Site Management Office

KLES
DR. PRABHAKAR KORE HOSPITAL
&
MEDICAL RESEARCH CENTRE
NEHRU NAGAR, BELAGAVI-590010

KLE Academy of Higher Education and Research

Belagavi - 10 [Formerly Known as KLE University]

KLES Dr.Prabhakar Kore Hospital

Nehru Nagar, Belgaum-590010, Karnataka

SOP Standard Operating Procedure

SOP Version: 3.0

In accordance with the Declaration of Helsinki (2000)
And ICH-GCP (E6) Guidelines
New Drugs and Clinical Trial Rules, 2019

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KLE Academy of Higher Education and Research

Site Management Office

KLES Prabhakar Kore Hospital Medical Research Center, Belgaum

Standard Operating Procedures- Version-3.0 (SOPs)

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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 will be discussed before initiating the trial.

Aims: To define Investigators' responsibilities and to provide instruction, when performing clinical study (ies) facilitated by KLES Dr. Prabhakar Kore Hospital & MRC, Belagavi

I. Objectives:

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

ii. To ensure that the study is 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 properly protected.

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

v. To ensure that the Investigator is acquainted with the study procedures, verification procedure, audits and inspection procedures.

vi. To responsible for the third-party staff (Site management organization employees), whoever working in the respective clinical trials.

Co-investigators:

Co-investigators are authorized healthcare professionals who work alongside the PI at a trial site, e.g. other Consultants in the department, Post Graduate Medical students). The co-investigator may conduct all or part of the PI's duties, and must be available to act up as PI if the PI is unavailable for any length of time (e.g. annual leave) or in an emergency situation that could affect the safe conduct or oversight of the trial.

Note: PI/Co-I not affiliated to the KAHER (KLE University), those cannot be delegated in the clinical trial team.

II. Prior to initiation of the study:

The Investigator should:

i. Be interested in the scientific aspects of the study and ensure that the study is responsive to the needs of public health within the country of the population in which it will be conducted.

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

iii. Have sufficient time free from other obligations to prepare and conduct the trial.

iv. Clinical trials are time consuming and the Investigator should ensure that sufficient time can be dedicated to the study, including for informing and supervising 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 investigators' SOPs 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 trial by providing retrospective data on numbers of patients who would have satisfied the proposed entrance criteria during proceeding time periods.

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

x. Make sure that there are sufficient medical, paramedical and clerical staffs to support the study and deal with foreseeable emergencies**.**

III. Make sure that the facilities are sufficient to allow the study to be undertaken efficiently.

Ensure:

- Confidentiality and safety conditions for trial subjects.
- Adequate equipment/facilities for subject follow-up, examination and care.
- Adequate facilities for Investigational Medicinal Products storage
- Adequate facilities for laboratory assay of the Subjects blood parameters investigations.
- Adequate facilities for retention of trial documents, ensuring confidentiality of all information about trial subjects and information supplied by KLEs Prabhakar Kore Hospital Medical research Centre, Belagavi /sponsoring agencies.
- Make sure 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 subjects' 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 will adhere to, the protocol, study procedures and ICH Good Clinical Practice, will collaborate with the monitor, and accords with Sponsoring agencies on publications policy.

Submit requested documents to the Site Management Office of KAHER, 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 Staff Form
- Product exportation/importation authorization.
- Laboratory certification/recent list of normal laboratory ranges, dated and signed by lab head/Investigator.
- Lab Accreditation certificate
- Final Clinical trial agreement
- Signed agreement that the product will not be used before the site Initiation Visit has been made and authorization obtained from the SMO Clinical Research Coordinator (if applicable).
- Ethics Committee accreditations
- Visit of archival facilities (situated at G-0 at KLES Dr. Prabhakar Kore Hospital and MRC, Belagavi

VI. During the Study:

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

i. Delegation of duties: PI can delegate the CRC/Sub-I/Phlebotomist when 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 by the PI. It is applicable for both observational and interventional clinical trial studies at KLES Dr.PK Hospital and MRC, Belagavi.

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 name of the person, their role and the activities they are delegated by the PI as well as being signed and dated by the 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 large department such as pharmacy, and the relevant trials pharmacist would then take responsibility for the conduct of that activity by the 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 tasks at a later date).

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

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

The Investigator should keep the File in a locked cabinet, in a secure area accessible only to the Investigator and authorized study staff. The Investigator 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. Written approval from sponsors and site administrations, PI must be obtained prior to destroying records.

- Lab kits
- IPs

- Study Documents (after completion of 15 years)

★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 KAHER, Belagavi
- IEC Accreditation details
- Lab head CV and MRC
- Local regulatory requirements.
- IEC and other authorities' written approval for all documents (protocol, informed consent(s) and any written information including advertisements for recruitment of study subjects).
- Protocol initial submission letter and initial IEC of KAHER 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 KAHER.
- 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-investigators' C.V.s.
- New Investigator and Sub-investigators' C.V.s 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 authority (ies).
- 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 authority (ies).
- The investigator should maintain a list of appropriately qualified persons to whom the investigator has delegated significant trial-related duties.
- PI should Signed confidentiality agreement

- PI should Signed agreement stating that products will not be used before the Trial Initiation.
- Monitoring Visit has been made and approval from the SMO Clinical Coordinator obtained.
- Sub investigator should be affiliated to KLES Dr. Prabhakar Kore Hospital and MRC, Belagavi and KLE's JN Medical College staff.

vii. Correspondence and Monitoring

- 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 Prior to Visit for site monitoring.
- Copies of the Investigator's interim report/written summaries of the trial to the IEC of KAHER and authorities.
- Monitoring visit of IEC members at site: PI/CRC should arrange/ready for the all study related documents for Monitoring. IEC secretariat will informed via mail/letter about the IEC monitoring visit. IEC members will select randomly which have approved and ongoing studies at site.
- To ensure to submit the SIV and SMV report to IEC of KAHER, Belagavi

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 authority (ies) and which were given approval/favorable opinion by the IEC of KAHER. 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 KAHER 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 KAHER 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 authority (ies)

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 available an adequate number of qualified staff and adequate facilities for the foreseen duration of the trial to conduct the trial properly and safely manner.

VII. After Completion of the study:

- The CRA has to confirm the close out visit in writing to the Investigator/study site. The letter will detail all persons expected to attend, and all administrative documents, IMP, and regulatory documents required for review at this visit. The CRA will confirm recruitment status at the end or premature end of the trial. If the site is closed prior to the end of the trial, a reason for early closure should be clearly documented.
- The CRA will ensure that all Serious Adverse Events (SAE's) have been reported by the Investigator to the Sponsor and that the investigator is aware of any future reporting requirements 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 will ensure that all outstanding data queries are resolved at the time of the close out visit.
- All outstanding issues from previous monitoring visits will be resolved or appropriately documented.
- The CRA will verify that final drug accountability is complete
- If applicable, the CRA will ensure that Sponsor authorization for IMP destruction has been obtained and that the destruction or return of unused or partially used IMP is appropriately commented and documented in the Pharmacy file.
- PI along with the study CRA review the all study related documents in study close out visit. After completion of the study, all the study documents should be archived. ***(Please Refer: title: 0012 SOP for archival study documents)***

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I. Policy:

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

II. Objective:

This SOP gives the procedure for obtain informed consent from 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 trial, after having been informed of all aspects of the study that are relevant to the subject's decision to participate. Informed consent is documented by means of a written, signed and dated informed consent form.

V. PROCEDURE:

1) All the clinical trial related ICFs should be obtained in the respective Principal investigator OPD.

2) Procedure for Obtaining Informed Consent from Volunteers for participation in study

3) The Subject Information sheet and the Informed Consent form will be given to the subject on the day of Screening.

4) The Study Coordinator/designated person will issue a copy of Institutional Ethics Committee of KAHER approved 'Subject Information Sheet and Informed Consent Form' (SIS/ICF) to the subject in the language best understood by him/her.

5) Investigator/designated person will give study related information from the Institutional Ethics Committee of KAHER approved 'Subject Information Sheet and Informed Consent Form' to the volunteer.

