10.3.6 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.

The CRA/Monitor will perform the independent drug accountability review and will seal the drug that need to be shipped back to the Sponsor/CRO.

The CRA/Monitor will arrange the preferred courier 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.

### **10.3.7 On-Site Destruction of IP**

If the sponsor/CRO request for on-site destruction of the IP, the CTC/delegated member should:

- Obtain a copy of the site's SOP of Waste Management from department of Microbiology for IP destruction/disposition, provide a copy to the monitor, and file a copy in the TMF.
- 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.
- Provide the 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.

#### **10.3.8 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.

#### **10.4 Applicable staff**

This SOP applies to those 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 Trial Coordinator (CTC)
- Pharmacist
- Research Nurse
- Support Staff

#### **10.5 Staff responsible for implementation**

DIRECTOR BBMCT, PI and delegated Site staff will ensure that at the time of implementation of the SOP, that the research team at the clinical research unit in AIIMS HOSPITAL 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 IRB that this site SOP will be implemented within the institution.

## References

1. 21 CFR 312.44 – Termination
2. 21 CFR 312.61 – Control of the Investigational Drug
3. 21 CFR 312.69 – Handling of Controlled Substances
4. CFR 312.59 – Disposition of Unused Supply of Investigational Drug
5. FR 312.60 – General Responsibilities of Investigators
6. ICH Guidelines for Good Clinical Practice (E6) section 4.6 – Investigational Products
7. Schedule Y - Investigational Product Management



## AX1-V1/ SOP 10/V1

### Drug Accountability Log

Project Title & Project No.:

Principal Investigator:

Drug /IP Name:

Sr. no.	Patient ID	Kit no./ Batch no	Date of Expiry	Quantity	Date	Dispensed by (Initials & Sign)	Return date	Quantity returned	Received by (Initials & Sign)	Remarks

**AX2-V1/SOP 10/V1**

**Protocol Title:** \_\_\_\_\_

**Subject Initials:** \_\_\_\_\_

Record from \_\_\_\_\_ to \_\_\_\_\_

**Date of next visit:** \_\_\_\_\_

**Prescribed dose:** \_\_\_\_\_

## Drug accountability diary (for Patient)

[illegible]

# **Standard Operating Procedure Clinical Trials**

**(Exclusive AIIMS Hospital,  
New Delhi)**



**Title: Archival of Essential Documents**

**SOP Code: SOP 11/V1**

**Date:13/November/2020**

**Pages: 87 to 102**

**British BioMedicine Clinical Trials (BBMCT)  
(2020)**

## **11.1 Purpose**

To describe the procedure of archiving essential documents during the entire course of the study and also to document the method to archive the essential document at AIIMS Hospital for the required period of time.

## **11.2 Scope**

This SOP will apply to all clinical trials conducted at AIIMS Hospital.

## **11.3 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 and with other applicable regulatory requirements.

Essential Documents are needed for Sponsor's independent audit function and inspection by the Regulatory Authority.

The Principal Investigator is responsible for archiving essential documents at the respective sites in accordance with the requirements of the Sponsor (or CI if appropriate), the institution and local requirements.

The Investigator should maintain documents as specified in the essential documents' list (AX1-V1/SOP 11/V1) and take measures to prevent accidental or premature destruction.

Filing space should be available for the storage of Trial Master File (TMF) during the conduct of the clinical trial. Investigator site files will normally be stored at PI's 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:

### **11.3.1 Archival of essential documents before the clinical phase of the study commences**

Before the study initiation visit, the CTC will create, or be given by the Sponsor/Contract Research Organization (CRO), a ring binder in which all required regulatory documents, forms and correspondence will be kept. If the Sponsor/CRO requires additional forms, or documents, these will be maintained in addition to the documents listed in AX2-V1/SOP11/V1.

The CTC will ensure that the appropriate documents are placed in the TMF on a regular basis. The CTC will make the file available for review by the Monitor at each site visit.

### **11.3.2 Archival 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 Form" and mention PI name, study number and title on the binder.

If the Sponsor/CRO has given no specific direction concerning storage of informed consents in the TMF, then they must be stored as specified by the Sponsor/CRO.

Original source documents (case file) will be kept at PI's department during the study. A copy of the source documents (case file) will be created once study is completed and the original source documents (case file) will be stored in the hospital medical record. Contracts such as the Confidentiality Agreement, Investigator Agreement, and Publication Policy Agreement can be stored separately in the investigators offices of Company (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 reimbursements document will be stored in separate file/binder.

A separate file/binder for each subject 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 subject's Case Report Form (CRF).

The CTC will ensure that the CRFs are stored in a secure location (i.e., Monitors should not have access to another study documents).

All site-related materials should be made available for review by the sponsor's representatives (monitors and auditors) or regulatory authority(s).

### **11.3.3 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 11/V1).

*(Note: Xerox copy of the subject 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, for humid conditions, pests 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\_11/V1– Archive Inventory) record for future reference.

The study documents must be archived for 15 years post the study close out or 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.

In case there is not enough space for storage of the study records, then PI can place the study record in a secure off-site facility i.e. in ACTREC where they may be readily accessed in the event of an audit.

If the Principal Investigator leaves Company, 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.

## **11.4 Applicable Staff**

This SOP applies to all the personals of the clinical research team who may be responsible archival of essential documents at AIIMS Hospital.

These include the following:

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

## **11.5 Staff responsible for Implementation**

Director BBMCT will ensure that the research team involved in the conduct of the study will comply with this site SOP.

Director BBMCT and PI at his level will ensure that at the time of implementation of the SOP, that the research team at AIIMS Hospital 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.

