1. PURPOSE

To provide a procedure for the accurate and timely reporting of serious adverse events (SAEs) from the Investigator to the study sponsor and Institutional Review Board (IRB). This Standard Operating Procedure (SOP) may be superseded by the sponsor's SOP, except when they conflict with federal regulations or other points of law.

2. SCOPE

Applies to Principal Investigator (PI) and, when delegated by the PI, additional Investigators, Study Coordinators (SCs), and other designated site personnel.

3. RESPONSIBILITIES

The PI is responsible for assessing the relationship between the study drug, device, or procedure(s) and an SAE, and for following the applicable documentation and reporting requirements.

4. BACKGROUND

SAE reporting generally includes the report of any adverse drug experience or device effect that is observed during an investigation and 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, whereas "severity" is a clinical definition.

PIs are obligated to report all SAEs to both the sponsor, if applicable, and to the IRB. Sponsors and IRBs may have specific requirements for reporting SAEs that must be followed by clinical research personnel. See IRB Policy 134, "Reportable New Information."

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

5. PROCEDURE

5.1. The PI or designee will promptly report any serious and/or unanticipated/unexpected AEs for drugs or biologics, or any changes significantly affecting the conduct of the clinical trial or increasing the risk to participants, to the sponsor and to the Creighton University IRB in accordance with 21 CFR 312.64 (b) and Creighton University IRB Policy 120, "Unanticipated Problems Involving Risks to Participants or Others." Unanticipated AEs with investigational devices will be reported to the sponsor and the Creighton University IRB in accordance with 21 CFR 812.150(a)(1).

5.2. For reported deaths, the PI or designee should supply the sponsor and IRB with any additional requested information (e.g., hospital records and autopsy reports, as applicable).

5.3. The investigator must review all IND/IDE safety reports. IND safety reports shall be submitted to the IRB only if the sponsor and/or the Data Safety Monitoring Board (DSMB) believe that the risk/benefit ratio has changed, and shall be accompanied by a plan of action, per IRB Policy 120, "Unanticipated Problems Involving Risks to Subject or Others."

5.4. In the case of investigational drugs, if upon further evaluation of the SAE, the sponsor or Investigator determines that the investigational drug presents an unreasonable and significant risk to subjects [21 CFR 312.56 (d)], the sponsor or PI may require:
- 5.4.1. Discontinuation of the investigation and notification of the FDA, IRBs, and participating PIs that the study is being discontinued
- 5.4.2. Notification to the Creighton University IRB and clinical site research personnel that the study is being discontinued
- 5.4.3. Documentation of the disposition of all outstanding stock of investigational product (IP)
- 5.4.4. Return of all outstanding stock of IP

5.5. In the case of devices, the Investigator and sponsor must evaluate any unanticipated adverse device effect immediately [21 CFR 812.46 (b)] and report the results to the FDA, IRBs, and participating Investigators within 10 working days after the sponsor first receives notice of it [21 CFR 812.150 (b)(1)].
- 5.5.1. If the sponsor or Investigator determines that an unanticipated adverse device event presents an unreasonable risk to SPs, the sponsor or Investigator will terminate part or all the investigation as soon as possible, but no later than five (5) working days after the sponsor or Investigator made the determination and no later than 15 working days after the sponsor or Investigator first received notice of the effect [21 CFR 812.46 (b)(2)].
- 5.5.2. The Investigator may terminate the investigation without prior agreement from the sponsor, but must inform the sponsor and the IRB no later than 15 working days after termination.
- 5.5.3. Sponsors must receive FDA and IRB approval to resume a terminated study of a significant risk device [21 CFR 812.46(c)]. The PI must submit to the sponsor a letter of approval from the Creighton University IRB.

6. TERMS & ABBREVIATIONS

AE Adverse Event
IP Investigational Product
IRB Institutional Review Board
PI Principal Investigator
SAE Serious Adverse Event
SOP Standard Operating Procedure

7. REFERENCES

7.1. Title 21 CFR 312.32 - IND Safety Reports
7.2. Title 21 CFR 803, Subpart B -Generally Applicable Requirements for Individual Adverse Events Reports
7.3. Title 21 CFR 812, Subpart G - Records and Reports
7.4. Title 21 CFR 812.140 - Investigational Device Exemptions – Records
7.5. Title 21 CFR 812.150 - Investigational Device Exemptions – Reports
7.6. ICH GCP Consolidated Guideline - Part 4.11 Safety Reporting
7.7. Creighton University Institutional Review Board Policies and Procedures
7.8. Creighton University IRB Policy 120, “Unanticipated Problems Involving Risks to Participants or Others”

8. ATTACHMENTS

None