6) Investigator/designated person will 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, 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 IEC/ approved 'SIS/ICF'. The name of the subject to whom the SIS/ICF is issued and sign and date of the person counseling the subject will be documented in the source document.

7) Investigator/ designated person will take the Informed Consent in one to one manner, the Investigator/ designated person will answer to all personal queries of the subject or their Legal Acceptable Representative (LAR) or Guardian during this session.

8) Investigator/designated person will inform that the eligible and interested subject or the volunteer's Legally Acceptable Representative (LAR) will 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 is independent of the study will be present during the entire informed consent discussion and will 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.

9) Each subject will 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.

10) The Investigator(s), Sponsor or the staff will not coerce or unduly influence the potential volunteer/subject to participate or to continue to participate in the study.

11) Investigator/Physician/ designated person will ensure that the subject as 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 KAHER approved 'SIS/ICF' and is participating in the study willingly.

12) Investigator/designated person will 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.

13) The volunteer/volunteer's legally acceptable representative (LAR) will 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.

14) In case of the volunteer/legally acceptable representative is unable to read/write then the subject will give the left thumb impression at the appropriate place and the impartial witness will 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 will 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.

15) 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 of the volunteer's legally representative or the guardian, and that the informed consent was freely given by the subject or the volunteer's legal representative.

16) The Investigator/Co-Investigator will sign and date and will put his/her name in the ICF.

17) Site coordinator will give photo copy of signed consent to Subjects/Legally Acceptable Representative.

18) The researcher has an obligation to convey details of how confidentiality will be maintained to the participant.

19) After the completion of consent process the study designee record the all protocol related information in sources documents.

20) If the patient is literate and unable to write in ICF then LAR can write the details on behalf of the patient and no LAR signature is required to authenticate the same. But reflection f the movement should be recorded in ICF process.

VI. Applicable rules and regulations:

- FDA 21 CFR 50.20—General Requirements for Informed Consents
- National Ethical Guidelines for Biomedical and Health Research Involving Human Participants-2017
- HHS 45 CFR 46.116—General Requirements for Informed Consent
- New Drugs and Clinical Trial Rules, 2019

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1. Purpose

This SOP defines the procedure and recommendation of training of study team members and adequate 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 research-related task(s).

The purpose of a handover is to ensure continuity of operations when the study team member, usually responsible, is not available due to temporary or permanent absence. A handover can be supported by a discussion to explain the status of the tasks, a summary of the work status in an email/ memorandum or, a more detailed file.

2. Scope:

This SOP will apply to all study research coordinator at site management office in KLEs Dr.Prabhakar Kore Hospital and MRC, Belagavi.

3. Responsibilities:

i. Study start up activities like Feasibility/Synopsis and Clinical disclosure agreements.
ii. Reviews and develops a familiarity with the study protocol (e.g. study procedures and timelines, inclusion/exclusion criteria, confidentiality).
iii. Document date of training and signatures of study personnel trained on study specific training log.
iv. Collect documents needed to initiate the study and submit to the sponsor (e.g. forms 1572, CVs, etc.)
v. Conduct or participates in the informed consent process, including interactions with the IEC and discussions with research participates, including answering any questions related to the study.
vi. Obtain appropriate signatures and dates on forms in appropriate places. Assures that amended consent forms are appropriately implemented and signed/Dated.
vii. Screen subjects for eligibility using protocol specific inclusion and exclusion criteria, documenting each potential subject eligibility or exclusion. Creates and utilizes Eligibility Checklist to inclusion/exclusion criteria.
viii. Coordinate participant tests and procedures, including scheduling and registration of subjects with hospital Outpatient/ in patient departments at site (e.g. radiology for CT scan).
ix. Collect data as required by the protocol. Assure timely completion of Case Report Forms
x. Maintain study timelines per the event schedule (e.g. subject visits, procedures and data entry are completed within the allotted time window per study protocol).
xi. Maintains adequate inventory of study supplies. If handling investigational drugs/devices, follows the sponsor protocol and/or UCSF Policy on Investigational Drug/Device Accountability.
xii. Complete study documentation and maintains 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.

xiii. Maintain effective communication with sponsor, research participants, IEC of KAHER and PI during the course of the study.

xiv. Work with the PI to manage the day-to-day activities of the study including problem solving, communication and protocol management.

xv. Report all findings and correspondence from external or internal study monitoring and audits to the research manager and department Chair in a timely manner.

xvi. Assist the PI in reporting of research-related incidents, including protocol deviations or potential violations, as well as findings and correspondence from external or internal study monitoring and audits to the IEC of KAHER, Belagavi in a timely manner.

xvii. Assist the Principal Investigator in submission of accurate and timely closeout documents to applicable Federal agencies, University entities, and the sponsoring agency in accordance with Federal regulations and Hospital/University policies and procedures.

xviii. **Study Handover:** If any study team member is planning for leave or to resign, he/she must ensure that the proper handover is given to concern person identified by the PI, the identified person should be briefed in time before the person goes on leave to allow for any follow up questions.

xix. 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 will change for the subjects.
- Provide a list of study-specific contacts (e.g., sponsor, monitor, vendors involved etc)
- Provide a list of outstanding issues
- The leaving person has to make sure that the documentations concerned for the tasks is up to date and easily available, and if needed, revise it when preparing the hand over.

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

- Inform Sponsor and IEC of KAHER regarding the change in PI in the Study team.
- Consider revising the protocol and informed consent form, as appropriate. Also consider notifying current subjects; correspondence sent to all subjects must be approved by the IEC, if applicable.
- Update the Form FDA 1572 or the Investigator Agreements, Investigator Undertaking and other required forms
- Update the Duty Delegation log
- Ensure that the new PI has completed the SOP required training and study-specific training

- Written hand over should be given in order to ensure the continuity of work. The format can be a briefing note, a check list, or a schedule prepared to give all information.

When the study member returns from leave a hand over should be prepared to give updates on the status of the tasks.

The existing and new study team member should document the study handover in a note to file or other documentation in the TMF. The note should contain some of the items above and the date of the handover. The new study team member should obtain documented study-specific training and any required approvals prior to being added to the duty delegation log.

4. Procedure:

Appointment Procedure:

The site clinical research coordinators have been appointed through respective site management organisations. Before assigning the CRC to KLEs Dr.PK Hospital, the Organisation has to intimate the site personnel via mail or letter for communication with proper appointment letter and period of agreement (If applicable).

Study Team Training:

1. On appointment, all study team members will be given an appropriate study depending on the job specification to possess the right experience and qualifications and further training may be provided to bring them up to the required level for specific tasks. Duty delegation / job responsibility document will be given to every Clinical research Coordinator/team member.

2. The Medical Director and department of clinical research recommend that all Investigators, CRC and other study team members must undergo training which will enable them to understand their responsibilities, applicable regulations, guidelines and research studies and training should be documented in the training log.

3. Each Investigator, CRC and study team members will review and learn the site's SOPs. It is recommended that SOP training must be included in the orientation of new clinical research personnel. All applicable clinical research personnel should be knowledgeable of new or revised SOPs.

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

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

6. Before study initiation the Sponsor/CRO will organize SIV meeting at site to train all study team members and all study team members should attend the meeting for thorough understanding of the study.

7. In the study start up activities like feasibility/study synopsis CRC should intimate to the site personnel.

8. 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 activation of each new study

9. Study team members should attend the course to acquire training or to update themselves.

10. PI can also train the study team and should maintain the training record.

11. It is recommended that the PI and study team must maintain the Site SOP training Record.

12. **Entry in to Study drug store at site:** The access will be given only blinded/unblinded pharmacist and who are delegated (Delegation log) in clinical study for the IP management. The entry access will 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
- Research Team (listed in the delegation log)
- Clinical Research Coordinator

Staff responsible for Implementation:

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

- The department and PI will ensure that at the time of implementation of the SOP, which the research team at the site management office (clinical research unit) in KLES Dr.Prabhakar Kore Hospital and MRC, Belagavi are trained and in the event that an SOP is modified, provide training regarding the change(s) and ensure their compliance with the changes.

- It is the responsibility of each individual who are about to go on short / long term absences or leave their current position / the Agency/third party employees to prepare a hand over file.