## References

1. 21 CFR 312.55 – Informing Investigators
2. 21 CFR 312.57 – Record Keeping and Record Retention
3. 21 CFR 312.58 – Inspection of Sponsor Records and Reports
4. 21 CFR 312.62 – Investigator Record Keeping and Record Retention
5. 21 CFR 312.64 – Investigator Reports
6. Appendix V-CDSCO guideline: Essential Documents
7. ICH Guidelines for Good Clinical Practice (E6) section 4.4 – Communication with IRB/IEC
8. ICH Guidelines for Good Clinical Practice (E6) section 4.9 – Records and Reports
9. ICH Guidelines for Good Clinical Practice (E6) section 5.22 – Clinical Trial/Study Reports

# AX1-V1/SOP 11/V1

## Essential Documents for Conduct of Clinical Trial

Legend :

I - Investigator / Institute,      S - Sponsor,      C - CRO,  
 E - IEC,      - - Yes,      ° - Not applicable

Title of the document		Purpose	Located in files of			
			I	S	C	E
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.						
1	Investigator's brochure	To document that relevant and current scientific information about the investigational product has been provided to the investigator	.	.	.	.
2	Signed protocol and amendments, if any, and sample case report form(CRF)	To document investigator and sponsor agreement to the protocol/amendment(s) and CRF	.	.	.	.
3	Information given to trial subject - informed consent form (including all applicable translations)	To document the informed consent	.	.	.	.
4	- Any other written information	To document that subjects will be given appropriate information (content and wording) to support their ability to give fully informed consent	.	.	.	.
5	-Advertisement for subject recruitment (if used)	To document that recruitment measures are appropriate and not coercive	.	.	.	.
6	Financial aspects of the trial	To document the financial agreement between the investigator/institution and the sponsor for the trial	.	.	.	.
7	Insurance statement (where required)	To document that compensation to subject(s) for trial-related injury will be available	.	.	.	.

Title of the document		Purpose	Located in files of			
			I	S	C	E
8	<p>Dated, documented approval / favourable opinion of independent ethics committee (IEC) of the following:</p> <ul style="list-style-type: none"> <li>- protocol and any amendments</li> <li>- CRF (if applicable)</li> <li>- informed consent form(s)</li> <li>- any other written information to be provided to the subject(s)</li> <li>- advertisement for subject recruitment (if used)</li> <li>- Subject compensation (if any)</li> <li>- any other documents given approval / favourable opinion</li> </ul>	<p>To document that the trial has been subject to IEC review and given approval / favourable opinion.</p> <p>To identify the version number and date of the document(s)</p>	.	.	.	.
9	Independent ethics committee composition	To document that the IEC is constituted in agreement with GCP	.	.	.	.
10	Regulatory authority(ies) authorisation / approval / notification of protocol (where required)	To document appropriate authorisation / approval / notification by the regulatory authority(ies) has been obtained prior to initiation of the trial in compliance with the applicable regulatory requirement(s)	.	.	.	.
11	Curriculum vitae and/or other relevant documents evidencing qualifications of Investigator(s) and Co-Investigator / Sub-Investigator(s)	To document qualifications and eligibility to conduct trial and/or provide medical supervision of subjects	.	.	.	.
12	Normal value(s) / range(s) for medical / laboratory / technical procedure(s) and/or test(s) included in the protocol	To document normal values and/or ranges of the tests	.	.	.	°

Title of the document		Purpose	Located in files of			
			I	S	C	E
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	.	.	.	°
14	Instructions for handling of investigational product(s) and trial-related materials  (if not included in protocol or Investigator's Brochure)	To document instructions needed to ensure proper storage, packaging, dispensing and disposition of investigational products and trial-related materials	.	.	.	°
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	.	.	.	°
16	Certificate(s) of analysis of investigational product(s) shipped	To document identity, purity, and strength of investigational product(s) to be used in the trial	°	.	.	°
	Decoding procedures for blinded trials	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	.	.	.	°
17	Master randomisation list	To document method for randomisation of trial population	°	.	.	°
18	Pre-trial monitoring report	To document that the site is suitable for trial (may be combined with Trial initiation monitoring report)	°	.	.	°
19	Trial initiation monitoring report	To document that the trial procedures were reviewed with the investigator and the investigator's trial staff  (may be combined with Pre-trial monitoring report)	.	.	.	°

Title of the document		Purpose	Located in files of			
			I	S	C	E
<b>During the Clinical Conduct of the Trial</b>						
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						
20	Investigator's brochure updates	To document that investigator is informed in a timely manner of relevant information as it becomes available	.	.	.	.
21	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	.	.	.	.
22	Dated, documented approval / favourable opinion of Independent ethics committee (IEC) of the following:  - protocol amendment(s)  - revision(s) of:  - informed consent form  - any other written information provided to subject  - advertisement for subject recruitment(if used)  - any other documents given approval / favourable opinion  - continuing review of trial (where required)	To document that the trial has been subject to IEC review and given approval / favourable opinion.  To identify the version number and date of the document(s).	.	.	.	.

Title of the document		Purpose	Located in files of			
			I	S	C	E
23	Regulatory authority(ies) authorisations / approvals / notifications where required for: - protocol amendment(s) and other documents	To document compliance with applicable regulatory requirements	.	.	.	.
24	Curriculum vitae for new investigator(s) and / or sub- investigator(s)	To document qualifications and eligibility to conduct trial and/or provide medical supervision of subjects	.	.	.	.
25	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	.	.	.	°
26	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	.	.	.	°
27	Documentation of investigational product(s) and trial-related material shipment	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	.	.	.	°
28	Certificate(s) of analysis for new batches of investigational products	To document identity, purity, and strength of investigational product(s) to be used in the trial	°	.	.	°
29	Monitoring visit reports	To document site visits by, and findings of, the monitor	°	.	.	°
30	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	.	°	.	°

Title of the document		Purpose	Located in files of			
			I	S	C	E
31	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	. (Original)	. ( Copy)	. (Copy)	°
32	Source documents	To document the existence of the subject and substantiate integrity of trial data collected. To include original documents related to the trials, to medical treatment, and history of subject	. (Original)	. (Copy)	. (Copy)	°
33	Signed, dated and completed case report forms (CRF)	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	. (Copy)	. (Copy)	. (Copy)	°
34	Documentation of CRF corrections	To document all changes / additions or corrections made to CRF after initial data were recorded	. (Original)	. (Copy)	. (Copy)	°
35	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	.	.	.	.
36	Notification by sponsor and/or investigator, where applicable, to regulatory authority(ies) and 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 IEC(s) of unexpected serious adverse drug reactions and of other safety information	.	.	.	.

