SITE MANAGEMENT ORGANIZATION

BLDE (DEEMED TO BE UNIVERSITY)'s

SHRI B.M.PATIL MEDICAL COLLEGE HOSPITL & RESEARCH CENTRE,

SMT.BANGARAMMA SAJJAN CAMPUS. B.M.PATIL ROAD, VIJAYAPUR-586103

(KARNATAKA STATE)

Site Management Office

STANDARD OPERATING PROCEDURE (SOP)

In accordance with the declaration of Helsinki (2000) and ICH-GCP (E6) guidelines

New Drug and Clinical Trial Rules (2019)

Dated: 29 May 2023

Effective Date: 29May 2023 through 29 May 2025

BLDE (DU)

SITE MANAGEMENT ORGANIZATION

BLDE (DU) SMO:

BLDE (DU) Site management organisation (SMO) is a reliable clinical trial related site service provider to Contract Research Organisation (CRO), Pharmaceutical, Biotechnology and Medical device companies and others to enable them to deliver their research in a time efficient and quality manner.

VISION

To provide quality and value based clinical trials related site services to the clients across the globe.

MISSION

- To ensure total quality management of Research projects and its deliverance within the stipulated timelines.
- Adherence to the dynamic regulatory standards driven through the component of integrity, proactively and transparency and trial subject centric work approach.
- To enhance collaborative and synergistic endeavors to create best professionals and skilled manpower to meet the global clinical research industry requirements.

BLDE (DU) SMO has an adequate hospital infrastructure and a team of dedicated, experienced and expertise staff in broader areas of therapeutics that will cater and meet the client's clinical trials research requirements in all domains of clinical research.

The SMO will aid in the deliverance of operational and administrative support services to the clinical investigator at the research site. This includes everything from handling regulatory and compliance activities to managing patient recruitment and data collection. It can also provide support with study start-up, monitoring, closeout and offer archival services as per client requirements. Our SMO offer the capability to ease operational complexity, regulatory compliance, and allow research teams to finish stipulated task on time.

BLDE (DU) SMO: -SITE STANDARD OPERATING PROCEDURES

BLDE (DU) SMO is committed to undertake and maintain highest scientific, clinical and ethical standards in conducting clinical research both regulated and funded at its constituent institution Shri B M Patil Medical College Hospital and Research Centre (SBMPMCHRC). The BLDE (DU) SMO is committed to comply with all applicable regulations and guidelines in clinical research. In view of the same, before agreeing to participate in a clinical research study, the Principal Investigator (PI) and the sponsors/CRO/Pharmaceutical/biotechnology company etc must agree to the scientific, clinical, and ethical merits of the study; operational feasibility of conducting the study; compliance with regulations and the financial impact to the hospital(BMPMCHRC). The Institutional Ethics Committee of BLDE (DU) will review, approve and monitor the clinical research done at BMPMCHRC. It is mandatory to register regulatory clinical studies in the Clinical Trial Registry of India (ctri.nic.in). The researchers are instructed to refer the policies and site SOPs of BLDE(DU)SMO for conducting a research study protocol and use the templates/formats provided for applying or submitting the report as necessary to the SMO/IEC.

This SOP describes the process for writing, reviewing, distributing, and amending SOPs within the SMO, BLDE (DU) and also to provide a tool for training new personnel in the procedures by which specific activities will be performed at BLDE(DU)SMO. This SOP will provide clear, unambiguous instruction to conduct activities of the clinical research in accordance with the ICMR guidelines 2006, Schedule “Y” (Drugs and Cosmetic Act 1940: Amendment 20th Jan 2005), ICH (International Conference on Harmonization) Good Clinical Practice (GCP),National Ethical Guidelines for Biomedical and Health Research Involving Human Participants, 2017; New Drugs and Clinical Trial Rules, 2019 and guidelines of Central Drugs Standard Control Organization (CDSCO) etc.

BLDE (DU) RESEARCH & DEVELOPMENT

BLDE (DU) Site Management Office (SMO)

Site Name	BLDE (DU) Shri B. M. Patil Medical College Hospital & Research Centre,Vijayapura-586103
Authorised by	Vice Chancellor of BLDE (DU), Smt. Bangaramma Sajjan Campus, Vijayapura-586103
SOP – 01/2023 **BLDE (DU) SMO - Site Management Office SOP**	
Version and Date	V1.0 and May 2023
Validity	29 May 2023 to 29 May 2025

Prepared by:

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Reviewed and Approved by:

Name	**Title**	**Signature**	**Date**
Dr.M.M.Patil	Director R & D Cell, Chairperson, SMO, BLDE(DU)		

List of Abbreviations

SOP : Standard Operating Procedure

PI : Principal Investigator

IEC : Institution Ethics Committee

ICF : Informed Consent Form

GCP : Good Clinical Practice

SAE : Serious Adverse Event

LIST OF SOPs at BLDE (DU) SMO
Site management office

BLDE(DU) SITE SOP	Version 1.0	Revision 0.0	Effective Date: 29/May/2023
SOP No	TITLE		
SOP 00/V1.0	SOP for Preparation of Standard Operating Procedures of BLDE(DU)SMO		

Purpose

This SOP describes the process for writing, reviewing, distributing, and amending SOPs within the BLDE(DU) SMO, and also to provide a tool for training new personnel in the procedures by which specific activities will be performed at BLDE(DU) SMO.

This SOP will provide clear, unambiguous instruction to conduct activities of the clinical research in accordance with the ICMR guidelines 2006, Schedule "Y" (Drugs and Cosmetic Act 1940: Amendment 20th Jan 2005), ICH (International Conference on Harmonization) Good Clinical Practice (GCP),National Ethical Guidelines for Biomedical and Health Research Involving Human Participants, 2017; New Drugs and Clinical Trial Rules, 2019 and guidelines of Central Drugs Standard Control Organization (CDSCO) etc.

Scope

This SOP covers the procedures of writing, reviewing, distributing, and amending SOPs within the BLDE(DU) SMO

Procedure

Dean R&D BLDE(DU) in consultation with BLDE(DU)SMO will determine the activity which requires SOPs and will appoint SOP team to formulate the SOPs. SOP team will prepare the draft of the SOPs with description of the procedure. The draft SOPs will be reviewed by BLDE(DU) SMO SOP review team. SOP team will be responsible to amend the SOPs as and when required. The finally reviewed SOP will be approved by Dean R&D, BLDE(DU)will then be signed. SOP team will also assess the request(s) for SOP revision Propose a new, or modification in existing SOPs as needed, Select the format and coding system for the SOPs, Draft the SOP, Review the draft SOP Submit the draft for approval.

Implementation, distribution and filing of SOPs

Approved SOPs will be implemented from the effective date. The Dean R&D and BLDE(DU) SMO will discuss the approved SOPs with the Investigators and instruct them to implement the SOP accordingly. Approved SOPs will be distributed to all the core committee and notified to the distribution list. When revised version is distributed, the old version will no longer be effective. A copy of the old version will be

archived in a master file. One complete original set of current SOPs will be archived in the SOP master file, by the SMO and maintained in the Office. Photocopies made from the paper versions of the SOP will be considered official only if stamped and signed by Dean R&D and BLDE (DU) SMO or authorized individual. A distribution log should be maintained.

Old SOPs should be retained and clearly marked “superseded” and archived in a file by the BLDE(DU) SMO.

Applicable Staff

This SOP applies to all the personnel’s of the BLDE(DU)SMO SOP team , clinical research team and the PI and others who may be responsible for making decisions regarding conduct of the research studies at Site.

Sno.	Contents
1.	Objectives
2.	Prior to Intimation of the study
3.	Make sure that the facilities should sufficient to allow the study to be undertaken efficiently.
4.	Arrange archiving of trial documents according to GCP and regulatory requirements. It should important to check
5.	If the IEC and others approve the trial, sign the final copy of the protocol and confirm in writing that he/she has read and understood, and should adhere to, the protocol, study procedures and ICH Good Clinical Practice, should collaborate with the monitor, and accords with Sponsoring agencies on publications policy.
6.	During the Study
7.	After Completion of the study

Note: *When a trial is sponsored by another agency/pharmaceutical company, the Investigator may also be requested to follow their procedures in order to comply with company obligations. Agreement between all parties should be discussed before initiating the trial.*

Aim:

To define Investigator responsibilities and to provide instruction, when performing clinical studies facilitated by BLDE (DU)'s Shri B.M.Patil Medical College Hospital & Research Centre, Vijayapura

Objectives:

i. To provide the Investigator with general instruction to ensure that he/she understands and accepts the obligations while undertaking the study.

ii. To ensure that the study should be planned, set up, conducted, documented and reported according to the protocol, related site SOPs, Recent IEC SOPs, ICMR Guidelines, ICH GCP and applicable local regulatory requirements.

iii. To ensure that the rights, safety, and wellbeing of study subjects/Participants are protected.

iv. To ensure that data generated, collected should be documented with accuracy, consistency and integrity.

v. To ensure that the Investigator should be familiar with the study procedures, verification procedure, audits and delegation of duties.

vi. To be responsible for the third party staff (Site management organization employees), involved in their respective clinical trials.

Co-investigators:

Co-investigators should be authorized health care professionals who work along with the PI at trial site, (e.g. other Consultants in the department, Post Graduate Medical students).The co-investigator may carry out all or part of the PI's duties, and must be available to act up as PI whenever the PI should unavailable for any length of time (e.g. annual leave) or in an emergency situation that could affect its safe conduct or over sight of the trial.

Note: *PI/Co-I not affiliated to the BLDE (DU) SBMPMC Hospital Vijayapura, cannot be delegated in the clinical trial team.*

II. Prior to initiation of the study: The Investigator should:

Investigator should:

i. Be interested in the scientific aspects of the study and ensure that the study full fill the needs of public health within the country or the population in which it should be conducted.

ii. Ensure the confidentiality of the product, the protocol and trial procedures by signing a confidentiality agreement in writing to sponsoring agencies/CRO.

iii. Have sufficient time free from other obligations to carry out the trial.

iv. As clinical trials are time consuming, the Investigator should ensure sufficient time dedicated to the study, including supervision of study staff.

v. Review Investigator's Brochure and any up-to-date information on the investigational product**.**

vi. The Investigator must be familiar with the product, including pre-clinical toxicology, pharmacology, pharmacokinetics and up-to-date clinical data.

vii. Review and discuss investigator's 'SOP's and protocol with the Clinical Monitor.

viii. The Investigator should clearly define; Factors that may alter the feasibility and acceptability of the trial. An adequate recruitment rate for the clinical trial, provide information about retrospective number of patients who would have satisfied the including.

ix. Make sure that the procedures stated in the study protocol in his/her center should fully under stood. The Investigator should ask the Clinical Monitor to clarify any points of possible misunderstanding.

x. Make sure the availability of adequate medical, paramedical and clerical staffs to support the study and to deal with foreseeable emergencies**.**

III. Make sure that the facilities should be sufficient to allow the study to be undertaken efficiently. Ensure:

- Confidentiality and safety of trial subjects.
- Facilities for subject follow-up /adequate equipment, care and examination.
- Adequate facilities for Investigational Medicinal Products storage
- Adequate facilities for laboratory assay of the Subject's blood parameters/investigations.
- Adequate facilities for retention of trial documents, ensuring confidentiality of all information about trial subjects and information supplied by BLDE(DU)'s Shri B.M.Patil Medical College Hospital & Research Centre, Vijayapura/sponsoring agencies.
- That the IPD trial subject should be in house in the Private Wards

IV. Arrange archiving of trial documents according to GCP and regulatory requirements. It is important to check.

- The duration of retention of patient records with the Institution's archive. In case the Institution's archive does not ensure retention of documents for the period of time requested by sponsor, the Investigator must arrange for the retention of the subject's source documents /records for the period requested by sponsor and regulatory requirements.

V. If the IEC and others approve the trial, sign the final copy of the protocol and confirm in writing that he/she has read and understood, and should adhere to, the protocol, study procedures and ICH Good Clinical Practice, should collaborate with the monitor, and accords with Sponsoring agencies on publications policy.

Submit required documents to the Site Management Organizations of SBMPMC Hospital Vijayapur, including:

- Signed agreement to comply with this SOP.
- Approved protocol, signed and dated.
- Approved informed consent form and other subject information, advertisement (Local language and English translation).
- Investigator's and co-investigator's Curriculum Vitae (CVs).
- Recent ICH-GCP training certificate.
- Authorized duties
- Product exportation/ importation authorization.
- Laboratory certification/ recent list of normal laboratory ranges, dated and signed by lab head/ Investigator.
- Lab Accreditation certificates
- Final Clinical trial agreement
- Signed agreement that the product should not be used before the site Initiation.
- Ethics Committee accreditations
- Visit to archival facilities (situated at second floor) at BLDE (DU) SBMPMC Hospital, Vijayapur

VI. During the Study:

The trial can be initiated (screening and/or enrolment of trial subjects) only after the Clinical trial Monitor has satisfactorily completed a Trial Initiation Monitoring Visit and the SMO Clinical Coordinator has been given written authorization.

i. **Delegation of duties:** PI can delegate the CRC/ Sub-I/ Phlebotomist whenever the study is ongoing at site. PI should provide a comprehensive list of study staff members and the duties that have been delegated to them. It is applicable for both observational and interventional clinical trial/studies at BLDE (DU)'s SBMPMC Hospital, Vijayapur

ii. Completion of the delegation log:

The Clinical trial delegation log provides documented evidence of the appropriate delegation of the PI's responsibilities. The delegation log must state clearly the names of the persons, their role and the activities they are delegated by the PI as well as being signed and dated by PI prior to the activity being undertaken by the individual. All key personnel must be on the delegation log. The PI may delegate activities to a named person in a larger department such as pharmacy, and the relevant trial pharmacist would then take responsibility for the conduct of that activity by that department. The dates of entries must be in chronological order and the PI must NOT pre-sign logs (for members of the research team to add names and delegated duties at a later date).

iii. Investigator's File, Including Storage and Retention:

On initiation of the study, the Investigator must maintain a file containing all the documents related to the trial. During the study, the Investigator is responsible for updating the File regularly adding trial-related documents.

The Investigator should keep the File in under lock and key, in a secure area accessible only to the Investigator and authorized study staff. The Investigator's File and associated source documents should be retained for the time agreed with sponsors. Patient identification codes should be kept for at least 15 years after completion of the trial.

iv. PI must obtain written approval from sponsors and site administrations, prior to destroying records.

- Lab. kits.
- IPs.
- Study Documents. (after completion of15years)

★ *Lab kits and IPs as per sponsor requirements, during the study*

v. The Investigator's File contains:

Administrative and Regulatory Documents

- Composition of IEC of BLDE (DU), Vijayapur
- IEC Accreditation details
- Lab. Head CV and MRC
- Local Regulatory Requirements.
- IEC and other authorities written approval for all documents (protocols/ Amendments, Informed consents and any written information including advertisements for recruitment of study subjects).
- Original Protocol submission letter and initial IEC of BLDE (DU) decision letter.

- Correspondence with the Ethics Committee and the Authorities, including Protocol submission, Amendment submission if any.
- SAE Initial, Follow Up and Final reports and SAE review report by IEC of BLDE (DU) Vijayapura.
- Protocol modification notification, if any.
- Interim report/written summaries of the trial, if applicable.
- Final Report/written summaries of the trial, if applicable.
- Product importation authorization.
- Correspondence about product importation.
- For studies under IND, a copy of the completed and signed Form FDA 1572 and FDA 3455.
- Investigator's and Co/Sub-investigator's C.Vs.
- New Investigator and Sub-investigator's C.Vs along with recent ICH-GCP certificate.
- Authorized Staff Form (ASF).

vi. Investigators /sub-Investigators qualifications and agreements.

- The investigator(s) should be qualified by education, training and experience to assume responsibility for the proper conduct of the trial. Should meet all the qualifications specified by the applicable regulatory requirement(s), and should provide evidence of such qualifications through up-to-date curriculum vitae and/or other relevant documentation requested by the sponsor, the IEC, and/or the Regulatory authorities.
- The investigator should be thoroughly familiar with the appropriate use of the investigational product(s), as described in the protocol, in the current Investigator's Brochure, in the product information and in other information sources provided by the sponsor.
- The investigator should be aware of and should comply with, GCP and New Drugs and Clinical Trial Rules 2019.
- The investigator /institution should permit monitoring and auditing by the sponsor, and inspection by the appropriate regulatory authorities.
- The investigator should maintain a list of appropriately qualified persons to whom the investigator has delegated significant trial-related duties.
- PI should Sign confidentiality agreement.
- PI should sign agreement stating that products will not be used before the Trial Initiation.
- Make arrangement for monitoring visit and obtain approval from the SMO Clinical Coordinator.
- Sub-investigator should be affiliated to BLDE (DU)'s BMPMC Medical College Vijayapura.

vii. Correspondence and Monitoring:

PI should maintain the record of:

- Correspondence with sponsoring agencies (including the telephone call, E-mail etc). Notes of meetings with sponsoring agencies.
- Summary list of site visits (copy).
- Site Initiation visit Report (copy).
- Notification by Investigator to Sponsor of serious adverse event and related reports.
- Documentation of serious adverse event reporting by/ Sponsor to other investigators.
- Investigator interim report/ summaries of the trial for/ sponsoring agencies if applicable.
- Investigator final report/summary of the trial for/ sponsoring agencies, if applicable.
- Sponsoring agencies should inform through Mail / telephonically in advance before visit for site monitoring.
- Copies of the Investigator's interim report/ written summaries of the trial to the IEC of BLDE (DU) and authorities.
- Monitoring visit of IEC members at site: PI/CRC should arrange for the all study related documents for Monitoring. IEC secretary will be informed via mail/ letter about the IEC monitoring visit. IEC members select randomly the studies which have been approved and ongoing studies at the site.
- Ensure to submit the SIV and SMV report to IEC of BLDE (DU) Vijayapura.

viii. Compliance with study protocol

- The investigator/ institution should conduct the trial in compliance with the protocol agreed by the sponsor and if required, by the regulatory authorities and which have been given approval / favorable opinion by the IEC of BLDE (DU). The investigator and the sponsor should sign the protocol, or an alternative contract, to confirm agreement.
- The investigator should not implement any deviation from, or changes in the protocol without agreement by the sponsor and prior review and documented approval/favorable opinion from the IEC of BLDE (DU) of an amendment, except where necessary to eliminate an immediate hazard(s) to trial subjects, or when the change(s) involves only logistical or administrative aspects of the trial.
    - ★ *(E.g. change in monitor(s), change of telephone number(s).*
- The investigator or person designated by the investigator should document and explain any deviation from the approved protocol.

