Title: Investigator Responsibilities	Version Number:#1	Effective Date: 14 MAY 2024	Page **1** of 6

Revision History		
Version No.	**Effective Date**	**Description**

1 Purpose

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

2 Scope

2.1 Investigators are responsible for ensuring that an investigation is conducted according to the signed investigator clinical trial agreement, the investigational protocol, and applicable regulations; for protecting the rights, safety, and welfare of subjects under the investigator's care; and for the control of drugs under investigation.

2.2 Except when an exemption is granted, investigators must obtain the informed consent of each human subject to whom the drug is administered. Exceptions to the informed consent requirements found in 21 CFR 50 are not described in this document. For more information regarding exceptions please refer to the IRB website or contact the IRB office. At the University of California, San Diego the Principal Investigator may delegate the informed consent to the study coordinator. However, the PI must be available to answer any questions prior to the completions of any assessments if necessary.

2.3 For studies that require an IND from the FDA, investigators may not commence with the study until a valid IND and IRB approval are in place. Usually, sponsors/investigators typically receive a letter from the FDA issuing an IND number within 30 days of submission. If this letter is not received within 30 days, the sponsor/investigator should follow-up with the FDA. For FDA-regulated studies conducted outside of the United States, an IND is not required provided the research is conducted under the Declaration of Helsinki and Good Clinical Practice guidelines.

3 Definitions and Abbreviations

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 related to the product or not. When an AE has been determined to be related to the investigational product, it is considered an Adverse Drug Reaction.

Deviation/Violation - a divergence from the protocol and/or IRB application This can be planned and requested in advance, or it can be unplanned and must be reported after it occurred. When unplanned it is considered non-compliance of the protocol.

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 in the conduct of a clinical trial.

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

4 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.

5 Procedures

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

5.1 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 (GCP, Human Subjects, HIPAA certificates).
  Be aware of and comply with all applicable regulations and Good Clinical Practice (GCP) guidelines.
- Maintain a list of appropriately trained and qualified staff who have been delegated trial-related duties and ensure their GCP, Human Subjects, and HIPAA certificates are current.

5.2 Compliance with the Protocol

- Conduct the trial in compliance with the protocol and be familiar with the appropriate use of the investigational products.
- Do not deviate from or 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 the protocol that occurs 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 ensure that the randomization code is broken only in accordance with the protocol.

5.3 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.

5.4 Medical Care of Trial Subjects

- A qualified physician who is an investigator or a sub-investigator for the trial, should be responsible for all trial-related medical 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.

5.5 Records and Reports

- Ensure data reported on the CRF/eCRF derived from source documents, are consistent with the source documents or the discrepancies should be explained. Any change or correction to a CRF/eCRF 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 have access to trial-related records, as requested.
- Ensure completeness, accuracy, legibility, and timeliness of the data reported to the sponsor in the CRFs/eCRFs 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.

5.6 Investigational drug/ device accountability

- Where allowed/required, the investigator/institution may/should assign some or all

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.

5.7 Informed Consent of the Subjects

- The investigator and study personnel will comply with current IRB policies and procedures on informed consent.

5.8 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.

5.9 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. The investigator should also comply with the applicable regulatory requirement(s) related to the reporting of unexpected adverse drug reactions to regulatory authorities and IRB.
- Reported deaths should be submitted to the sponsor and the IRB with any additional requested information, within the required time frame.

5.9.1 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 a written explanation.

6 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

7 Document Approval

- Name and Title of Approver
- Date in the format (MM/DD/YYYY)
- Insert Name and Title below Signature

Approved By: Date:

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Insert Name and Title