Center for Clinical and Translational Research Standard Operating Procedure

Section: **Clinical Research Center**
Date Created: **November 1, 2010**
Title: **Adverse Events**
Version Date: **January 1, 2023**
SOP Number: **SM42**

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 the University of Nebraska Medical Center (UNMC) and Nebraska Medicine (NM).

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

DEFINITIONS:

- **Adverse Event (AE) –** (adapted from the FDA definition) An adverse event is any undesirable experience associated with the use of a medical product in a patient.
- **Medical Terms to Code:** A set of criteria for the standardized classification of adverse effects of drugs or devices used in therapy (e.g., CTCAE, MedDRA, DAIDS).
- **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.
- **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/permanent damage,
  - results in congenital anomaly/birth defect
  - 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/SAEs

- Adverse events may be reported from patient report, laboratory reports (both local and central), hospitalizations, provider notes, or by any other means.
- 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 an AE is to be reported, 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, grade the adverse event as appropriate per protocol guidelines and note if the adverse event was expected or unexpected.
- 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/SAEs

- **Reporting of AEs/SAEs 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 by the time designated in 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/SAEs to the FDA or other applicable outside agencies**- If the study is sponsored, the sponsoring company is responsible for 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 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 SAEs to the IRB**- All reporting should go through the IRB of record based on their policies and procedures.
    - It is the responsibility of the IRB of record to then report to the UNMC IRB following the reliance agreement. The UNMC IRB may then do their own investigation.

The only exception to this is if subject has a related or possibly related, and unexpected SAE it should be reported to both the IRB of record and the UNMC IRB.

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: https://www.unmc.edu/irb/
    - **HRPP Policy 8.1 IRB Review of Adverse Events &Adverse Device Effects**
- WCG CIRB: https://www.wcgirb.com
- Advarra CIRB: https://www.cirbi.net/
- National Cancer Institute (NCI) CIRB: https://www.ncicirb.org

CTCAE Guidelines:
https://ctep.cancer.gov/protocolDevelopment/electronic_applications/ctc.htm

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Department Approval

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Signed: 5/3/2023

Signed
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Signed: 5/3/2023