Title: 004- SOP for Check in and check out of the subject

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Title: 004- SOP for Check in and check out of the subject

I. **OBJECTIVE:** This SOP gives the procedure for check-in and check –out of subject, from the housing area 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 Make sure to avoid dosing schedules on Sundays (on Sunday Registration counter will be remains closed/Unavailability of the Study Nurses/PIs)

III. **PROCEDURE:**

1.0 Procedure for Subject Check-In (in the First period 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's as mentioned in the study protocol, and who are found negative in breath alcohol, Urine screen for drug of abuse and urine pregnancy test or any other screening procedure as mentioned in the study protocol will be checked-in into the private/Semi Private wards as per direction from the Medical Director of KLES Dr,Prabhakar Kore Hospital and MRC, Belagavi.

1.2 The Study coordinator/designated person will 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 will check the subject's belongings, clothing and pockets for any prohibited products like gum, medication, cigarettes and tobacco or sharp instruments.

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

2.1 The PI will perform the medical checks (history from the last visit), vital sign measurement and well being assessment, Clinical examination or any other investigation requirements as specified in the study protocol for the subject, before enrolling for subsequent Period of the study.

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

2.3 PI will review the above reports and will 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 will be checked-in into the housing area as mentioned in point 1.2.

2.5 The subject who is found to be unfit in any of the above parameters will be withdrawn from the study and will 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 will be documented in the format for 'Subject Dropout/Withdrawal /Termination Form' of the CRF.

3.0 Procedure for Check-Out

3.1 Subject will 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 is 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 will be recorded in the format 'Discharge summary' of the CRF of the respective subject.

3.3 The Physician/designated person will measure the vital signs and assess the well being of subject and will perform the Clinical examination before discharge from the Clinical facility.

3.4 The Subject Custodian/designated person will return the subjects belongings from the locker; will 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 will be recorded in the form in the CRF.

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

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

3.7 Physician and/or Clinical Investigator/Co-Investigator will check the ECG report of respective subject and will 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 will be collected and sent to the Clinical laboratory.

3.9 The subject will 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 will 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 will be checked and reviewed by the Physician/designated person and the details of observation will be recorded in the Post study evaluation form of the CRF of the respective subject. The Physician/designated person will 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**.**

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

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3.	PROCEDURE: • Monitoring Restriction • Dosing the subject	22

I) OBJECTIVE

This SOP gives the procedure for dosing the subjects and Monitoring Restrictions in compliance to the study Protocol for the Clinical study.

II) SCOPE

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

III) PROCEDURE:

1.0 Monitoring Restriction

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

1.2 The Subject Custodian/designated person will monitor these restrictions and will 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 will be documented in the CRF and will be justified appropriately.

2.0 Dosing the subject

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

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

2.3 Staff responsible for dosing will ensure that gloves, dosing fluid (as per Protocol), flash light, 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 will be administered in a staggered manner to maintain subsequent blood collection schedule.

2.5 The designated person will 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 will call subject by subject number for dosing prior to the scheduled time of dosing.

2.7 The Designated person will 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 will 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 will assess the well being of the subject verbally before dosing, and will also briefly explain the procedure to be followed for dosing and the restriction to be followed thereafter.

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

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

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

2.15 The Designated person will collect unused IP(s) (due to subject dropout/terminated before dosing) and will take it to the IP storage room and will 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 will be followed as per respective Study Protocol/Pack Insert/on the IP container.

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3.	PROCEDURE: • Procedure for blood sample collection • Precaution to be taken for Photo sensitive and Temperature Sensitive Drug Product • Transfer of samples from the Clinical Facility to the Bio-analytical Facility.	25

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:

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

III. PRECAUTIONS:

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

IV. PROCEDURE:

A. Procedure for Blood Sample Collection

1. The Phlebotomist/Nursing Staff/designated person will 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 will ensure the availability of the required medical accessories like labeled vacutainers/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 will check the pre-labeled vacutainers/centrifuge tubes and will arrange them in sequence on the rack for each sample collection station and will enter the details in ‘Pre-Sample Collection Vacutainer/Tube Check format’
4. Intravenous cannula will be inserted in the fore arm of the subject for collection of the blood samples for Pharmacokinetic study.
5. The Subject custodian will call the subject(s) by their subject number in sequence and will 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 will be done as per requirement or if stated in the study protocol.
7. The Phlebotomist/Nursing staff/designated person will verify the vaccutainer/centrifuge tube label for the study code, sampling time and the subject number and will 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 will be staggered as per the dosing time of each subject. Phlebotomist/Nursing staff/designated person will 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 will discard the initial saline mixed blood (approximately 0.3 mL or volume as per Study specific protocol) from the intravenous canula using a 2 mL syringe before collecting the blood sample.
10. The Phlebotomist/Nursing staff/ designated person will secure the disposable (10 mL/5 mL/2 mL) syringe to the intravenous cannula, will open the three-way stop-cock and will 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 will be as per the Study Protocol. After collection of blood samples, the vacutainer/tube with samples will be shaken mildly for mixing with the anticoagulant in the vaccutainer/tube.
11. After collecting the blood sample, the 3-way stop cock will be closed and the blood sample will 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 will 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 will be injected into the 3-way stop cock to avoid blockage of cannula. The 3-way stop cock will be kept closed till the next scheduled sample collection of the subject.
14. The Phlebotomist/Nursing staff/ designated person will record the actual time of each sampling time point for each subject and will sign and date in the format for ‘Blood Sample Collection Details’ of the CRF.
15. In case of cannula blockage observed during the sample collection, the blood sample will be collected by direct vein puncture using a syringe with needle, thereafter the subject can be recanulate, 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 (canula block/canula replaced/direct prick/poor blood flow) will be recorded in the ‘Blood Sample Collection Details’ of the CRF of respective subject.
16. The Phlebotomist/Nursing staff/designated person will transfer the vacutainer /centrifuge tubes with blood samples at each sampling time from each sampling station(s) to the sample processing area.
17. The Technician/designated person will receive the vacutainer/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 will be processed as specified in the respective Study Protocol.
19. The Technician/designated person will place the vacutainer/centrifuge tubes in the centrifuge machine.
20. The Technician/designated person will set the speed (RPM), time and temperature (as mentioned in the study protocol) of centrifuge machine and will 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 will be recorded in ‘Centrifugation and Separation of Biological Samples Record’.

21. After completion of the centrifugation, the Technician/designated person will remove the vacutainer/centrifuge tubes carefully (without disturbing the contents) from the centrifuge machine and will arrange it in vacutainer/centrifuge tube stand.
22. The Technician/designated person will arrange the pre labeled vials of respective sampling hour sequentially in the rack/tray.
23. The Technician/designated person will harvest the plasma/serum from each centrifuged vacutainer/centrifuge tube using micro pipette with disposal tips without disturbing the sediment layer and will 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 will cap the vials.
24. The Technician/designated person will 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 will 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.
26. The Technician/designated person will 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 will 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 will 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 will be taken or will follow the measures/procedures mentioned in the respective Study Protocol.
4. The blood sample will be collected into pre-chilled vacutainer /centrifugation tube. This vacutainer/centrifugation tube with blood samples will be placed in ice water bath till it is centrifuged. After centrifugation at the set parameters the plasma/serum will be harvested using micropipettes with disposable tips into pre-labeled vials as 'Analytical' and 'Replicate' sample, these vials containing the harvested plasma/serum will be placed into deep-freezer maintained at a temperature specified in the Study Protocol.
5. The Phlebotomist/Nursing staff/designated person will record the sample time point deviation in the 'Deviation Reporting Form'. The responsible Physician/designated person will 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.

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

1. Study Coordinator/designated person will take the authorization from Clinical investigator/designated person for transfer of biological samples to the bio-analytical

facility and will get the name and address of the bio-analytical facility where the sample has to be transferred.

