1. OBJECTIVE

To ensure that the Principal Investigator (PI) and all research team members assisting in the conduct of clinical research are informed about their obligations and responsibilities as they pertain to Good Clinical Practices (GCP), the investigational plan, applicable regulations, guidance, and institutional policies. This Standard Operating Procedure (SOP) applies to the written procedures followed by all members of a clinical research team involved in the conduct of human subjects' research at LSU Health New Orleans, including the Health Sciences Center (HSC), the Stanley S. Scott Cancer Center (SSSCC) and the Healthcare Network (HN), hereafter called the investigational site. These detailed instructions promote compliance in conducting clinical research.

SOP 2.10 describes the process for adverse event reporting for clinical research.

2. RESPONSIBILITY

The HSC, SSSCC and HN Clinical Trials Offices develop, implement, and maintain SOPs. The need to write a new or revise an existing SOP is based upon changes to federal regulations, guidelines, institutional policies, or procedures. These documents will be provided to departments and research teams conducting human subjects' research. Departments or research teams may develop additional research SOPs or a Research Procedure Addendum (RPA) to expand on an existing SOP, however this need should be limited.

The PI is ultimately accountable for all clinical research activities and is responsible for the appropriate delegation of tasks to individuals with adequate training and education to perform such tasks. It is the responsibility of all members of the clinical research team involved in supervising, managing, or conducting study-related activities to follow the SOPs. The clinical research team may include but is not limited to the following members:

Research Team Members

Principal Investigator (PI)	Clinical Research Coordinator (CRC)
Sub-Investigator (Sub-I)	Other Research Staff
Clinical Research Nurse Coordinator (CRNC)	Administrative and Support Staff

3. DEFINITIONS

Adverse Drug Reaction or Experience (ADR or ADE): an ADR is a response to a drug which is noxious and unintended and which occurs at doses normally used in man for prophylaxis, diagnosis or therapy of diseases or for modification of physiological function

Adverse Event (AE): any unfavorable or unintended event, including abnormal laboratory findings, symptom or disease, or death associated with the research or the use of a medical investigational test article.

Life-Threatening Adverse Drug Experience: any adverse drug experience that places the subject, in the view of the investigator, at immediate risk of death from the reaction as it occurred, i.e., it does not include a reaction that, had it occurred in a more severe form, might have caused death.

Serious Adverse Event (SAE): an adverse event or suspected adverse reaction 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

Unanticipated Adverse Device Effect: Any serious adverse effect on health or safety, or any life threatening problem or death caused by (or associated with) a device, if that effect, problem, or death was not previously identified in nature, severity, or degree of incidence in the investigational plan or application; any other unanticipated, serious problem associated with a device that relates to the rights, safety, or welfare of subjects.

Unexpected Adverse Drug Experience (Reaction): An adverse reaction, the nature or severity of which is not consistent with the applicable product information

Please refer to the SOP Glossary document for other detailed definitions of commonly used clinical research terminology.

4. PROCEDURES

The PI is responsible for:

- Ensuring an investigation is conducted according to the signed investigator statement, the investigational plan, applicable regulations, and any conditions of approval imposed by an IRB or FDA;
- Protecting the rights, safety, and welfare of subjects under the investigator's care; and
- The control of IP under investigation.

The PI and delegated research team members will conduct the clinical research study in compliance with the IRB approved protocol. The investigator/institution and the sponsor will sign the signature page of the protocol or an alternative contract to confirm their agreement, as applicable.

The PI and delegated members of the research team will not implement any deviation from or changes to the protocol without agreement by the sponsor and prior review and documented approval from the IRB of an amendment, except where necessary to eliminate an immediate hazard to clinical research study subjects, or when the changes involve only logistical or administrative aspects of the clinical research study (e.g., change of monitor, change of telephone numbers). The implemented deviation or change should be submitted to:

- The IRB for review and approval;
- The sponsor for agreement; and
- If required, the appropriate regulatory authorities within the required timeframe.

The PI or delegated research team members will document and explain any deviation from the approved protocol and report the deviation promptly to the sponsor, IRB and other regulatory agency, as applicable.

The investigator should promptly provide written reports on any changes significantly affecting the conduct of the clinical research study, and/or increasing the risk to subjects to the sponsor, the IRB, and where required by the applicable regulatory requirements, the institution.

A. Adverse Events

The PI and delegated research team members will conduct a review of systems and document the subject’s baseline state, per the protocol, prior to any clinical research study intervention.

They will review the subject's systems at regular intervals as outlined by the protocol and document any adverse change in health or wellbeing.

All adverse events observed will be documented noting the event description, seriousness, severity, relationship to the clinical research study intervention, start date, outcome, stop date and any medical care given to manage the adverse event. All adverse events will be recorded on case report forms (CRFs) or as outlined in the protocol. The site will maintain any supportive documentation as source documentation.