- The investigator may implement a deviation from or a change of the protocol to eliminate an immediate hazard(s) to trial subjects without prior IEC of BLDE (DU) approval /favorable opinion. As soon as possible, the implemented deviation or change, the reasons for it, and if appropriate, the proposed protocol amendment(s) should be submitted:
  - **a.** To the IEC for review and approval/ favorable opinion,
  - **b.** To the sponsor for agreement and, if required,
  - **c.** To the regulatory authorities

xi. Adequate sources:

- The investigator should be able to demonstrate (e.g., based on retrospective data) a potential for recruiting the required number of suitable subjects within the agreed recruitment period.
- The investigator should have sufficient time to conduct and complete the trial within the agreed trial period.
- The investigator should have an adequate number of qualified staff and adequate facilities for the given duration of the trial to conduct the trial properly and safely manner.

VII. On Completion of the study:

- The CRA has to confirm the close out visit with the Investigator/study site. The letter should detail all persons expected to attend and all administrative documents, IMP and regulatory documents required for review at this visit. The CRA should confirm recruitment status at the end or premature end of the trial. If the site is to be closed prior to the end of the trial, a reason for early closure should be clearly documented.
- The CRA should ensure that all Serious Adverse Events (SAEs) have been reported by the Investigator to the Sponsor and that the investigator should be aware of any future communication and follow up on any ongoing SAEs. If applicable, a line listing of all SAEs/SUSARs that have occurred at the site should be filed in the TMF. If closing the lead site in a multi-center trial, a line listing for all the SAEs/SUSARs at each site should be filed in the TMF.
- The CRA should ensure that all outstanding queries regarding data should be resolved at the time of the close out visit.
- All Outstanding issues raised during from previous monitoring visits should be resolved or appropriately documented.
- The CRA should verify that final drug accountability is complete
- If applicable, the CRA should ensure that Sponsor authorization for IMP destruction has been obtained and the destruction or return of unused or partially used IMP should appropriately be commented and documented in the Pharmacy appropriate file.
- PI along with the study CRA Should review the all study related documents in study close out visit. On completion of the study, all the study documents should be archived.
- *(**Please Refer: SOP15/V1.0 for archival study documents**)*

Sno.	Contents
1.	Purpose
2.	Scope
3.	Procedure

Purpose

To describe the procedures for assessing the feasibility of conducting a study at Shri B M Patil Medical College Hospital and Research Centre (BMPMCHRC) (referred as Site) in compliance with standard protocol. Site is committed to maintain the highest scientific, clinical and ethical standards while conducting research at Site. Further, Site 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 Site. This standard operating procedure (SOP) describes the steps for assessing the feasibility of conducting a research study at Site.

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 SITE research network.

Scope

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

Procedure

Protocol Assessment

When a Sponsor/CRO contacts the study Site about a potential study, the Principal Investigator (PI) will assess whether or not it would be feasible to conduct the protocol with the existing staff and facilities.

Clinical/Scientific/Ethical Feasibility

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

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.

Regulatory Feasibility

The PI reviews the protocol to determine whether there is anything required that may be problematic when submitting the project to the Institutional Ethics Committee of BLDE (DU) [referred as IEC BLDE (DU)]. As part of the review the Clinical Trial Coordinator (refereed as CTC) can consult with IEC BLDE (DU).

- The PI must check the following points before submitting the protocol to the IEC BLDE(DU) for approval, as IEC BLDE(DU) 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.

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.
- The PI and CTC prepare the budget worksheet.
- The budget worksheet is compared with the sponsor's budget.
- The PI and CTC will negotiate with the sponsor to establish a feasible budget. Once an agreement is made, the budget will be signed by the PI and sent to the sponsor.
- If an agreement cannot be reached with the study sponsor to cover all costs of the study, the PI and CTC will work together to determine whether the study will be conducted at SITE.
- The Legal expert will facilitate legal review of the contract.

Decision

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

Applicable Staff

This SOP applies to all the personnel's of the BLDE(DU)SMO clinical research team and the PI and others who may be responsible for making decisions regarding conduct of the research studies at Site.

Prepared by		**Page no: 18-20**
Reviewed & Approved by		**BLDE(DU)SMO**

BLDE(DU) SITE SOP	Version 1.0	Revision 0.0	Effective Date: 29/May/2023
SOP No	**TITLE**		
SOP 03/V1.0	**SOP for Communication with Sponsor or Contract Research Organization (CRO)**		

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2.	Scope
3.	Procedure

Prepared by		**Page no: 21-25**
Reviewed & Approved by		**BLDE(DU)SMO**

Purpose

This standard operating procedure (SOP) describes the communication between BLDE(DU)SMO 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 Site and to ensure proper documentation of communications with the Sponsor/CRO concerning study activities.

Scope

This SOP applies to communications between the BLDE(DU) SMO 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.

Procedure

General communications

- Provide the sponsor/CRO a contact list of BLDE(DU)SMO site personnel involved in study start up, along with each individual's role and responsibilities.
- Communicate regularly, courteously and in accordance with Site 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 BLDE(DU) SMO's SITE MASTER FILE.
- Retain all sponsor-generated communications regarding conduct of the study (e.g., teleconference announcement) in the correspondence section of the SITE MASTER FILE.
- 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.

Pre-Study communication

- The Clinical Trial Coordinator 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 at Site.
- 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 Site Master File.
- 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 Site Master File.
- 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.

Communications while the study is ongoing

- Investigator/Clinical Trial Coordinator 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 Site Master File.
- Communicate significant regulatory changes as per the sponsor's requirements (e.g., SEC acknowledgement of an unanticipated issues or protocol deviation, IEC BLDE (DU) 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 BLDE (DU).. 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 BLDE (DU) as per IEC BLDE (DU) SOP. Notification of other key research personnel and/or enrolled subjects may be necessary (e.g., new risk identified related to investigational treatment).

Communication after study is completed

- Inform IEC BLDE (DU) regarding scheduled site close out visit.
- Communicate with sponsor and confirm the close out date.
- Provide the sponsor/CRO with any IEC BLDE (DU) required correspondence (e.g. information requires in the SVIEC 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 BLDE (DU) in the required IEC BLDE (DU) format.
- File all the communication in the appropriate section of the SITE MASTER FILE.

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 CLINICAL TRIAL COORDINATOR or delegate will file the Telephone Contact copy in the SITE MASTER FILE.
2. Letters and Faxes – All study personnel will make copies of all correspondence written to the Sponsor/CRO. The CLINICAL TRIAL COORDINATOR or delegate will file this correspondence in the SITE MASTER FILE.
3. E-mails – All study personnel will print out copies of critical e-mails with the Sponsor/CRO. The Clinical Trial coordinator or delegate will file this correspondence in the Site Master File 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.

Applicable Staff

This SOP applies to all the personals of the BLDE(DU) SMO clinical research team involved in communication with the Sponsor/CRO and responsible for the management of the data.

These include the following:

- BLDE(SMO) office
- Principal Investigator
- Co-Investigator
- Clinical Trial Coordinator
- Pharmacist
- Support Staff

Sno.	Contents
1.	Purpose
2.	Scope
3.	Procedure

Purpose

To describe the procedures related to communication with the IEC BLDE (DU) 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 BLDE (DU).

Scope

This SOP will apply to all studies being conducted at Site.

Procedure

Interactions with the Institutional Ethics Committee [IEC BLDE (DU)] continue throughout the duration of a research study. Establishing effective ongoing IEC BLDE (DU) communication and reporting procedures are essential to the successful management of research studies. An effective working relationship with the IEC BLDE (DU) 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 SVIEC required during the entire course of the research study, the phases could be:

Initial Submission of project to IEC BLDE (DU)

1. Detailed description of project submission

- The PI/ Co-I/CTC should submit all study related documents to the IEC BLDE (DU), no fewer than fourteen (14) days before the scheduled meeting.
- The PI/Co-I/CTC should complete the IEC BLDE (DU) submission form (Refer IEC BLDE (DU)) and PI must sign and date in the form wherever required.
- PI/Co-I/CTC must check the submissions as per the IEC BLDE (DU) checklist (Refer IEC BLDE (DU) SOP) to ensure that all mandatory forms and documents are enclosed.
- The CTC will submit the signed forms and documents to the IEC BLDE (DU). These include, but are not limited to:
    - Covering letter with brief description regarding the list of documents enclosed for IEC BLDE (DU) approval, including the no. of copies submitted, document enclosed relevant version number and date of all the documents.
    - Project submission Form as mentioned above
    - Study protocol
    - Other related documents necessary for initial review as mentioned in the IEC BLDE (DU)
    - Curriculum Vitae and updated GCP certificate of the investigator and study team.

- IEC BLDE (DU) fees cheque in the favor of "Member Secreatry", in case of sponsored studies.
- Number of copies required for IEC BLDE (DU) submission will be as per IEC BLDE (DU) SOP

Note: One additional copy for PI Acknowledgement

The PI/CTC should keep a copy of the acknowledged IEC BLDE (DU) stamp with sign and date) submission letter of the above mentioned documents in the Site Master File (SMF) and send scan or copy to the sponsor (via mail or courier as required by the sponsor).

PI/CTC must document the unique "Project no." given by the IEC BLDE (DU) after project submission for future communication and collect updated SVIEC membership roster and IEC BLDE (DU) registration number and should place in the Site Master File (SMF).

2. EC Response

The PI and CTC should ensure that the letter of response from the IEC BLDE (DU) includes the following information:

- Clinical study identification, protocol number and title;
- Name and version date of all documents reviewed by the IEC BLDE (DU).
- Date of review by the IEC BLDE (DU)
- 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 BLDE (DU) in case of any suggested modifications)
- If conditional approval given, it is not valid for more than 6 months (Refer IEC BLDE (DU) SOP)
- Procedures for appealing the decision/opinion of the committee;
- Any other information, if applicable, as described in the IEC BLDE (DU) SOP
- Date of renewal of approval;
- Signature of the IEC BLDE (DU) 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 PI/CTC should keep an original copy of the SECs approval letter in the SMF and provide one copy to the sponsor/CRO (via email/fax).
- Immediately after receiving IEC BLDE (DU) approval, register the study on CTRI and if applicable on ClinicalTrials.gov
- Notify IEC BLDE (DU) after receiving registration number.

Study Progress

PI can start project at site after receiving approval letter from IEC BLDE (DU) and as study progress at site PI must communicate with IEC BLDE (DU) for all required notification and reporting such as:

Protocol Amendments

a. Major Amendments

- Notify the IEC BLDE (DU) 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 BLDE (DU) SOP)
- Number of copies required for IEC BLDE (DU) submission will be as per IEC BLDE (DU) SOP
- Note: One additional copy for PI Acknowledgement
- The PI/CO-I/CTC should obtain a copy of the acknowledged (IEC BLDE (DU) stamp with sign and date) amendment submission letter of the above mentioned documents, and file the same in relevant section of SMF 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 BLDE (DU) approval, and should immediately implement the documents at the site after approval.
- Document the approval letter in the relevant section of the SMF 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 BLDE (DU) (Refer IEC BLDE (DU) SOP).

This may include but may not restrict to:

- Renewed insurance policy
- DCGI and DGFT approvals
- Administrative notes
- Documents of administrative nature

Deviations/Violation and Waivers

- Submit protocol deviations/violations and waivers to the IEC BLDE (DU) for review and approval according to IEC BLDE (DU) 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 BLDE (DU) requests
- PI/CO-I//CTC must submit the deviations /violations/waiver reports as per the site SOP.
- Protocol deviation/ non-compliance/ violation/waiver can be detected during monitoring visit for the investigator initiated study by IEC BLDE (DU) and for sponsored studies by the monitor/ CRA also. Sometimes it can be detected by PI /study team member.
- The SVIEC 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 BLDE (DU) within reasonable time limit
    - fail to adhere to protocol required procedures
- Protocol Waiver is analogous to a Protocol Deviation, except that prior IEC BLDE (DU) 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 BLDE (DU) action could include one or more of the following:
    - IEC BLDE (DU) will inform the PI that IEC BLDE (DU) has noted the violation / noncompliance /deviation and inform the PI to ensure that deviations / noncompliance / violations do not occur in future and follow IEC BLDE (DU) recommendations.
    - IEC BLDE (DU) 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 BLDE (DU) are implemented by the PI and found to be satisfactory by the IEC BLDE (DU) Suspend the study for a fixed duration of time
    - Inform the Director, SITE
    - 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 BLDE (DU) acknowledged deviations/violations and waivers forms submitted in relevant file and send one copy to the sponsor/CRO.

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 BLDE (DU) according to the IEC BLDE (DU) 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 BLDE (DU) correspondence, if any, in the SMF.
- Copies of the associated IEC BLDE (DU) correspondence should be provided to the sponsor according to sponsor requirements.
- Report any other information to the IEC BLDE (DU) 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 BLDE (DU) /DSMSC/Sponsor.
- 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 BLDE (DU) 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 BLDE (DU) /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 BLDE (DU) SOP) will be reported to IEC BLDE (DU) /DSMSC
- Sponsor/CRO will send two sets of the offsite SAE, CTC will submit one to the DSMSC (as per the IEC BLDE (DU) SOP) and file acknowledged (Stamped, signed and dated by the IEC BLDE (DU) /DSMSC) copy in the SMF 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 BLDE (DU) /DSMSC.
- PI/Co I may receive email or letter as applicable, if any queries are raised by the SEC/DSMSC Secretary. PI/Co I must reply to the query immediately.

b. Onsite SAE reporting:

Kindly Refer SOP for Safety Reporting

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.
- PI/Co I/CTC must submit continuing review report/annual report to the IEC BLDE (DU) annually, subsequent to the date of IEC BLDE (DU) approval to renew approval before two months of expiry.
- All information must be provided to IEC BLDE (DU) /DSMSC, as requested in the continuing review application form (Refer IEC BLDE (DU) SOP)
- The Investigator/CTC should submit the continuing review application well in advance i.e. 12 months after IEC BLDE (DU) 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 BLDE (DU), and file the same in SMF and send a copy to sponsor (via email/fax).
- The IEC BLDE (DU) Secretary 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 BLDE (DU) /DSMSC, if the continuing review report/annual report is approved / accepted.
- The letter should be file in the SMF 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 BLDE (DU) approval, the PI cannot recruit any patient during that phase, till IEC BLDE (DU) /DSMSC, approve the continuing review report.

Study Termination

a. Premature Termination / Suspension /Discontinuation of the study

- Research studies are usually terminated as per the recommendation of the IEC BLDE (DU),PI, Sponsor or other authorized bodies wherein subject enrollment and subject follow-up are discontinued before the scheduled completion of the study.
- The IEC BLDE (DU) /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 BLDE (DU) secretary can send a notification letter for termination/suspension/discontinuation or query letter to request additional information to the PI.
- In case Sponsor is terminating the study, PI will receive a letter from Sponsor/CRO for the termination/suspension/discontinuation with the explanation for the same.
- PI and CTC will prepare the protocol termination package along with covering letter, Premature Termination Report (Refer IEC BLDE (DU) SOP) signed and dated by PI and another material (e.g. letter received from the Sponsor/PI/ IEC BLDE (DU))
- CTC must obtain acknowledgment of the IEC BLDE (DU) member secretary on the covering letter and file it in the SMF.
- PI/CTC must reply immediately in case of any query generated or any further information requested from the IEC BLDE (DU).
- PI will receive acceptance letter from the IEC BLDE (DU), 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.

Study completion

- On the Study completion the PI/ CTC will notify the IEC BLDE (DU) of the study completion using study completion form (Refer IEC BLDE (DU) SOP)
- Additionally PI and CTC must submit letter provided by the sponsor/CRO to give adequate and sufficient information.
- CTC must submit one hard copy + soft copy of Study Completion Reports

Applicable Staff

This SOP applies to all the personals of the BLDE (DU) clinical research team and others who may be responsible for the interaction with the IEC BLDE (DU)

These include the following:

- Investigator
- Research Team (listed in the delegation log)
- CTC
- IEC BLDE (DU) staff/member

I. Policy:

The ethical conduct of clinical trial designed should base on the voluntary consent of the subject, who has been appropriately informed about risks and benefits of the study and should be designed to protect the rights, safety and wellbeing of participants. It is responsibility of the investigator to ensure compliance with all ethical standards, guidelines and federal and state regulations have been met with through the language of the informed consent document. It is responsible of PI to ensure that informed consent has been properly obtained from the subject or the subject's legal representative.

II. Objective:

This SOP gives the procedure for obtaining informed consent form all trial subjects.

III. Scope:

Applicable for all Clinical trials at the site.

IV. Definition-

Informed Consent: A process by which a subject voluntarily confirms his or her willingness to

Participate in a particular clinical trial, after having been informed of all aspects of the study that should relevant to the subject's decision to participate. Informed consent is documented by means of a written, signed and dated informed consent form.

V. Procedure:

Following should be followed:

- All the clinical trial related ICF should be obtained in the respective Principal investigator OPD / Work station.
- The Subject Information sheet and the Informed Consent form should be given to the subject on the day of Screening.
- The Study Coordinator/ designated person should use a copy of Institutional Ethics Committee of BLDE (DU) approved 'Subject Information Sheet and Informed Consent Form' (SIS/ICF) to the subject in the language best understood by him/her.
- Investigator/designated person should give study related information from the Institutional Ethics Committee of BLDE (DU) approved 'Subject Information Sheet and Informed Consent Form to the Participants.

- Investigator/designated person should inform and explain the subject about the purpose of the study, the study procedure, the risk and discomforts associated with the study procedure and restrictions, the adverse effects of study drug, housing period, duration of the study, the remuneration, number of volunteers to be included in study, voluntary participation, withdrawal from the study, identity confidentiality etc., from the IEC/ approved 'SIS/ICF'. The name of the subject to whom the SIS/ ICF is issued, signature should of the person counseling the subject should be documented in the source document.
- Investigator/ designated person should take the Informed Consent in one to one manner. The Investigator/ designated person should answer to all personal queries of the subject or their Legal Acceptable Representative (LAR) or Guardian during this session.

- Investigator/designated person should inform that the eligible and interested subject or the volunteer's Legally Acceptable Representative (LAR) should have to sign the SIS/ ICF and if the subject is unable to read and if the Legally Acceptable Representative (LAR) is unable to read then an impartial witness who should independent of the study should be present during the entire informed consent discussion and should explain the contents of the SIS/ ICF to the subject or the volunteer's legally acceptable representative in the best language understood to the volunteer.
- Each subject should be given sufficient time and opportunity to enquire about the study drug or the study procedure or consult his/her family physician to decide for his/her participation in the study.