2. Study Coordinator/designated person or the Contract Courier person (who will be shipping the samples) will arrange insulated boxes with appropriate coolant before initiation of the transfer activity.
3. Study Coordinator/designated person or the Contract Courier person will place the temperature monitoring device to record the temperature during the transfer of biological samples.
4. Study Coordinator/designated person will identify and remove the biological sample boxes/polybags from the deep-freezer and will record the retrieval of samples in respective format.
5. Study Coordinator/designated person will transfer these labeled samples boxes/polybags as per the specified requirements, into the insulated box with sufficient coolant to maintain the storage condition of the biological sample during transportation and will seal the box (es).
6. Study Coordinator/designated person will 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 will paste appropriate labels {e.g. warning label as "Biological Samples", "Handle with Care", "Light Sensitive samples" (if any)} and will also paste label mentioning the complete address of the bio-analytical facility where samples are to be transferred, on the box. If Applicable.
8. Study Coordinator/designated person will 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 will sign the transfer format as 'Received by' and will write the time of receipt. The Contract Courier person will 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 will 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 will acknowledge the receipt of the samples.
11. A copy of this transfer format will be maintained in the Study File at the Clinical site.
12. The person receiving the sample at bio-analytical facility/Contract Courier service person will remove the temperature monitoring device and the print of the temperature record during transportation will be maintained along with the Sample transfer format.
13. If it is genetic samples (Please submit the Material transfer agreement and Data Transfer Agreement to the Institution/IEC.

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I. OBJECTIVE:

This SOP gives the procedure for handling and reporting the Adverse Events and Serious Adverse Events encountered during the clinical studies at KLES Dr. Prabhakar Kore Hospital & MRC, Belagavi

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, is life-threatening, requires inpatient hospitalization or prolongation of existing hospitalization, results in persistent or significant disability/incapacity, or is 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 is otherwise life threatening.

- **Adverse Event**: An AE is 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 is not consistent with either:**

a) The known or foreseeable risk of adverse event associated with the procedures involved in the clinical study that are described in (a) the protocol-related documents, such as the IEC-approved Study protocol, any applicable investigator brochure, and the current IEC-approved informed consent document and (b) other relevant sources of information, such as product labeling and package inserts; or

b) 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 will 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 intake • Cannot be explained by disease or other drugs • Response to withdrawal plausible (pharmacologically, pathologically) • Event definitive pharmacologically or phenomenologically (i.e. an objective and specific medical disorder or a recognized pharmacological phenomenon) • Rechallenge satisfactory, if necessary
Probable/ Likely	• Event or laboratory test abnormality, with reasonable time relationship to drug intake • Unlikely to be attributed to disease or other drugs • Response to withdrawal clinically reasonable • Rechallenge not required
Possible	• Event or laboratory test abnormality, with reasonable time relationship to drug intake • 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
Un assessable/ Unclassifiab	• Report suggesting an adverse reaction • Cannot be judged because information is insufficient or contradictory • Data cannot be supplemented or verified

*All points should be reasonably complied with

2) Severity: The degree of an adverse event is divided into mild, moderate, or severe.

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

V) PROCEDURE:

1.0 Handling of Adverse Event

a. The Clinical Investigator/Medical Officer will 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 will monitor the subject(s) for any untoward or unfavorable and unintended sign (including abnormal Clinical laboratory finding), symptom during the

Visits and study housing. The designated person will 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 will examine the subject and will give assurance or provide appropriate medical care to ensure well being of the subject in accordance with currently acceptable clinical standards and guidelines.
d. The designated person will 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 will also inquire about the progress of the adverse events to the subject telephonically. The subject is also requested to report the Adverse Event at any time to the designated person.
f. The designated person will review the post study clinical laboratory report (pathological report) for any out of range values, these values will be compared with the baseline reports values to determine its significance for evaluation of any Adverse event. If any clinically significant observation(s) are found in the Clinical laboratory reports then it will recorded in the Adverse Event Form of the CRF, attached as Annexure-01, and the designated person will inform the subject about the evaluation and will request him/her to report to the Study center for follow up.
g. The designated person will 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 is required for the management of the adverse event, will be done on the discretion of the Clinical Investigator/Co-Investigator.
i. The designated person will monitor the subject or follow up with the subject till the resolution of the Adverse Event.
j. designated person will 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.
k. If in the judgment of the Clinical Investigator/Co-Investigator the continuation of the subject proves harmful to him/her, then will take the decision to terminate the subject from the study. The termination details will be recorded in the 'Subject Drop-Out/Withdrawal/Termination Form' of the CRF of the respective subject. Handling of Serious Adverse Event (SAE).
l. In case of occurrence of any Serious Adverse Event, Clinical Investigator/Co-Investigator/Medical Officer will 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 will shift the subject to the emergency facility (if required).
m. The subject will be monitored till the resolution of the Serious Adverse Event or on the discretion of the Clinical Investigator/Co-Investigator.
n. The Medical Officer will 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 will keep all the relevant medical record including the hospital record along with the CRF of the respective subject.

o. The Medical Officer will also record details in the 'Logbook for Serious Adverse Event details.
p. Clinical Investigator/Co-Investigator will review the details recorded in respective subject's CRF and in 'Logbook for Serious Adverse Event Details'.
q. The termination of the subject from the study due to a Serious Adverse Event will be documented in the 'Subject Drop-Out/Withdrawal/Termination Form' of the CRF of the respective subject.

2.0 Reporting of Adverse event:

Reporting of the adverse event by the Investigator:

- Unanticipated problems involving risks to subjects should be reported promptly.
- 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 a serious, unexpected event that is uncommon and strongly associated with drug exposure (e.g agranulocytosis, hepatic injury)
- A single occurrence, or more often a small number of occurrences, of a serious, unexpected event that is not commonly associated with drug exposure, but uncommon in the study population.
- Multiple occurrence of an AE that, based on an aggregate analysis, is 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 is described or addressed in the investigator's brochure, protocol, or informed consent documents, but occurs at a specificity or severity that is inconsistent with prior observations.
- A Serious Adverse Event that is 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.

2.1 Reporting of the adverse event by the Investigator to Sponsor:

There is 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 is 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 is alarming, in which case, to be reported immediately;
- Serious adverse events, to be reported immediately unless the protocol or other document indicates otherwise. It is essential to specify clearly in the protocol and the adverse event reporting section of the protocol, what is and is not expected as well as what is and is 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.2019 is within 24 hours of identifying the event

2.2. 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 are associated with the use of the drug and that are 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 is 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 is 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 will get the compensation and in case of death, the nominee of the subject will get the compensation.
- In post marketing studies, sponsors must not only report under MedWatch (The FDA's safety information and adverse event reporting program, which provides information about safety issues and provides an online gateway 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.

2.3. PI Reporting of the serious adverse event to the IEC of KAHER

- It is 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 checklist detailed by Licensing Authority.
- IEC will perform Causality Assessment with reasoning for Relatedness/Un-relatedness and will 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

2.4. Reporting of the adverse event by the Sponsor to other Investigators:

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

- Adverse events those are 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.

2.5. 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 New Drugs 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) is 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 is the template of covering letter.

e) Instructions are provided 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 is 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. DCGI CT file number
ii. Complete address of Sponsor and CRO (if any) including phone & e-mail address
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 exceeding 10 lines. A detailed narrative may be enclosed, if available.

Code	SAEs occurring in clinical trial
CT-1-IND	New Drug - Investigational New Drug (IND) study (where IND is filed in India and is 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

viii. Unexpected SAEs have to be submitted to the office as per Schedule Y of Drugs and Cosmetics Rules, 1945.
ix. Causality assessment by investigator and the medical monitor of Sponsor /CRO.
x. The assessment report should clearly mention whether the SAE occurred is related or not related (Situations like unlikely, possibly, suspected, doubtful etc should not be used).
xi. Whether the outcome is fatal
xii. Details of compensations provided for injury or death. In case no compensation has been paid, reason for the same should be submitted. It is 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.
xiii. Mention whether it is "initial" or "follow-up" report. For follow-ups, clearly mention the follow-up report number e.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.
xiv. 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.
xv. Relevant supportive documents may be enclosed

NOTE: Submission of same SAE in different forms/ format, in different occasions has to 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 whosoever have obtained permission from CDSCO in a time bound manner.

ii. As per this procedure, each SAE including death will be examined by the CDSCO and decision regarding causality of death and quantum of compensation (if any) will 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 is due to following reasons, which are 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.

a) Adverse effect of Investigational product (s)
b) Violation of the approved protocol, scientific misconduct or negligence by the Sponsor or his representative or the investigator;
c) Failure of investigational product to provide intend therapeutic effect;
d) Use of placebo in a placebo –controlled study

e) Adverse effects due to concomitant medication excluding standard care, necessitated as part of approved protocol;
f) For injury to a child in-utero because of the participation of parent in clinical study.
g) 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 the report 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 is considered as clinical study related injury.
Note: CDSCO has option to constitute as independent Expert Committee, wherever considered 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 within thirty (30) days of the receipt of such order.

viii. As per this procedure the preliminary scrutiny of the SAE reports will be done by CDSCO Officer (s) based on laid down checklist attached as Annexure -06. During the preliminary examination, the CDSCO Officer(s) will 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 will only accept the SAE reports for further examination, if it is submitted in accordance with the format and the checklist.

