Standard Operating Procedure (SOP)

SOP number: SOP CW AHC 246	**SOP Name:** Adverse Event Review and Documentation for Research
Location: *Company-Wide Policies	**Responsible Department:** Research Services
SOP Owner/Executive Owner Executive Director Research Services	**Original Creation Date (If applicable)** 6/15/2022
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I. SCOPE: This standard operating procedure (SOP) describes the options available for documenting Adverse Events (AE) and the processes for reviewing and documenting AEs including the options available in Epic, common terminology criteria for Adverse Events (CTCAE) and non-common terminology criteria for Adverse Events (Non-CTCAE) for research.

II. PURPOSE: This SOP is intended to describe the procedure for reviewing and documenting AEs or Serious Adverse Events (SAEs) at AdventHealth for research.

III. QUALIFIED PERSONNEL: This SOP applies to all Investigators and Research Personnel conducting a research study within an AdventHealth system facility, utilizing paper, the Epic electronic medical record (EMR), or any other electronic platforms which are 21 CFR Part 11 compliant, as source.

IV. TRAINING: CITI training as required per CW AHC 112 Investigator Obligations in Research and Epic training and access.

V. SUPPLIES & EQUIPMENT: Epic

VI. PROCESS/PROCEDURE: Investigators are responsible for conducting human subjects research in accordance with all applicable federal and state regulations, AdventHealth research policies, guidance, and procedures. During the conduct of a study, unanticipated events may occur, or be discovered, in the form of AEs or SAEs. Therefore, these events must be well documented in accordance with protocol and institutional review board (IRB) of record requirements.

For any AdventHealth sponsored Investigator initiated prospective, interventional Clinical Trials, where AdventHealth holds regulatory sponsor responsibilities or clinical trials as part of a federal grant in which AdventHealth is the prime recipient, AEs must be documented in Epic following this SOP.

For all other prospective interventional Clinical Trials (industry sponsored Clinical Trials, grant funded, etc.) AEs may be documented in the Epic research record and will be considered Source Data, utilizing the Epic CTCAE form or the Epic smart form for Non-CTCAE reported AE's.

If Epic does not satisfy sponsors specific requirements, the AdventHealth Adverse Event Log for IND-Drug Studies (AE Log) template or the sponsor

required forms may be utilized.

Legacy studies planning to utilize Epic for AE documentation:

- Continue to maintain all previously documented AEs in their original format up to the date that the protocol goes live in Epic.

- After go-live: all AEs will be captured in Epic and paper forms will no longer be used. Legacy paper versions will remain in the original study records.

- Legacy studies that remain paper will continue to follow the same procedures for AE documentation and assessment of AEs.

A. Forms

1. **Epic AE form:** The AE form in Epic will only be used when using CTCAE version 4.3 or 5 grading. If other grading is used, you will need to use a Non-CTCAE smart form.
2. **Epic Non-CTCAE smart form:** A smart form is available for Non-CTCAE grading documentation in Epic through the use of the data capture module.
3. **AE Log paper source document:** AE Log is available through our SharePoint site. This form is modifiable to meet protocol requirements.
4. **Electronic AE form or log:** Form or log must be 21 CFR part 11 compliant.

B. Adverse Event Documentation

1. If AE information is currently entered in other systems for reporting purposes, such as a sponsor's electronic data capture system, please continue to do so.
2. AEs should be documented promptly upon the study team becoming aware. At each study visit, the participant should be asked if they have experienced any new complaints, changes to their health, new medications, visits to a physician or emergency room, etc. since their last study visit. Documentation of this conversation should be documented in the research chart. All source data should be reviewed to ensure all AEs are captured, such as review of symptom diaries, pill diaries, medical records, etc. The study team member who obtains the information will document in the applicable AE form and progress note. The initial grading of the AE will be entered by the research study team member as delegated by the principal Investigator of the study and must include documentation to support the grading selected. The Investigator must be notified to review and assess the AE.
3. The Investigator is responsible to confirm the initial AE grading provided and determine causality. The Investigator may make revisions to the initial information provided prior to signing off on the form. The AE causality determination is not final until the Investigator signs off.
4. AEs will be followed until resolution or as required per the IRB approved protocol. Upon AE changes, research study team will update the event in the AE form whether paper or electronic. Investigator will be notified to review and assess the AE revisions and sign off.