Title of the document		Purpose	Located in files of			
			I	S	C	E
37	Notification by sponsor to investigators of safety information	Notification by sponsor to investigators of safety information	.	.	.	.
38	Interim or annual reports to IEC and authority(ies)	Interim or annual reports provided to IEC and to authority(ies)	.	.	.	.
39	Subject screening log	To document identification of subjects who entered pre-trial screening	.	(Where required)	(Where required)	°
40	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	.	.	.	°
41	Subject enrolment log	To document chronological enrolment of subjects by trial number	.	.	.	°
42	Investigational products accountability at the site	To document that investigational product(s) have been used according to the protocol	.	.	.	°
43	Signature sheet	To document signatures and initials of all persons authorised to make entries and / or corrections on CRFs	.	.	.	°
44	Record of retained body fluids/ tissue samples (if any)	To document location and identification of retained samples if assays need to be repeated	.	.	.	°

Title of the document		Purpose	Located in files of			
			I	S	C	E
After Completion or Termination of the Trial						
After completion or termination of the trial, all of the documents identified should be in the file together with the following						
45	Investigational product(s) accountability at site	To document that the investigational product(s) have been used according to the protocol. To documents the final accounting of  investigational product(s) received at the site, dispensed to subjects, return by the subjects, and returned to sponsors	.	.	.	°
46	Documentation of investigational product destruction	To document destruction of unused investigational products by sponsor or at site  (if destroyed at site)	.	.	.	°
47	Completed subject identification code list	To permit identification of all subjects enrolled in the trial in case follow-up is required. List should be kept in a confidential manner and for agreed upon time	.	.	.	°
48	Audit certificate (if available)	To document that audit was performed	°	.	.	°
49	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	°	.	.	°
50	Treatment allocation and decoding documentation	Returned to sponsor to document any decoding that may have occurred	°	.	.	°
51	Final report by investigator to IEC where required, and where applicable, to the regulatory authority(ies)	To document completion of the trial	.	.	.	.
52	Clinical study report	To document results and interpretation of trial	.	.	.	.

## AX2-V1/SOP11/V1

### Contents of Trial Master File

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
4. Investigator's Brochure (if any)
5. Investigational product Information (if any)
6. IP accountability
7. Duty delegation log
8. CV,MRC , GCP certificates of all study team members
9. Investigator's Undertaking
- 10.DCGI submission Acknowledgement (if applicable)
- 11.CTRI Details
- 12.IEC communication
- 13.SAE reporting details
- 14.Contracts and Agreements (if any)
- 15.Laboratory details (if any)
- 16.Others

## AX3-V1/SOP 11/V1

### Archiving box labels

Study Reference Number OR TMH project no:	
Study Title	
Name of Sponsor Name	
Name of Principal Investigator	
Archival Date	
Archive Until	
Contents of BOX 1:	
1.	
2	
3	
4	
5	
6	
7	
8	
9	
10	

## Archive Inventory

Study Reference Number OR TMH Project Number	
Study Title	
Name of Sponsor	
Name of Principal Investigator	
Archival Date	
Archive Location	On-site/Off-site/Storage area
<b>Archive Until</b>	

BOX Number 1	Content
Box Number 2	

# **Standard Operating Procedure Clinical Trials**

**(Exclusive AIIMS Hospital,  
New Delhi)**



**Title: Safety Reporting**

**SOP Code: SOP 12/V1**

**Date:13/November/2020**

**Pages: 103 to 116**

**British BioMedicine Clinical Trials (BBMCT)  
(2020)**

## 12.1 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

## 12.2 Scope

This SOP will apply to all clinical trials conducted at AIIMS Hospital.

## 12.3 Procedure

### 12.3.1 Managing AEs and SAEs during study

PI must educate the study team about adverse events (expected and non-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, subjects must be given 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) and in the source documents at the site.

When a subject reports an adverse event (at each clinical visit/telephonic contact), it should be informed to the PI/Col who must provide the necessary and appropriate medical care to the subject.

In the event that the PI/study team learn about the adverse event/SAE from the subject/relative over telephone; e-mail, fax etc. then the PI/Study team must collect all the information about the event from the subject/relative and document it in the subject file and include details such as

- Date and time of the discussion
- Date and time of the event occurred (start and stop date).
- Any medicine or advice taken or offered.
- Details of the person provided the information.

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 subject's file.

In events where original records are not available an attested copy must be obtained and maintained. The subject on recovery may be invited for an unscheduled visit if deemed necessary by the PI/ Co I.

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. mild, moderate or severe).

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/CTC must document the event start and stop date and whether study medication prescribed was continued/interrupted/discontinued, 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 (eg SAE Reporting Form provided by the IEC) and inform the same to the IEC, CDSCO and sent to the sponsor/designee and Institutional Head within time frame of the study team getting to know of the event.

### **12.3.2 Reporting SAE to CDSCO**

As per the Drugs & Cosmetics Rules amended vide GSR no 53 (E) dated 30-01-2013 inserting a Rule 122DAB, and a new Appendix-XII in Schedule 'Y' along with other amendments 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 appendix-XI of Schedule Y (AX1-V1/SOP 12/V1) of D&C Rules.

PI/Co I must report the SAE to CDSCO and make sure it contains all the required administrative as well as technical information in proper manner as per the checklist (AX2-V1/SOP 12/V1)

The SAE reports must be submitted with proper binding, indexing and page number. Without indexing of page number, no SAE report will be accepted.

The PI/Co I must select the proper cover to submit the SAE, as mentioned below

- The reports of SAEs of deaths should be prepared and submitted in red cover.
- The reports of SAE of injury other than deaths should be prepared and submitted in blue cover.
- The SAE report other than that mentioned in (a) & (b) above is to be prepared and submitted in white cover.

Clear and unequivocal information should be provided in the SAE report.

Text and tables should be prepared using margins that allow the document to be printed clearly without losing any information and the left-hand margin should be sufficiently large so that information is not obscured by the method of binding. The documents printed on both sides of a page, can be submitted. However, one should take care that the information is not obscured when the page is placed in a binder.

While submitting reply to a query, the applicant should always enclose with the reply, a copy of query letter issued by CDSCO.