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

a) The Sponsor or his representative conducting clinical studies in India will have to prepare the SAE reports for submission to CDSCO as per New Drugs and CT rules, 2019
b) The SAE reports must be submitted with proper binding, indexing and page number.
a) The reports of SAEs of death should be prepared and submitted in red cover.
b) The reports of SAE of injury other than death should be prepared and submitted in blue cover.
c) The SAE report other than that mentioned at (i) & (ii) above is to be prepared and submitted in white cover.
c) Clear and unequivocal information should be provided in the SAE report.
d) Text and tables should be prepared using margins that allow the document to be printed clearly without losing any information and the left-hand margin should be sufficiently large so that information is not obscured by the methods of binding. The documents printed on both sides of a page, can be submitted. However care should be taken that the information is not obscured when the page is placed in a binder.
e) While submitting reply to a query, the applicant should always enclose with the reply, a copy of query letter issued 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

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Title: 008- Instruction for filling of screening form and CRF

I. OBJECTIVE: This SOP gives the procedure for recording of the Screening & Case Report Form in the all the 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 will be used for recording **the clinical studies**

2.0 Investigator/ designated person will 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 will be done by black ballpoint pen.
2. The date should be written in the format of DD/MM/YY, e.g. for 27th Feb 2017 - 27/02/17.
3. The time should be written in the format of 24 hours by HH:MM, e.g. for 3 hours 15 minutes P.M. – 15:15.
4. Hand-write all data on all pages of the CRFs. Do not type data onto the forms.
5. Do not use any type of correction fluid (white-out), pencil, or erasable pen on the CRFs.
6. Open boxes are for entry of numerical or alphabetical (in block letters) data. The boxes should be completely filled-up.
7. Closed boxes are for tick mark (inside the box) purpose only. Many items have a box or series of boxes for recording a response. Mark the box clearly with an only. Do not shade in the box or mark it with a slash or other character.
8. If data is written on the form incorrectly and the error is noticed, draw a single line through the incorrect entry, place the correct answer near the box, and sign and date the correction. If errors are identified again, find the appropriate space and do the same correction method.
9. Blank items on data forms are considered missing data and will therefore result in a query unless they are blank due to skip pattern requirements. To avoid a query on items where the answer to an item is unknown or is not available, or where the participant refuses to answer an item.
   - In case of unknown, write “UNK”, then initial and date the item.
   - In case of answer not available, write “N/A”, then initial and date the item.
   - DO NOT enter a line through items that are blank due to skip patterns.
10. 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 a review checklist.
    - Review all completed CRFs before being sent to Sponsor/CRO.
    - Make sure all items are 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, then initial and date the item.
    - Make sure only one response box per item is marked, unless instructed otherwise.
    - Make sure all written entries are clear enough to be legible for data entry.

- Check for common errors. The largest percentages of avoidable queries are 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 will be as first two boxes will be Centre No. (Allotted by the CRO) and the rest three box will be the Sequence no.
2. Record Date of visit in DD/MM/YY Format.
3. Record date Patient Initials i.e. first letter of First, Middle & Last name

Footer

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

Informed Consent form:

1. Record date when subject/ LAR/witness signs the Informed Consent.

Demography:

1. Record Date of birth in DD/MM/YYYY format. Year should be provided at minimum.
2. Check gender as either 'Male' or 'Female'
3. Age will be recorded as completed years.
4. Record the Body Weight in kilograms in the box provided.
5. Record height in meters.
6. Calculate and record BMI.
7. Tick the smoking and tobacco Chewing Habit of the subject as Mild, Moderate & Severe.
8. Tick alcohol consumption details.
9. Orally take the history of any drug abuse and tick the appropriate box.
10. Considering DSM-IV tick 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. Tick the appropriate box for Mode of diagnosis of epilepsy and add if any comments are there.
2. Tick the appropriate box depending upon Type of Partial (Focal/localized) Epilepsy and
3. Add if any comments are there.
4. Tick the YES and NO box depending upon Diagnosis of Refractory Partial Epilepsy.

Medical History:

1. Check 'YES' or 'NO' depending upon the presence of any relevant Medical/ Surgical History.
2. If YES, please record 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 is currently/potentially active. Use a separate line for each condition.
3. Record clinical condition in the condition column. Preferably provide diagnosis rather than symptom.
4. Record Start and End dates of the recorded condition.\

Previous and concomitant medications

1. Record all the details of the Prior and concomitant Medications on the Previous and concomitant medications page.
2. If Yes, Record Medication Name (Generic/Brand name)
3. Record 'Start' and 'End' dates for the medication. Check ongoing, if the medication is still being consumed and leave End date blank.
4. Record 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 is not available or not applicable.
5. Record Route of drug administration and frequency of drug.

Physical examination

In Physical Check table, check all the given system and tick the appropriate corresponding box and if any abnormality is found, specify the same in given adjacent space.

Systemic examination

During systemic examination, check all the given system in the table during subject examination and tick the appropriate box, and if any abnormality is found then specify the same in given adjacent space.

Vital sign measurements and wellbeing

Vital Signs to be performed at Screening & other scheduled visits.

1. Record the Pulse Rate value in bpm (beats per minute) in the box provided.
2. Record the Systolic and Diastolic Blood Pressure value in the box provided.
3. Record Respiratory rate value in /min in the box provided.
4. Record axillary Temperature in ^{o}F in the box provided

Sample collection

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

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

After receiving the Pathological report

1. Record results of the analysis in the values column.
2. Check 'Normal' or 'Clinically Significant' or 'Clinically Non significant' values in the check box depending upon the value, if the value is out of acceptable range or not.
3. Specify any relevant information in the comment section, if necessary.
4. Check 'reactive' or 'non reactive' box depending upon the result of serological examination and specify any relevant information in the comment section, if necessary.
5. Check 'Positive' or 'negative' box depending upon the result of serum pregnancy test. If result is Positive, exclude the subject from study.

12-Lead ECG and Chest X-Ray

1. Fill the date of ECG and X-RAY done in space provided for date in DD/MM/YY format.
2. Check 'Normal' or 'Abnormal' box depending upon the report.
3. If abnormality is found the put the comments in the space provided.

Any Additional Laboratory Test / Procedure

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

Inclusion Criteria:

1. Check 'Yes', 'No' or 'N/A' boxes 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. Check 'Yes', 'No' or 'N/A' boxes 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 is not done mention the same and reason in space for comment.
2. Tick 'Yes' Or 'No' as per the eligibility of the subject for the Inclusion /Exclusion criteria status. If any answer is 'NO' then specify the reason in the comment box.

Onset of Clinical Up-Titration/Down titer and Issuance Record

1. Mention the dosage of Felbamate in the mg
2. Put the total number of Felbamate tablet(s) dispensed to the subject.
3. Tick one box of qd or bd or od depending upon the frequency prescribed to consume felbamate tablet to the subject.
4. Tick the name of prescribed medication concomitantly used by the subject.
5. Mention Dosage frequency and route of the concomitant medication prescribed along with Felbamate to the subject.
6. Tick 'YES' or 'NO' depending upon the dosing instruction is explained or not explained to the subject.
7. Tick 'YES' or 'NO' depending whether the patient Dairy card has been issued or not issued to the subject.
8. Tick 'YES' or 'NO' depending upon the Patient dairy card filling instruction is explained or not explained to the subject.
9. Put the date on which the patient is asked to visit the centre and then tick YES if you have conveyed the next visit date to subject.

