[SITE NAME]

STANDARD OPERATING PROCEDURE

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<tr><td colspan="2">Title:</td><td colspan="2">No.: ISCORE-RC 109.00</td></tr>
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<tr><td>Prepared by:</td><td>Reviewed by:</td><td colspan="2">Approved by:</td></tr>
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Purpose:
This standard operating procedure (SOP) describes the operations followed by the [SITE] [SITE LOCATION] and affiliated health systems for the management safety reporting for all human subject research.

Scope:
This SOP describes the procedural pathways that should be followed at this site for recording and reporting serious and non-serious adverse events, device adverse effects and deviations according to Good Clinical Practice (GCP), protocol, regulations and institutional policies.

Materials:
NA

Responsibility:

This SOP applies to the [SITE] Institutions and associated clinical departments involved in ensuring the appropriate management of adverse events, adverse device effects and protocol deviations.

Definitions:

Adverse event (AE): Any untoward medical occurrence in a patient or clinical investigation subject administered a pharmaceutical product and which does not necessarily have a causal relationship with the

treatment. An adverse event (AE) can therefore be of any unintended sign including an abnormal laboratory finding), symptom, or disease temporarily associated with the use of a medicinal (investigational product, whether or not related to the medicinal (investigational) product.

Adverse Device Effect (ADE): Described as a device related adverse event having a causal relationship between the device and an adverse event.

Deviation: A protocol deviation/violation is generally an unplanned excursion from the protocol that is not implemented or intended as a systematic change.

Serious Adverse Event (SAE): Any untoward medical occurrence that at any dose:

- results in death,
- is life threatening,
- requires inpatient hospitalization or prolongation of existing hospitalization,
- results in persistent or significant disability/incapacity,
- or is a congenital anomaly/birth defect.

Suspected Unexpected Serious Adverse Reaction (SUSAR): Serious adverse reaction where the severity and nature are not consistent with the information regarding the medicinal product or device.

Unanticipated Adverse Device Effect (UADE): Any serious adverse effect on health or safety or any life-threatening problem or death caused by or associated with a device.

Unanticipated Problem Involving Risks to Subjects or Others (UPIRTSO): Any problem or event which, in the opinion of the investigator, was unanticipated, places subjects or others at a greater risk of harm than was previously known or recognized and was possibly related to the research procedures.

Procedure:

Adverse events (AEs) are categorized as non-serious (AEs), serious (SAEs), suspected unexpected serious adverse reaction (SUSAR), unanticipated adverse device effects (UADE), definitions noted above. Regardless of the category, the principal investigator (PI) and the delegated research team are responsible to record and report adverse events/effects in accordance with the protocol, the institutional review board (IRB) and regulatory requirements.

Also refer to the IRB of Record and/or [SITE] IRB definitions and procedures for safety reporting as needed.

1. Recording AEs/SAEs/UADE

    a. The PI may delegate the recording and reporting of adverse events to qualified research team members.

    b. The PI and the research team shall be trained on and familiar with the IRB approved protocol and pertinent study documentation about the requirements of recording and reporting of AEs/SAEs/UADE for the trial.

    c. All IRB approved safety monitoring processes and procedures for the review of safety information, including the frequency of the reviews should be followed.

    d. A review of the source documentation for the subject, including review of systems and/or laboratory

values will be assessed at regular intervals as per protocol and any change from baseline and/or the current health status shall be evaluated.

e. Record the AEs/SAEs/UADEs on the appropriate adverse event form. All adverse events observed shall be documented noting the severity, serious/unexpected, causal relationship to the research which may include the investigational product, start date, stop date, resolution and the intervention provided to manage the AE.

f. AEs/SAEs/UADEs shall be continually monitored and followed up at subsequent study visits or assessed, by the investigator or delegated research team until the AE has stabilized or has been resolved as per protocol to ensure that all appropriate resources are directed toward subject safety and well-being.

2. Reporting AEs/SAEs/UADEs

Note: For Investigator Initiated studies the principal investigator would assume the role as the sponsor referenced below.

a. Adverse events (AEs)

- AEs shall be reported to the IRB, sponsor and regulatory agencies according to the requirements and within the time periods specified by the protocol and applicable IRB policies and regulations.

b. Serious Adverse Events (SAEs) / Unanticipated adverse device effects (UADEs)

- SAEs/UADEs shall be promptly reported completely, accurately and in a timely manner to the sponsor according to protocol requirements. These will also be reported to the IRB according to IRB and regulatory requirements. The sponsor is responsible to reporting to the FDA or regulatory agency.
- For SAE/UADEs including reported deaths, the PI should supply the sponsor and the IRB with any additional requested and/or follow up information (e.g. autopsy reports if available).
- Primary Documentation of the SAE/UADEs can be completed in [SITE Clinical Trials Monitor System]/Internal form, sponsor provided and/or IRB templates. Only one method of documentation is advised.
- Originals or copies of all relevant documentation shall be maintained in the regulatory file.

Note: Where [SITE] is the sponsor or lead site the PI is responsible for submitting the progress/safety reports, Regulations require that progress reports/safety reports including a summary of anticipated and unanticipated adverse effects, be submitted to the regulatory agency on an annual basis, at a minimum or per the direction of the regulatory agency.

Note: The blind for the subject may need to be broken for emergency reasons to establish the best course of treatment. If the blinded code is broken, the investigator should promptly document and notify the sponsor. If possible, the sponsor should be consulted before unblinding occurs.

3. Reporting Unanticipated Problem Involving Risks to Subjects or Others (UPIRTSO)

    a. The investigator shall determine the event has met ALL three of the following:
        - **Serious** event that result in significant harm or places subjects or others at a greater risk of harm than previously determined.
        - **Unanticipated** occurrence meaning not previously determined as a potential risk, not included in the Investigator's Brochure, not part of the underlying disease or occurred more frequently or more severe than expected.
        - **Related** to the research procedures

    b. The investigator shall report the event to the sponsor promptly and in accordance to the protocol.

    c. Notify the IRB of record and upon completion of the IRB review and confirmation that the event is an UPIRTSO, the applicable regulatory agency shall be notified. [SITE] IRB must also be notified once confirmed, if not the IRB of record.

4. Reporting Deviations

The investigator should conduct the trial in compliance with the protocol agreed to by the sponsor and, if required, by the regulatory authority(ies) and which was given approval/favorable opinion by the IRB.

The investigator is responsible to ensure that deviation(s) from the protocol are assessed, recorded and reported in accordance with the protocol, IRB and regulatory requirements.

    a. Clinical research staff should be familiar with the defined reporting requirements and timelines in the protocol and with the IRB of record.

    b. The investigator shall report all protocol deviations/violations to the sponsor, IRB and in accordance to regulatory requirements. Prompt reporting of serious non-compliance may be required per IRB guidelines.

    c. Any deviation from the protocol to protect the life or physical well-being of a subject in an emergent situation must be reported promptly after the emergent deviation occurred in accordance to regulatory requirements.

References

E6 (R2) Good Clinical Practice: Integrated Addendum to ICH E6 (R1) Guidance for Industry
FDA Guidance for Industry and Investigators, Safety Reporting Requirements for INDs and BA/BE Studies
FDA Guidance for Clinical Investigators, Sponsors and IRBs- Adverse Event Reporting to IRBs – Improving Human Subject Protection
21 CFR 312.32 IND Safety Reporting
21 CFR 812.150 Reports
21 CFR Part 803 Medical Device Reporting
21 CFR 56.108 IRB Functions and Operations

History of Revisions to SOP

Effective Date	Nature of Revision