PURPOSE: The purpose of this standard operating procedure (SOP) is to explain the responsibilities of the principal investigator as related to investigational trials.

SCOPE: This SOP applies to sponsored clinical trials and outlines the principal investigator’s (PI) responsibilities for these types of trials.

PERSONNEL RESPONSIBLE: Principal Investigator (PI) is responsible for protecting the rights, safety, and welfare of subjects under the investigator's care; and for the control of drugs under investigation.

DEFINITIONS:

- **Adverse Event (AE)** - (adapted from the ICH definition) any undesirable medical occurrence in a clinical trial subject administered a pharmaceutical product and which does not necessarily have a causal relationship with this treatment. An AE can include any unfavorable and unintended signs, symptoms, or the exacerbation of a pre-existing condition associated with the use of an investigational product, whether or not related to the product. When an AE has been determined to be related to the investigational product, it is considered an Adverse Drug Reaction.

- **Documentation**—All records, in any form (including, but not limited to, written, electronic, magnetic, and optical records; and scans, x-rays, and electrocardiograms) that describe or record the methods, conduct, and/or results of a trial, the factors affecting research, and the actions taken.

- **Food and Drug Administration (FDA)** - Department within the United States Department of Health and Human Services. Enforces Food, Drug and Cosmetics Act and related federal public health laws.

- **Good Clinical Practice (GCP)** - A standard for the design, conduct, performance, monitoring, auditing, recording, analyses, and reporting of clinical trials that provides assurance that the data and reported results are credible and accurate, and that the rights, integrity, and confidentiality of trial subjects are protected.

- **Institutional Review Board (IRB)**—An independent group made up of medical, scientific, and non-scientific members, whose responsibility is to ensure the protection of the rights, safety and well-being of human subjects involved in a trial by reviewing and approving the clinical protocol, informed consent forms, and the methods and materials used in the trial.

- **Protocol**—A document that describes how a clinical trial will be conducted to include the objective(s), design, methodology, statistical considerations and organization. It works to ensure the safety of study participants and integrity of the data collected.
• **Source Documents** - Original documents, data and records (e.g., hospital records, clinical and office charts, laboratory results, memoranda, subjects' diaries or evaluation checklists, pharmacy dispensing records) that contain the first recording of pertinent information.

• **Sponsor**—An individual, company, institution, or organization that takes responsibility for the initiation, management, and/or financing of the research.

**PROCEDURES:**
The principal investigator is responsible for the conduct of the study in all ways, which includes, but is not limited, to the following:

**Maintain Qualifications and Adhere to Agreements**
• Be qualified by education, training and experience to be responsible for the proper conduct of the trial as supported by an up-to-date CV, current license and other relevant documents.
• Be aware of, and comply with all applicable regulations and Good Clinical Practice (GCP) guidelines.
• Adhere to the written protocol and be familiar with the appropriate use of the investigational products.
• Maintain a list of appropriately trained and qualified staff whom have been delegated trial-related duties.

**Compliance with the Protocol**
• Conduct the trial in compliance with the protocol.
• Do not deviate from, change the protocol without agreement by the sponsor and documented approval from the IRB/IEC of an amendment, except where necessary to ensure safety of the trial subjects.
• Report any deviation from the approved protocol to the sponsor and IRB.
• Any deviation from or a change of the protocol to eliminate an immediate hazard(s) to trial subjects should be followed by a report to the IRB, sponsor and regulatory authority(s).
• Ensure that only subjects meeting eligibility criteria are enrolled.
• Follow the trial’s randomization procedures, if any, and should ensure that the randomization code is broken only in accordance with the protocol.

**Adequate Resources**
• 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 properly 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.
The investigator should ensure that all persons assisting with the trial are adequately informed about the protocol, the investigational product(s), and their trial-related duties and functions.

The Investigator will need adequate space & appropriate equipment to conduct the trial.

Medical Care of Trial Subjects

- A qualified physician (or dentist, when appropriate), who is an investigator or a sub-investigator for the trial, should be responsible for all trial-related medical (or dental) decisions.
- Ensure that adequate medical care is provided to a subject for any adverse events, including clinically significant laboratory values, related to the trial.
- If the subject agrees, the investigator should inform the subject's primary physician about the subject's participation in the trial.
- The investigator should make a reasonable effort to ascertain the reason(s) for a subject withdrawal, while fully respecting the subject's rights.

Records and Reports

- Ensure data reported on the CRF derived from source documents, are consistent with the source documents or the discrepancies should be explained. Any change or correction to a CRF should be dated, initialed, and explained. Sponsors should provide guidance to investigators and/or the investigators' designated representatives on making such corrections.
- Ensure that monitor, auditor, IRB/IEC, or regulatory authority, and regulatory authorities have access to trial-related records, as requested.
- Ensure completeness, accuracy, legibility and timeliness of the data reported to the sponsor in the CRFs and required reports.
- Maintain all trial documents as specified by GCP recommendations and regulatory requirements. Take measures to prevent accidental or premature destruction of these documents.
- All essential trial documents should be retained until at least 2 years after the last approval of a marketing application or at least 2 years have elapsed since the formal discontinuation of clinical development of the investigational product. Documents should be retained for a longer period however if required by the applicable regulatory requirements or by an agreement with the sponsor.

