Standard Operating Procedure (SOP)

SOP number	SOP Name
851.020	Investigational New Drug (IND) Safety Reports
Location	**Responsible Department**
AdventHealth Orlando	Research Services
SOP Owner/Executive Owner	**Original Creation Date (If applicable)**
Executive Director of Research Services	2/28/2022
Effective Date	**Review Date**
2/28/2022	2/28/2022

I. SCOPE: This SOP describes how <Research Personnel> at AdventHealth Orlando Research Institute process external safety letters/Investigational New Drug (IND) safety reports submitted by pharmaceutical or investigator-sponsors for clinical research conducted at AdventHealth Orlando Research Institute.

II. PURPOSE: The sponsor of a research study must notify the Food and Drug Administration (FDA) and all participating investigators in an IND safety report of potential serious risks, from clinical trials or any other source, as soon as possible, but in no case later than 15 calendar days after the sponsor determines that the information qualifies for reporting. To ensure the safety of our research subjects, <Research Personnel> at AdventHealth Orlando Research Institute review safety reports (e.g., adverse events, serious adverse events, suspected adverse reactions, or unexpected adverse reactions) when a determination has been made that the event meets the criteria set forth in 21 CFR 312.32 (c) (1) as it relates to conduct of the research study.

This SOP outlines the review process for IND safety reports received by <Research Personnel> at AdventHealth Orlando Research Institute.

III. QUALIFIED PERSONNEL: AdventHealth Orlando Research Institute <Research Personnel>

IV. TRAINING: Training will be conducted through review of this SOP and Institutional Review Board (IRB) reporting requirements.

V. SUPPLIES & EQUIPMENT: Not applicable

VI. PROCESS/PROCEDURE:

A. Background

a. As outlined in 21 CFR 312.55, the sponsor is required to keep each participating investigator informed of new observations discovered by or reported to the sponsor on the drug, particularly with respect to adverse effects and safe use. The sponsor must make the determination as to whether an event meets the criteria set forth in 21 CFR 312.32 (c)(1). This includes reports that outline:
   - Serious and unexpected suspected adverse reaction;
   - Findings from other studies that suggest a significant risk in humans;
   - Findings from animal or in vitro studies that suggest a significant risk in humans; or

- Increased rate of occurrence of serious expected adverse reactions.

b. IND safety reports submitted to AdventHealth Orlando Research Institute by a sponsor (either Pharmaceutical or Investigator-Sponsor) must include a detailed explanation of the event or series of events determined to meet the above mentioned criteria. All the safety reports will be reviewed by principal investigator (PI) and assessed by the Investigator and/or designee to determine if the report meets the criteria described above..
c. The sponsor must notify the Principal Investigator (PI) and applicable <Research Personnel> of any protocol or consent changes related to the IND safety report to prompt review and signature of the IND safety report..
   - For research studies opened after September 1st, 2019 all IND safety reports that require a change to the protocol or consent will be saved in the electronic regulatory system, Florence; and routed for electronic signature in Florence. IND safety reports may also be maintained in an electronic platform where the PI and study coordinator can access the reports.
   - For research studies opened prior to September 1st, 2019 all IND safety reports that require a change to the protocol or consent will be routed for signature via wet ink or other Part 11 Compliant electronic signature method and stored in the regulatory binder per department processes.
   - This process may vary depending on the specific protocol or department obligations. Additional requirements may be necessary to the information above.

B. Study Activation

a. At the time of new study activation, the sponsor must inform the applicable <Research Personnel> regarding how safety reports will be delivered to site in the case there is an IND Safety report that requires a change to the protocol or consent. The PI and applicable <Research Personnel> must be granted access to any applicable portals that house IND safety reports.

C. Study Status

a. Safety reports will be assessed and acknowledged while the study is open to enrollment or with active subjects receiving the study drug or in follow-up.

D. 6-Month SUSAR reports

a. When a 6-month Suspected Unexpected Serious Adverse Reaction (SUSAR) summary report is received, these will be filed in the regulatory binder. No PI acknowledgement is required. If provided by sponsor, the site will file into the investigator study file a summary in lieu of the individual safety reports. The individual safety reports will not be acknowledged or filed by site.

E. Institutional Review Board (IRB) reporting

a. Reporting for studies relying on the AdventHealth Orlando IRB: IND safety reports will only be reported to the AdventHealth Orlando IRB if they meet reporting criteria as outlined in 400.069 - HRP-069 Prompt Reporting Requirements in Research.
b. Reporting for studies relying on an External IRB: If the study is under an External IRB, the sponsor or Contract Research Organization (CRO) is required to submit any applicable IND safety reports to the External IRB of Record on the site's behalf.

The <Research Personnel> will file any IRB approval letters for IND safety reports that are approved at the site level.

VII. DEFINITION(S):

Adverse Event: means any untoward medical occurrence associated with the use of a drug in humans, whether or not considered drug related. (21 CFR 312.32(a))

Research Personnel: Individuals involved in designing, conducting, or reporting of research.

Serious Adverse Event or Serious Suspected Adverse Reaction: An adverse event or suspected adverse reaction is considered "serious" if, in the view of either the investigator or sponsor, it results in any of the following outcomes: Death, a life-threatening adverse event, inpatient hospitalization or prolongation of existing hospitalization, a persistent or significant incapacity or substantial disruption of the ability to conduct normal life functions, or a congenital anomaly/birth defect. Important medical events that may not result in death, be life threatening, or require hospitalization may be considered serious when, based upon appropriate medical judgment, they may jeopardize the patient or subject and may require medical or surgical intervention to prevent one of the outcomes listed in this definition. (21 CFR 312.32(a))

Suspected Adverse Reaction: any adverse event for which there is a reasonable possibility that the drug caused the adverse event. Reasonable possibility means there is evidence to suggest a causal relationship between the drug and adverse event. Suspected adverse reaction implies a lesser degree of certainty about causality than adverse reaction, which means any adverse event caused by a drug. (21 CFR 312.32(a))

Unexpected Adverse Event or Unexpected Suspected Adverse Reaction: An adverse event or suspected adverse reaction is considered "unexpected" if it is not listed in the investigator brochure or is not listed at the specificity or severity that has been observed; or, if an investigator brochure is not required or available, is not consistent with the risk information described in the general investigational plan or elsewhere in the current application, as amended. "Unexpected," as used in this definition, also refers to adverse events or suspected adverse reactions that are mentioned in the investigator brochure as occurring with a class of drugs or as

anticipated from the pharmacological properties of the drug, but are not specifically mentioned as occurring with the particular drug under investigation. (21 CFR 312.32(a))

VIII. EXCEPTION(S): Not applicable

IX. REFERENCE(S):

21 CFR 50 Protection of Human Subjects

21 CFR 312 Investigational New Drug Application

45 CFR 46 Protection of Human Subjects

X. RELATED DOCUMENT(S) / ATTACHMENT(S):

400.069 - HRP-069 Prompt Reporting Requirements in Research
HRP-204 Form: Prompt Reporting Requirements