- The Investigator(s), Sponsor or the staff should not force or unduly influence the potential volunteer/ subject to participate or to continue to participate in the study.

- Investigator/Physician/ designated person should ensure that the subject has understood all the aspects of the study including the purpose of the study, the study procedure, the risk and discomforts associated with the study procedure and restrictions, the adverse effects of study drug, housing period, total blood loss, duration of the study, the remuneration, number of volunteers to be included in study, voluntary participation, withdrawal from the study, identity confidentiality etc, from the Institutional Ethics Committee Of BLDE (DU) approved 'SIS/ICF' and should participating in the study willingly.

- Investigator/designated person should document the name of the subject to whom the SIS/ICF is issued and the name of Investigator/designated person counseling the volunteer, in the source document.

- The volunteer/ volunteer's legally acceptable representative (LAR) should write all the details like his/her name, address, date of birth, qualification, occupation, annual income of the volunteer, name of nominee(s), relation of the nominee with the subject, address of the nominee and sign the ICF(declaration)with date.
- In case of the volunteer/legally acceptable representative is unable to read/write then the subject should give the left thumb impression at the appropriate place and the impartial witness should write volunteer's name and date below the thumb impression and all the respective details as mentioned above in the ICF, with the consent of the volunteer. The impartial witness should write his/her name, address and contact details, sign and date the declaration for witnessing the entire process of obtaining the informed consent of the volunteer.
- The impartial witness by signing the consent form attest that the information in the consent form and any other written information is accurately explained and is apparently understood by the subject's legally representative or the guardian, and that the informed consent was freely given by the subject or the volunteer's legal representative.
- The Investigator /Co-Investigator should sign and date and should put his / her name in the ICF.
  - ★ Site coordinator should give photo copy of signed consent to Subjects/Legally Acceptable Representative.
  - ★ The researcher has an obligation to convey details of how confidentiality should be maintained to the participant.
    - After the completion of consent process the study delegated person should record the all protocol related information in sources documents.
    - If the patient is illiterate and unable to write in ICF then LAR can write the details on behalf of the patient and no LAR signature should require authenticating the same. But reflection of the movement should be recorded in ICF process.

- **Applicable rules and regulations:**
  - FDA21CFR50.20—General Requirements for Informed Consents
  - National Ethical Guidelines for Biomedical and Health Research Involving Human Participants-2017
  - HHS45CFR46.116—General Requirements for Informed Consent New Drugs and Clinical Trial Rules, 2019

BLDE(DU) SITE SOP	Version 1.0	Revision 0.0	Effective Date: 29/May/2023
SOP No	TITLE		
SOP 06/V1.0	SOP for Roles and Responsibilities of Clinical Research Coordinators (CRC)		

1. **Purpose**

This SOP defines the procedure and recommendation for training of study team members and appropriate handover to CRC/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 members 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 trial-related task(s).

The purpose of a handover should to ensure continuity of operations when the study team member, usually responsible, should 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.

2. **Scope:**

This SOP should apply to all study research coordinators at site management Organization in BLDE (DU) SBMPMC Hospital Vijayapura.

3. **Responsibilities:**

- Study startup activities like Feasibility/Synopsis and Clinical disclosure agreements.
- Review and develop a familiarity with the study protocol (e.g. study procedures and timelines, inclusion/ exclusion criteria, confidentiality).
- Documentation of date of training and signatures of study personnel trained on study specific in training log.
- Collection of documents needed to initiate the study and submit to the sponsor (investigators CV along with relevant supportive documents).
- Conduct or participation in the informed consent process, interactions with the IEC and discussions with research participates, including answering any questions related to the study.
- Obtaining appropriate signatures and dates on forms at appropriate places. Assuring that amended consent forms are appropriately implemented and signed/dated.
- Screening of subjects for eligibility using protocol specific inclusion and exclusion criteria, documenting each potential subject eligibility or exclusion. Creating and utilizing eligibility Checklist for inclusion/exclusion criteria.
- Coordinating for participant’s tests and procedures, including scheduling and registration of subjects with hospital Outpatient/ inpatient departments at site (e.g. Radiology for CT scan).

- Collecting data as required as per protocol requirement. Assuring timely completion of Case Report Forms.
- Maintaining study timelines as per the event schedule (e.g. subject visits, procedures and data entry is completed within the allotted time as per protocol).
- Maintaining adequate inventory of study supplies. While handling investigational drugs/devices, following the sponsor protocol and/or UCSF Policy on Investigational Drug/Device Accountability.
- Completing study documentation and maintaining study files in accordance with sponsor requirements and University policies and procedures including, but not limited to, consent forms, source documentation, narrative notes if applicable, case report forms, and investigational material accountability forms.
- Maintaining effective communication with sponsor, research participants, IEC of BLDE (DU) and PI during the course of the study.
- Working with the PI to manage the day-to-day activities of the study including problem solving, communication and protocol management.
- Reporting all findings and correspondence from external or internal study monitoring and audits to the research manager and department Chair in a timely manner.
- Assisting the PI in reporting of research-related incidents, including protocol deviations or potential violations, and correspondence from external or internal study monitoring and audit teams to the IEC of BLDE (DU), Vijayapura in a timely manner.
- Assisting the Principal Investigator in submission of accurate and timely closeout documents to applicable Federal agencies, University IEC, and the sponsoring agency in accordance with Federal regulations and Hospital/University policies and procedures.
- **Study Handover:** If any study team member planning for leave or to resign, he/she must ensure that the proper handover should be 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
    - ★ 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 is changing for the subjects.

- Provide a list of study-specific contacts (e.g., sponsor, monitor, vendors involved etc)
- Provide a list of outstanding.
- The leaving person has to make sure that the documentations related to delegated duties should be up to date and easily available, and if needed, revise when preparing the handover.

If there is a change in PI, the following documents need to be revised and completed;

- Inform Sponsor and IEC of BLDE (DU), regarding the change of 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 handover should be given in order to ensure the continuity of work. The format can be a briefing note, a checklist 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 delegated of duties.
- 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 mentioned above and the date of the handover. The new study team member should undergo documented study-specific training and obtain any required approvals prior to being added to the duty delegation log.

4. Procedure:

Appointment Procedure:

1. The site clinical research coordinators should be appointed in gap pointed through respective site management Organization. Before assigning the CRC to SBMPMC Hospital Vijayapura, the Organization has to intimate the site personnel via mail or letter for communication with proper appointment, specific training letter and period of agreement (If applicable).
2. Study Team Training:
3. On appointment, all study team members should be given an appropriate Specific training study depending on the job specification to possess the right experience. Duty delegation /job responsibility document should be given to every Clinical research Coordinator/ team member.

4. The Medical Superintendent and Director (R & D Cell) recommend that all Investigators, CRC and other study team members must undergo training which should enable them to understand their responsibilities, applicable regulations, guidelines and training should be documented in the training log.
5. Each Investigator, CRC and study team members should 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 acquire knowledge of new or revised SOPs.
6. Good Clinical Practice (GCP) is a universal standard in clinical research that must be followed in every research protocol. GCP training and education is recommended for research team members, especially the Investigator and CRC. However, any member of the research team with a significant role in the conduct of clinical trial must have knowledge of GCP. All members of the clinical research team should be GCP trained and certified.
7. If scheduled, the PI and CRC should attend the Investigator Meeting (IM) (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.
8. Before initiation of study the Sponsor/CRO should organize SIV meeting at site to train all study team members. All study team members should attend the meeting for understanding of the study.
9. In the study start up activities like feasibility/study synopsis, CRC should intimate to the site personnel.
10. The 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 initiation of each new study.
11. Study team members should attend the course to acquire training or to update themselves.
12. PI can also train the study team and should maintain the training record.
13. It is recommended that the PI and study team must maintain the Site SOP training Record.

14. **Entry in to Study drug store at site:** The access should be given only blinded/unblended pharmacist and who should delegated (Delegation log) in clinical study for the IP management. The entry access should be restricted.

5. 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/s
- Research Team (listed in the delegation log)
- Clinical Research Coordinator/s

Staff responsible for Implementation:

- The department and Investigator should ensure that the research team involved in the conduct of the study should comply with this site SOP.
- The department and PI should ensure that at the time of implementation of the SOP, all members of research team at the site management Organization (clinical research unit) in BLDE (DU) Shri B. M. Patil Medical College Hospital & Research Centre, Vijayapura are trained and in an event SOP is be modified, training is provided regarding the change(s) to ensure their compliance with the changes.
- It is the responsibility of each individual who should about to go on short / long term absences or leave their current position / the Agency/third party employees to prepare a hand over file.

BLDE(DU) SITE SOP	Version 1.0	Revision 0.0	Effective Date: 29/May/2023
SOP No	TITLE		
Sop 07/V1.0	SOP for Check-In and Check-Out of the Subject		

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Reviewed & Approved by		BLDE(DU)SMO

I. **Objective:** This SOP gives the procedure for check-in and check–out of subject, from the housing should a before the start and the completion of the hospitalization period in a PK/PD studies.

II. **Scope:** This SOP is applicable to all volunteer/subjects participating in a PK/PD studies. All the PK/PD should be preplanned and made sure to avoid dosing schedules on Sundays (on Sunday Registration counter should be remained closed /Unavailability of the Study Nurses/PIs)

III. **Procedure:**

1.0 Procedure for Subject Check-In (in the first phase (Run) of the study):-

1.1 The subjects who have given the written (signed) Informed Consent and have found eligible for the study in Screening, pre-enrollment checks and are complying with the inclusion and exclusion criteria as mentioned in the study protocol, and who are found negative for alcohol breath testing, Urine screen for drug of abuse and urine pregnancy test or any other screening procedure as mentioned in the study protocol should be checked-in into the private/Semi Private wards as per direction from the Medical Superintendent of BLDE (DU) Shri B. M. Patil Medical College Hospital Research Centre, Vijayapura.

1.2 The Study coordinator/designated person should allot the subject number to each subject in ascending order (01 onwards) in first period of study or as specified in the respective study protocol on a first come first basis.

1.3 Study coordinator/ designated person/ Subject Custodian should check the subject's belongings, clothing and pockets for any prohibited products like gum, medication, cigarettetes and tobacco or sharp instruments.

2.0 Procedure for Check-In For Subsequent Period(s):-

2.1 The PI should carry out the medical check-up (history from the last visit), vital sign measurement and wellbeing assessment, Clinical examination or any other investigation required as specified in the study protocol for the subject, before enrolling for subsequent period of the study.

2.2 Blood/urine samples should be collected and for testing in the Clinical laboratory as specified in the study protocol (if applicable).

2.3 PI should review the above reports and shall record the status of subject's fitness in the CRF.

2.4 If the subject is found to be eligible in all the above procedures, then he/she should be checked-in into the housing area as mentioned in point 1.2.

2.5 The subject who found to be unfit in any of the above parameters should be withdrawn from the study and should be checked-out as per the procedure mentioned in point 3.0. If the subjects have not reported to the study center for subsequent period or if the subject withdrew his/her consent from the study then the details of his/her withdrawal should be documented in the format for Subject Dropout/ Withdrawal/ Termination Form of the CRF.

3.0 Procedure for Check-Out

3.1 Subject should be checked out after completion of the study /after completion of the housing period of each study period or due to withdrawal/ termination of subjects from the study.

3.2 In case subject should discharged after completion of the housing period of each study period or due to withdrawal/ termination of the subjects from the study then the details should be recorded in the format 'Discharge summary' of the CRF of the respective subject.

3.3 The Physician/ designated person should record the vital signs and assess the wellbeing of subject and should perform the Clinical examination before discharge from the Clinical facility.

3.4 The Subject Custodian/ designated person should return the subjects belongings from the locker; should ensure that all the items provided by clinical facility are returned by the subject and also ensure that the subjects are informed about the schedule date and time of subsequent period or ambulatory sample (if applicable). The details of the check-out activity should be recorded in the form in the CRF.

3.5 After completion of the study the Physician/designated person should perform the post study safety evaluation as mentioned in the study protocol.

3.6 Physician/designated person should measure the vital sign, assess the wellbeing of subject, take the 12 lead ECG, perform the Clinical examination and should record details in the 'Post study evaluation form of the CRF of the respective subject.

3.7 Physician and or Clinical Investigator / Co-Investigator should check the ECG report of respective subject and should put the appropriate comment on the same after interpretation.

3.8 As per the requirements of the protocol, the blood and /or urine samples for Post-study Clinical laboratory investigations should be collected and sent to the Clinical laboratory.

3.9 The subject should be advised to contact the responsible person of the study center if any health-related problem arises after discharge from the study center. The details of the telephonic communication should be recorded in the 'Telephonic communication and Subject follow-up form of the CRF.

3.10 After receipt of Post-study Clinical laboratory investigation reports from the laboratory, it should be checked and reviewed by the Physician/ designated person and the details of observation should be recorded in the Post study evaluation form of the CRF of the respective subject. The Physician/ designated person should review the Post study Clinical laboratory report values with the base line (Screening report) values and determine its significance to judge if any Adverse Event has occurred /or any follow-up is required to resolve the same**.**

If any significant abnormal results are found then the subject should be followed up to resolve the same and to ensure subject safety. The details should be recorded as adverse event in the CRF of the respective subject.

I) Objective:

This SOP provides the details of the procedure for dosing the subjects and Monitoring Restrictions incompliance to the study Protocol for the Clinical study.

II) Scope:

The SOP should applicable to PK/PD studies at the site

III) Procedure:

1.0 Monitoring Restriction

1.1 The Subject Custodian/designated person should be responsible for monitoring the compliance of diet, water or any other restriction to be followed by the subjects in compliance with the Study protocol during the hospitalization period of the PK/PD study.

1.2 The Subject Custodian/designated person should monitor these restrictions and should record the details of the pre-dose and post-dose restriction compliance, in the Format for 'Dosing and Restriction monitoring Record' of the CRF of the respective subject. Any deviation should be documented in the CRF and should be justified appropriately.

2.0 Dosing the subject

2.1 The dosing activity during the hospitalization period for Pharmacokinetic studies should be performed under the supervision of the Principal Investigator/ Co-Investigator.

2.2 The Principal Investigator /Co-Investigator should assign the responsibility of dosing to the trained staff.

2.3 Staff responsible for dosing should ensure that gloves, dosing fluid (as per Protocol), flashlight, tongue depressor, scissors (if applicable) and format 'Dosing and Restriction monitoring Record' for the subjects is kept ready on the dosing station well before scheduled time of dosing.

2.4 The dose for each subject should be administered in a staggered manner to maintain subsequent blood collection schedule.

2.5 The designated person should arrange the container containing the dispensed IP as per the subject number in the dosing station before initiation of dosing activity.

2.6 The Subject Custodian should call subject by subject number for dosing prior to the scheduled time of dosing.

2.7 The Designated person should give IP container of the respective subject to the respective staff dosing the subject in the dosing station.

2.8 Staff responsible for dosing activity should verify the subject number and photo on ID card and the subject number on the label on the dispensed IP container before dosing.

2.9 Staff responsible for dosing should assess the wellbeing of the subject verbally before dosing, and should also briefly explain the procedure to be followed for dosing and the restriction to be followed thereafter.

2.10 Staff responsible for dosing activity should administer the IP directly in mouth of subject along with water/dosing fluid or as per the procedure mentioned in the respective study protocol at the scheduled dosing time for the respective subject.

2.11 Staff responsible for dosing activity should remove the duplicate label from the dispensed IP container and stick it on the 'Dosing and Restriction monitoring Record' of the CRF of the respective subject.

2.12 Staff responsible for dosing activity should store the empty IP container/ syringe/ dosing cup/ glass/ tongue depressor used for the subject.

2.13 Staff responsible for dosing activity should record the actual time of dosing and dosing details in the 'Dosing and Restriction monitoring Record' of the CRF of the respective subject and should sign and date it.

2.14 The Clinical Investigator/ Co-Investigator should verify the dosing activity and the compliance of the restrictions and should sign and date this record.

2.15 The Designated person should collect unused IP(s) (due to subject dropout/terminated before dosing) and should take it to the IP storage room and should record in the IP accountability Record as per the respective SOP.

2.16 In case of formulation where there is any specific requirement for administration/ application of the IP, the procedure for dosing/dose administration should be followed as per respective Study Protocol/ Pack Insert/on the IP container.

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1	Objective
2	Scope
3	PROCEDURE: - Procedure for blood sample collection. - Pre caution to be taken for Photo sensitive and Temperature Sensitive Drug Product. - Transfer of samples from the Clinical Facility to the Bio-analytical Facility.

I. Objective:

This SOP defines the procedure for collection and processing of blood samples, separation of plasma/ serum from blood samples, storage and transfer of plasma/ serum/ whole blood samples.

II. Scope:

This SOP is applicable to PK/ PD and Phase I, II, III and IV studies.

Precautions:

Proper care should be taken while handling the blood sample/ plasma/ serum during transfer to avoid spillage. (trained Phlebotomist should be appointed from Sponsor/ Hospital if Applicable) Correctness of the Vacutainer type and capacity and to be used for the collection as per the study protocol should be checked.

III. PROCEDURE:

A. Procedure for Blood Sample Collection

1. The Phlebotomist/ Nursing Staff/ designated person should arrange the labeled Vacutainer/ centrifuge tubes in the racks in each blood sample collection station as per the sampling time point.
2. The Phlebotomist/Nursing staff/designated person should ensure the availability of the required medical accessories like labeled Vacutainer /centrifuge tubes with appropriate anticoagulant as mentioned in the study protocol, syringes, cotton, tourniquet, Vacutainer/centrifuge tube stands, needles, gloves and blood sample collection formats, or any other requirement(s) as specified in the study protocol, on the sample collection table before the start of the blood sample collection activity.
3. The Phlebotomist/ Nursing staff/ designated person of standby collection station should check the pre-labeled Vacutainer /centrifuge tubes and should arrange them in sequence on the rack for each sample collection station and should enter the details in 'Pre-Sample Collection Vacutainer/Tube Check format'.
4. Intravenous cannula should be inserted in the fore arm of the subject for collection of the blood samples for Pharmacokinetic study.
5. The Subject custodian should call the subject(s) by their subject number in sequence and should direct them to the respective sample collection station, at least 2 minutes before the scheduled blood sample collection time.
6. Bed-side blood sample collection should be done as per requirement or if stated in the study protocol.