Follow-up for laboratory investigations, Safety & Concomitant medications

1. Tick YES or NO depending upon if investigator doubts about any laboratory values and if he wants to repeat that particular investigation and if response of investigator is YES then he has to fill the form
2. Tick YES or NO depending upon if subject has consumed any medication other than apart from Felbamate and Levetiracetam, Valproic acid, Gabapentin or Pregabalin and response is YES then filling the form
3. Tick YES or NO after inquiring the subject about whether he/she suffered any adverse event.
4. Tick YES or No depending on whether the subject has suffered any Serious Adverse Event.

Checking for Dosing Compliance

1. Fill the details for quantity of Felbamate tablet and concomitant medication issued, any dose missed and quantity returned. And tick YES or NO depending upon the dosing compliance.
2. Tick YES or NO depending upon the Investigator's discretion whether the patient can continue the study or not.

Randomization

1. Put the date of Informed consent Taken
2. Fill Screening ID
3. Put the Date of Randomization
4. Fill the Enrollment ID which will consist of centre code and Randomization ID.
5. Tick either Test or Reference arm depending upon the randomization obtain telephonically from the CRO during period I and tick reverse arm for Period II.
6. Put Sign and Date who has conducted this activity.
7. Put Sign & Date who has checked this activity.

Clinical stabilization and issuance record

1. Tick Test or Reference box as per randomization.
2. Mention the Quantity of Felbamate Issued and then Tick 'YES' or 'NO' depending upon the Patient stabilized on dose (mg) & frequency.
3. Fill the details like Quantity issued frequency of dose dosage and route of concomitant medication

Check In & Out Procedure

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

In House Dosing

1. Fill Pre determined Schedule Time by in 24 Hrs Format
2. Tick 'YES' or 'NO' after properly checking ID no of the subject.
3. Tick either 'YES' Or 'NO' depending upon the instruction is conveyed to the subject or not**.**
4. Tick Test or Reference depending upon the subject's randomization arm
5. Tick either YES or NO after ensuring that subject has drank 240 ml of water for dosing.
6. Tick YES or NO depending upon checking the mouth of subject.
7. Record the time of actual dosing in 24 Hr format.
8. Put Remark about if any deviation occurs or any spillage is there etc.

Meal Record

1. Record predetermined Schedule time for meal in 24 Hr Format.
2. Record the time as Start time when subject Start Eating the meal in 24 Hr Format.
3. Record the time as 'END' time when subject finishes the meal in 24 Hr Format.
4. Put comment for any unscheduled event happens.

Pre-Dose Blood Sample

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

Pharmacokinetic Blood Sampling

1. Below will be applicable for All PK sampling point
2. Record predetermined Schedule time for blood collection in 24 Hr format.
3. Record Actual time for blood collection in 24 Hr format.
4. Designated Person who collected the blood sample will Put Sign and date in collected by column

Removal or Replacement of Cannula

1. Record The time of recannullation if cannulla is removed or change and specify the reason in comment space and
2. Designated Person who has carried out the activity will Put Sign and date in done by column

Pre-dose Compliance

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

Post dose Compliance

1. Tick Yes or NO depending upon Drinking water not permitted 1.00 hr post-dose
2. Tick Yes or NO depending upon Posture restricted for 2.00 hrs post-dose.
3. Tick Yes or NO depending upon Maintenance of fasting for 4.00 hrs post-dose

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

1. If Patient needs further down titration then Investigator has to fill Annexure F form
2. If Response is NO fill the study completion status.

Study Completion Status

1. Tick YES or NO depending upon whether the patient completed the study.
2. And if response is NO complete the questionnaire of Part A by ticking the reason for withdrawal & then complete the part B by mentioning the date of when subject was out of the study.

Investigator's Declaration

1. Investigator will Sign and Date in checked by box after checking the entire Screening form and CRF for its correctness and completeness.

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Introduction: the **KLE Research Pharma** [Clinical Trial IMPs] is constituted by KLE College of Pharmacy/Registrar respectively under Drugs and Cosmetic Act, 1940 at KLE Research Pharma, , 02nd Floor, site management office, KLES Dr.PK Hospital and MRC.

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 traceability;

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 generated in the trial.

e) To ensure to maintain the Temperature of IMPs

2. Communications:

a) Periodic GCP/Protocol Training will be conducted for the site Research pharmacists by the Sponsors/CROs/Site
b) The purposes of these GCP/Protocol training are to keep abreast 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 also communicate via email, fax and telephone as needed.
d) Electronically transmitted documents will be password protected.
e) Pharmacists will conduct cross-site visits as appropriate.

3. ROLES AND RESPONSIBILITIES:

➢ ROLES AND RESPONSIBILITIES OF SITE

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

a) IP Shipment and receipt
b) IP Storage
c) IP Repackaging and Relabelling
d) IP Dispensing 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 will be documented in a Signed Signature Sheet. Study staff/Pharmacist will be trained on IP management procedures.

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

➢ ROLES AND RESPONSIBILITIES OF SPONSOR

a) This clinical trial will be monitored by the Sponsor monitor.

(For sites involved in IP repackaging and relabelling, describe that there will be two separate monitors:

a) The blinded monitor will 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]

b) The unblinded monitor will 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. <u>Pharmacy Procedures:</u>

a) **Pharmacy procedures specific to the protocol**

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

b) Drug Supply Statement

a. New drug supply statements are added as they are received from Sponsors/CROs/WHO

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)

d) Shipments

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

e) Return Records

a. Records of all medications returned to Sponsors/CROs/WHO

f) Correspondence

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

g) IMP/Devices Request Procedure: Flow Chart

IMP/Devices Request Procedure: Flow Chart

Received 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

↓

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, issued 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 will 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 will take 15-20 days to complete the Process) if sponsors have provision can send the Used and Unused IMPs/Kits.

- **Request letter contains – No of IPs, quantity, batch no and date of Expiry**

↓

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

Annexure: 01- Prescription Form

✈----------

PRCICRIPTION FORM-Only for clinical trial purpose

Clinical trial Prescription- Dispensary	**KLES Dr.Prabhakar Kore Hospital and MRC, Belagavi**	
KLE Research Pharma, CTS No: 5434, 2nd Floor, SMO office, Room No: 04	SOP version 3.0	Page no 01 of 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 Pharmacist sig

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/Unblinded study:

Sponsored by:

Manufactured by:

Sl.No	No. of IMPs Requested/date	Recommended storage condition	No of IMPs received	Dispensed/Date	Balance
1.					
2.					
3.					
4.					

6. Participant Consultation and Counselling: if Applicable

At the KLE site, the pharmacist is responsible for ensuring that all participants are adequately counselled when 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 counselling can be done by the pharmacist or by someone delegated by the pharmacist and will be documented. At the KLE Hospital, the study nurse is responsible for medication and compliance counselling at the entry visit. After the initial counselling, the pharmacists will continue to serve as a resource at the KLEs D.PK Hospital and MRC will be available to the participant and the study nurse to provide further counselling and consultation as needed. The pharmacists at the site dispense medications to the patient and provide counselling at each study visit. The pharmacist will notify the study nurses/CRC if there is a problem with adherence based on estimated measurements/accurate counts of returned medication

7. IP SHIPMENT AND RECEIPT:

7.1. The Blinded CRC / Unblinded 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 / Unblinded CRC / Study Pharmacist should ensure that the contents of the <receipts of purchase / IP Shipping Documentation are in compliance with Section 4.6.3 of ICH E6 Guideline for Good Clinical Practice.

