Center for Clinical and Translational Research Standard Operating Procedure

Section **Clinical Research Center** Date Created: **November 1, 2010**

Title: **Adverse Events** Date Reviewed/Modified: **July 7, 2021**

SOP Number: **SOP- 1** Version Number: **5**

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

- other serious important medical event
- any event that requires treatment to prevent one of the outcomes listed above

- **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

- **Reporting of AEs to the sponsor-** AEs are to be reported according to the protocol. In most cases AEs will be reported through the sponsors data entry system. If there is an SAE, reporting to the sponsoring company of the research must be done within 24 hours of learning of the event or time designated by the protocol. 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. Some sponsors may require SAE reports to be faxed or emailed.
- **Reporting of AEs to the FDA or other applicable outside agencies**- If the study is sponsored, the sponsoring company typically handles reporting to the FDA or other applicable outside agencies. The protocol should give details on the reporting requirements to the FDA or other applicable outside agencies. If not a sponsored study or the investigator is the sponsor, the reporting requirements will fall on the investigator. The investigator should follow the safety reporting requirements outlined by the agency. In the case of the FDA this would be following their safety reporting requirements.
- **Reporting of AEs to the IRB**- AEs should be reported to the IRB of record for the study. This will be done by following that IRBs policies and procedures for reporting of AEs. SAEs for the IRB of record may require expedited reporting.

RESOURCES:

- FDA/ website: 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/
- wcgIRB: https://www.wcgirb.com
- Advarra: https://www.cirbi.net/
- Central IRB for the National Cancer Institute: https://www.ncicirb.org

Staff Accountability:

Developed By: Director of Clinical Research Operations, Clinical Research Center
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Department Approval

Signed LuAnn Larson Date: Jul 8, 2021
Director of Clinical Research Operations

Signed Matt Lunning Matt Lunning (Aug 2, 2021 11:08 CDT) Date: Aug 2, 2021
Medical Director of Clinical Research Center

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