Every report (both initial as well as follow-up reports) should be submitted along with a covering letter. A template of covering letter is available in AX3-V1/SOP 12/V1.

### **12.3.3 Reporting SAE to Institutional Ethics Committee (IEC)**

PI/Col shall report all SAE to the IEC /DSMSC that accorded approval to the study protocol within 24 hours of their occurrence in the format required by the IEC/DSMSC (as per IEC SOP).

If the outcome of an SAE is 'Death' the IEC/DSMSC 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 progressive disease the event should be reported in the SAE reporting format unless specified in the protocol.

If the patient is out of trial and on Survival follow up the event should be reported unless specified in the protocol.

PI must complete the required information in the SAE reporting Form (as per IEC SOP) and sign and date the same.

Serious Adverse Event should be graded as per CTCAE guidelines and the SAE causality and relatedness must be marked carefully by the investigator

Investigator/CTC must submit one original + 2 photo copies + soft 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 gets timely and appropriate medical attention/intervention as required.

If the outcome of the SAE is death and found to be related to the investigational product the IEC/DSMSC will discuss the SAE in the IEC meeting and will take a decision regarding compensation.

Follow-up reports on the SAEs should be submitted within 10 days of the initial report or when any additional information regarding the event is available, whichever is earlier.

IEC/DSMSC 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/DSMSC and PI/Co I must respond to the query letter immediately.

#### **12.3.4 Reporting SAE to Sponsor/CRO**

PI/Col/CTC 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/DSMSC 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/CTC should collect as much of the information as possible for completing the SAE reporting form.

PI/Co I must documents 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 send 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 gets timely and appropriate medical attention/intervention as required.

PI must inform the Sponsor/CRO regarding the progress report of the subject till the subject recovered or discharge from the hospital or till death.

The CTC will ensure that the SAE is properly documented in the subject'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. \* for regulated studies)*

## **12.4 Applicable areas of the Hospital**

(AIIMS Hospital) IEC/DSMSC

## **12.5 Applicable Staff**

This SOP applies to all the personals of the clinical research team who may be responsible for reporting SAE.

These include the following:

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

## 12.6 Staff responsible for Implementation

Director BBMCT and Investigators will ensure that the research team involved in the conduct of the study will comply with this site SOP.

Director BBMCT will ensure that at the time of implementation of the SOP, that the research team at the clinical research unit in AIIMS Hospital are trained and in the event that an SOP is modified, provide training regarding the change(s) and ensure their compliance with the changes.

## References

1. Appendix XI-Schedule Y
2. Draft Guideline on Reporting Serious Adverse Event (Dated 11-5-2011) F.No. 12-01/13-DC (Pt-13A ) Office of Drugs Controller General (India) New Drugs Division
3. ICH Guidelines for Good Clinical Practice (E6) section 4.11 – Safety Reporting
4. ICH Guidelines for Good Clinical Practice (E6) section 4.3 – Medical Care of Trial Subjects
5. AIIMS HOSPITAL-IRB SOP: SOP Code: SOP 09/V1 Date : 05/09/2012
6. Add gazette reference

## AX1-V1/SOP 12/V1

### Appendix XI – Schedule Y

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

#### 1. Patient Details

Initials & other relevant identifier (hospital/OPD record number etc.)\*

Gender:

Age and/or date of birth:

Weight:

Height:

#### 2. Suspected Drug(s)

Generic name of the drug\*

Indication(s) for which suspect drug was prescribed or tested

Dosage form and strength

Daily dose and regimen (specify units - e.g., mg, ml, mg/kg)

Route of administration

Starting date and time of day

Stopping date and time, or duration of treatment

#### 3. Other Treatment(s)

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

#### 4. Details of Suspected Adverse Drug Reaction(s)

Full description of reaction(s) including body site and severity, as well as the criterion (or criteria) for regarding the report as serious. In addition to a description of the reported signs and symptoms, whenever possible, describe a specific diagnosis for the reaction.\*

Start date (and time) of onset of reaction

Stop date (and time) or duration of reaction

Dechallenge and rechallenge information

Setting (e.g., hospital, out-patient clinic, home, nursing home)

## 5. Outcome

Information on recovery and any sequelae; results of specific tests and/or treatment that may have been conducted

For a fatal outcome, cause of death and a comment on its possible relationship to the suspected reaction; Any post-mortem findings.

Other information: Anything relevant to facilitate assessment of the case, such as medical history including allergy, drug or alcohol abuse; family history; findings from special investigations etc.

## 6. Details about the Investigator\*

Name

Address

Telephone number

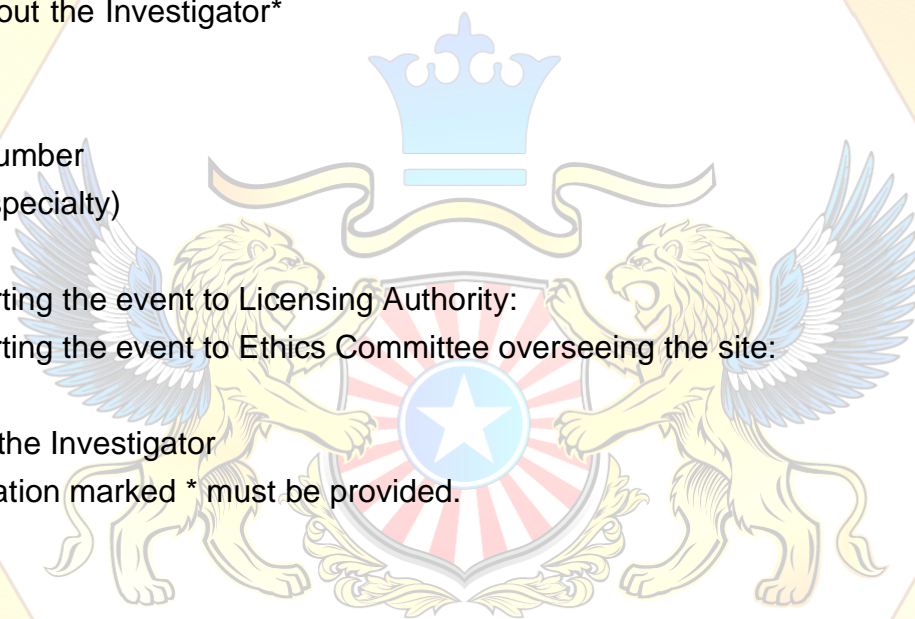
Profession (specialty)

Date of reporting the event to Licensing Authority:

Date of reporting the event to Ethics Committee overseeing the site:

Signature of the Investigator

Note: Information marked \* must be provided.