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

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

8. <u>IP STORAGE:</u>

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

8.1.1. IP Storage Temperature Logs will 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 / Unblinded 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 KLEs Dr.PK Hospital and MRC connected to an emergency generator backup power system. At the KLE Hospital the system is activated automatically if the main power is interrupted. The generators are being set up to come on automatically within 22 seconds

8.6. **Temperature Monitoring**: At KLE Hospital refrigerator and freezer temperatures are checked daily when the pharmacy is open and recorded on a manual/electronic temperature log. In addition the room, refrigerator and freezer temperatures are monitored by a constant temperature monitoring, data logging, and alarm system. If the temperature varies outside the defined range, an alarm will go off in the hospital room. This room is manned 24 hours a day, seven days a week. Checked two times daily when the pharmacy is open and recorded on temperature logs. A 24-hour recording device that records the temperature on a paper chart monitors each KLE site Management office [KLE-Research Pharma]

8.7. If the temperature varies out of range an audible alarm will sound and the system will automatically and immediately call to the site research pharmacist/study designee. If an

alarm is activated, pharmacy personnel will take action to either correct the malfunction or move product to an area of appropriate temperature.

9. IP REPACKAGING AND RELABELLING (if applicable)

9.1. ***IP repacking and relabelling*** of IMPs, the Study Team Should Be Notified to Site Ethics Committee.

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

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

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

9.3.2. IP repackaging and relabelling should be witnessed by an unblinded study staff.

9.3.3. Line clearance should be observed during IP repackaging and relabelling whereby one IP will be repackaged and relabelled at a time.

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

9.3.5. The IP Repackaging and Relabelling will be documented on the IP Repackaging and Relabelling Form.

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

9.4. The unblinded study team will perform IP repackaging and relabelling <prior to study initiation / at each subject visit/ etc.>.

9.5. The unblinded study team will assign a dummy batch number and dummy expiry date for the repackaged and relabelled IP and document it on the relevant IP Repackaging and Relabelling Form.

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

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

10. <u>IP DISPENSING AND ACCOUNTABILITY</u>

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 IP Dispensing 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 are in compliance with Section 4.6.3 of ICH E6 Guideline for Good 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 is documented on the IP Return and Destruction Forms. The IP Return and Destruction Forms will 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 are in compliance with Section 4.6.3 of ICH E6 Guideline for Good 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 paperwork concerning destruction of the drug that is required in the site's Waste Management SOPs and place a copy in the TMF.
- Provide the CRA/Monitor with written proof of IP destruction at site.
- Complete the Drug Return/Destruction Form or similar form provided by the sponsor/CRO.
- Provide a signed copy of the form to the CRA/Monitor and retain the original in the TMF.

12. REFERENCES

12.1. Health Products (Clinical Trials) Regulations
12.2. Medicines (Clinical Trials) Regulations
12.3. ICH E6 Guideline for Good Clinical Practice
14.4. New Drugs and Clinical Trial Rules, 2019

Title: 010- for screening and enrollment of subjects

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I) OBJECTIVE: This SOP gives the procedure for screening and enrollment of subject in the all clinical trials at KLES Dr.PK Hospital and MRC, Belagavi

II) SCOPE : This SOP is applicable for all clinical studies conducted in the facility.

III) PROCEDURE :

1) It is 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 is likely to be longer than the time required for normal consultation.

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

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

5) The Study Coordinator/designated person will issue the IEC of KAHER approved 'Inform Consent Form' to the subject s who have come for the screening procedure.

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

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

8) If the subject / Legally Acceptable Representative's (LAR) is unable to read, then an impartial witness present during the presentation of the screening and study related activities will 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 will sign /put thumb impression on the consent form and then the witness will 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 will ask him to return if he/she is willing to participate in the particular study.

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

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

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

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

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

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

17) The Laboratory Technician (pathology)/Phlebotomist/Nursing staff will request the subject to collect the urine sample and will 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 will make appropriate entry of the collection in the 'Test Requisition form' and the 'Screening form'. The biological samples will 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 will 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 will review the reports and if any significant observations then it will be recorded in the clinical investigation details of the 'Screening form' of the respective subject. The Clinical Laboratory Investigation report will be attached to the 'Screening form' of the CRF of the respective subject.

20) The Investigator/designated person will 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 are found fit in all the above procedures to avoid unnecessary exposure to radiation hazard.

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

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

a) Screening Consent Form
b) Screening form (including the Demographic profile, medical history of subject s, 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 shall inform the eligibility of the subject to the subject or the LAR of the subject.

2.0 Laboratory Technician (pathology)/Phlebotomist/Nursing staff will request the subject to collect urine in labeled container and will 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 will be recorded in the respective Pre-Enrollment Day Activity format of the subject. If the Test is found to be negative then the subject will be sent for further procedures.

3.0 If any additional test has to perform on this pre-enrollment day, then it will 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 will be reviewed by the Investigator/designated person and the comments/discrepancy will be noted and recorded in the 'Pre-enrollment day activity' format of the respective subject . The Clinical Laboratory Investigation reports will be attached to this format.

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

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

7.0 Randomization Procedures and Unblinding

- The Investigator must follow the randomization procedures, if any In the case of a randomized, Controlled, double-blinded trial, the code is 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 is broken only in accordance with the Protocol and mainly for medical reason(s).
- Premature unblinding must be reported to the Clinical Monitor immediately and should be documented in the File. The reason for premature unblinding 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

AF-I/SMO/SOP-010/V2.0

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										
	56	57	58	59	60	61	62	63	64	65	66
145	26.6	27.1	27.6	28.1	28.5	29.0	29.5	30.0	30.4	30.9	31.4
146	26.3	26.7	27.2	27.7	28.1	28.6	29.1	29.6	30.0	30.5	31.0
147	25.9	26.4	26.8	27.3	27.8	28.2	28.7	29.2	29.6	30.1	30.5
148	25.6	26.0	26.5	26.9	27.4	27.8	28.3	28.8	29.2	29.7	30.1
149	25.2	25.7	26.1	26.6	27.0	27.5	27.9	28.4	28.8	29.3	29.7
150	24.9	25.3	25.8	26.2	26.7	27.1	27.6	28.0	28.4	28.9	29.3
151	24.6	25.0	25.4	25.9	26.3	26.8	27.2	27.6	28.1	28.5	28.9
152	24.2	24.7	25.1	25.5	26.0	26.4	26.8	27.3	27.7	28.1	28.6
153	23.9	24.3	24.8	25.2	25.6	26.1	26.5	26.9	27.3	27.8	28.2
154	23.6	24.0	24.5	24.9	25.3	25.7	26.1	26.6	27.0	27.4	27.8
155	23.3	23.7	24.1	24.6	25.0	25.4	25.8	26.2	26.6	27.1	27.5
156	23.0	23.4	23.8	24.2	24.7	25.1	25.5	25.9	26.3	26.7	27.1
157	22.7	23.1	23.5	23.9	24.3	24.7	25.2	25.6	26.0	26.4	26.8
158	22.4	22.8	23.2	23.6	24.0	24.4	24.8	25.2	25.6	26.0	26.4
159	22.2	22.5	22.9	23.3	23.7	24.1	24.5	24.9	25.3	25.7	26.1
160	21.9	22.3	22.7	23.0	23.4	23.8	24.2	24.6	25.0	25.4	25.8
161	21.6	22.0	22.4	22.8	23.1	23.5	23.9	24.3	24.7	25.1	25.5
162	21.3	21.7	22.1	22.5	22.9	23.2	23.6	24.0	24.4	24.8	25.1
163	21.1	21.5	21.8	22.2	22.6	23.0	23.3	23.7	24.1	24.5	24.8
164	20.8	21.2	21.6	21.9	22.3	22.7	23.1	23.4	23.8	24.2	24.5
165	20.6	20.9	21.3	21.7	22.0	22.4	22.8	23.1	23.5	23.9	24.2
166	20.3	20.7	21.0	21.4	21.8	22.1	22.5	22.9	23.2	23.6	24.0
167	20.1	20.4	20.8	21.2	21.5	21.9	22.2	22.6	22.9	23.3	23.7
168	19.8	20.2	20.5	20.9	21.3	21.6	22.0	22.3	22.7	23.0	23.4
169	19.6	20.0	20.3	20.7	21.0	21.4	21.7	22.1	22.4	22.8	23.1
170	19.4	19.7	20.1	20.4	20.8	21.1	21.5	21.8	22.1	22.5	22.8
171	19.2	19.5	19.8	20.2	20.5	20.9	21.2	21.5	21.9	22.2	22.6
172	18.9	19.3	19.6	19.9	20.3	20.6	21.0	21.3	21.6	22.0	22.3
173	18.7	19.0	19.4	19.7	20.0	20.4	20.7	21.0	21.4	21.7	22.1
174	18.5	18.8	19.2	19.5	19.8	20.1	20.5	20.8	21.1	21.5	21.8
175	18.3	18.6	18.9	19.3	19.6	19.9	20.2	20.6	20.9	21.2	21.6
176	18.1	18.4	18.7	19.0	19.4	19.7	20.0	20.3	20.7	21.0	21.3
177	17.9	18.2	18.5	18.8	19.2	19.5	19.8	20.1	20.4	20.7	21.1
178	17.7	18.0	18.3	18.6	18.9	19.3	19.6	19.9	20.2	20.5	20.8
179	17.5	17.8	18.1	18.4	18.7	19.0	19.4	19.7	20.0	20.3	20.6
180	17.3	17.6	17.9	18.2	18.5	18.8	19.1	19.4	19.8	20.1	20.4
181	17.1	17.4	17.7	18.0	18.3	18.6	18.9	19.2	19.5	19.8	20.1
182	16.9	17.2	17.5	17.8	18.1	18.4	18.7	19.0	19.3	19.6	19.9
183	16.7	17.0	17.3	17.6	17.9	18.2	18.5	18.8	19.1	19.4	19.7
184	16.5	16.8	17.1	17.4	17.7	18.0	18.3	18.6	18.9	19.2	19.5
185	16.4	16.7	16.9	17.2	17.5	17.8	18.1	18.4	18.7	19.0	19.3

