# UNIVERSITY OF TENNESSEE GRADUATE SCHOOL OF MEDICINE
# INSTITUTIONAL REVIEW BOARD
# SERIOUS ADVERSE EXPERIENCE REPORTING

## I. PURPOSE

To provide a procedure for the accurate and timely reporting of serious adverse experiences (SAE) from the clinical site to University of Tennessee Graduate School of Medicine Institutional Review Board (UTGSM IRB).

## II. SCOPE

Applies to all personnel involved in the review of studies by UTGSM IRB.

Personnel responsible: IRB administrative staff and IRB members

## III. BACKGROUND

SAE reporting generally includes the report of any adverse drug experience or device effect observed during an investigation that is considered to be serious, regardless of causality or severity. The term serious is a regulatory definition as defined in the code of federal regulations whereby severity is a clinical definition. Principal investigators are obligated to report all serious adverse experiences to both the sponsor and to the IRB. Sponsors and IRB may have specific requirements and / or forms for reporting serious adverse experiences that must be followed by clinical site research personnel.

Sponsors must report to the FDA and participating investigators all serious, expected or unexpected adverse experiences with the use of an investigational drug during a clinical investigation [21 CFR 312.32 (c)(4)(a)].

In the case of investigational drugs, if upon further evaluation of the SAE, the sponsor determines that the investigational drug presents an unreasonable and significant risk to subjects [21 CFR 312.56 (d)), the sponsor may:

a. Discontinue the investigation and notify the FDA, IRB and participating investigators that the study is being discontinued
b. Assure FDA of the disposition of all outstanding stock of clinical trial materials
c. Furnish FDA with a full report of its actions

In the case of devices, the sponsors must evaluate any unanticipated adverse device effect immediately [21 CFR 812.46 (b)] and report the results to the FDA, IRB and participating investigators within 10 working days after the sponsor first receives notice of it [21 CFR 812.150 (b)(1)]. If the sponsor determines that an unanticipated adverse device event presents an unreasonable risk to study subjects, the sponsor will terminate part or all the investigation as soon as possible, but no later than 5 working days after the sponsor made

the determination and no later than 15 working days after the sponsor first received notice of the effect [21 CFR 812.46 (b)(2)]. Sponsors must receive FDA and IRB approval to resume a terminated study of a significant risk device [21 CFR 812.46(c)].

SAE reporting is in accordance with the following regulatory requirements and industry guidelines:
Title 21 CFR 312.32 –IND Safety Reports
Title 21 CFR 803, Subpart B -Generally Applicable Requirements for Individual Adverse Events Reports
Title 21 CFR 812, Subpart G - Records and Reports
Title 21 CFR 812.140 - Investigational Device Exemptions - Records
Title 21 CFR 812.150 - Investigational Device Exemptions - Reports
ICH GCP Consolidated Guideline - Part 4.11 Safety Reporting

## DEFINITIONS

Adverse event: is an untoward medical occurrence that may present itself during the course of a research study.

Unanticipated adverse event: is a medical occurrence whose nature, severity or frequency is not consistent with existing information regarding the risk profile of the study procedure or test article. For pharmaceutical studies, this usually reflects inconsistency with information contained in the current investigator's brochure.

Serious Adverse Event: is a medical condition that results in death, is life-threatening, requires inpatient hospitalization or prolongs an existing hospitalization, creates persistent or significant disability or incapacity, or results in a congenital anomaly or birth defect. An important medical event that may not result in death, be life threatening, or require hospitalization may be considered a serious adverse event when, based upon appropriate medical judgment, it may require medical or surgical intervention to prevent one of the outcomes noted above.

Unanticipated problems other than adverse events include: occurrences such as (but not limited to) accidental overdoses of study medications, deviations from study inclusion/exclusion criteria, failure to follow criteria for subject withdrawal, stolen laptop or hard drive that contained PHI, falsified data or information relating to informed consent or patient safety, or improper refrigeration of study drug,

An adverse event may be related to the study intervention if it may reasonably be regarded as possibly, probably, or clearly caused by the intervention. Alternatively, the relationship of adverse events to study interventions may be characterized as either "unrelated" or as "unlikely related".

## IV. PROCEDURES

1. Reports of adverse events at local sites should be submitted **only if** they are determined by the principal investigator to be: unanticipated; serious; and possibly, probably or clearly caused by the research intervention (rather than unrelated or unlikely related to the research intervention).

2. External adverse events (such as "IND Safety Reports" provided by the sponsor of the research) which meet UTGSM reporting criteria must be reported to the IRB within 10 working days of their receipt by the principal investigator. (See SOP #18 Review of External Reports)

3. Local adverse events, other than deaths, meeting UTGSM reporting criteria must be reported by the principal investigator to the IRB within 5 working days of their occurrence.

4. Deaths occurring locally that are unanticipated and are possibly, probably, or clearly caused by the research intervention must be reported by the principal investigator to the IRB within 24 hours of their occurrence.

5. Unanticipated problems other than adverse events must be reported by the principal investigator to the IRB within 5 working days of their occurrence.

6. The Investigator will report the Adverse Events and Unanticipated Problems through iMedRIS, the electronic system. Information should include the facts of the case, including subject identifier, adverse event or problem description, the event relationship to the test article or underlying condition, seriousness assessment, whether the event was anticipated or unanticipated, type of report, date of injury, whether it is a UTGSM subject, whether the intervention was stopped, and, if so, whether it was re-started, and whether the event provides new risk information that alters the risk-benefit assessment and/or should be added to the informed consent disclosure.

| | **Local Event** | **External Event** |
|---|---|---|
| **SAE other than death** | 5 working days | |
| **Death** | 24 hours | |
| **Unanticipated Problem** | 5 working days | 10 working days |

7. All reported events must include a summary of how the reported event affects the study's overall risk profile.

8. The investigator will maintain a cumulative summary of reported events (sorted by event type) and include an updated copy with the annual renewal.

9. For reported deaths, the principal investigator or designee should supply the sponsor and IRB with any additional requested information (e.g., hospital records and autopsy reports).

10. In the case of investigational drugs, if upon further evaluation of the SAE, the sponsor determines that the investigational drug presents an unreasonable and significant risk to subjects [21 CFR 312.56 (d)], the sponsor may require the principal investigator to:
    a. Discontinue the investigation
    b. Notify the IRB and clinical site research personnel that the study is being discontinued
    c. Return all outstanding stock of clinical trial materials

11. The principal investigator is responsible for immediately discontinuing a trial upon receipt of notification from the sponsor in the event that the sponsor determines that an unanticipated adverse device event presents an unreasonable risk to study subjects. In order to resume a previously terminated study of a significant risk device, the principal investigator must submit a request to the IRB and copy all IRB correspondence / approval to the sponsor.

12. Upon receipt of a serious adverse event report, the administrative staff will review the event and send to the Chairperson for review.

13. Should the IRB require additional information, a correspondence will be sent to the investigator requesting additional information.

14. All reported adverse events will be placed on the agenda for review by the full board.

15. A copy of all correspondence / reports will be maintained in iMedRIS.