# SERIOUS ADVERSE EVENT REPORTING STANDARD OPERATING PROCESS

## PROCESS:

Investigators are responsible for conducting human-subjects research in accordance with all applicable federal and state regulations, CHRISTUS Health Institutional Review Board (IRB) policies, guidance, and procedures. In the event that CHRISTUS Health IRB is not the IRB of record the specific requirements of the IRB that reviewed the research study must be followed as well. During the conduct of the study, unanticipated events may occur, or be discovered, in the form of adverse events (AE) or serious adverse events (SAE). Reporting of AEs and SAEs are governed by federal regulations and CHRISTUS IRB policies and procedures. The guidance can be found at https://www.fda.gov/downloads/regulatoryinformation/guidances/ucm126572.pdf.

The federal regulations specifically require the IRB to review local AEs and SAEs [21 CRF 56.108, 21 CRF 312.66, 21 CRF 312.53, 21 CRF 312.60].

## OVERVIEW:

The CHRISTUS health IRB requires reporting of SAEs in order to monitor for research subject protection.

Any related, unexpected, and serious adverse event must be reported to the CHRISTUS Health IRB as per the Serious Adverse Event Reporting Standard Operating Process (SOP).

**DEFINITIONS:** The following definitions apply throughout this guidance document:

**ADVERSE EVENT (AE):** Adverse event (AE) 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)).

**SPONSOR OR CONTRACT RESEARCH ORGANIZATION (CRO) EXPECTED ADVERSE EVENT:** Adverse events that are listed in the protocol, informed consent form, or Investigator's Brochure as expected events or know adverse events to the drug or device. These events should be reported to the CHRISTUS Health IRB as per sponsor or CRO guidelines and SOPS.

**IND SAFETY REPORTS:** While the Sponsor is required to collect all IND Safety Reports for a given protocol, only a small subset of those reports should be submitted to the IRB. Only those IND Safety Reports that may, in the opinion of the Sponsor/CRO/SMO or Principal Investigator, represent an unanticipated problem involving risks to subjects or others should be reported to CHRISTUS Health IRB.

**SERIOUS ADVERSE EVENT (SAE):** The FDA defines an SAE as: An AE is considered "serious" (SAE) if, in the view of either the investigator or sponsor, it results in any of the following: Death, Is considered Life-threatening, Results in Hospitalization or Prolongation of hospitalization, Results in a disability or permanent damage, Causes a congenital anomaly or birth defect, Requires or Required intervention to prevent permanent impairment or damage, Other Important medical event

**LIFE-THREATENING:** The patient was at substantial risk of dying at the time of the adverse event, or use or continued use of the device or other medical product might have resulted in the death of the patient.

**HOSPITALIZATION OR PROLONGATION OF HOSPITALIZATION:** Admission to the hospital or prolongation of hospitalization was a result of the adverse event. Emergency room visits that do not result in admission to the hospital should be evaluated for one of the other serious outcomes (e.g., life-threatening; required intervention to prevent permanent impairment or damage; other serious medically important event).

**DIABILITY OR PERMANENT DAMAGE:** The adverse event resulted in a substantial disruption of a person's ability to conduct normal life functions, i.e., the adverse event resulted in a significant, persistent

or permanent change, impairment, damage or disruption in the patient's body function/structure, physical activities and/or quality of life.

**CONGENITAL ANOMALY OR BIRTH DEFECT:** Exposure or suspected exposure to a medical product prior to conception or during pregnancy may have resulted in an adverse outcome in the child.
**REQUIRED INTERVENTION TO PREVENT PERMANENT IMPAIRMENT OR DAMAGE:** Medical or surgical intervention was necessary to preclude permanent impairment of a body function, or prevent permanent damage to a body structure, either situation suspected to be due to the use of a medical product.

**OTHER SERIOUS OR IMPORTANT MEDICAL EVENTS:** The event does not fit the other outcomes, but the event may jeopardize the patient and may require medical or surgical intervention (treatment) to prevent one of the other outcomes. Examples include allergic bronchospasm (a serious problem with breathing) requiring treatment in an emergency room, serious blood dyscrasias (blood disorders) or seizures/convulsions that do not result in hospitalization. The development of drug dependence or drug abuse would also be examples of important medical events.