7. The Phlebotomist /Nursing staff/designated person should verify the Vacutainer/centrifuge tube label for the study code, sampling time and the subject number and should also verify the identity of the subject by checking photograph and subject number on the Identity card and the subject number on the wrist band, before the start of each blood sample collection.
8. The sample collection timings should be staggered as per the dosing time of each subject. Phlebotomist/ Nursing staff/ designated person should record the schedule time of each sample time point mentioned in the 'Blood Sample Collection Details' of the CRF for each subject.
9. The Phlebotomist/Nursing staff/ designated person should discard the initial saline mixed blood (approximately 0.3 ml. or volume as per Study specific protocol) from the intravenous cannula using a 2 ml syringe before collecting the blood sample.
10. The Phlebotomist/ Nursing staff/ designated person should secure the disposable (10ml/ 5 ml/ 2 ml) syringe to the intravenous cannula, should open the three-way stop-cock and should collect the blood sample on the scheduled time within two minutes (or as mentioned in the study protocol The volume of the blood sample to be collected should be as per the Study Protocol. After collection of blood samples, the Vacutainer/ tube with samples should be shaken mildly for mixing with the anticoagulant in the Vacutainer/ tube.
11. After collecting the blood sample, the 3-way stop cock should be closed and the blood sample should be transferred into the respective Vacutainer/centrifuge tubes of the subject.
12. At the time of transfer of blood samples the Phlebotomist/Nursing staff/ designated person should ensure that the samples are transferred into the correct Vacutainer/ centrifuge tubes of the respective subject.
13. After each sample, 1 ml isotonic saline solution should be injected into the 3-way stopcock to avoid blockage of cannula. The 3-way stop cock should be kept closed till the next scheduled sample collection of the subject.
14. The Phlebotomist/Nursing staff/ designated person should record the actual time of each sampling time point for each subject and should sign and date in the format for 'Blood Sample Collection Detail's of the CRF.
15. In case of cannula blockage observed during the sample collection, the blood sample should be collected by direct vein puncture using a syringe with needle, there after the subject can be re-cannulated, if required. Any deviation in the sample collection, time of more than two minutes (or as mentioned in the study protocol) and the reason for the same (cannula block/cannula replaced/ direct prick/ poor blood flow) should be recorded in the 'Blood Sample Collection Details of the CRF of respective subject.

16. The Phlebotomist/Nursing staff/designated person should transfer the vacutainer /centrifuge tubes with blood samples a teach sampling time from each sampling station(s) to the sample processing should.

17. The Technician/designated person should receive the vacationer/centrifuge tubes with blood samples and check for the time point, receiving time, total number of samples received, and record the details in 'Centrifugation and Separation of Biological Samples Record'.

18. In case of requirement of whole blood or serum, the sample should be processed as specified in the respective Study Protocol.

19. The Technician/designated person should place the vacationer/centrifuge tubes in the centrifuge machine.

20. The Technician/designated person should set the speed (RPM), time and temperature (as mentioned in the study protocol) of centrifuge machine and should operate the centrifuge machine as per the Standard operating procedure for Centrifuge machine. The details of the set parameters and the centrifugation start and end time should be recorded in 'Centrifugation and Separation of Biological Samples Record'.

21. After completion of the centrifugation, the Technician/designated person should remove the Vacutainer/centrifuge tubes carefully (without disturbing the contents) from the centrifuge machine and should arrange it in Vacutainer/centrifuge tube stand.

22. The Technician/ designated person should arrange the pre-labeled vials of respective sampling hour sequentially in the rack/tray.

23. The Technician/ designated person should harvest the plasma/ serum from each centrifuged Vacutainer/centrifuge tube using micro pipette with disposal tips without disturbing the sediment layer and should transfer the harvested plasma/serum to respective subject's pre-labeled vials into two aliquots as 'Replicate' (1 ml) and 'Analytical' (remaining quantity) sample. Or as specified in the Study Protocol, and should cap the vials.

24. The Technician/designated person should record the observation [like hemolysed samples (H), missing sample (M), subject not reported (N)], or any other observation as remark in the 'Centrifugation and Separation of Biological Samples Record'.

25. The Technician/designated person should pack these vials with plasma/serum samples of each sampling time point into labeled zip-lock bags (each for Analytical and Replicate samples) of all the subjects, and store in the deep freezer maintained at suitable storage temperature as specified in Study Protocol. The Technician/designated person should record details of samples stored in the deep-freezer.

B. Precaution to be taken for Photo sensitive and Temperature Sensitive Drug Product.

1. For study of Photosensitive molecules, appropriate measures should be taken (like use of sodium vapor lamp/covering the glass windows with dark paper) to avoid exposure to light while performing all the procedures done in sample collection and processing area.
2. The Technician/designated person should use pre labeled amber colored vials for storage of Plasma/Serum samples of light sensitive drug product.
3. For temperature sensitive drug products, the following measures should be taken or should follow the measures/procedures mentioned in the respective Study Protocol.
4. The blood sample should be collected into pre-chilled Vacutainer /centrifugation tube. This Vacutainer/centrifugation tube with blood samples should be placed in ice water bath till it is centrifuged. After centrifugation at the set parameters the plasma/serum should be harvested using micropipettes with disposable tips into pre-labeled vials as 'Analytical' and 'Replicate' sample, these vials containing the harvested plasma/serum should be placed into deep-freezer maintained at a temperature specified in the Study Protocol.
5. The Phlebotomist/Nursing staff/designated person should record the sample time point deviation in the 'Deviation Reporting Form'. The responsible Physician/designated person should also give the details of sample time point deviation, missing samples and the delay in sample time for ambulatory samples to the Statistical Department for considering in the statistical analysis.

A. Transfer of samples from the Clinical Facility to the Bio-analytical Facility.

1. Study Coordinator/ designated person should take the authorization from Clinical investigator/ designated person for transfer of biological samples to the bio-analytical facility and should get the name and address of the bio-analytical facility where the samples have to be transferred.
2. Study Coordinator/ designated person or the Contract Courier person (who should be shipping the samples) should arrange insulated boxes with appropriate coolant before initiation of the transfer activity.
3. Study Coordinator/ designated person or the Contract Courier person should place the temperature monitoring device to record the temperature during the transfer of biological samples.
4. Study Coordinator/ designated person should identify and remove the biological sample boxes/ poly bags from the deep- freezer and should record the retrieval of samples in respective format.

5. Study Coordinator/ designated person should transfer the labeled samples boxes/ poly bags as per the specified requirements, into the insulated box with sufficient coolant to maintain the storage condition of the biological sample during transportation and should seal the box(es).
6. Study Coordinator/designated person should record the details of samples to be transferred in the format for 'Transfer of Biological Samples from Clinical facility to Bio-analytical Facility'.
7. Study Coordinator/designated person or the Contract Courier service person should paste appropriate labels {e.g. warning label as "Biological Samples", "Handle with Care" "Light Sensitive samples" (if any)} and should also paste label mentioning the complete address of the Bio-analytical facility where samples are to be transferred, on the boxes. If Applicable.
8. Study Coordinator/designated person should handover the samples/insulated box(es), the format for 'Transfer of Biological Samples from Clinical facility to Bio-analytical Facility' and the covering letter with the details of the samples, to Contract Courier service person or the person shipping the samples(in case the samples are hand delivered).
9. The Contract Courier service person should sign the transfer format as 'Received by' and should write the time of receipt. The Contract Courier person should also fill the details in the shipment tracking form, and submit a copy of it to the Study Coordinator/designated person.
10. In case the samples are hand delivered the person receiving the sample at Bio-analytical facility should verify details of the sample from the covering letter and/or from the transfer format and sign as 'Received by' write the time of receipt on the format and should acknowledge the receipt of the samples.
11. A copy of this transfer format should be maintained in the Study File at the Clinical site.
12. The person receiving the sample at Bio-analytical facility/ Contract Courier service person should remove the temperature monitoring device and the print of the temperature record during transportation should be maintained along with the Sample transfer format.
13. If it is genetic samples, the Material transfer agreement and Data Transfer Agreement to the Institution/ IEC should be submitted

BLDE(DU) SITE SOP	Version 1.0	Revision 0.0	Effective Date: 29/May/2023
SOP No	TITLE		
SOP 10/V1.0	SOP for Handling and Reporting of AE and SAE		

Sno.	Contents
1.	Objective
2.	Scope
3.	Precautions
4.	Definitions
5.	Procedure - Handling of Adverse Events - Reporting of Adverse Events - System of Pre-Screening for submission of reports of SAE to CDSCO
6.	References

I. Objective:

This SOP gives the procedure for handling and reporting the Adverse Events and Serious Adverse Events encountered during the clinical studies at BLDE (DU) Shri B.M.Patil Medical College Hospital & Research Centre, Vijayapura.

II. Scope:

Applicable to all Clinical studies.

***III.* Precaution:** *Nil*

IV. Definition:

a. Definitions:

★ **Serious Adverse Event:**

Any untoward medical occurrence that at any dose results in death, life-threatening, requires inpatient hospitalization or prolongation of existing hospitalization, results in persistent or significant disability/ incapacity, or should a congenital anomaly/ birth defect.

★ **Serious Adverse Event or Serious Adverse Drug Reaction:**

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 should otherwise life threatening.

★ **Adverse Event:**

An AE should any untoward medical occurrence in a patient or clinical investigation of subject administered a pharmaceutical product and that does not necessarily have a causal relationship with this treatment. An AE can therefore be any unfavorable and unintended sign (including an abnormal laboratory finding), symptom, or disease temporally associated with the use of a medicinal (investigational) product, whether or not related to the medicinal (investigational) product.

★ **Unexpected Adverse Event:**

- ★ Any adverse event occurring in one or more subjects such that, the nature, severity or frequency of which should not consistent with either:
- ★ The known or foreseeable risk of adverse event associated with the procedures involved in the clinical study that should described in (a) the protocol-related documents, such as the IEC-approvedStudyprotocol,anyapplicableinvestigatorbrochure,andthecurrentIEC-approved informed consent document and (b) other relevant sources of information, such as product labeling and package inserts; or

★ The expected natural progression of any underlying disease, disorder, or condition of the subject(s) experiencing the adverse event and the subject's predisposing risk factor profile for the adverse event (if applicable).

1. Relatedness/ Causality assessment of Adverse Event to an Investigational Drug:

Relatedness/ Causality assessment of Adverse Events should be as per the WHO-UMC causality assessment system as mentioned.

WHO-UMC Causality Categories

Causality term	Assessment criteria*
Certain	• Event or laboratory test abnormality, with plausible time relationship to drug in take • Cannot be explained by disease or other drugs • Response to withdrawal plausible (pharmacologically, pathologically) • Event definitive pharmacologically or phenomenological (i.e.an objective and specific medical disorder or are cognized • Pharmacological phenomenon) • Re-challenges at is factory, if necessary
Probable/ Likely	• Event or laboratory test abnormality, with reasonable time relationship to drug in take • Unlikely to be attributed to disease or other drugs • Response to withdrawal clinically reasonable • Re-challenge not required
Possible	• Event or laboratory test abnormality, with reasonable time relationship to drug in take • Could also be explained by disease or other drugs • Information on drug withdrawal may be lacking or unclear
Unlikely	• Event or laboratory test abnormality, with a time to drug intake that makes a relationship improbable (but not impossible) • Disease or other drugs provide plausible explanations
Conditional/Unclassified	• Event or laboratory test abnormality • More data for proper assessment needed, or • Additional data under examination
Unassessable/ Unclassifiable	• Report suggesting an adverse reaction • Cannot be judged because information Should in sufficient or contradictory • Data cannot be supplemented or verified

All points should be reasonably complied with

Severity: The degree of an adverse event should divided in to mild, moderate, or severe.

- **Mild:** Minimal interference in day-to-day activities, Special treatment may not be required to treat adverse event, Symptoms should transient.
- **Moderate:** Discomforting event, interference in day-to-day activities, the rapeutic intervention should required to treat adverse
- **Severe: (As mentioned in the 'Definitions' section above)** Severe discomfort, Day-to-day activities should impossible, major therapeutic intervention should required to treat adverse event.

V) PROCEDURE:

1.0 Handling of Adverse Event

a. The Clinical Investigator /Medical Officer should explain the expected adverse events identified in the Study Protocol/product literature or package insert in the study meeting held prior to the conduction of the Clinical study.

b. The designated person should monitor the subject(s) for any untoward or unfavorable and unintended dsign (including abnormal Clinical laboratory finding), symptom during the Visits and study housing. The designated person should also consider any Adverse Event occurring after discharge of the subject from the clinical facility (during washout period, during the anticipated duration of action of the drug(s) or also thereafter at the discretion of the Clinical Investigator).

c. On occurrence of an Adverse Event the designated person should examine the subject and should give assurance or provide appropriate medical care to ensure wellbeing of the subject in accordance with currently acceptable clinical standards and guidelines.

d. The designated person should further ask the subject about the adverse event in detail to ascertain the severity and/or circumstances contiguous to the adverse event, including any medication taken (if any) after discharge from the study center, so that the event can be judged clinically.

e. Whenever required, the designated person should also inquire about the progress of the adverse events to the subject telephonically. The subject should also requested to report the Adverse Event at any time to the designated person.

f. The designated person should review the post study clinical laboratory report (pathological report) for any out of range values, these values should be compared with the baseline reports values to determine its significance for evaluation of any Adverse event. If any clinically significant observation(s)should found in the Clinical laboratory reports then it should recorded in the Adverse Event Form of the CRF, attached as Annexure-01, and the designated person should inform the subject about the evaluation and should request him/her to report to the Study center for follow-up.

g. The designated person should record the follow ups in the 'Telephonic Communication and Subject Follow-up Form of the CRF, attached as Annexure-02

h. The decision for any further diagnostic test(s) or specialist consultation should required for the management of the adverse event, should be done on the discretion of the Clinical Investigator/Co-Investigator.

i. The designated person should monitor the subject or follow up with the subject till there solution of the Adverse Event.

j. Designated person should record the Adverse Event, time of occurrence, time /date of resolution, the assessment of causality, severity, expectedness/ unexpectedness and course of treatment or action (if appropriate), in the 'Adverse Event Form' of the CRF of the respective subject. If in the judgment of the Clinical Investigator/Co-Investigator the continuation of the subject proves harmful to him/her, then should take the decision to terminate the subject from the study. The termination details should be recorded in the 'Subject Drop-Out/ Withdrawal/ Termination Form' of the CRF of the respective subject. Handling of Serious Adverse Event (SAE).

k. In case of occurrence of any Serious Adverse Event, Clinical Investigator/Co-Investigator/Medical Officer should give preliminary treatment (if required) to the subject in the Emergency Care Unit (ECU) of Hospital. As per the 'Standard Operating Procedure for ECU maintenance and handling Emergency Situation' and then should shift the subject to the emergency facility (if required).

l. The subject should be monitored till the resolution of the Serious Adverse Event or on the discretion of the Clinical Investigator/Co-Investigator.

m. The Medical Officer should record the Serious Adverse Event, time of occurrence, time/date of resolution, the assessment of causality, severity, expectedness/ unexpectedness and course of treatment or action (if appropriate), in the 'Serious Adverse Event Form' of the CRF of the respective subject, The Medical Officer should keep all the relevant medical record including the hospital record along with the CRF of the respective subject.

n. The Medical Officer should also record details in the 'Logbook for Serious Adverse Event details.

o. Clinical Investigator/ Co-Investigator should review the details recorded in respective

p. Subject's CRF and in 'Log book for Serious Adverse Event Details'.

q. The termination of the subject from the study due to a Serious Adverse Event should be documented in the 'Subject Drop-Out/Withdrawal/Termination Form' of the CRF of the respective subject.

2.0 Reporting of Adverse event:

a. Reporting of the adverse event by the Investigator:

- Unanticipatedproblemsinvolvingriskstosubjectsshouldbereportedpromptly.
- Summary of the adverse events and any unanticipated problems involving risks to the subjects should be reported at continuing review.
- Any information about risks associated with the clinical study, should be reported at continuing review.
- A single occurrence of as serious, unexpected event that should un common and strongly associated with drug exposure (e.g agranul ocytosis, hepatic injury)
- A single occurrence, or more of ten a small number of occurrences, of a serious, unexpected event that should not commonly associated with drug exposure, but uncommon in the study population.
- Multiple occurrence of an AE that, based on an aggregate analysis, should determined to be an unanticipated problem. There should be a determination that series of AEs represents a signal that the AEs were not just isolated occurrence and involve risk to human subjects. A summary and analyses supporting the determination should accompany the report.
- An AE that should described or addressed in the investigator's brochure, protocol, or informed consent documents, but occurs at a specificity or severity that should inconsistent with prior observations.
- A Serious Adverse Event that should described or addressed in the investigator's brochure, protocol, or informed consent documents, but for which the rate of occurrence in the study represents a clinically significant increase in the expected rate of occurrence.
- Any other AE or safety finding that would cause the sponsor to modify the investigator's brochure, study protocol, or informed consent documents or would prompt other action by the IEC to ensure protection of human subjects.
- An AE observed during the conduct of a study should be considered an unanticipated problem involving risk to human subjects, and reported to the IEC, only if it were unexpected, serious, and would have implication for the conduct of the study (e.g. requiring a significant, and usually safety-related, change in the protocol such as revising inclusion/exclusion criteria or including a new monitoring requirement, informed consent, or Investigator's brochure). An individual AE occurrence ordinarily does not meet these criteria because, as an isolated event, its implications for the study cannot be understood. Many types of AEs generally require an evaluation of their relevance and significance to the study, including an aggregate analysis of other occurrence of the same (or similar) events, before they can be determined to be an unanticipated problem involving risk to human subjects.

a. Reporting of the adverse event by the Investigator to Sponsor:

There should no severity or expectation threshold to trigger the investigator's responsibility to report to the sponsor adverse events related to the drug. The sponsor however should required to report only serious, unexpected and related adverse event experiences to the Regulatory.