## AX2-V1/SOP 12/V1

### CHECKLIST FOR SUBMISSION OF SERIOUS ADVERSE EVENT REPORT (SAE) OCCURRING IN CLINICAL TRIAL

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

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

<b>17</b>	<b>Details about the Investigator</b>		
<b>a)</b>	CT Site Number, if any		
<b>b)</b>	Name		
<b>c)</b>	Address		
<b>d)</b>	Telephone/Mobile Number & Email		
<b>e)</b>	Profession (speciality)		
<b>f)</b>	Date of reporting the event to Licensing Authority:		
<b>g)</b>	Date of reporting the event to Ethics Committee overseeing the site:		
<b>h)</b>	Signature of the Investigator		
<b>18</b>	<b>Details about the Ethics Committee</b>		
<b>a)</b>	Name & Address		
<b>b)</b>	Name of Chairman & Address		
<b>c)</b>	Telephone/Mobile Number		
<b>d)</b>	Email		
<b>19</b>	Adverse Event Term / Details of SAE		
<b>20</b>	Causality Assessment (Related/Unrelated) by Investigator		
<b>21</b>	Causality Assessment (Related/Unrelated) by Sponsor/CRO		
<b>22</b>	Details of compensation provided for injury or death. In case no compensation has been paid, reason for the same :		
<b>23 a)</b>	Duly filled SAE Form as per Appendix XI of Schedule Y		
<b>b)</b>	Laboratory investigations report /Discharge summary (if available and applicable)		
<b>c)</b>	Post-mortem report (if applicable)/ Any additional documents)		

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

## AX3-V1/SOP 12/V1

### Covering letter template for SAE reporting in CTs

<Please print on company / CRO letter head>

Ref No.: <Insert Company's letter ref

Date: <DDMMYYYY>

/tracking No., if any>

**To**

The Drugs Controller General (India)  
CDSCO, FDA Bhawan, CHEB Campus  
Kotla Road, New Delhi - 110002

**Subject:** Reporting Serious Adverse Event (SAE)

<b>CT File No. (CDSCO File No.):</b>	<b>Sponsor Address:</b>	<b>CRO Address (if any):</b>
<b>Trial ID/Protocol No./Study code:</b>	<b>Phone:</b>	<b>Phone:</b>
<b>Phase of Study:</b>	<b>E-mail :</b>	<b>E-mail :</b>
<b>Investigational Drug(s):</b>	<b>Study Title:</b>	
<b>Initial Report <input type="checkbox"/> / Follow-up #</b> __		
<b>CT Category</b> <(Please select appropriate category from the list)>	<input type="checkbox"/> CT-1-IND <input type="checkbox"/> CT-2-Reg <input type="checkbox"/> CT-3-GCT <input type="checkbox"/> CT-4-rDNA <input type="checkbox"/> CT-5-Vac <input type="checkbox"/> CT-6-Oth <input type="checkbox"/> CT-7-Dev <input type="checkbox"/> CT-8-Oth	
<b>Adverse Event term / Diagnosis:</b>	<b>Whether the event is an Unexpected</b>	<b>Causality Assessment</b> (Related/Not related)
	Investigator	Medical Monitor
	<b>SAE:</b> <input type="checkbox"/> Yes <input type="checkbox"/> No	
	<b>Fatal:</b> <input type="checkbox"/> Yes <input type="checkbox"/> No	
<b>Details of compensation provided for injury or death . In case no compensation has been paid , reason for the same :</b>		

Dear Sir,

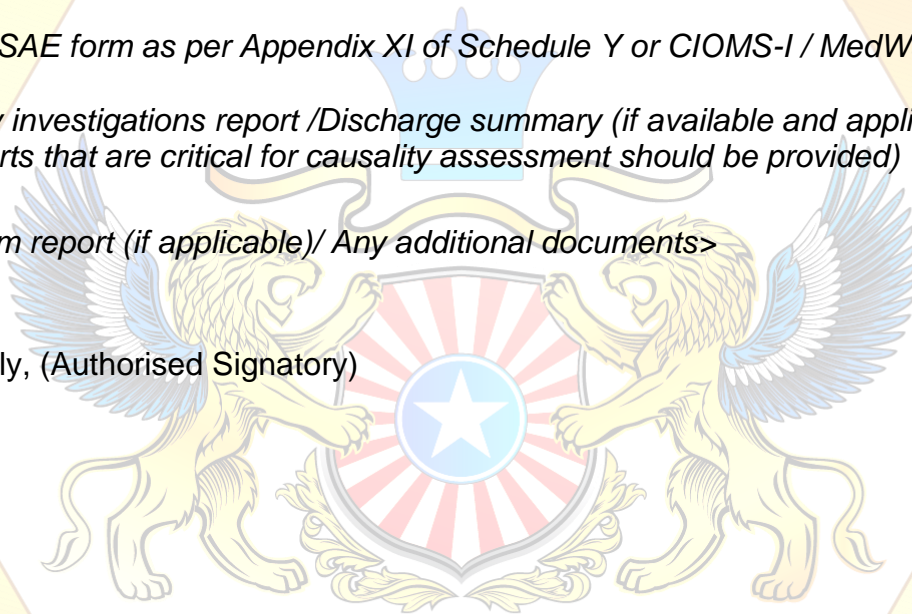
This is to bring to your kind notice that <Dr. \_\_\_\_\_>, investigator at <\_\_\_\_\_>, has informed us that a subject with initials <“ \_ \_ ”> has suffered with a SAE on <DDMMYYYY>. Brief details are as below:

*<Insert a brief narrative - not exceeding 10 lines> <Incase, this is a follow-up report, please capture the date of submission of initial report in the narrative>*

Following documents are enclosed for your perusal, < (please edit the list as appropriate)

1. Duly filled SAE form as per Appendix XI of Schedule Y or CIOMS-I / MedWatch form
2. Laboratory investigations report /Discharge summary (if available and applicable i.e. only the reports that are critical for causality assessment should be provided)
3. Postmortem report (if applicable)/ Any additional documents>

Yours faithfully, (Authorised Signatory)



# **Standard Operating Procedure Clinical Trials**

**(Exclusive AIIMS Hospital,  
New Delhi)**



**Title: Managing Biological Samples**

**SOP Code: SOP 13/V1**

**Date:13/November/2020**

**Pages: 117 to 120**

**British BioMedicine Clinical Trials (BBMCT)  
(2020)**

## **13.1 Purpose**

This SOP describes the procedures for collection, preparation, storage and shipment of biological sample.