## REPORTING REQUIREMENTS AND PROCESS

The Principal Investigator (PI) or designee is required to collect all AEs and SAEs from subject histories, interviews, medical records, assessments, test results, other medical providers, family and friends (as applicable).

The PI is responsible to assign severity, seriousness, relationship, and if applicable, the unexpected nature of AEs and SAEs identified from the subject's medical records. This safety information is then reported to the sponsor according to the protocol.

Reporting requirements to the sponsor and or CRO can be found in the protocol.

In cases of Investigator-Initiated Trials, where the investigator is also the Sponsor, safety reporting should be submitted to the Food and Drug Administration (FDA) in accordance with federal regulations (21 CRF 312.32 (C)(V)).

Reporting requirements for CHRISTUS Health IRB:

- In the event that an AE is found the study personnel should report the event in the subject's source documents, on the CRFS, eCRFS, and to the sponsor or CRO as per the study guidelines.
- In the event that an AE or SAE results in suspension of the study must be reported to the CHRISTUS Health IRB within 7 days of awareness of the site.
- In the event that a subject is deceased, a SAE the death should be reported to the CHRISTUS Health IRB within 24 hours of awareness.
- In the event that an SAE occurs and is both unexpected and related the site should report the event to the CHRISTUS Health IRB:
    - Within 24 Hours of awareness in the event of death (All deaths of study subjects should be reported within 24 hours of awareness – regardless of study phase, treatment status, or relatedness to the study)
    - Within 10 business days of awareness for all events other than death

All SAE forms submitted to the CHRISTUS Health IRB via iRIS should include the following information:

- Date the SAE was reported to the IRB (Date of SAE Report)
- Date of awareness of SAE

- Onset date of SAE
- Cessation date of SAE if known
- Number of patients enrolled in the study to date (site enrollment)
- Number of SAE's reported to date, including the current event being reported
- Number of SAEs "related" to date, including the current event being reported
- Report Type (Initial or Follow-Up report)
- Type of SAE being reported
- Subject's initials
- Subject's study number (or ID)
- Subject's gender
- Subject's age
- If the subject is still an active participation
- If the event should be added to the risks section of the informed consent form or if protocol modifications are required due to the event
- A description of the SAE and the current status of the subject
- What actions were taken with regards to the treatment, follow-up, dose modifications, etc.
- If the report was submitted more than 24 hours after awareness for all deaths or more than 10 days after awareness on all other SAEs and reason for delay in reporting should be given
- The principal diagnosis of the SAE
- Confirmation that the sponsor has been notified of the event
- The name of the individual that reported the event

**CHRISTUS HEALTH IRB SERIOUS ADVERSE EVENT REVIEW PROCESS:** Upon receipt of the SAE submitted to iRIS, a CHRISTUS Health IRB Coordinator will review the submission for completeness. If clarifications or corrections are required the coordinator will send the submission back to the study team as a stipulation. The stipulation will need to be met prior to continuing review by the CHRISTUS Health IRB. Once the coordinator has verified that the submission is complete and all clarifications (if any) have been received, the coordinator will send the submission for review by the CHRISTUS Health IRB Chair, Vice-Chair, Compliance Officer, Director, or designated CHRISTUS Health IRB member. The SAE reviewer may request further information in order to complete the review of the reported SAE. All SAEs will be reviewed at the next fully convened CHRISTUS Health IRB Board meeting after submission. After review the CHRISTUS Health IRB Board may take one or more of the following actions prior to indicating in writing the determination of the Board to the SAE. The investigator should receive notification in writing of the CHRISTUS Health IRB Board determination within ten (10) days of the fully convened CHRISTUS Health IRB Board meeting.

**IRB ACTIONS**:

- No further action is required

- Require modifications to the informed consent form
- Require modifications to the protocol when permissible
- Require the investigator to re-consent enrolled subjects
- Notification of previously enrolled and/or currently enrolled subjects of new information
- Increase monitoring of subjects by the CHRISTUS Health IRB and CHRISTUS Health Compliance Officer
- Increase frequency of continuing review reporting
- Observation or monitoring of the research by the CHRISTUS Health IRB or CHRISTUS Health Compliance Officer
- Educational of study staff interventions
- Suspension of all or parts of the research
- Termination of CHRISTUS Health IRB approval of the research
- Refer to the appropriate institutional entity