- Adverse events that could be reasonably regarded as caused by or probably caused by the drug, to be reported promptly unless the event should alarming, in which case, to be reported immediately;
- Serious adverse events, to be reported immediately unless the protocol or other document indicates otherwise. It should essential to specify clearly in the protocol and the adverse event reporting section of the protocol, what should and should not expected as well as what should and should not regarded as serious.
- The time lines for notifying of SAE both death and other than death events by the Investigator to Sponsor as per 122 DAC of New Drugs and Clinical Trial Rules.2019shouldwithin24 hours of identifying the event

b. Reporting of the serious adverse event by the Sponsor to the Regulatory authorities:

Reporting requirements for the Sponsors to the Regulatory include time frames as follows:

- Adverse experiences that should associated with the use of the drug and that should both Serious and Unexpected, Unexpected fatal or life-threatening experience associated with use of the drug, to be reported within 24 hours of the occurrence;
- Any adverse experience with a licensed product that should serious and unexpected, whether domestic or export, to be reported by the license holder within 24 hours of the occurrence, by the licensed manufacturer.
- The time lines for reporting of SAE-death and other than death events by the Sponsor (after due analysis) to the Licensing authority (DCGI) as per 122 DAC of New Drugs and Clinical Trial Rules. 2019 should within 10 days of occurrence of SAE and reporting of death to chairman of the expert committee at CDSCO office within 10 calendar days of occurrence of SAE.
- As per 122 DAC of New Drugs and Clinical Trial Rules,2019 the Sponsor/ representative shall pay the compensation in case of clinical study related injury or death within 30 days of receiving the order from licensing authority (DCGI). For SAE other than death, the study subject should get the compensation and in case of death, the nominee of the subject should get the compensation.

- In post marketing studies, sponsors must not only report under Med Watch (The FDA's safety information and adverse event reporting program, which provides information about safety should sues and provides an online gate way for reporting adverse events) requirements but also be consistent with reporting obligations for IND research that require reporting serious consequence or adverse effects of an already approved and legally marketed drug.

♦ **PI Reporting of the serious adverse event to the IEC of BLDE (DU).**

- **It should the responsibility of the Principal Investigator should submit within 24 hours SAE report or the unexpected adverse event report to the Sponsor, IEC, DCGI by hard copy / by email.**
- The report of SAE of due analysis shall be forwarded by the Investigator to IEC, DCGI, sponsor and Head of the institution within 14 calendar days of occurrence SAE.
- The report should be accompanied by detailed narrative of the SAE and New Drugs and Clinical Trial Rules.2019
- It should be submitted as per check list detailed by Licensing Authority.
- IEC should perform Causality Assessment with reasoning for Relatedness/Un-relatedness and should communicate to DCGI within 30 days of Occurrence of SAE (as per CDSC Rules)
- PI also communicate the SAE initial report to the Medical director of the Institution

♦ **Reporting of the adverse event by the Sponsor to other Investigators:**

Sponsors should required to report to other investigator in a multisite trial. The requirements should similar to those for sponsors reporting to the Regulatory. The reporting obligations include the following:

- Adverse events those should serious, unexpected, and associated with the drug, to be reported promptly.
- Any new observations discovered by or reported to the sponsor about the drug (other than the other safety information) as the investigation processed.
- The Ethic Committee shall forward its report of death and/or any other SAE after due analysis on SAE with its opinion on the financial compensation (if any) to be paid by the Sponsor to DCGI office, and the report of death to the Chairperson of expert committee –at CDSCO office within 30 calendar days.

- **Reporting of the Serious Adverse Event (SAE) by the Investigator to DCGI/CDSCO:**

a) All SAEs occurring in clinical studies should be reported as per the details provided in NewDrugs and Clinical Trial Rules.2019 within the applicable timeline to,The Drugs Controller General (India).Directorate General of Health Services Central Drugs Standard Control Organization (CDSCO) FDA, Bhawan, Kotla Road, New Delhi – 110 002

b) Pharmaceutical company /the Sponsor / CRO (Investigator in investigator-initiated studies) should responsible for reporting SAEs within the applicable timelines.

c) Every report (both initial as well as follow-up reports) should be submitted along with a covering letter.

d) Covering letter should be prepared using the template as guide, and printed on the Company /CRO's letter head, attached should the template of covering letter.

e) Instructions should provide in the template as highlighted text in *"Italics"*. Delete all instructions from the final letter.

f) All the sections of the covering letter should be completed. When some information should not available at the time of report e.g. causality assessment by medical monitor of Sponsor / CRO, compensation provided for study related injury or death, the same has to be provided as a follow-up report.

g) Covering letter of every report arising from the clinical trials (CT) has to capture, (at stipulated box provided in the template) as per the format.

i. DCGICT file number

ii. CompleteaddressofSponsorandCRO(ifany)includingphone&e-mailaddress

iii. Phase of clinical trial

iv. Category of clinical trial as per the codes mentioned below. Mark the appropriate Code from this list provided in the covering letter using below details.

v. Protocol or Study No. /Code / ID and the study title.

vi. Adverse event term/ diagnosis (Whenever possible provide a 'preferred' term)

vii. A brief narrative of the event, not exceeding10 lines. A detailed narrative may be closed, if available.

Code	SAEs occurring in Clinical Trial
CT-1-IND	New Drug-Investigational New Drug (IND) study (where IND should filed in India and should an NCE)
CT-2-Reg	New Drug–Local Clinical Trial–For product approval in India
CT-3-GCT	New Drug– Global CTs
CT-4rDNA	Biological–Recombinant products (Global CTs, India IND and study for product approval)
CT-5-Vac	Biological–Vaccines (Global CTs, India IND and study for product approval)
CT-6-Oth	Biological–Others(e.g. stem cell studies)
CT-7-Dev	Device study (Global CTs, India IND and study for product approval)
CT-8-Oth	Others

i. Unexpected SAEs must be submitted to the office as per Schedule Y of Drugs and Cosmetics Rules, 1945.

ii. Causality assessment by investigator and the medical monitor of Sponsor / CRO.

iii. The assessment report should clearly mention whether the SAE occurred should related or not related (Situations like unlikely, possibly, suspected, doubtful etc should not be used).

iv. Whether the outcome should fatal

v. Details of compensations provided for injury or death. Incase no compensation should paid reason for the same should be submitted. It should pertinent to mention that in case of study related injury or death, complete medical care as well as compensation for the injury or death should be provided.

vi. Mention whether it should "initial" or "follow-up" report should be maintained. For follow-ups, it should be clearly mention thefollow-upreportnumbere.g.Follow-up#01, Follow-up # 02, etc. In case of follow-up reports, mention the date of submission of initial (first) report, as narrative should be clearly mentioned.

vii. Forms should be completed in legible English, illegible forms, incomplete with respect to critical information and improperly scanned /fax copies would be rejected by DCGI office.

viii. Relevant supportive documents may be enclosed

ix. **NOTE:** Submission of same SAE in different forms/ format, in different occasions should be avoided (e.g. submitting CIOMS forms and then later submitting the same event details as per New Drugs and Clinical Trial Rules, 2019

3.0. System of Pre-screening for submission of reports of SAEs to CDSCO

i. In order to streamline the submission of reports of SAEs a pre-screening of reports of SAE submitted to CDSCO, this SAE includes death occurring during the clinical study to arrive at the cause of death/injury to the subject, as the case may be and to determine the quantum of compensation, if any to be paid by the Sponsor or his representative who so ever have obtained permission from CDSCO in a time bound manner.

ii. As per this procedure, each SAE including death should be examined by the CDSCO and decision regarding causality of death and quantum of compensation (if any) should be taken by CDSCO in a time bound manner as per the procedure specified in the **New Drugs and Clinical Trial Rules, 2019**

iii. As per this New Drugs and CT rules 2019, the investigator shall report all serious and unexpected adverse events to CDSCO, the Sponsor or his representative whosoever had obtained permission from the CDSCO for conduct of the clinical study and the Ethics committee within 24 hours of their occurrence.

iv. In case of serious adverse event of death, the reports shall be examined by an Independent expert committee constituted by DCG(I) to determine if the cause of death should duet o following reasons, which should considered as clinical study related death and gives recommendation to CDSCO. In case of clinical study related death, the committee shall also recommend the quantum of compensation to be paid by the sponsor or his representative, to CDSCO.

- Adverse effect of Investigational product(s)
- Violation of the approved protocol, scientific misconduct or negligence by the Sponsor or his representative or the investigator;
- Failure of investigational product to provide intend the rapeutic effect;
- Use of place boina place bo–controlled study
- Adverse effects due to concomitant medication excluding standard care, necessitated as part of approved protocol;
- For injury to a child in-utero because of the participation of parent in clinical study.
- Any clinical study procedures involved in the study.

v. CDSCO shall consider the recommendations of the expert committee and shall determine the cause of the death and also the quantum of compensation in case of clinical studies related death within three months of receiving there port of SAE of death.

vi. In cases of serious adverse event other than death, CDSCO shall determine the cause of injury, if any, due to any of the reasons mentioned above as in the case of death, which should considered as clinical study related injury.

Note: CDSCO has option to constitute as independent Expert Committee, where reconsidered necessary, to examine such serious adverse event. In case of clinical study related injury, CDSCO shall also determine the quantum of compensation within three (3) months of receiving of the SAE)

vii. In case of clinical study related injury or death, the Sponsor or his representative concerned shall pay the compensation as per the order of CDSCO with in thirty (30) days of the receipt of such order.

viii. As per this procedure the preliminary scrutiny of the SAE reports should be done by CDSCO Officer (s) based on laid down checklist attached as Annexure -06. During the preliminary examination, the CDSCO Officer(s) should scrutinize the SAE report to ensure that it contains all the required administrative as well as technical information in proper manner as per the checklist. CDSCO should only accept the SAE reports for further examination, if it should submitted in accordance with the format and the checklist.

ix. Once the report of SAE should accepted by the CDSCO, the information in the report should be reviewed by CDSCO as per the specified procedures:

- The Sponsor or his representative conducting clinical studies in India should have to prepare the SAE reports for submission to CDSCO as per New Drugs and CT rules, 2019
- The SAE reports must be submitted with proper binding, indexing and page number.
- There ports of SAEs of death should be prepared and submitted in red cover.
- There ports of SAE of injury other than death should be prepared and submitted in blue cover.
- The SAE report other than that mentioned at (i) & (ii) above should 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 than information should not obscured by the methods of binding.
- The documents printed on both sides of a page, can be submitted. However care should be taken that the information should not obscured when the page should place in a binder.
- While submitting reply to a query, the applicant should always enclose with the reply, a copy of query letter should use by CDSCO.

VI) RFERENCES:

1. Standards and Operational Guidance for Ethics Review of Health-Related Research with Human Participants-2011
2. WMA Declaration of Helsinki –Ethical Principles for Medical Research Involving Human Subjects 2013
3. National Ethical guidelines for Biomedical and health research involving research participants Guidelines – ICMR -2017
4. New Drugs and Clinical Trial Rules,2019

BLDE(DU) SITE SOP	Version 1.0	Revision 0.0	Effective Date: 29/May/2023
SOP No	TITLE		
SOP 11/V1.0	SOP for Instruction for Filling of Screening Form and CRF		

Sno.	Contents
1.	Objectives
2.	Scope
3.	Procedures
4.	Screening form & CRF Filling guidelines

I. Objective:

This SOP gives the procedure for recording of the Screening & Case Report Form in the all clinical studies.

II. Scope:

This SOP is applicable to all the clinical studies at site.

III. Procedure:

1.0 The approved Screening Form and Case Report Form should be used for recording **the clinical studies.**

2.0 Investigator /designated person should fill the Screening Form /CRF as per the details mentioned in the IEC approved Study Protocol and Screening Form/CRF.

3.0 General Instruction for Filling the Screening Form/ CRF

1. Filling of the Screening/CRF should be done by black ballpoint pen.
2. The date should be written in the format of DD/MM/YY, e.g. for27th Feb 2012 -27/02/22.
3. The time should be written in the format of 24hours by HH:MM, e.g. for 3 hours 15 minutes P.M. – 15:15.
4. All data on all pages of the CRFs, should be and should not be typewritten.
5. Any type of correction fluid (white-out), pencil, or erasable pen on the CRFs should not be used.
6. Open boxes should for entry of numerical or alphabetical (in block letters) data. The boxes should be completely filled-up.
7. Closed boxes should for tick mark (inside the box) purpose only. Many items have a box or series of boxes for recording a response. Box should be clearly marked. Do not shade in the box or mark it with a slash or other character.
8. If data is be written on the form incorrectly, the error should be noticed and single line should be drawn. Incorrect entry the correct answer should be placed with near the box, and sign, date of correction. If errors is identified again, should be used appropriate space and do the same correction method.
9. Blank items on data forms should considered missing data and should therefore result in a query unless they should blank due to skip pattern requirements. To avoid a query on items where the answer to an item should unknown or should not available, or where the participant refuses to answer an item.
10. In case of unknown, write “UNK”, should be written initial and date the item.
11. In case of answer not available, write “N/A” then initial and date the item.
12. DONOT enter a line through items that should blank due to skip patterns.

13. The assigned staff must review each completed form for completeness and legibility. This could include the clinician or coordinator completing the forms and the Data Management Coordinator (DMC). The following list can be used as are view check list.

- Review of all completed CRFs before being sent to Sponsor/CRO.
- Make sure all items should answered, unless skipped according to the instructions on the form. If a question cannot be answered, write "UNK" for unknown or "N/A" for Not Available, with initial and date the item.
- Mark only one response box per item should be marked, unless instructed otherwise.
- Make sure all written entries should clear enough to be legible for data entry.
- Should be checked for common errors.(The largest percentages of avoidable queries should associated with:
    - Missing dates
    - Transposed or incorrectly transcribed patient screening or enrolment IDs.
    - Invalid site numbers
    - Missed skipped pattern)

VI. Screening form & CRF Filling Guidelines Header (Applicable to all the Pages)

1. Screening ID / Enrollment ID should be as first two boxes should be Centre No. (Allotted by the CRO) and the rest three box should be the Sequence no.
2. Record Date of visit should be in DD/MM/YY Format.
3. Record Date should be recreated as Patient Initials i.e. first letter of First, Middle & Last name.

Footer

1. Signed and Date should be in 'Done by' box.
2. Signed and Date in 'checked by' box after checking the entire page for correctness and completeness.

Informed Consent form:

1. Date when subject /LAR/witness signs the Informed Consent should be recorded

Demography:

1. Record Date of birth should be in DD/MM/YYYY format. Year should be provided at minimum.
2. Check gender as either 'Male' or 'Female'.
3. Age should be recorded as completed years.
4. Record the Body Weight in kilograms should be in the box provided.
5. Record height shall be in meters.

6. Should be Calculated and recorded BMI.
7. The smoking and tobacco Chewing Habit of the subject as Mild, Moderate & Severe should be tick marked.
8. Should be tick marked alcohol consumption entails.
9. Should be taken the history of any drug abuse and tick the appropriate box.
10. Considering DSM-IV marked the appropriate 'YES' or 'NO' box for presence of significant alcoholism and Drug dependency.
11. Put Remarks if any in given space.

Diagnosis and Type of Epilepsy

1. In the appropriate box mode of diagnosis of epilepsy and should be tick marked, if any comments, should be shared.
2. The appropriate box depending upon Type of Partial (Focal/localized) Epilepsy and
3. Should be added if any comments shall be tick marked.
4. The YES and NO box depending upon Diagnosis of Refractory Partial Epilepsy.

Medical History:

1. Should be checked 'YES' or 'NO' depending upon the presence of any relevant Medical / Surgical History.
2. If YES, should be recorded appropriate body system number from corresponding code provided on the CRF page. E.g. record 07 for Neurological system and give the details of state if the condition should currently/potentially active. Use a separate line for each condition.
3. Record clinical condition in the condition column. Preferably provide diagnosis rather than symptom should be preferably provide.
4. Record Start and End date soft he recorded condition.

Previous and concomitant medications

1. All the details of the Prior and concomitant Medications should be recorded on the Previous and concomitant medications page. If Yes, should be recorded Medication Name (Generic/Brand name)
2. Should be recorded 'Start' and 'End' dates for the medication. Check ongoing, if the medication should still being consumed and leave End date blank.
3. Should be recorded the value of Dose and Unit of the medication in the space provided. E.g. for unit, record the unit as mg, ml, etc. Record 'NA' for Dose & Unit where data should not available or not applicable.
4. Should be recorded Route of drug administration and frequency of drug.

Physical examination

In Physical Check table, should be checked and marked all the given system and the appropriate corresponding box and if any abnormal found should be specified in given adjacent space.

Systemic examination

During systemic examination, should be checked and finally recorded all the given system in the table during subject examination and should be ticked appropriate box, and if any abnormality found should be specify the same in given adjacent space.

Vital sign measurement sand wellbeing

Vital Signs should be measured at Screening & other scheduled visits.

1. Pulse Rate value in b pm (beats per minute) should be recorded in the box provided.
2. The Systolic and Diastolic Blood Pressure value in the box provided should be recorded.
3. Respiratory rate value in /min in the box provided should be recorded.
4. Axillary Temperature in ^{o}F should be recorded the box provided

Sample collection

1. In this section the date and quantity of blood sample collected for Pathological examination during screening should be recorded.
2. Designated Person who has done the above activity should sign and date in 'Collected by' box.

Hematology, Urine Analysis, Biochemistry, Serology and Serum Pregnancy Test

After receiving the Pathological report

1. Results of the analysis should be the values column.
2. 'Normal' or 'Clinically Significant' or 'Clinically Non significant' should be checked values in the check box depending upon the value, if the value should out of acceptable range or not.
3. Any relevant information should be the comment section, if necessary.
4. 'Reactive' or 'non-reactive' box depending upon the result of serological examination and specify any relevant information in the comment section, if necessary.
5. 'Positive' or 'negative' should be checked depending upon the result of serum pregnancy test. If result should Positive, should be excluded the subject from study.

12-Lead ECG and Chest X-Ray

1. The date of ECG and X-RAY done in space provided for date in DD/MM/YY format.
2. 'Normal' or 'Abnormal' box should be checked depending upon the report. If abnormality should found the same should be put in the comments in the space provided

Any Additional Laboratory Test/ Procedure

1. In this section If Investigator feels any additional investigation should needed other than protocol specific should be recorded the name of test/procedure.
2. Add Values or observations in the space and write if any comments.

Inclusion Criteria:

1. 'Yes' , 'No' or 'N/A' boxes should be checked as appropriate for every criterion.

Note: For Subject to be eligible for the study, all respective criteria for inclusion should be either 'Yes' and/ or 'N/A'.

Exclusion Criteria:

1. 'Yes' , 'No' or 'N/A' boxes should be as appropriate for every criterion.

Note: For Subject to be eligible for the study, all respective criteria for exclusion should Be either 'No' and /or 'N/A'.