## **13.2 Scope**

This SOP will apply to all biological samples collected, processed, stored and shipped by AIIMS Hospital, unless alternate directions are provided by the sponsor or Contract Research Organization (CRO).

## **13.3 Procedure**

### **13.3.1 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 13/V1)

### **13.3.2 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 is unusable immediately inform to Sponsor/CRO (in case of sponsored study) and report deviation to IEC and document the same in the source note, if required.

### **13.3.3 Storage of Samples**

Before shipments, site personnel will store both urine and plasma samples at a temperature of at least - 20°C – or at a temperature mentioned in the protocol

Other biological samples should be stored as mentioned in the protocol.

### **13.3.4 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 AIIMS Hospital policy.
- Keep a photocopy of the Biological Sample Inventory page in the TMF.

### **13.4 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 study related activities as mentioned in this SOP( per the delegation log). These include following

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

### **13.5 Staff responsible for Implementation**

Director BBMCT and Investigator will ensure that the research team involved in the conduct of the study will comply with this site SOP.

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

### **References**

None

## AX1-V1/SOP 13/V1

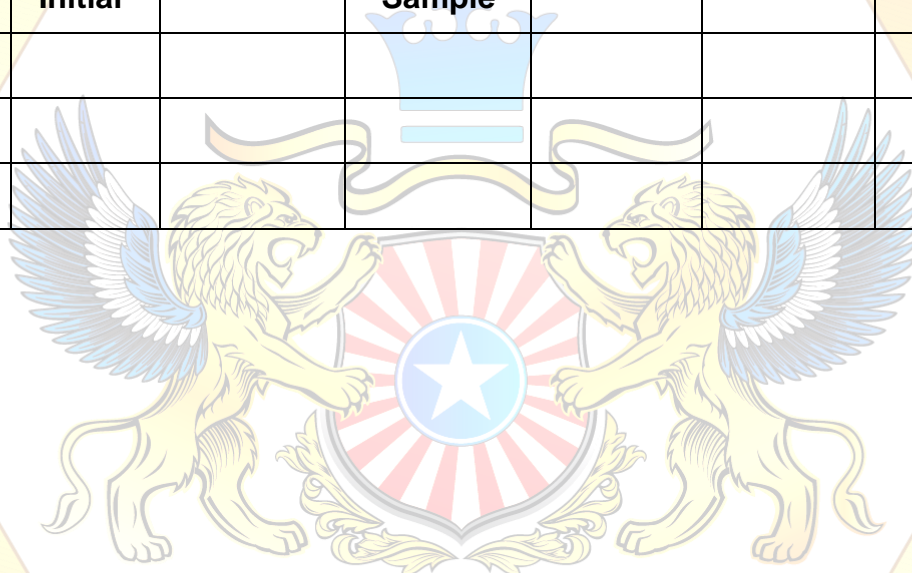
(Note: Template for investigator-initiated studies. For sponsored studies, refer the sponsor template.)

Protocol no:

Protocol Title:

PI name:

Trial ID no	Subject Initial	Sample ID	Type of Sample	Date	Time	Collected by



# **Standard Operating Procedure Clinical Trials**

**(Exclusive AIIMS Hospital,  
New Delhi)**



**SOP Code: SOP 14/V1**

**Date:13/November/2020**

**Pages: 121 to 124**

**British BioMedicine Clinical Trials (BBMCT)  
(2020)**

## **14.1 Intent / Purpose**

This SOP describes the procedures involved in reimbursement to the study subject for their involvement in the research and research related activities as agreed in CTA and mentioned in ICF.

## **14.2 Scope**

This SOP applies to all study team member who are engaged in study related activities and delegated in the delegation log for research related reimbursement (if applicable) to all subject participated in the studies being conducted in AIIMS Hospital.

## **14.3 Procedure**

### **14.3.1 Information regarding reimbursement**

Subjects may be paid for the inconvenience and time present, and should be reimbursed for expenses incurred, in connection with their participation in research. They may also receive free medical services. However, payments should not be so large or the medical services so extensive as to induce prospective subjects to consent to participate in research against their better judgement (inducement). All payments, reimbursement and medical services to be provided to research subjects should be approved by the IEC. Care should be taken:

- When a guardian 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 subject is withdrawn from research for medical reasons related to the study the subject should get the benefit for full participation;
- When a subject withdraws 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 as defined in the Informed consent document.

### **14.3.2 Procedure for reimbursement**

CTC as designated will reimburse the amount to the patient as mentioned below:

- Should open a particular study account in the AIIMS Hospital accounts department and maintain the account number. Always deposit the cheque in the same account received by the sponsor/CRO.
- Keep a track of patient's 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) or bills of the protocol specified visits or unscheduled visits if any.
- Must collect the original bills from the patient for above listed things for reimbursement
- Payment voucher must be prepared for the same; it will include patient hospital case number, name, amount to be paid, study account number and reason for reimbursement.
- Investigator or designee will approve and sign the voucher. Patient will sign or put his/her thumb impression in case patient is illiterate on the copy of the voucher (patient will sign/thumb while submitting the voucher to the accounts department).
- Copy of signed voucher (by investigator/designee and subject) 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 AIIMS Hospital.
- The competent authority from accounts department will sanction and release the amount.

In case of Serious Adverse Event (SAE) which found to be related to the IP, PI/ Co I will make sure that subject 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.