Investigational drug/device accountability

- Where allowed/required, the investigator/institution may/should assign some or all of the investigator's/institution's duties for investigational product(s) accountability at the trial site(s) to an appropriate pharmacist under the supervision of the investigator.
- The designated pharmacist, should maintain accurate records of investigational product received, dispensed, returned or destroyed. Records should include dates, quantities,
batch/serial numbers, expiration dates and the unique code numbers assigned to the investigational product(s) and trial subjects.

- Provide secure storage of study drug to meet requirements specified by the sponsor.
- Ensure that the investigational product(s) are used only in accordance with the approved protocol.
- The investigational product(s) correct use should be explained to each subject and should check, at intervals appropriate for the trial, that each subject is following the instructions properly.

Informed Consent of the Subjects

- The investigator should comply with the applicable regulatory requirement(s), and should adhere to GCP and to the ethical principles that have their origin in the Declaration of Helsinki.
- The investigator should have the IRB/IEC's written approval of the written informed consent form and any other written information to be provided to subjects.
- Informed consent form and any other written information provided to the subject(s) should be revised whenever important new information becomes available that may be relevant to the subject’s consent. Any revision must receive IRB approval before use.
- No subject should be coerced or unduly influenced to participate or to continue to participate in a trial.
- No materials given to the subject should contain any language that causes the subject or the subject’s legally authorized representative to waive or to appear to waive any legal rights, or that releases or appears to release the investigator, the institution, the sponsor, or their agents from liability for negligence.
- All subjects (or subjects LAR) should be fully informed of all pertinent aspects of the trial and the language used in the oral and written information about the trial, including the written informed consent form, should be as non-technical as practical.
- Before giving consent, subjects (or subjects LAR) should be given ample time and opportunity to inquire about details of the trial and to decide whether or not to participate in the trial.
- Prior to a subject’s participation in the trial, the written informed consent form should be signed and personally dated by the subject (or subjects LAR) and by the person authorized to document consent.
- The informed consent discussion and the written informed consent form and any other written information to be provided to subjects should include all the basic and additional elements of informed consent as outlined in the regulations.
- The subject (or subjects LAR) should receive a copy of the signed and dated written informed consent form and any other written information provided to the subjects. Including the patient rights as research subjects and “What you should know before entering a research study”.

Page 4 of 6
• If there is an amendment to the protocol that changes the patients obligations or if the new information becomes available that may influence the subject(s) decision to stay in the study they must be re-consented with the new information.

• Subjects who are cognitively impaired and must use an LAR (e.g., minors, or patients with dementia), the subject should be informed about the trial to the extent compatible with the subject's understanding.

• A non-therapeutic trial (i.e., a trial in which there is no anticipated direct clinical benefit to the subject), should only be conducted in subjects who personally give consent and who sign and date the written form, except in certain conditions - objectives of the trial cannot be met by means of a trial in subjects who can give informed consent personally; risk to subjects is low; trial is not prohibited by law; etc

• In emergency situations, when prior consent of the subject (or LAR) is not possible, enrollment of the subject should follow the exact process described in the protocol and by IRB approval to protect the rights, safety and well-being of the subject and to ensure compliance with applicable regulatory requirements.

Communicate with IRB

• Before initiating a trial, submit protocol, investigator’s brochures, amendments, consents, and recruitment procedures (advertising) and written materials to IRB for approval

• Annually provide the IRB all documents subject to review, including annual trial status summary, any changes affecting the conduct of the trial or increasing the risk to subjects and study completion.

• Maintain record of all communication with IRB

Safety Reporting

• All serious adverse events (SAEs) should be reported immediately to the sponsor. The investigator should also comply with the applicable regulatory requirement(s) related to the reporting of unexpected serious adverse drug reactions to regulatory authorities and IRB

• Adverse events and/or laboratory abnormalities identified in the protocol as critical to safety evaluations should be reported to the sponsor

• Reported deaths should be submitted to the sponsor and the IRB with any additional requested information, within the required time frame.

Premature Termination or Suspension of a Trial

• If the trial is prematurely terminated or suspended for any reason, the investigator should promptly inform the trial subjects, and assure appropriate therapy and follow-up for the subjects

• The IRB should be promptly informed and provided a written explanation of the termination.
• If the IRB terminates or suspends a trial, the investigator should inform the sponsor and provide written explanation

**RESOURCES:**
21 CFR 54 Financial Disclosure by Clinical Investigators
21 CFR 56.109 IRB Review of Research
21 CFR 312.60 General responsibilities of investigators
21 CFR 312.62 Investigator recordkeeping and record retention
21 CFR 312.64 Investigator reports

ICH Guidelines for Good Clinical Practice (E6) document – Section 4 Investigator responsibilities

**Staff Accountability:**

Developed By: Director of Clinical Research Operations, Clinical Research Center
Associate Vice Chancellor for Clinical Research, Clinical Research Center
Reviewed By: Director of Clinical Research Operations, Clinical Research Center

**Department Approval**

Signed: [Signature]
Director of Clinical Research Operations

Signed: [Signature]
Medical Director of Clinical Research Center