End of Visit Checklist:

1. Tick 'Yes' Or 'No' depending upon completion of the screening procedure and if any procedure should not done mention the same and reason should be mentioned in space for comment.
2. Tick 'Yes' Or 'No' should be ticked as per the eligibility of the subject for the Inclusion/ Exclusion criteria status. If any answer should 'NO' then should be specified the reason in the comment box.

Onset of Clinical Up- Titration /Down titer and should suance Record

1. The dosage of test drug should be mentioned in the mg
2. The total number of test drug dispensed to the subject should be marked
3. Tick one box of qdorbdorod should be depending upon the frequency prescribed to consume test drug to the subject.
4. The name of prescribed medication concomitantly used by the subject should be ticked.
5. Mention Dosage frequency and route of the concomitant medication prescribed along with test drug to the subject should be
6. 'YES' or 'NO' depending upon the dosing in struction should explained or not explained to the subject.
7. 'YES' or 'NO' should be ticked depending whether the patient Dairy card has been should sued or not should sued to the subject.
8. 'YES' or 'NO' should be ticked depending upon the Patient dairy card filling in struction should explained or not explained to the subject.
9. The date on which the patient has been asked to visit the Centre should be maintained and should be ticked YES if you have conveyed the next visit date to subject.

Follow-up for laboratory investigations, Safety & Concomitant medications

1. YES or NO depending upon should be ticked investigator doubts about any laboratory values and if he desires to repeat that particular investigation and if response of investigator should YES then in response for should be filled.
2. YES or NO should be ticked depending upon if subject has consumed any medication other than test drug should be ticked at appropriate space provided.
3. YES or NO should be ticked after inquiring the subject about whether he/she suffered any adverse event.
4. YES or No should be ticked depending on whether the subject has suffered any Serious Adverse Event.

Checking for Dosing Compliance

1. The details for quantity of test drug and concomitant medication should sued, any dose missed and quantity returned. And should be ticked YES or NO depending upon the dosing compliance.
2. YES or NO should be ticked depending upon the Investigator's discretion whether the patient can continue the study or not.

Randomization

Should be marked on the date of Informed consent Taken

1. Should be filled Screening ID
2. Should be filled the Date of Randomization
3. Should be mentioned Enrolment ID which should consist of centre code and Randomization ID.
4. Either Test or Reference arm depending upon the randomization obtain telephonically from the CRO during period I and tick reverse arm for Period II should be mentioned.
5. Sign and Date should be filled who has conducted this activity
6. Put Sign & Date who has checked this activity.

Clinical stabilization and issuance record

1. Tick Tester Reference box as per randomization.
2. Mention the Quantity of test drug issued and should be ticked 'YES' or 'NO' depending upon the Patient stabilized on dose (mg) & frequency.
3. The details like Quantity should sued frequency of dose dosage and route of concomitant medication should be filled.

Check In & Out Procedure

1. 'YES' or 'NO' should be ticked depending upon patient satisfies inclusion and exclusion criteria.
2. 'YES' or 'NO' should be ticked depending upon patient fit for check-in.
3. 'YES' or 'NO' should be ticked after should suance of ID to subject.
4. 'YES' or 'NO' should be ticked after checking body and belongings of the subject.
5. 'YES' or 'NO' should be ticked depending upon should suance of personal kit to subject.
6. Subject's Check-in-time in 24 Hours format should be recorded.

In House Dosing

1. Pre-determined Schedule Time by in 24Hrs Format should be filled.
2. 'YES' or 'NO' should be ticked after properly checking ID no of the subject.
3. Either 'YES' Or 'NO' should be ticked depending upon the instruction should conveyed to the subject or not**.**
4. Test or Reference depending upon the subjects randomization arm.
5. Either YES or NO after ensuring that subject has d rank 240ml of water for dosing should be ticked.
6. YES or NO depending upon checking the mouth of subject should be ticked.
7. The time of actual dosing in 24 Hr format should be recorded.
8. Comment about if any deviation occurs or any spillage should there etc. should be put.

Meal Record

1. Re-determined Schedule time for meal in 24 Hr Format should be recorded.
2. The time as Start time when subject Start Eating the meal in24 Hr Format should be recorded.
3. The time as 'END' time when subject finishes the meal in 24 Hr Format should be recorded.
4. Comment for any unscheduled event happens should be put.

Pre-Dose Blood Sample

1. The time of 5ml Blood sample collection which prior to morning dosing should be recorded.
2. Designated Person who collected the blood sample Put Sign and date in done by column

Pharmaco kinetic Blood Sampling

1. Below applicable for All PK sampling point
2. Pre-determined Schedule time for blood collection in 24 Hr format should be recorded.
3. Actual time for blood collection in 24Hr format should be recorded.
4. Person who collected the blood sample Put Sign and date in collected by column should be designated.

Removal or Replacement of Cannula

1. The time of re cannullation if cannula s h o u l d removed or change and specify the reason in comment space should be and
2. Person who has carried out the activity Put Sign and date in done by column should be designated.

Pre-dose Compliance

1. Yes or NO depending upon the whether patient has maintained fasting for 8 hours prior to dosing should be ticked.
2. Yes or NO depending upon restriction for not allowing to drink water should be ticked.

Post dose Compliance

1. Yes or NO depending upon Drinking water not permitted 1.00hrpost-dose should be ticked.
2. Yes or NO depending upon Posture restricted for 2.00 hr spost-dose should be ticked.
3. Yes or NO depending upon Maintenance of fasting for4.00 hrs post-dose should be ticked.

Is Patient to Needs to be Further Down-Titrated for test drug Dose Study?

1. Whenever Patient needs further down titration Investigator to fill Annexure F form
2. If Response should NO fill the study completion status should be filled.

Study Completion Status

1. YES or NO depending upon whether the patient completed the study should be ticked.
2. And if response should NO questionnaire of Part should be completed by the reason for withdrawal & then the part B by with the date when subject has been out of the study.

Investigator's Declaration

1. Signature with Date should put in "checked by" box after checking the entire Screening form and CRF for its correctness and completeness.

Introduction: The BLDE (DU) Research Pharma [Clinical Trial IMPs] should be constituted by BLDE (DU) Registrar respectively under Drugs and Cosmetic Act, 1940 at BLDE (DU) Research Pharma, Second Floor, Site Management Organization, BLDE (DU) SBMPMC Hospital Vijayapur.

1. **Goals of Investigational Product (IP) Management**

1.1. The goals of IP management for this clinical trial include the following:

- **a.** To ensure protection of the subject and trace ability;
- **b.** To enable identification of the product and the trial;
- **c.** To facilitate proper use and storage of the product;
- **d.** To ensure the reliability and robustness of data generate din the trial.
- **e.** To ensure to maintain the Temperature of IMPs

2. **Communications:**

- **a.** Periodic GCP/Protocol Training should be conducted for the site Research pharmacists by the Sponsors/ CROs/ Site
- **b.** The purposes of these GCP/Protocol training should to keep updated of new information and protocol changes, to follow up on action items, to problem solve, to coordinate and collaborate on activities, to build relationships, and to review the results of pharmacy audits.
- **c.** Pharmacists should communicate via-email, fax and telephone as needed.
- **d.** Electronically transmitted documents should be password protected.
- **e.** Pharmacists should conduct cross-site visits as appropriate.

3. **Roles and Responsibilities:**

- **Roles and Responsibilities of Site**

3.a.1. The following, Pharmacist should be responsible for IP management:

a) IP Shipment and receipt

b) IP Storage

c) IP Repackaging and Relabeling

d) IPD is pensing and Accountability

e) IP Return and Destruction

3.a.2. The roles and responsibilities of the Pharmacist / study staff involved in IP management for this clinical trial should be documented in a Signed Signature Sheet. Study staff / Pharmacist should be trained on IP management procedures.

3.a.2.1. Training should be documented and maintained in the Investigator Site Files.

- **Roles and Responsibilities of Sponsor**

a. This clinical trial should be monitored by the Sponsor monitor.

(For sites involved in IP repackaging and relabeling, describe that there should be two separate monitors

- ★ *The blinded monitor should be responsible for monitoring all aspects of the clinical trial except IP management. [to be intimated to site pharmacist prior to one week of the Monitoring]*
- ★ *The unblinded monitor should be responsible for monitoring the IP management of this clinical trial). [to be intimated to site pharmacist prior to one week of the Monitoring]*

4. Pharmacy Procedures:

a) Pharmacy procedures specific to the protocol

- Forms and Labels**:** Pre-printed medication labels and forms should to be used in the study.
- Pharmacist's Prescription List Provided by the Study Investigators on the Study Identification Number, should be used.
- Additional treatment assignment lists should added as they should Received from Sponsors / CRO / PI

b) Drug Supply Statement

a. New drug supply statements should be added as they should received from Sponsors /CROs.

c) Prescriber Information

a. Copy of the signed FDA form 1572 or Investigator of Record Agreement and a Prescribers List and Signature Log (names and signatures of providers authorized to prescribe) should be available.

d) Shipments

a. Completed order forms and packing slips for each shipment stapled together and filed after the drug shipment received, verified and should be entered on drug accountability /logs records.

e) Return Records

a. Records of all medication should be returned to Sponsors /CROs / WHO

f) Correspondence

a. Letters and memos to and from Sponsors / CROs / PIs and other study- specific correspondence should be appropriate maintenance.

g) IMP/ Devices Request Procedure: Flow Chart

IMP/ Devices Request Procedure: Flow Chart

Receive from the courier personnel from the sponsors By Blinded/ Unblended/ site personnel

⬇

Checking the Present temperature of the IMPs (If applicable)

⬇

Temp. Registration (Any excursion / deviations)

⬇

If No. Proceed to next step /if yes Notify to sponsors should be notified.

⬇

Store as per the requirements of sponsors and site SOP [Location and label]

⬇

Stored by the bin card system [Bin Card implies a document which records the quantity of material received by, should sued to and remained in stores]

⬇

Request for IMP / Indent or Prescription by the study designee / Principal Investigator through annexure [Prescription Form]

⬇

Dispensing by the registered research pharmacist

⬇

Received by the CRC/ Study Designee

⬇

Return of used trips / vials / bottles→ ← Return of unused IMPs/ devices

⬇

Sponsors should be intimated about the same if they have facility to destruct the study Drugs Used / Unused

Destruction of used /unused IMPs at site level

Letter would be written to head of the institution/Clinical services administrators by the Principal Investigator for permission to destruct - (it may take15-20 days to complete the Process) if sponsors have provision can send the Used and Unused IMPs/ Kits should be send.

Request letter contains – No. of IPs, quantity, Batch no and date of Expiry

⬇

Destruction certificate from the Hospital administrators should be generated a copy of certificate to be maintained

Annexure: 01-Prescription Form

→----------

PRCICRIPTION FORM- Only for Clinical Trial purpose

Clinical Trial Prescription-Dispensary	**BLDE (DU) Shri B.M.Patil Medical College Hospital & Research Centre, Vijayapur**	
BLDE (DU) Research Pharma, CTS No:5434, 2nd Floor, SMO Office, Room No.00	SOP Version1.0	Page no 01of 01

Protocol No:

Hospital/ Site Code:

CTRI No:

Subject Initial		**Prescriber / PI name**	
IWRS/ IVRS number		**Contact No**	
Visit No		**CRC Name**	
Visit Date		**Randomization no**	

Rx.,

Date/Time	**Quantity**	**Drug**	**Route**	**Dose**	**Checked by**	**Received by**

Study designee/ PI signature and date

Chief Pharmacist sign Pharmacists sign

5. Source of IP:

5.1. Table 1 summarizes the name(s), manufacturer(s), source(s) and recommended storage temperature(s) of the IP(s) used in this clinical trial.

Research Office Use: {individual study}

IMPs Dispense tracker

Protocol No:

PI Name:

Blinded/ Un-blinded study:

Sponsored by:

Manufactured by:

Sno.	No. of IMPs Requested/ date	Recommended Storage Condition	No of IMPs Received	Dispensed/ Date	Balance
1.					
2.					
3.					
4.					

6. Participant Consultation and Counseling: if Applicable

At the BLDE DU site, the pharmacist should responsible for ensuring that all participants should adequately counseled whenever they receive their first supply of study medication with information on proper use and storage of each medication and possible side effects and adherence. The pharmacist provides written materials that explain proper use and storage of each medication, the possible side effects and contact information for the study team at the site. This counseling should be done by the pharmacist or by delegated personnel by the pharmacist and should be documented. At the BLDE (DU) SBMPMC Hospital, the study nurse should be responsible for medication and compliance counseling at the entry visit. After the initial counseling, the pharmacists should continue to serve as a resource at the BLDE (DU) SBMPMC Hospital Vijayapur should be available to the participant and the study nurse to provide further counseling and consultation as needed. The pharmacists at the site dispense medications to the patient and provide counseling at each study visit. The pharmacist should notify the study nurses/CRC if there should be a problem with adherence based on estimated measurements/ accurate counts of returned medication

7. IP Shipment and Receipt:

7.1. The Blinded CRC/ Un-blinded CRC/ Study Pharmacist should file<receipts of purchase /IP Shipping Documentation> and the GMP certificate/ Certificate of Analysis (COA)/ Product Insert of the IP in the Pharmacy Binder. If possible SMPC.

7.1.1. The Blinded CRC / Un-blinded CRC / Study Pharmacist should ensure that the contents of the <receipts of purchase/IP Shipping Documentation should incompliance with Section 4.6.3 of ICHE 6 Guideline for Good Clinical Practice.

7.2. The Blinded CRC / Un-blinded CRC / Study Pharmacist should verify the inventory of the IP and update the IP Inventory Log(s). The IP Inventory Log(s) should be filed in the Pharmacy Binder.

7.2.1. The Blinded CRC / Un-blinded CRC / Study Pharmacist should ensure that the contents of IP Inventory Log(s) should in compliance with Section 4.6.3 of ICH E6 Guideline for Good Clinical Practice.

8. IP Storage:

8.1. The Blinded CRC / Un-blinded CRC /Study Pharmacist should monitor the storage temperature of the IP on daily twice.

8.1.1. IP Storage Temperature Logs should be maintained in the Pharmacy Binder.

8.2. In the event of excursions from the recommended storage temperature of the IP as referenced in Table 1, the Blinded CRC / Un-blinded CRC / Study Pharmacist should complete the IP Storage Temperature Excursion Report and notify the Principal Investigator and/ or Sponsor for appropriate action to be taken.

8.3. The IP affected by the temperature excursion should be quarantined until a decision has been made by the Principal Investigator and /or Sponsor to use or destroy the IP.

8.4. All relevant documentation and correspondences pertaining to temperature excursions should be filed in the Pharmacy Binder.

8.5. Power Loss: Refrigerators and Freezers at BLDE (DU). SBMPMC Hospital Vijayapur connected to an emergency generator backup power system. At the BLDE (DU) SBMPMC Hospital the system should activated automatically if the main power should interrupted. The generators should being setup to come on automatically within 22 seconds

8.6. Temperature Monitoring: At BLDE DU SBMPMC Hospital refrigerator and freezer temperatures should checked daily when the pharmacy should open and recorded on a manual / electronic temperature log. In addition the room, refrigerator and freezer temperatures s h o u l d monitored by a constant temperature monitoring, data logging, and alarm system. If the temperature varies outside the defined range, an alarm should go off in the hospital room. This room should manned 24 hours a day, seven days a week. Checked two times daily when the pharmacy should open and recorded on temperature logs. A 24-hour recording device that records the temperature on a paper chart monitors each BLDE (DU) SBMPMC Hospital Site Management office [BLDE (DU) –Research Pharma]

8.7. If the temperature varies out of range an audible alarm should sound and the system should automatically and immediately call to the site research pharmacist /study designee. If an alarm should activated, pharmacy personnel should take action on either correct the mal function or move product to and should a of appropriate temperature.

9. IP RE PACKAGING AND RELABELLING (if applicable)

9.1. IP repacking and relabeling of IMPs, the Study Team Should be notified to Site Ethics Committee.

9.2. The unblended study team should perform IP repackaging and relabeling in accordance with the protocol and Good Manufacturing Practice (GMP) guidelines.

9.3. The unblended study team should apply the following GMP principles during IP repackaging and relabeling :

9.3.1. IP repackaging and relabeling should be performed by delegated and trained unblended study staff.

9.3.2. IP repackaging and relabeling should be witnessed by an un-blinded study staff.

9.3.3. Line clearance should be observed during IP repackaging and relabeling where by one IP should be repackaged and relabeled at a time.

9.3.4. Label reconciliation should be performed and documented on the IP Repackaging and Relabeling Form.

9.3.5. The IP Repackaging and Relabeling should be documented on the IP Repackaging and Relabeling Form.

9.3.6. The IP Inventory Logs for the IP(s) should be updated accordingly.

9.4. The un-blinded study team should perform IP repackaging and relabeling <prior to study initiation/ at each subject visit/etc.>.

9.5. The un-blinded study team should assign a dummy batch number and dummy expiry date for the repackaged and relabeled IP and document it on the relevant IP Repackaging and Relabeling Form.

9.5.1. For example, the dummy batch number should be set as 'YYYYMMDD' in accordance with the date of IP repackaging, and the dummy expiry date should be set as the earlier expiry date of the IP.

9.6. The unblended study team should ensure that all documentation pertaining to IP shipment, receipt, inventory, storage, repackaging and relabeling, transfer, return and destruction should be filed in the Pharmacy Binder with access secure and limited to the unblended study team.

10. IP Dispensing and Accountability:

a. The Blinded CRC / Unblinded CRC / Study Pharmacist should dispense the IP to the subject with prescription from the PI / study designee.

b. The Blinded CRC / Unblinded CRC /Study Pharmacist should advise the subject on the proper use of the IP in accordance with the protocol.

c. The Blinded CRC / Unblinded CRC / Study Pharmacist should advise the subject to return all used and unused to the site at the next study visit for determination of compliance.

d. The Blinded CRC / Unblinded CRC /Study Pharmacist should train the subject how to fill subject dairy on daily basis.

e. The < Blinded CRC / Unblinded CRC/ Study Pharmacist should update the IPD is pen sing and Accountability Logs and file it in the Investigator Site File/ Subject CRF.

f. The Blinded CRC / Unblinded CRC / Study Pharmacist should ensure that the contents of the IP Dispensing and Accountability Logs should in compliance with Section 4.6.3 of ICHE6GuidelineforGood Clinical Practice.

