PURPOSE: The purpose of this SOP is to describe how all adverse events are captured, recorded and reported to all the necessary agencies in a timely fashion and ensure adequate follow up is performed.

SCOPE: This procedure applies to all research conducted at University of Nebraska Medical Center (UNMC) and Nebraska Medicine (NM).

PERSONNEL RESPONSIBLE: Principal Investigator (PI), Sub-investigators, Study Coordinator and/or other pertinent staff conducting research visits and follow-up visit/phone calls with research subjects.

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.

- **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.

- **Serious Adverse Event (SAE)** - Any untoward medical occurrence that:
  - results in death,
  - is life-threatening,
  - requires inpatient hospitalization or prolongation of existing hospitalization,
  - results in persistent or significant disability/incapacity,
  - Congenital anomaly/birth defect
  - fetal death/spontaneous abortion
  - pregnancy
• **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 notes, memoranda, subjects’ diaries or evaluation checklists, pharmacy dispensing records, etc.) 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:**

**Capturing and Recording AEs**

• All pertinent staff conducting an “interview” of a research subject shall use “open-ended” questions to inquire about any adverse events. Example: “Have you experienced any health problems or changes in your health since your last contact with the research staff?”

• If answer is yes, staff will document:
  - Type of adverse event
  - Date of onset
  - Time of occurrence (if pertinent to report)
  - Severity (mild, moderate, severe)
  - If study intervention changed
  - Date the event resolved
  - Treatment, if any

• The principal investigator and/or sub-investigator will assess the relationship of the adverse event to the study intervention.

• All adverse events shall be documented in source documents and case report forms.

• Supporting documentation for adverse events will be collected and included in the source documents and case report form such as:
  - Laboratory reports
  - Emergency room notes
  - Hospital discharge summary
  - Death certificate
  - Autopsy report
Reporting AEs

- Typically, only SAEs require reporting to outside agencies. If there is an SAE, reporting to the FDA and/or sponsoring company of the research must be done within 24 hours of learning of the event. If the sponsoring company requests source documentation relevant to an SAE, all patient records being transferred to the sponsor must first be de-identified to maintain patient confidentiality.

- Internal serious adverse events that related to the investigational product are to be reported to the IRB within 24 hours of becoming aware of the event, if they meet reporting criteria. All SAEs are submitted through the UNMC RSS system. If an SAE occurs at another site conducting the same research (External AE), the FDA/sponsor will make available a safety report detailing the event. A copy of the report is filed in the regulatory binder. The UNMC IRB will NOT accept, acknowledge or review external safety reports if there are no changes required in the protocol, IRB application and/or ICF. If it is determined by the PI and/or sponsor that a change in the protocol or revision to the consent is needed as a result of the External AE, then investigators must submit a Request for Change along with a revised IRB application and consent form for review and approval by the IRB.

RESOURCES:

- FDA/ website: [http://www.fda.gov](http://www.fda.gov)
- 21 CFR 312. 32- IND Safety Reports 21 CFR 312.64—Investigator Report
- ICH GCP Consolidated Guideline E6 (R1)
- UNMC IRB website: [https://www.unmc.edu/irb/](https://www.unmc.edu/irb/)

Staff Accountability:

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