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

AF-II/SMO/SOP-010/V2.0

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 (if enrolled)	Screening Failure Reason	Signature & Date

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In the drugs and cosmetics rules, 1945, in schedule, (Gazette notification New Delhi the 31 st 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 will be done at site management office.

I. Principle of Privacy and Confidentiality

1. During the audio-visual recording of informed consent process, the identity and records of the trial subjects are as far as possible kept confidential; and that no details about identity of said subjects, which would result in the disclosure of their identity, are 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 does 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 videographer should be engaged 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 shall 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 Investigator will 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 videography 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 is recognizable and the audio is 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 is not possible to maintain the same permanently.

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I. PURPOSE:

The purpose of this Standard Operating Procedure (SOP) is to describe the standard procedures to be followed when archiving essential paper/electronic documents related to clinical research/trial of sponsored and conducted at KLEs Dr. Prabhakar Kore Hospital and Medical Research centre, Belagavi.

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

II. INTRODUCTION

Archiving is 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 are no pending or contemplated marketing applications in an ICH region or at least 5-10 years (total 15 Years) 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 Will applies to all Clinical trials conducted at KLE's Dr.Prabhakar Kore Hospital &MRC, Nehru Nagar, and Belagavi.

IV. RESPONSIBILITY:

- Archivist or designated personnel are responsible to follow this SOP during archival retrieval and re-archival of documents / data.
- Relevant department personnel has to follow this SOP while submitting documents for archival / re-archival and requesting for retrieval of documents / data.
- It is responsibility of the Site Management of KAHER, KLES Dr.Prabhakar Hospital to conduct periodic audit to assure the implementation of this SOP.

V. DEFINATION

- **Archival:** The procedure of preserving documents in any media for longer storage, in a safe 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 is 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 ascertaining the safety or efficacy of those products.

- **International Council for Harmonisation (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 Harmonisation.
- **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 are those documents that individually and collectively permit evaluation of the conduct of a trial and the quality of the data produced. Essential documents include the Trial Master File, source documents and Case Report Forms (CRFs).
- **Trial Master File:**The Trial Master File is 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 are 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

- õ Access to the archival room shall be controlled and tracked.
- õ Access to archives is 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 logbook as per Annexure 01 – Entry and Exit of Archives.
- õ Archival room is provided with the CCTV Camera, fire extinguisher, Heat and smoke detector.
- õ The temperature of 23(+/-) 4oC and humidity 30-70% RH shall be maintained in archival room.
- õ Pest control activity shall be performed quarterly or as whenever required

- The archivist shall 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 are taken.

ii. Archival period:

- All essential documents relating to clinical study including monitoring documents, projects files and audit documents shall be archived in accordance with the requirements of the applicable regulations / guidelines as follows:
  - As defined in protocol or/ 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 are no pending or contemplating marketing applications in an ICH region.
- Documents relating to clinical study documents shall be archived for a minimum period of 10 to 15 years (or) in accordance Regulatory guidelines and KLES Dr.Prabhakar Kore Hospital and MRC which shall be decided by the management team as per requirement.

iii. Location of Archival Documents:

- Archived material shall be stored in a legible condition at KLES Dr.Prabhakar Hospital and MRC in Ground floor (G+2), opposite of Free X-Ray Department, Belagavi.
- 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, shall be assigned the archival location as “I1”
- Each cabinet shall have register maintained by the archivist as per Annexure 07 – Format of archival register
- The register shall 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 KLES Dr.Prabhakar Kore Hospital and MRC, Belagavi 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 is completed, project documents shall be returned to the client or archived according to the terms and conditions as per regulations/site policies.
- Study documents shall 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 KHAER, Nehru Nagar, Belagavi.

ii. Non-Study related documents:

Superseded SOPs shall be archived within 10 working days from the date the y become obsolete.

iii. Archival of paper documents:

- The respective department head/designee is responsible for notifying the archivist in writing, the intent to archive study documents.
- All records related to the project shall be retained in a manner that shall preserve the security, integrity and authenticity.
- All study related documents shall be given to archivist in appropriately labelled files by the concerned department as shown below: *AF-I/012/SOP- V3.0*
- The contents in the files shall be verified against the index given in the respective files by the archivist before archival.
- Upon completion of the contracted archival period, the sponsor shall be informed/intimated in writing. If the archival period is extended by the sponsor
- Archive master copies of the superseded versions or absolute of the SOPs/Work procedures in the labelled box files
- While archiving do not compile all versions of single SOPs/Work Procedures of different departments together.
- The details of archive shall 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 KLES Dr.Prabhakar Kore Hospital and MRC, Belagavi, all the created electronically or received electronically by KLES Dr.PK Hospital shall 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 labelled by the concerned department as shown as below: Annexure-III

Name of the study document:

Study title/Number:

Name of Principal investigator/Co-I:

Date of creation:

- Appropriate security measures shall be taken to avoid my unauthorised access to the electronic data.
- If the responsibility of electronic archival is not delegated to KLES Dr.PK Hospital and MRC, Belagavi, 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 be removed/ destroyed by the Clinical services administrators of KLEs Dr.PK Hospital 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 shall be informed/intimated in writing. If the archival period is not extended by the sponsor then the study documents shall be returned to the sponsor and a list of documentation provided to the sponsor shall be created. A sponsor acknowledgment copy of this shall be retained.
- If required, disposition of study documents/data shall be out sourced to an external vendor by KAHER's Site Management office, KLES Dr.Prabhakar Kore Hospital and MRC, Belagavi

VIII. References:

1. 21 CFR 312.55-Informing Investigators
2. 21 CFR 312.57- Record Keeping and Record Retention
3. 21 CFR 312.58- Inspection of Sponsor records and Reports
4. 21 CFR 312.62- Investigator Record Keeping and Record retention
5. 21 CFR 312.64- Investigator Reports
6. Appendix V-CDSCO guideline: Essential Documents
7. ICH Guidelines for 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 Tail/Study Reports

Annexure: I *AF-I/012/SMO/SOP- V3.0*

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

AF-II/012/SMO/SOP-V3.0

Retrieval Data Form

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

Annexure: III *AF-III/012/SOP- V3.0*

Destruction Form

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

Annexure: IV *AF-V/012/SMO/SOP- V3.0*

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 performed by:	
Name	
Designation:	
Signature:	

Annexure: V *AF-V/012/SMO/SOP- V3.0*

Document location Form

Cabinet ID:

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