University of Nebraska Medical Center

Center for Clinical and Translational Research Standard Operating Procedure

Nebraska Medicine

Section **Clinical Research Center**

Title: **Review of Safety Reports**

SOP Number: **SOP- 53**

Date Created: **October 1, 2019**

Date Last Reviewed/Modified:

Version Number: **1**

PURPOSE: This standard operating procedure (SOP) describes the process for evaluating and reporting External Safety Reports to the Institutional Review Board (IRB) for trials working with the Clinical Research Center (CRC).

SCOPE: This SOP applies to the evaluating and reporting of Adverse Events External Safety Reports.

NOTE: For University of Nebraska Medical Center (UNMC) sponsored trials where the Principle Investigator (PI) is the Sponsor-Investigator, all adverse events (internal and external) that occur in association with the trial, must be reviewed and assessed by the UNMC PI.

PERSONNEL RESPONSIBLE: Principle Investigator (PI)—and when delegated by the principal investigator—Sub-investigators, Study Coordinator and/or other pertinent CRC staff.

The Clinical Investigators have the responsibility to ensure compliance with the University of Nebraska Medical (UNMC) IRB policy #8.1. Investigator review of individual safety reports are not prohibited and may be done by the Investigator at his or her discretion, however this review will not be the responsibility of the research staff, unless the Investigator determines that the report(s) require submission to the IRB.

DEFINITIONS:

- **Adverse Event (AE)** – 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.
- **Food and Drug Administration (FDA or USFDA) -** Is a federal agency of the United States Department of Health and Human Services, one of the United States federal executive departments. The FDA is responsible for protecting and promoting public health through the control and supervision of food safety, tobacco products, dietary supplements, prescription and over-the-counter pharmaceutical drugs (medications), vaccines, biopharmaceuticals, blood transfusions, medical devices, electromagnetic radiation emitting devices (ERED), cosmetics, animal foods & feed and veterinary products.
- **Office for Human Research Protections (OHRP) -** provides clarification and guidance, develops educational programs and materials, maintains regulatory oversight, and

provides advice on ethical and regulatory issues in biomedical and behavioral research conducted or supported by the U.S. Department of Health and Human Services (HHS).

- **Serious Adverse Event (SAE)** – A serious AE is one which results in any of the following outcomes:
  - Death
  - A life-threatening adverse event
  - Inpatient hospitalization or prolongation of existing hospitalization
  - Required intervention to prevent permanent impairment or damage
  - Persistent or significant disability or incapacity
  - Congenital anomaly or birth defect
  - One which requires medical or surgical intervention to prevent one of the outcomes listed above.
- **Serious UADE -** An UADE which results in any of the outcomes listed in UADE definition, or one in which required intervention to prevent permanent impairment or damage.
- **Unanticipated Adverse Device Effect (UADE) -** Any serious adverse effect on health or safety or any life-threatening problem or death caused by, or associated with, a device, if that effect, problem, or death was not previously identified in nature, severity, or degree of incidence in the investigational plan or application (including a supplementary plan or application), or any other unanticipated serious problem associated with a device that relates to the rights, safety, or welfare of subjects (per 21 CFR 812.3(s)).

  Note: The FDA device regulations at 21 CFR 812.3(s) define an adverse device effect which is different than the definition of an adverse event in FDA IND regulations at 21 CFR 312.32(a). Significantly, an AE may be expected or unexpected, related or unrelated, or serious or not serious. An UADE is related ("caused by, or associated with") and unexpected ("not previously identified").

PROCEDURES:

The FDA and OHRP state that it is neither useful nor necessary that reports of individual adverse events occurring in subjects enrolled in multicenter studies (e.g., MedWatch, CIOMS, SUSARs, other expedited reports) be distributed routinely to investigators or IRBs at all institutions conducting the research.

The UNMC CRC, their Investigators and designated research staff, and the UNMC IRB will not acknowledge, review, nor retain these types of reports. This includes accessing sponsor web portals.

Should the sponsor, or UNMC Sponsor-Investigator if applicable, ascertain through their assessment of these reports that an unanticipated problem involving risk to subjects or others exists and that there are implications for the protocol, the report(s) and the related protocol, consent and Investigator Brochure changes will be submitted to the IRB. The events must meet the following criteria, as established in 21CFR 312.32(c)(A):

1. Unexpected
2. Related or possibly related to participation in the research, and
3. Serious or otherwise suggests that the research places the subjects or others at a greater risk of physical or psychological harm than was previously known or recognized.

The Sponsor's or UNMC Sponsor-Investigator's report will include:

- A clear explanation of why the adverse event or series of adverse events has been determined to be an unanticipated problem; and
- The implications for the conduct of the study (e.g., requiring a significant, and usually safety related, change in the protocol and/or the consent).

ASSOCIATED FORMS:

MEMO TO FILE

RESOURCES:

- 21 CFR 312.32(c)(A)
- 21 CFR 56.108(b)(1)
- 21 CFR 812.3(s)
- 45 CFR 46.103(b)(5)(i), b)
- Bienkowski, R. S., & Broome, B. J. (2013 march). What to Do with External Safety Reports: *Journal of Clinical Research Best Practices,* 9(3), 1-5.
- *Guidance for Clinical Investigators, Sponsors, and IRBs: Adverse event reporting to IRBs: Improving human subject protection.* (2009). Rockville, MD: U.S. Dept. of Health and Human Services, Food and Drug Administration, Office of the Commissioner.
- ICH GCP section 1.2
- UNMC IRB: #8.1 IRB Review of Adverse Events and Adverse Device Effects

Staff Accountability:

Developed By: Director of Clinical Research Operations, Clinical Research Center
Medical Director, Clinical Research Center

Reviewed By: Director of Clinical Research Operations, Clinical Research Center

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Department Approval

Signed _____
Director of Clinical Research Operations

Signed _____
Medical Director of Clinical Research Center

October 1, 2019

MEMO TO FILE

RE: External Adverse Events

To Whom It May Concern:

Please see the attached process regarding review of external adverse events which is effective today. External safety reports will no longer be reviewed or retained and web safety portals will no longer be accessed for Clinical Trials conducted by Investigators in the Clinical Research Center unless there are implications for the protocol and/or consent form as determined by the sponsor.

Sincerely,

Lunning

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