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 2.09 describes the process for ensuring protocol compliance and documenting and reporting protocol deviations 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 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.

Protocol: A document that describes the objective(s), design, methodology, statistical considerations and organization of a study.

Regulatory Authorities: Bodies having the power to regulate. In the ICH GCP Guidelines, regulatory authorities include those authorities that review submitted clinical data and those that conduct inspections, such as the FDA.

Source Documents: Original documents, data and records (e.g., hospital records, clinical and office charts, laboratory notes, memoranda, subjects' diaries or evaluation checklists, pharmacy dispensing records, recorded data from automated instruments, copies or transcriptions certified

after verification as being accurate and complete, microfiches, photographic negatives, microfilm or magnetic media, x-rays, subject files and records kept at the pharmacy, the laboratories and medico-technical departments involved in the clinical study).

Statement of Investigator: An agreement signed by the Investigator to provide certain information to the sponsor and assure that he/she will comply with FDA regulations related to the conduct of a clinical investigation of an investigational drug or biologic.

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

4. PROCEDURES

A. Protocol Compliance

The PI's responsibility includes, but is not limited to the following:

- Ensuring that clinical research is conducted according to the signed investigator statement, the investigational plan, and applicable regulations and any conditions of approval imposed by an IRB, sponsor, or other regulatory body.
- Protecting the rights, safety, and welfare of subjects under the investigator's care.
- Control of investigational product.
- Accurate and adequate data and case histories.
- Timely reporting of adverse events and study data.
- Assurance of IRB review 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 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, except where necessary to eliminate an immediate hazard to a subject, or when the changes involve only logistical or administrative aspects of the study (e.g., change of monitor, change of telephone numbers).

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 PI or delegated research team members may implement a deviation from, or a change in, the protocol to eliminate an immediate hazard to clinical research study subjects without prior IRB approval. The implemented deviation or change should be submitted to the IRB for review and approval, to the sponsor for agreement, and (if required) to the appropriate regulatory authorities within the required timeframe.

Noncompliance with the protocol, SOPs, GCP, and/or applicable regulatory requirements by an investigator or by members of the research team may lead to prompt action by the sponsor, IRB, and/or FDA to ensure compliance.

If monitoring and/or auditing identifies serious and/or persistent noncompliance on the part of an investigator or members of the research team, the research may be terminated at the site. If

investigational site participation is terminated because of noncompliance, the regulatory authorities should be promptly notified.

B. Preventative Measures

If not already provided by the sponsor, the delegated research team member will appropriately create worksheets, flow sheets, study calendars, electronic health record smart phrases, paper orders, electronic order sets and other tools to be used for source documentation and/or as a reminder to clinical research team members to perform protocol specific evaluations, assessments and tests.

These tools will be developed and shared with key personnel and clinical support staff prior to protocol implementation to ensure that all key members of the protocol management team are trained and educated on the expectations of the protocol.

The delegated research team members will meet regularly with the key personnel and clinical support staff involved in the conduct of the clinical research study. This will ensure that the tools created are utilized appropriately and are successful in preventing protocol deviations. Delegated research team members will ensure tools remain current should protocol changes arise and that appropriate approvals are obtained by the IRB, if applicable.

C. Protocol Deviations

If the PI or Sub-Investigator foresees the need for a protocol deviation waiver they must receive sponsor approval prior to the deviation and, if necessary, obtain IRB approval. Protocol waivers should be used in very rare situations where compliance is not feasible and where the protocol cannot be amended in a timely manner to avoid the deviation.

The PI or Sub-Investigator may deviate from the protocol to eliminate immediate hazard to the patient without prior sponsor or IRB approval. The delegated research staff will document the deviation in a note to file or as part of the subject medical record as a research note and appropriately report the deviation to the sponsor and IRB, as applicable.

If a member of the research team discovers a protocol deviation or subject non-compliance, they will document the deviation as part of the study records, subject medical record or research chart. They will appropriately report the deviation to the sponsor, IRB and other regulatory authorities, as applicable, and as specified in the reporting requirements of the protocol.

Protocol deviations will be reviewed at regular intervals with the PI, delegated research team members and clinical support staff. If consistent deviations are noted, attempts should be made to implement a new process or create tools to prevent future deviations. If the implementation of a new process or tools is unable to correct the problem, the PI should work with the sponsor to assess whether a protocol amendment is feasible

5. APPLICABLE REGULATIONS AND GUIDANCE

LSU Health Guidance/Policy	Title
LSUHSC HRP Policies & Procedures	2.03 Criteria for IRB Approval of Research
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
LSUHSC Institutional Review Board	Reportable New Information
LSUHSC Office of Compliance Programs	Penalties for Violating HIPAA Regulations

Federal/International Regulation/Guidance/Policy	Title
21 CFR 50.20	General Requirements for Informed Consent
21 CFR 50.25	Elements of Informed Consent
21 CFR 56.109	IRB Review of Research
21 CFR 56.111	Criteria for IRB Approval of Research
21 CFR 312.60	Investigational New Drug Application: General Responsibilities of Investigators
21 CFR 312.62	Investigational New Drug Application: Investigator Recordkeeping and Record Retention
21 CFR 812.20	Investigational Device Exemptions: Application
ICH E6(R2)	Guideline for Good Clinical Practices E6 Integrated Addendum
FDA Guidance for Industry	Recruiting Study Subjects – Information Sheet
FDA Guidance for Industry	Payment and Reimbursement to Research Subjects – Information Sheet
FDA Guidance for Industry	Considerations When Transferring Clinical Investigation Oversight to Another IRB
FDA Guidance for Industry	Investigator Responsibilities- Protecting the Rights, Safety, and Welfare of Study Subjects
FDA Guidance for Industry	Adverse Event Reporting to IRBs – Improving Human Subject Protection
FDA Guidance for Industry	Oversight of Clinical Investigations – A Risk-Based Approach to Monitoring

6. MATERIALS

6.1. Note to File: PI Privileges

6.2. Note to File: Event

6.3. Note to File: Misc.

6.4. Event Tracking Log

Approved by:

Jawed Alam, PhD, MBA
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