#### **14.4 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 as mentioned in this SOP (as per the delegation log).

These include the following:

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

## 14.5 Staff responsible for Implementation

Director BBMCT 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 unit in AIIMS Hospital 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.

## References

1. Good clinical practice.
2. Schedule Y



# **Standard Operating Procedure Clinical Trials**

**(Exclusive AIIMS Hospital,  
New Delhi)**



**Title: Study Team Training and Study Handover**

**SOP Code: SOP 15/V1**

**Date:13/November/2020**

**Pages: 125-150**

**British BioMedicine Clinical Trials (BBMCT)  
(2020)**

## 15.1 Purpose

This SOP defines the procedure and recommendation of training of study team members and adequate handover to CTC/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 to explain the status of the tasks, a summary of the work status in an email/ memorandum or, a more detailed file.

## 15.2 Scope

This SOP will apply to all study team members conducting studies in AIIMS Hospital.

## 15.3 Procedure

### 15.3.1 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.

The Director and OIC, CRS recommend that all Investigators, CTC and 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.

Each Investigator, CTC and study team members will review and learn 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.

If scheduled, PI and CTC will attend the Investigator Meeting (organized by Sponsor) and complete all required training for a study. If PI is unable to attend the meeting, PI can recommend other study team member(s) to attend the IM. PI should be informed regarding the study contents discussed in IM.

Before study initiation 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.

Clinical Research Secretariat (CRS) Department annually conducts two training programmes namely Clinical Research Methodology (CRM) and GCP. Study team member should attend the course to acquire training or to update themselves.

CRS will arrange a SOP training workshop to train PI and study team in addition PI can also train the study team and should maintain the training record (AX1-V1/SOP15/V1).

It is recommended that the PI and study team must maintain the Site SOP training Record (AX1-V1/SOP15/V1) at their respective unit and should make available whenever asked by the OIC, CRS.

### **15.3.2 Study Handover**

If any study team member is planning for leave or to resign, he/she must ensure that the proper handover is given to concern 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 on protocol and procedures e.g. SOPs and explanation of relevant documents
- Information regarding study subjects, 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 of the study team changes if the research team contact information will change for the subjects.
- Provide a list of study-specific contacts (e.g., sponsor, monitor, vendors involved etc)
- 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; correspondence sent to all subjects 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. 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.

## **15.4 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 (listed in the delegation log)
- CTC

## 15.5 Staff responsible for Implementation

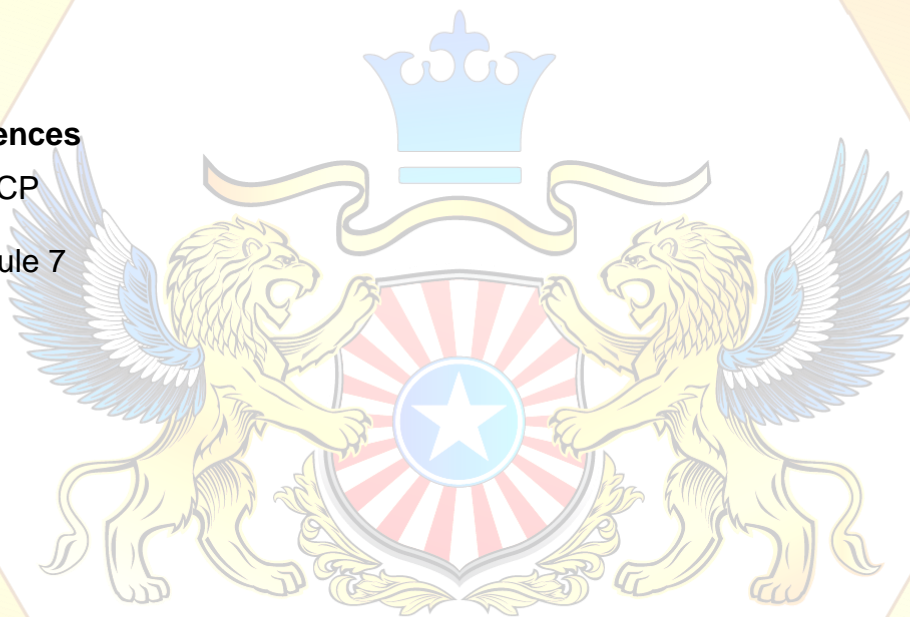
Director BBMCT and Investigator will ensure that the research team involved in the conduct of the study will comply with this site SOP.

Director BBMCT and PI will ensure that at the time of implementation of the SOP, that the research team at the clinical research unit in AIIMS Hospital are trained and in the event that an SOP is modified, provide training regarding the change(s) and ensure their compliance with the changes.

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.

## 15.8 References

- 1) ICH GCP
- 2) Schedule 7



## TRAINING Record

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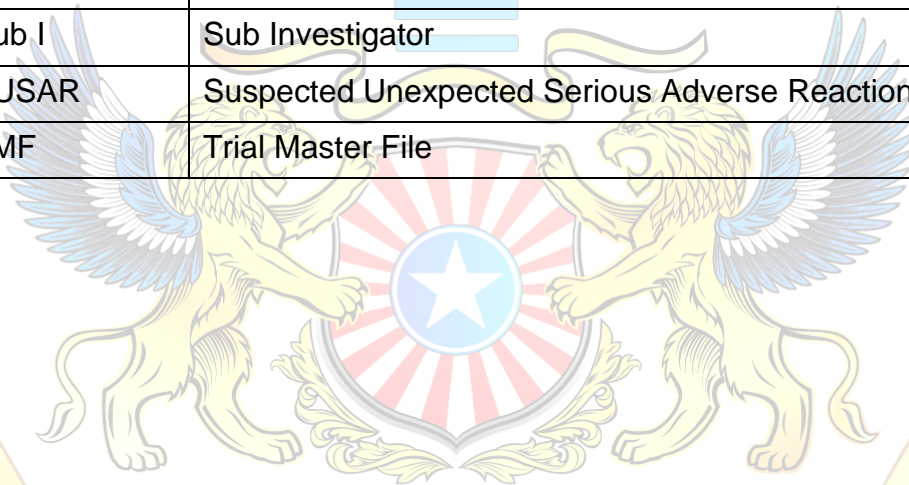
# Appendix A