All adverse events that are unexpected, related or possibly related, and increase the potential for harm to subjects will be reported to the IRB, sponsor, and other regulatory bodies (e.g., FDA) according to the reporting requirements and within the time periods specified by the protocol and applicable policies and regulations. Adverse events, including laboratory abnormalities, identified in the protocol as critical to safety evaluations should be reported according to the reporting requirements and within the timeline specified by the sponsor.

During and following a subject's participation in a clinical research study, the PI should ensure that adequate medical care is provided to a subject for any adverse events, including clinically significant laboratory values, related to the clinical research study.

The PI and research team members will follow up appropriately when a research subject experiences any adverse change from baseline or pretreatment condition, ensuring all appropriate resources are directed toward subject safety and well-being. The subject should be followed until the event has resolved, or as specified in the protocol.

B. Serious Adverse Events

A serious adverse event (SAE) may include, but is not limited to, an adverse event that is fatal or life threatening, permanently disabling, requires or prolongs hospitalization, or results in significant disability, congenital anomaly, or birth defect.

In addition to SAEs, other events also requiring prompt reporting to the IRB may be unanticipated problems involving risks to subjects or others such as:

- Adverse events or injuries that are unexpected, related or possibly related, and increase the potential for harm to subjects.
- Adverse device effects that are unanticipated.
- Major protocol deviations or violations involving risks or with the potential to recur.
- Major or continuing non-compliance
- Events requiring prompt reporting according to the protocol, sponsor, and IRB.

All serious adverse events observed will be documented noting, at a minimum, the date of occurrence, the date the research team learned of the SAE, the involved participant(s) ID, the involved participant age, the involved participant's date of enrollment, a description of the SAE, a description of any immediate action taken, steps taken to correct the SAE, and a description of the preventative action plan.

The PI and the delegated research team members will immediately report all SAEs to the sponsor according to protocol requirements, and will also comply with the applicable regulatory requirements related to the reporting of unexpected serious adverse drug/device reactions to the FDA and the IRB.

The initial report should be followed promptly by detailed, written reports. The immediate and follow-up reports should identify subjects by unique code numbers assigned to the clinical research study subjects and protocol number. Subjects should not be identified by name or initials.

For reported deaths, the investigator should supply the sponsor and the IRB with any additional requested information (e.g., autopsy reports, death certificates, and terminal medical reports).

Event reporting information and a link to the event reporting form for LSUHSC's IRB can be found at https://www.lsuhsc.edu/administration/academic/ors/irb/reportable_new_information.aspx.

Event reporting information and a link to the event reporting form at Western Institutional Review Board can be found at www.wirb.com.

For all other reviewing IRBs, please refer to their event reporting guidelines.

The PI and delegated research team members will ensure the IRB is notified of all serious or reportable events occurring at this site during the approval period for the ongoing study. The PI should ensure all adverse events are reviewed as part of the site's periodic or annual reporting requirements.

C. Managing Safety Reports

The PI and research team will review all safety reports which are sent from the sponsor regarding SAEs experienced at other sites. All safety reports received from sponsors will be promptly submitted to the IRB according to the IRB's reporting requirements and timelines for review. The PI will sign and date each IND report as acknowledgement of review. In the case of electronic reporting, the PI will log in to the portal for acknowledgement and review. A copy of all safety reports will be maintained and filed appropriately with the regulatory files for each protocol.

D. Emergency Unblinding

The research team should follow the clinical research study's randomization procedures, if any, and should ensure that the code is broken only in accordance with the protocol. If the clinical research study is blinded, the investigator should promptly document and explain to the sponsor any premature unblinding (i.e. accidental unblinding, unblinding due to a serious adverse event) of the investigational product(s). If possible, the sponsor should be consulted before unblinding occurs.

5. APPLICABLE REGULATIONS AND GUIDANCE

LSU Health Guidance/Policy	Title
LSUHSC HRP Policies & Procedures	4.01 Assessment of Risks to Subjects
LSUHSC HRP Policies & Procedures	4.02 Unanticipated Problems Involving Risks to Subjects and Others
LSUHSC HRP Policies & Procedures	4.03 Non-Compliance by Investigators
LSUHSC HRP Policies & Procedures	4.04 Notification of Termination of the Study

Federal/International Regulation/Guidance/Policy	Title
21 CFR 50.25	Elements of Informed Consent
21 CFR 56.108	IRB Functions and Operations
21 CFR 56.109	IRB Review of Research
21 CFR 56.115	IRB Records
21 CFR 312.32	Investigational New Drug Application – IND Safety Reporting
21 CFR 312.33	Investigational New Drug Application – Annual Reports
21 CFR 312.44	Investigational New Drug Application - Termination
45 CFR 46.103	Assuring Compliance with this Policy - Research Conducted or Supported by any Federal Department or Agency
45 CFR 46.109	IRB Review of Research
45 CFR 46.115	IRB Records
45 CFR 46.116	General Requirements for Informed Consent
ICH E6(R2)	Guideline for Good Clinical Practice E6 Integrated Addendum
FDA Guidance for Industry	Continuing Review after Study Approval – Information Sheet

6. MATERIALS

6.1. None

Approved by:

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