11. IP Return and Destruction:

a) The Blinded CRC / Unblinded CRC / Study Pharmacist should collect the used and unused IP from the subject at the next study visit.

b) The Blinded CRC / Unblinded CRC / Study Pharmacist should document the returns in the IP Dispensing and Accountability Logs.

c) The Blinded CRC / Unblinded CRC / Study Pharmacist should return the used and unused IP to the Sponsor for destruction /send the used and unused IP for destruction in accordance with institution policy.

d) The Blinded CRC / Unblinded CRC / Study Pharmacist should send the used and unused IP for destruction once a final IP Accountability has been performed by the monitor; all discrepancies have been investigated, satisfactorily explained and reconciliation accepted; and written approval has been sought from the Sponsor/ Principal Investigator.

e) The Blinded CRC/ Unblinded CRC/ Study Pharmacist> should ensure that IP Return and / or Destruction should documented on the IP Return and Destruction Forms. The IP Return and Destruction Forms should be filed in the Pharmacy Binder.

f) The Blinded CRC / Unblinded CRC / Study Pharmacist should ensure that the contents of the IP Return and Destruction Forms should in compliance with Section 4.6.3 of ICH E6GuidelineforGood Clinical Practice.

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

- Obtain a copy of the site's SOP of Waste Management from Clinical services administrators 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 paper work concerning destruction of the drug that should 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.
- CompletetheDrugReturn/DestructionFormorsimilarformprovidedbythesponsor/CRO.
- Provide a signed copy of the form to the CRA/Monitor and retain the original in the TMF.

12. References:

12.1. Health Products (Clinical Trials) Regulations

12.2. Medicines (Clinical Trials) Regulations

12.3. ICHE6 Guideline for Good Clinical Practice

14.4. New Drugs and Clinical Trial Rules, 2019

Sno.	Contents

I) Objective:

This SOP provides the details of the procedure for screening and enrollment of subject in the all clinical trials BLDE (DU) Shri B.M.Patil Medical College Hospital & Research Centre, Vijayapur.

II) Scope: This SOP should applicable for all clinical studies conducted in the facility.

III) Procedure:

1) It should important that the principal investigator resolves all questions from his/her staff concerning the interpretation of Exclusion/ Inclusion criteria.

2) The investigator should be able to dedicate time to the recruitment of each subject should likely to be longer than the time required for normal consultation.

3) The Clinical Investigator /Co-investigator should inform the subject (s) by word of mouth about the recruitment of subjects for the study.

4) The Clinical Investigator/Co-investigator should schedule the screening dates and should inform the subject (s).

5) The Study Coordinator/designated person should share the should sue the IEC of BLDE (DU) approved 'Inform Consent Form' to the subjects who have come for the screening procedure.

6) The Designated person should give the information of the screening and the study related activity to the subjects.

7) Clinical Investigator/Co-investigator/Medical Officer should request the interested subjects and the subject's Legally Acceptable Representative's (LAR) to sign the IEC of BLDE (DU) approved "Informed Consent Form" in the language best under stood by them.

8) If the subject / Legally Acceptable Representative's (LAR)should unable to read, then an impartial witness present during the presentation of the screening and study related activities should explain the contents of the Informed Consent Form in the best language understood by the subject. After the subject consent for participation in the study the subject and/or the LAR should sign

/put thumb impression on the consent form and then the witness should sign and date the 'Informed Consent Form' as per 'Standard Operating Procedure for Obtaining Informed Consent from Subject'.

9) In case the subject requires more than the allotted time to inquire about the details of the study/drug product/or to consult his family Physician to decide about the participation in the Clinical trials, then the Investigator shall permit him/her to leave the study center and should ask him to return if he/she should willing to participate in the particular study.

10) The subject who should found eligible for participation in the study should be given a unique Screening identification number for identification of subject.

11) The responsible Person should measure the height, weight, and calculate the BMI of subject as per the BMI chart (Refer APPENDIX 1). The details of the demographic data should be recorded in the Screening Form of the CRF designed for the study.

12) Investigator/designated person should take the medical history, should conduct the physical examination (General and Systemic examination) and the vital measurement and record the details in the 'Screening Form' of the CRF.

13) Technician / designated person should take the 12 lead ECG of the subjects. The Technician / designated person should sign and date the ECG print and should attach the same to the respective subject's 'Screening form' of the CRF.

14) Investigator/designated person should review the ECG of respective subject and should put the appropriate comment on the same after interpretation.

15) During the entire process of screening if the subject should found to be ineligible at any point of time, then the subject should not be considered for further screening procedure and should be excluded at that stage.

16) If the ECG of the subject should within normal limits then he/she should be sent for collection of blood and urine samples for Clinical Laboratory Investigations.

17) The Laboratory Technician (pathology)/Phlebotomist/Nursing staff should request the subject to collect the urine sample and should collect the blood sample after verifying the screening identification number of the subject from the 'Screening form', and on the labeled container/ vial / vacationers used for collection of the respective sample and should make appropriate entry of the collection in the 'Test Requisition form' and the 'Screening form'. The biological samples should be then transferred to the Clinical Pathological Laboratory.

18) In case the Clinical Laboratory Investigation has to be done in an outsourced facility then the Study Coordinator/designated person should give the details of subject 's identification (screening identification number, initial, gender and age) and other required test information(s) to the respective Clinical laboratory person in the 'Test requisition form'.

19) After receiving Clinical Laboratory Investigation reports the Investigator/ designated person should review the reports and if any significant observations then it should be recorded in the clinical investigation details of the 'Screening form' of the respective subject. The Clinical Laboratory Investigation report should be attached to the 'Screening form' of the CRF of the respective subject.

20) The Investigator/designated person should review the complete screening record forms for the health status of the subject.

21) The X-ray has to be done for the subjects who should found fit in all the above procedures to avoid unnecessary exposure to radiation hazard.

22) The Investigator/designated person should record the observations reported by the radiologist in the 'Screening Form'. The X-ray film should be kept along with the screening documents and the report should be attached to the respective subject's 'Screening form'.

23) Study coordinator should compile the screening documents in following sequence:

a) Screening Consent Form

b) Screening form (including the Demographic profile, medical history of subjects, Vital Sign and physical examination form, ECG and Clinical Investigation details form)

c) Clinical Laboratory Report(s), X-Ray reports

d) Other Investigation Report (if any)

1.0 Study Coordinator/designated person should inform the eligibility of the subject to the subject or the LAR of the subject:

2.0 Laboratory Technician (pathology) / Phlebotomist / Nursing staff should request the subject to collect urine in labeled container and should perform the 'Urine Screen for Drugs of abuse' test for Urine Screen for Drug of Abuse and Serum Pregnancy test (for female subjects).The results should be recorded in the respective Pre-Enrollment Day Activity format of the subject. If the Test should found to be negative then the subject should be sent for further procedures.

3.0 If any additional test has to perform on this pre-enrollment day, then it should be performed as per the requirements specified in the Study protocol.

4.0 The Clinical laboratory Investigation report obtained from the in house/ outsourced laboratory should be reviewed by the Investigator/ designated person and the comments/ discrepancy should be noted and recorded in the 'Pre-enrollment day activity' format of the respective subject . The Clinical Laboratory Investigation reports should be attached to this format.

5.0 After enrollment of the subject in the study the Study coordinator/designated person should should sue Subject identification number/Subject number (ID card) and should be checked-in to the clinical facility.

6.0 The Study coordinator / responsible person should prepare the list of subjects enrolled in the format for 'Screening and Enrollment Log' (Refer APPENDIX 2).

7.0 Randomization Procedures and Un-blinding.

- The Investigator must follow the randomization procedures, if any In the case of a randomized, Controlled, double-blinded trial, the code should usually prepared in the form of numbered envelopes, each containing the identification of the corresponding treatment in order to enable the Investigator to open the code when needed, without identifying other patients' treatment
- Ensure that the code should broke only in accordance with the Protocol and mainly for medical reason(s).
- Premature un-blinding must be reported to the Clinical Monitor immediately and should be documented in the File. The reason for premature un-blinding of the investigational product should be given, e.g. due to a serious adverse event.
- At the end of the trial, the Investigator must return all the unbroken codes to the Clinical Monitor to prove that the study was blinded throughout.

Height in Centimetres	Weight in Kilograms										
	45	46	47	48	49	50	51	52	53	54	55
145	21.4	21.9	22.4	22.8	23.3	23.8	24.3	24.7	*25.2*	*25.7*	*26.2*
146	21.1	21.6	22.0	22.5	23.0	23.5	23.9	24.4	24.9	*25.3*	*25.8*
147	20.8	21.3	21.8	22.2	22.7	23.1	23.6	24.1	24.5	25.0	*25.5*
148	20.5	21.0	21.5	21.9	22.4	22.8	23.3	23.7	24.2	24.7	*25.1*
149	20.3	20.7	21.2	21.6	22.1	22.5	23.0	23.4	23.9	24.3	24.8
150	20.0	20.4	20.9	21.3	21.8	22.2	22.7	23.1	23.6	24.0	24.4
151	19.7	20.2	20.6	21.1	21.5	21.9	22.4	22.8	23.2	23.7	24.1
152	19.5	19.9	20.3	20.8	21.2	21.6	22.1	22.5	22.9	23.4	23.8
153	19.2	19.7	20.1	20.5	20.9	21.4	21.8	22.2	22.6	23.1	23.5
154	19.0	19.4	19.8	20.2	20.7	21.1	21.5	21.9	22.3	22.8	23.2
155	18.7	19.1	19.6	20.0	20.4	20.8	21.2	21.6	22.1	22.5	22.9
156	*18.5*	18.9	19.3	19.7	20.1	20.5	21.0	21.4	21.8	22.2	22.6
157	*18.3*	18.7	19.1	19.5	19.9	20.3	20.7	21.1	21.5	21.9	22.3
158	*18.0*	*18.4*	18.8	19.2	19.6	20.0	20.4	20.8	21.2	21.6	22.0
159	17.8	*18.2*	18.6	19.0	19.4	19.8	20.2	20.6	21.0	[redacted]	21.8
160	17.6	18.0	*18.4*	18.8	19.1	19.5	19.9	20.3	20.7	21.1	21.5
161	17.4	17.7	*18.1*	18.5	18.9	19.3	19.7	20.1	20.4	20.8	21.2
162	17.1	17.5	17.9	*18.3*	18.7	19.1	19.4	19.8	20.2	20.6	21.0
163	16.9	17.3	17.7	*18.1*	*18.4*	18.8	19.2	19.6	19.9	20.3	20.7
164	16.7	17.1	17.5	17.8	*18.2*	18.6	19.0	19.3	19.7	20.1	20.4
165	16.5	16.9	17.3	17.6	*18.0*	*18.4*	18.7	19.1	19.5	19.8	20.2
166	16.3	16.7	17.1	17.4	17.8	*18.1*	18.5	18.9	19.2	19.6	20.0
167	16.1	16.5	16.9	17.2	17.6	17.9	*18.3*	18.6	19.0	19.4	19.7
168	15.9	16.3	16.7	17.0	17.4	17.7	*18.1*	*18.4*	18.8	19.1	19.5
169	15.8	16.1	16.5	16.8	17.2	17.5	17.9	*18.2*	18.6	18.9	19.3
170	15.6	15.9	16.3	16.6	17.0	17.3	17.6	*18.0*	*18.3*	18.7	19.0
171	15.4	15.7	16.1	16.4	16.8	17.1	17.4	17.8	*18.1*	*18.5*	18.8
172	15.2	15.5	15.9	16.2	16.6	16.9	17.2	17.6	17.9	*18.3*	18.6
173	15.0	15.4	15.7	16.0	16.4	16.7	17.0	17.4	17.7	*18.0*	*18.4*
174	14.9	15.2	15.5	15.9	16.2	16.5	16.8	17.2	17.5	17.8	*18.2*
175	14.7	15.0	15.3	15.7	16.0	16.3	16.7	17.0	17.3	17.6	18.0
176	14.5	14.9	15.2	15.5	15.8	16.1	16.5	16.8	17.1	17.4	17.8
177	14.4	14.7	15.0	15.3	15.6	16.0	16.3	16.6	16.9	17.2	17.6
178	14.2	14.5	14.8	15.1	15.5	15.8	16.1	16.4	16.7	17.0	17.4
179	14.0	14.4	14.7	15.0	15.3	15.6	15.9	16.2	16.5	16.9	17.2
180	13.9	14.2	14.5	14.8	15.1	15.4	15.7	16.0	16.4	16.7	17.0
181	13.7	14.0	14.3	14.7	15.0	15.3	15.6	15.9	16.2	16.5	16.8
182	13.6	13.9	14.2	14.5	14.8	15.1	15.4	15.7	16.0	16.3	16.6
183	13.4	13.7	14.0	14.3	14.6	14.9	15.2	15.5	15.8	16.1	16.4
184	13.3	13.6	13.9	14.2	14.5	14.8	15.1	15.4	15.7	15.9	16.2
185	13.1	13.4	13.7	14.0	14.3	14.6	14.9	15.2	15.5	15.8	16.1

Height in Centimetres	Weight in Kilograms										
	67	68	69	70	71	72	73	74	75	76	77
145	31.9	32.3	32.8	33.3	33.8	34.2	34.7	35.2	35.7	36.1	36.6
146	31.4	31.9	32.4	32.8	33.3	33.8	34.2	34.7	35.2	35.7	36.1
147	31.0	31.5	31.9	32.4	32.9	33.3	33.8	34.2	34.7	35.2	35.6
148	30.6	31.0	31.5	32.0	32.4	32.9	33.3	33.8	34.2	34.7	35.2
149	30.2	30.6	31.1	31.5	32.0	32.4	32.9	33.3	33.8	34.2	34.7
150	29.8	30.2	30.7	31.1	31.6	32.0	32.4	32.9	33.3	33.8	34.2
151	29.4	29.8	30.3	30.7	31.1	31.6	32.0	32.5	32.9	33.3	33.8
152	29.0	29.4	29.9	30.3	30.7	31.2	31.6	32.0	32.5	32.9	33.3
153	28.6	29.0	29.5	29.9	30.3	30.8	31.2	31.6	32.0	32.5	32.9
154	28.3	28.7	29.1	29.5	29.9	30.4	30.8	31.2	31.6	32.0	32.5
155	27.9	28.3	28.7	29.1	29.6	30.0	30.4	30.8	31.2	31.6	32.0
156	27.5	27.9	28.4	28.8	29.2	29.6	30.0	30.4	30.8	31.2	31.6
157	27.2	27.6	28.0	28.4	28.8	29.2	29.6	30.0	30.4	30.8	31.2
158	26.8	27.2	27.6	28.0	28.4	28.8	29.2	29.6	30.0	30.4	30.8
159	26.5	26.9	27.3	27.7	28.1	28.5	28.9	29.3	29.7	30.1	30.5
160	26.2	26.6	27.0	27.3	27.7	28.1	28.5	28.9	29.3	29.7	30.1
161	25.8	26.2	26.6	27.0	27.4	27.8	28.2	28.5	28.9	29.3	29.7
162	25.5	25.9	26.3	26.7	27.1	27.4	27.8	28.2	28.6	29.0	29.3
163	25.2	25.6	26.0	26.3	26.7	27.1	27.5	27.9	28.2	28.6	29.0
164	24.9	25.3	25.7	26.0	26.4	26.8	27.1	27.5	27.9	28.3	28.6
165	24.6	25.0	25.3	25.7	26.1	26.4	26.8	27.2	27.5	27.9	28.3
166	24.3	24.7	25.0	25.4	25.8	26.1	26.5	26.9	27.2	27.6	27.9
167	24.0	24.4	24.7	25.1	25.5	25.8	26.2	26.5	26.9	27.3	27.6
168	23.7	24.1	24.4	24.8	25.2	25.5	25.9	26.2	26.6	26.9	27.3
169	23.5	23.8	24.2	24.5	24.9	25.2	25.6	25.9	26.3	26.6	27.0
170	23.2	23.5	23.9	24.2	24.6	24.9	25.3	25.6	26.0	26.3	26.6
171	22.9	23.3	23.6	23.9	24.3	24.6	25.0	25.3	25.6	26.0	26.3
172	22.6	23.0	23.3	23.7	24.0	24.3	24.7	25.0	25.4	25.7	26.0
173	22.4	22.7	23.1	23.4	23.7	24.1	24.4	24.7	25.1	25.4	25.7
174	22.1	22.5	22.8	23.1	23.5	23.8	24.1	24.4	24.8	25.1	25.4
175	21.9	22.2	22.5	22.9	23.2	23.5	23.8	24.2	24.5	24.8	25.1
176	21.6	22.0	22.3	22.6	22.9	23.2	23.6	23.9	24.2	24.5	24.9
177	21.4	21.7	22.0	22.3	22.7	23.0	23.3	23.6	23.9	24.3	24.6
178	21.1	21.5	21.8	22.1	22.4	22.7	23.0	23.4	23.7	24.0	24.3
179	20.9	21.2	21.5	21.8	22.2	22.5	22.8	23.1	23.4	23.7	24.0
180	20.7	21.0	21.3	21.6	21.9	22.2	22.5	22.8	23.1	23.5	23.8
181	20.5	20.8	21.1	21.4	21.7	22.0	22.3	22.6	22.9	23.2	23.5
182	20.2	20.5	20.8	21.1	21.4	21.7	22.0	22.3	22.6	22.9	23.2
183	20.0	20.3	20.6	20.9	21.2	21.5	21.8	22.1	22.4	22.7	23.0
184	19.8	20.1	20.4	20.7	21.0	21.3	21.6	21.9	22.2	22.4	22.7
185	19.6	19.9	20.2	20.5	20.7	21.0	21.3	21.6	21.9	22.2	22.5