## List of Abbreviations

Sr. No.	Acronym	Full Title/Description
1	AE	Adverse Event
2	AIIMS	All India Institute of Medical Sciences
3	BBMCT	British BioMedicine Clinical Trials
4	CA	Confidentiality agreement
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	CS	Clinically significant
16	CT scan	Computerized Tomography Scan
17	CTA	Clinical Trial Agreement
18	CTCAE	Common Terminology Criteria for Adverse Events
19	CTRI	Clinical Trial Registry India
20	CV	Curriculum Vitae
21	DCGI	Drugs Controller General of India
22	DGFT	Directorate General of Foreign Trade

Sr. No.	Acronym	Full Title/Description
23	DNA	Deoxyribonucleic Acid
24	DSMSC	Data Safety Monitoring Subcommittee
25	EC	Ethics Committee
26	ECG	Electrocardiogram
27	EDC	Electronic Data Capture
28	EMR	Electronic Medical Record
29	FDA	Food and Drug Administration
30	FDF	Financial Disclosure Form
31	GCP	Good Clinical Practices
32	GLP	Good Laboratory Practices
33	HOD	Head of Department
34	IB	Investigator's Brochure
35	ICF	Inform Consent Form
36	ICH GCP	International Conference on Harmonization Good Clinical Practices
37	IEC	Institutional Ethics Committee
38	IM	Investigator Meeting
39	IND	Investigation New Drug
40	INR	Indian National Rupees
41	IP	Investigational Product
42	ISF	Investigational Site File
43	IU	Investigator Undertaking
44	IVRS	Interactive Voice Response System
45	IW	Impartial Witness
46	IWRS	Interactive Web Response System
47	LAR	Legally Authorized Representative
48	MRI	Magnetic Resonance Imaging
49	NCS	Non Clinically Significant

Sr. No.	Acronym	Full Title/Description
50	OPD	Out Patient Department
51	PET	Positron Emission Tomography
52	PI	Principle Investigator
53	PIS	Patient Information Sheet
54	PSUR	Periodic Safety Update Report
55	QA	Quality Assurance
56	SAE	Serious Adverse Event
57	SDV	Source Data Verification
58	SIV	Site Initiation Visit
59	SOP	Standard Operating Procedure
60	Sub I	Sub Investigator
61	SUSAR	Suspected Unexpected Serious Adverse Reactions
62	TMF	Trial Master File



# 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 subject administered a pharmaceutical products and which does not necessarily have a casual relationship with the treatment.

**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 subjects 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):** Is the national regulatory body for Indian pharmaceuticals and medical devices, and serves parallel function to

the European Medicines Agency of the European Union. Within the CDSCO, the Drug Controller General of India (DCGI) regulates pharmaceutical and medical devices. This is coming under the ministry of health and family welfare India.

**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 subjects 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 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 patients 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 Research Coordinator (CRC):** 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](http://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.

**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 Monitoring Subcommittee (DSMSC):** A subcommittee of the IEC, essentially responsible for monitoring patient safety and assessing data during the course of the study in a manner that contributes to the scientific and ethical integrity of the study

**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 (safety, 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.

**Disease Management Group (DMG):** It is a group of clinicians from different specialties involved in the multidisciplinary management of a particular site of cancer.

**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 Director BBMCT and by Director, AIIMS HOSPITAL, 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 to 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 Productll 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 projects.

**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 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.

This definition contains four parts, all of which must be met. Here they are presented separately for emphasis and analysis:

1. —Who is independent of the trial: This could be a person who is a family member. It would not be a member of the site staff involved with the study.
2. —Who cannot be unfairly influenced by people involved with the trial: This would be a person free from potential coercion or undue influence or conflicted interest.
3. —Who attends the informed consent process if the subject or the subject's legally acceptable representative cannot read: This emphasizes the participation of the witness throughout the consent process, not just when the subject signs. A robust informed consent process will likely result, on the part of the person obtaining consent.
4. —Who reads the informed consent form and any other written information supplied to the subject: This responsibility has the witness confirming the subject was presented sufficient information to assure truly informed consent of 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 trials, 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.

**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):** An independent ethics committee comprising of medical / scientific and non-medical / non-scientific members, whose responsibility is to verify the protection of the rights, safety and well-being of human subjects involved in a study. The independent review provides public reassurance by objectively, independently and impartially reviewing and approving the —Protocoll, the suitability of the investigator(s), facilities, methods and material to be used for obtaining and documenting —Informed Consentll of the study subjects and adequacy of confidentiality safeguards.

**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'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):** An individual or juridical or other body authorized under applicable law to consent, on behalf of a prospective subject, to the subject's participation in the clinical trial

**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.

**Major Protocol deviation/violation:** A protocol deviation that may affect the subject's rights, safety, or well being or alter the risk benefit ratio, and/or affect the subjects' willingness to participate in the study, and/or impact the completeness, accuracy and reliability of the study data.

**Master SOP files:** An official collection of the Standard Operating Procedures (SOP) of BBMCT 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 after 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:** The extent of harm or discomfort anticipated from a clinical trial/research which is not greater than the routine practice.

**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.

**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, ICH GCP, FDA 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 Deviations:** Refer to non-compliance with the protocol schedule of events.

**Protocol Feasibility:** An analysis of the ability to complete a project successfully, taking into account 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:** Any planned or unintended changes or deviations from the IRB approved study protocol, consent document, recruitment process, or study materials that were not approved by the IRB prior to implementation.

**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 pre set 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 is 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 Trial 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 performed to check that the patient is eligible for enrolment in the trial or not.

**Serious Adverse Event (SAE) :** An AE or ADR that is associated with death, inpatient hospitalization (in case the study was being conducted on out-patients), prolongation of hospitalization (in case the study was being conducted on in-patients), persistent or significant disability or incapacity, a congenital anomaly or birth defect, or is otherwise life threatening.

**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 DIRECTOR BBMCT who oversee the creation, preparation, review and periodic revision of the CRS, AIIMS HOSPITAL 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

**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 individual 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.

**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 trail.

**Voluntary:** The act of giving one's own free will without any coercion or undue inducement.

**Thank you for your kind attention**