5. Investigators and study research coordinators will be automatically notified through the Epic system should a study patient check-in to the AdventHealth emergency department or admitted as an inpatient. Investigators will be reminded through the in-basket in Epic to sign off on an AE.
6. The coordinator should view the audit history in Epic or AE Log at least twice a week to ensure the Investigator has signed off on these events.
7. The notification must be reviewed and AE assessed by the Investigator within 5 business days. SAEs should be reviewed within 24 hours or as required per sponsor.
8. Please note recording AE data within the Epic or any EMR system is not equivalent to reporting to the sponsor, IRB or Food and Drug Administration (FDA). These events will still need to be reported to all applicable parties per protocol reporting requirements.
9. All AEs are followed until resolution or for the duration specified in the IRB approved protocol. All relevant follow-up information, such as treatment and findings, should be recorded in the subject's medical record.

C. AE Reporting

1. Reporting of AEs and SAEs are governed by federal regulations and the IRB of record policies and procedures.
2. Monitors will be given access to review AE/SAEs through the EpicCare link from any browser or other applicable source.

VII. DEFINITION(S):

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

Attribution: The determination of whether there is a causal relationship between an adverse event and the investigational product or intervention.

Epic: Single integrated software platform for AdventHealth's EMR and revenue cycle.

EpicCare: A free, web-based portal offering physicians secure access to their patients' medical records, 24/7. Access includes:

a) Patient demographics and visit information
b) Lab results
c) Diagnostic imaging results and PACS images
d) Scanned/Imported documents
e) Inpatient and outpatient record data from physicians using Epic Electronic Medical Record
f) Notification of important patient events: test results, hospital admissions, discharges, and ER visits

g) Convenient messaging between physicians

Clinical Trials as defined by FDA: Clinical Trials, also known as clinical studies, test potential treatments in human volunteers to see whether they should be approved for wider use in the general population. A treatment could be a drug, medical device, or biologic, such as a vaccine, blood product, or gene therapy.

Clinical Trial(s): Per the Common Rule, a research study in which one or more human subjects are prospectively assigned to one or more interventions (which may include placebo or other control) to evaluate the effects of the interventions on biomedical or behavioral health-related outcomes.

Common Rule: A 1981 rule of ethics in the United States regarding biomedical and behavioral research involving human subjects.

Investigator: A person responsible for the conduct of the Clinical Trial at a trial site. If a trial is conducted by a contains nonbinding recommendations team of individuals at a trial site, the Investigator is the responsible leader of the team and may be called the principal Investigator. (See also Subinvestigator.) ICH GCP E6R3 1.34

Serious Adverse Event (SAE): An AE 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))

Source Data: All information in original records and certified copies of original records of clinical findings, observations, or other activities in a Clinical Trial necessary for the reconstruction and evaluation of the trial. Source data are contained in source documents (original records or certified copies). ICH GCP E6 R2 1.51

Source Document: Original documents, data, and records (e.g., hospital records, clinical and office charts, laboratory notes, memoranda, subjects' diaries or evaluation checklists, pharmacy dispensing records, recorded data from automated instruments, copies or transcriptions certified after verification as being accurate copies, microfiches, photographic negatives, microfilm or magnetic media, x-rays, subject files, and records kept at the pharmacy, at the laboratories and at medico-technical departments involved in the Clinical Trial). ICH GCP E6 R2 1.52

Subinvestigator: Any individual member of the Clinical Trial team designated and supervised by the Investigator at a trial site to perform critical trial-related procedures and/or to make important trial-related decisions (e.g., associates, residents, research

fellows). See also Investigator. ICH GCP E6 R2 1.56

VIII. EXCEPTION(S): See CW AHC 101 Research Oversight

IX. REFERENCE(S):

E6(R2)Good Clinical Practice: Integrated Addendum to ICH E6(R1) Guidance for Industry (https://www.fda.gov/media/93884/download)

21 CFR § 56.108
21 CFR § 312.66
21 CFR § 312.53
21 CFR § 312.60

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

- Research Oversight
- Human Research Protection Program
- Prompt Reporting Requirements in Research
- Investigator Obligations in Research
- Adverse Event Log for IND-Drug Studies