Height in Centimetres	Weight in Kilograms										
	78	79	80	81	82	83	84	85	86	87	88
145	37.1	37.6	38.0	38.5	39.0	39.5	40.0	40.4	40.9	41.4	41.9
146	36.6	37.1	37.5	38.0	38.5	38.9	39.4	39.9	40.3	40.8	41.3
147	36.1	36.6	37.0	37.5	37.9	38.4	38.9	39.3	39.8	40.3	40.7
148	35.6	36.1	36.5	37.0	37.4	37.9	38.3	38.8	39.3	39.7	40.2
149	35.1	35.6	36.0	36.5	36.9	37.4	37.8	38.3	38.7	39.2	39.6
150	34.7	35.1	35.6	36.0	36.4	36.9	37.3	37.8	38.2	38.7	39.1
151	34.2	34.6	35.1	35.5	36.0	36.4	36.8	37.3	37.7	38.2	38.6
152	33.8	34.2	34.6	35.1	35.5	35.9	36.4	36.8	37.2	37.7	38.1
153	33.3	33.7	34.2	34.6	35.0	35.5	35.9	36.3	36.7	37.2	37.6
154	32.9	33.3	33.7	34.2	34.6	35.0	35.4	35.8	36.3	36.7	37.1
155	32.5	32.9	33.3	33.7	34.1	34.5	35.0	35.4	35.8	36.2	36.6
156	32.1	32.5	32.9	33.3	33.7	34.1	34.5	34.9	35.3	35.7	36.2
157	31.6	32.0	32.5	32.9	33.3	33.7	34.1	34.5	34.9	35.3	35.7
158	31.2	31.6	32.0	32.4	32.8	33.2	33.6	34.0	34.4	34.9	35.3
159	30.9	31.2	31.6	32.0	32.4	32.8	33.2	33.6	34.0	34.4	34.8
160	30.5	30.9	31.3	31.6	32.0	32.4	32.8	33.2	33.6	34.0	34.4
161	30.1	30.5	30.9	31.2	31.6	32.0	32.4	32.8	33.2	33.6	33.9
162	29.7	30.1	30.5	30.9	31.2	31.6	32.0	32.4	32.8	33.2	33.5
163	29.4	29.7	30.1	30.5	30.9	31.2	31.6	32.0	32.4	32.7	33.1
164	29.0	29.4	29.7	30.1	30.5	30.9	31.2	31.6	32.0	32.3	32.7
165	28.7	29.0	29.4	29.8	30.1	30.5	30.9	31.2	31.6	32.0	32.3
166	28.3	28.7	29.0	29.4	29.8	30.1	30.5	30.8	31.2	31.6	31.9
167	28.0	28.3	28.7	29.0	29.4	29.8	30.1	30.5	30.8	31.2	31.6
168	27.6	28.0	28.3	28.7	29.1	29.4	29.8	30.1	30.5	30.8	31.2
169	27.3	27.7	28.0	28.4	28.7	29.1	29.4	29.8	30.1	30.5	30.8
170	27.0	27.3	27.7	28.0	28.4	28.7	29.1	29.4	29.8	30.1	30.4
171	26.7	27.0	27.4	27.7	28.0	28.4	28.7	29.1	29.4	29.8	30.1
172	26.4	26.7	27.0	27.4	27.7	28.1	28.4	28.7	29.1	29.4	29.7
173	26.1	26.4	26.7	27.1	27.4	27.7	28.1	28.4	28.7	29.1	29.4
174	25.8	26.1	26.4	26.8	27.1	27.4	27.7	28.1	28.4	28.7	29.1
175	25.5	25.8	26.1	26.4	26.8	27.1	27.4	27.8	28.1	28.4	28.7
176	25.2	25.5	25.8	26.1	26.5	26.8	27.1	27.4	27.8	28.1	28.4
177	24.9	25.2	25.5	25.9	26.2	26.5	26.8	27.1	27.5	27.8	28.1
178	24.6	24.9	25.2	25.6	25.9	26.2	26.5	26.8	27.1	27.5	27.8
179	24.3	24.7	25.0	25.3	25.6	25.9	26.2	26.5	26.8	27.2	27.5
180	24.1	24.4	24.7	25.0	25.3	25.6	25.9	26.2	26.5	26.9	27.2
181	23.8	24.1	24.4	24.7	25.0	25.3	25.6	25.9	26.3	26.6	26.9
182	23.5	23.8	24.2	24.5	24.8	25.1	25.4	25.7	26.0	26.3	26.6
183	23.3	23.6	23.9	24.2	24.5	24.8	25.1	25.4	25.7	26.0	26.3
184	23.0	23.3	23.6	23.9	24.2	24.5	24.8	25.1	25.4	25.7	26.0
185	22.8	23.1	23.4	23.7	24.0	24.3	24.5	24.8	25.1	25.4	25.7

SCREENING AND ENROLLMENT LOG (if applicable)

Protocol No.:	
Investigator	**Centre No.:**

Screening No.	Screening Date (DD/MM/YY)	Subject Initial	Enrolled Yes / No	Patient ID allocated (ifenrolled)	Screening Failure Reason	Signature & Date

Prepared by		**Page no: 89-97**
Reviewed & Approved by		**BLDE(DU)SMO**

BLDE(DU) SITE SOP	Version 1.0	Revision 0.0	Effective Date: 29/May/2023
SOP No	**TITLE**		
SOP 14/V1.0	**SOP for Audio-Video Recording of ICF Process**		

Sno.	Contents
1.	Principle of Privacy and Confidentiality
2.	Procedure of Audio-Visual Recording
3.	Quality of Audio-Visual Recording
4.	Storage & Archival of Audio-Visual Recordings

In the drugs and cosmetics rules, 1945, in schedule, (Gazette notification New Delhi the 31st July, 2015

- An A-V recording of the informed consent process in cases of vulnerable subjects in clinical trials of New chemical entity or new molecular Entity including procedure of providing information to the subject and his understanding on such consent, should maintained by the Principal Investigator.
- In case of anti-HIV and anti-leprosy drugs, only audio recording of the informed consent process of individual subject and his understanding on such consent should maintained by Principal Investigator and team.

  Note: The A-V consenting procedure should be done in the respective PIs OPD / in some cases it should be done at site management organization.

I. Principle of Privacy and Confidentiality

1. During the audio-visual recording of informed consent process, the identity and records of the trial subjects should be kept confidential; and that no details about identity of said subjects, which would result in the disclosure of their identity, should be disclosed without valid scientific and legal reasons which may be essential for the purposes of therapeutics or other interventions, without the specific consent in writing of the subject concerned, or someone authorized on their behalf, and after ensuring that the said subject would not suffer from any form of hardship, discrimination or stigmatization as a consequence of having participated in the trial.
2. The Investigator must safeguard the confidentiality of trial data, which might lead to the identification of the individual subjects. Data of individual subjects can be disclosed only in a court of law under the orders of the presiding judge or in some cases may be required to communicate to Drug regulatory/ Health authority.
3. In order to maintain the confidentiality, the video grapher should been gaged as part of the study team. Prior to initiation of the study, the Investigator should define and allocate the activities of audio-video recording of informed consent process to the respective identified person as videographer. The Investigator should maintain the details of the person to whom he has delegated the duties of audio video recording.

II. Procedure of Audio-Visual Recording

1. At the beginning of the video recording process, the Investigators ho identify the protocol, the subject / LAR/IW and the language understood by the subject/LAR/IW. If the Investigator does not know the language of the subject/LAR/IW a member of the study team who understands the language, would become the interpreter.
2. In order to identify the subject/LAR/IW his/her photo ID may be documented. The video camera for the audio-visual recording should be of adequate capability to simultaneously capture the facial details of subject, LAR/Impartial Witness (if any), Investigator/ authorized person present during the consent process. The audio-visual recording should be conducted in a room conducive to recording of disturbance- free audio and video of the consent process.

   During the video graphy process, care should also be taken not to include unrelated persons/ patients at the hospital within the field of vision.

III. Quality of Audio-Visual Recording

The Video recording of informed consent may not serve the intended purpose if the quality of the recording fails to meet a minimum standard required for the purpose. The video recording should be done using video camera of appropriate resolution and in a room free from any disturbance to ensure that the image should recognizable and the audio should clearly audible.

IV. Storage &Archival of Audio –Visual Recordings

Audio visual recording of informed consent process and other related documents should be preserved safely after the completion / termination of the study for at least a period of 03 years if it should not possible to maintain the same permanently.

BLDE(DU) SITE SOP	Version 1.0	Revision 0.0	Effective Date: 29/May/2023
SOP No	**TITLE**		
SOP 15/V1.0	**SOP for Archival of Study Documents**		

Sno	Contents
1.	Purpose
2.	Introduction
3.	Scope
4.	Responsibility
5.	Definition
6.	Procedure
7.	Frequency of Archival
8.	References
9.	Annexures *AF-I/012/SMO/SOP-V3.0*Entryandexitregisterofarchives
	*AF-II/012/SMO/SOP-V3.0*RetrievalDataform
	*AF-III/012/SMO/SOP-V3.0Destruction*Form
	*AF-IV/012/SMO/SOP-V3.0*ArchivalroomvisualAuditlog
	*AF-V/012/SMO/SOP-V3.0*Documentlocationform

I. PURPOSE:

The purpose of this Standard Operating Procedure (SOP) should to describe the standard procedures to be followed when archiving essential paper/ electronic documents related to clinical research /trial of sponsored and conducted at BLDE (DU) SBMPMC Hospital Vijayapur.

All trial data must be kept so that the data can be accessed after the trial should finished. This may be necessary in the event of unexpected side effects after the trial drug has been approved. It should the responsibility of the Sponsor and the Principal Investigator/ Institution to keep these records.

II. INTRODUCTION

Archiving should the act of storing and preserving non-active records with an enduring value .the archivist coordinates and ensures quality storage and easy retrieval of the records.

As specified in GCP, the sponsor as well as the investigator / institution (i.e. investigational site) should maintain essential trial documents in accordance with applicable regulatory requirements. Essential study documents should be retained until at least 2 years after the last approval of a marketing application in an ICH region and until there should no pending or contemplated marketing applications in an ICH region or at least 5-10years (total 15Years) have elapsed since the formal discontinuation of clinical development of the investigational product. However, these documents should be retained even longer if required by applicable regulatory requirements or else agreed with the sponsor.

III. SCOPE:

This SOP applies to all Clinical trials conducted BLDE DU Shri B.M.Patil Medical College Hospital Research Centre, Vijayapura.

IV. RESPONSIBILITY:

- Archivist or designated personnel should be responsible to follow this SOP during archival retrieval and re-archival of documents / data.
- Relevant department personnel should follow this SOP while submitting documents for archival/ re-archival and requesting for retrieval of documents/ data.
- It should responsibility of the Site Management of BLDE DU Shri B.M.Patil Medical College Hospital Vijayapur to conduct periodic audit to assure the implementation of this SOP.

V. DEFINITION

- **Archival:** The procedure of preserving documents in any media for longer storage, in as a environment with controlled access.
- **Retrieval:** The procedure of getting the documents from the archives for reference, regulatory requirements etc.
- **Re-archival:** The procedure of re-archiving the documents after the purpose of retrieval should completed.
- **Clinical Trial**- Any investigation in human subjects, other than a non-interventional trial intended to discover or verify the clinical, pharmacological or other Pharmacodynamic effects of one or more medicinal product or to identify any adverse reactions to one or more such products and to study absorption, distribution metabolism and excretion in one of more such products with the object of as curtaining the safety or efficacy of those products.
- **International Council for Harmonization (ICH)** –Produced a series of guidelines in 1996, E6 being the guideline on Good Clinical Practice, otherwise known as ICH-GCP. Formerly known as International Conference on Harmonization.
- **Investigator Site File (ISF)**- A standard filing system which contains all essential documents held by Principal investigator(s) conducting a trial. Which individually and collectively permit the evaluation of the conduct of a trial and the quality of the data produced.
- **Principal Investigator (Pl):** A Registered Physician, Dentist who has responsibility for the conduct of the trial at a host site.
- **Essential Documents:** Essential documents should 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).
- **Trial Master File:**The Trial Master File should a file that consists 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 of Good Clinical Practice and with the applicable regulatory requirements.
- **Source Documents:** Source documents should original documents, data, and records (e.g., hospital records, clinical and office charts, laboratory notes, subjects' diaries or evaluation checklists, pharmacy dispensing records, recorded data from automated instruments, copies or transcriptions certified after verification as being accurate copies, microfiches, photographic negatives, x-rays, subject files and records kept at the pharmacy, at the laboratories and at medico-technical departments involved in the clinical trial).
- **Case Report Forms (CRFs):** A printed, optical or electronic document designed to record all of the protocol required information on each trial subject.

VI. PROCEDURE:

i. Archival Room Maintenance and Access control

- Access to the archival room should be controlled and tracked.
- Access to archives should restricted to Archivist and Administration. Entry of other individuals Third Party employees and external personnel such as Auditors / Clients into the archival facility shall be escorted by the archivist during visit. Entry and exit details shall be captured in the log book as per Annexure 01– Entry and Exit of Archives.
- Archival room should provided with the CCTV Camera, fire extinguisher, Heat and smoked etector.
- The temperature of 23 (+/-) 4oC and humidity 30-70% RH should be maintained in archival room.
- Pest control activity should be performed quarterly or as whenever required
- The archivist should perform quality check of the archives once in 06 months by visual audit for any signs of deterioration.
- The minimum signs of deterioration for visual evaluation includes the following but not limited to:
  - Presence of Paper Mites
  - Presence of Dust in the storage cabinets Presence of Rodents /
  - insects Excreta Presence of any growth of moulds
  - Presence of any self – deterioration of paper documents / files
- For any deterioration noticed, ensure immediate remedial actions should be taken.

ii. Archival period:

- All essential documents relating to clinical study including monitoring documents, projects files and audit documents should be archived in accordance with the requirements of the applicable regulations / guidelines as follows:
  - As defined in pro to color/ and as per the contract agreement with the sponsor
  - Until at least 2 years after the last approval of a marketing application in a region where the ICH guidelines applies.
  - Until there should no pending or contemplating marketing applications in an ICH region.

Documents relating to clinical study documents should be archived for a minimum period of10 to 15 years (or) in accordance Regulatory guidelines and BLDE (DU) Shri B.M.Patil Medical College Hospital Research Centre, Vijayapura. Which should be decided by the management team as per requirement.

iii. Location of Archival Documents:

Archived material should be stored in a legible condition at BLDE (DU) Shri B.M.Patil Medical College Hospital Research Centre, Vijayapura.

- In second floor opposite to SMO, Hospital Building
- The documents shall be archived in fire proof steel cabinets and shall be identified as I, II, III…etc.

  For example if the documents archived in cabinets – I and shelf–1, should be assigned the Archival location as "I1"
- Each cabinet should have register maintained by the archivist as per Annexure 07–Format of archival register.
- The register should contain the details of documents or materials archived in each shelf.

VII. Frequency of archival:

i. Study documents:

During the conduct of a study, study documents and data can be retained in Archival room at BLDE (DU) Shri B.M.Patil Medical College Hospital Research Centre, Vijayapura. And stored in the project file and/or e-directory, or otherwise as specified in the contract/work order with the sponsor.

- Once the trial should completed, project documents shall be returned to the client or archived according to the terms and conditions as per regulations/ site policies.

Study documents should be archived after the completion of the study and within 30 days. The Study completion letter along with study progress to submitted to the IEC of BLDE DU Vijayapura.

ii. Non-Study related documents:

Superseded SOPs should be archived within10 working days from the date they become obsolete.

iii. Archival of paper documents:

- The respective department head/ designee should responsible for notifying the archivist in writing, the intent to archive study documents.
- All records related to the project should be retained in a manner that should preserve the security, integrity and authenticity.
- All study related documents should be given to archivist in appropriately labeled files by the concerned department as shown below: *AF-I/012/SOP-V3.0*

- The contents in the files should be verified against the index given in the respective files by the archivist before archival.
- Upon completion of the contracted archival period, the sponsor should be informed / intimated in writing. If the archival period should extended by the sponsor
- Archive master copies of the superseded versions or absolute of the SOPs / Work procedures in the labeled box files

- While archiving do not compile all versions of single SOPs/ Work Procedures of different departments together.
- The details of archive should be captured in *AF-III/012/SOP- V3.0* archival inventory log by the archivist

iv. Archival of Electronic Documents /data (if applicable)

- Once the study completed at BLDE(DU)'s Shri B.M. Patil Medical Hospital Research Centre, Vijayapura, all the created electronically or received electronically by **BLDE (DU) SBMPMC Hospital** should be archived on appropriate electronic media in read only format duplicate copies or as per procedure specified in the contract with sponsor.
- After that the data shall be deleted from the shared network directories and individual computers.
- All the electronic documents/ data shall be appropriately labeled by the concerned department as shown as below: Annexure-III
-

Name of the study document:
Study title/Number:

Name of Principal investigator/Co-PI:
Date of creation:

- Appropriate security measures shall be taken to avoid my unauthorized access to the electronic data.
- If the responsibility of electronic archival should not delegated to BLDE (DU) SBMPMC Hospital Vijayapur, the protocol specific electronic data, along with details of e-Data, shall be returned to sponsor.

v. Disposition of archived data/ documents:

- Under circumstances, shall any archived material should be removed/ destroyed by the Clinical services administrators of BLDE (DU) SBMPMC Hospital Vijayapur, without intimation from sponsor or any other specified in the contract with the sponsor.
- Processes for identifying materials that have reached the end of their retention period
- Upon completion of the contracted archival period, the sponsor should be informed / intimated in writing. If the archival period should not extended by the sponsor then the study documents should be returned to the sponsor and a list of documentation provided to the sponsor should be created. A sponsor acknowledgment copy of this shall be retained.
- If required, disposition of study documents/data should be out sourced to an external vendor by SBMPMC Hospital Site Management Organization, BLDE (DU) Shri B.M.Patil Medical Hospital & Research Centre, Vijayapura.

VIII. References:

1. 21CFR312.55-Informing Investigators

2. 21CFR312.57-Record Keeping and Record Retention

3. 21CFR312.58- Inspection of Sponsor records and Reports

4. 21CFR312.62-Investigator Record Keeping and Record retention

5. 21CFR312.64-Investigator Reports

6. Appendix V-CDSCO guideline: Essential Documents

7. ICH Guidelines for GCP (E6) Section 4.4- communication with IRB/IEC

8. ICH Guidelines for GCP (E6) Section 4.9- Records and reports

9. ICH Guidelines for GCP (E6) Section 5.22- Clinical Trial /Study Reports

ANNEXURES

Annexure: I

Entry and Exist register of Archives:

Sl. No.	Name of the Person	Department /Sponsor / Regulators	Purpose	Time in	Time out	Sign and date	Authorized by

Annexure II

Retrieval Data Form

SI. No.	Protocol No.	Request for &Date	Retrieved by/ signature	Returned Date and signature	Authorized by

Annexure: III

Destruction Form

Sl.No.	File /Document No	Box/ Shelf No	No. of Boxes	Date of destruction	Verified by

Annexure: IV

Archival room–Visual Audit log

Archival room visual audit for the quarter of_____(MM/DD/YYYY)

Location of damage/ Deterioration and remedial actions taken (if any observed)

Observations:

Visual Audit per formed by:	
Name	
Designation:	
Signature:	

Annexure: V

Document location Form

Cabinet ID:

Shelf ID	*Contents*	*Shelf ID*	*Contents*