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), 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 2.05 describes the process for creating and maintaining study regulatory files, subject records, and record retention which are periodically reviewed by the sponsor and may be requested by the FDA or other regulatory authorities.

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.

Case Report Form (CRF): A printed, optical or electronic document designed to record protocol-required data for each study subject and sent to the Sponsor for purposes of statistical analysis.

Confidentiality (*Regulatory Perspective*): The prevention of disclosure, other than to authorized individuals, of a subject's data or medical information. Privacy concerns people, whereas confidentiality concerns data.

Data Safety Monitoring Committee (DSMC): A committee of clinical research experts, such as

physicians and statisticians, and patient advocates who monitor the progress of a clinical trial and review safety and effectiveness data while the trial is ongoing.

HIPAA Authorization: A detailed document that gives covered entities permission to use protected health information for specified purposes, which are generally other than treatment, payment or healthcare operations, or to disclose protected health information to a third party specified by the individual.

Informed Consent Form (ICF): The form on which the process of conducting and achieving informed consent from potential study subjects is documented.

Investigational Device Exemption (IDE): An application that permits a device that would otherwise be required to comply with a performance standard (e.g., 510(k) submission) or to have pre-market approval by the FDA to be legally shipped for a clinical investigation.

Investigational New Drug (IND): Refers to the regulations in 21 CFR 312. An IND that is in effect means that 30 days have elapsed from the date that a complete IND application was submitted to the FDA and an appropriate IRB has reviewed and approved the Sponsor's clinical study, all the requirements under 21 CFR 312 are met and an investigational product can be distributed to investigators.

Investigator's Brochure (IB): A document that is provided by a clinical study Sponsor to investigators participating in that study. It is a compilation of the clinical and non-clinical data on the investigational product(s) relevant to the study of the investigational product(s) in human subjects.

IRB of Record: The IRB that is responsible for the ethical review of Human Research on behalf of an institution/organization or individual investigator.

Monitor: The person who periodically oversees the progress of a clinical study and ensures that it is conducted, recorded and reported in accordance with the protocol, SOPs, GCP and applicable regulatory requirement(s).

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

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).

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

4. PROCEDURES

A. Prior to Clinical Research Implementation

The PI or delegated research team members will create and maintain study regulatory files (electronic or paper) for each clinical research study that will contain required, original, and revised essential documents.

All study-related essential regulatory and subject case history documents will be kept confidential and stored in a secure and limited access location, meeting institutional privacy and security policy expectations. Upon request of the monitor, auditor, IRB, sponsor or regulatory authority, the PI and delegated research team members will make all essential documents available for review.

The PI or delegated research team members will provide the IRB with a complete IRB application, a current copy of the protocol, investigator brochure, investigator manual, consent/assent forms, HIPAA authorization form, IND or IDE FDA information, data collection forms (if required), recruitment materials and any additional required documentation for review. The PI and delegated research team members should refer to LSUHSC IRB Policies & Procedures as well as the policies of the IRB of record (if other than LSUHSC IRB) for details on what to documents should be submitted.

A research study will be registered to ClinicalTrials.gov if deemed an Applicable Clinical Trial by study design or funding source (e.g., NIH). Studies may also register for publication purposes.

The investigational site will receive a copy of the dated approval from the IRB and other regulatory bodies, if required, for the protocol, Informed Consent Form, HIPAA authorization, subject recruitment procedures (e.g., advertisements), and any other written information to be provided to subjects prior to implementing any study activities.

B. During the Conduct of the Research Study

The PI or delegated research team members will create and maintain study specific subject files for each consented clinical research subject. These files will contain required original essential documents such as source documents used for case report form data elements, original signed Informed Consent Forms (ICF) and HIPAA authorization forms, protocol deviations, adverse events (AE) , Case Report Forms (CRF) and Serious Adverse Event (SAE) reports.

During the conduct of the study the PI and delegated research team members will provide to the IRB all documents subject to review, such as:

- Amendments to the protocol, Informed Consent Form, Investigator's Brochure, or other approved materials
- Addition/removal of Sub-Investigators and key personnel
- Continuing Review documents
- Subject safety information
- IND safety reports meeting LSUHSC IRB or IRB of record reporting requirements, protocol deviations, Data Safety Monitoring Committee (DSMC) reports (if required)
- Adverse Events and Serious Adverse Events

The PI or delegated research team member will submit written summaries of the study's status to the reviewing IRB, as part of the annual renewal process, which will occur at least annually. Under specific conditions IRB-approved research may undergo annual continuing review via expedited or administrative review. In some cases, a brief annual status report can be submitted for administrative review. The PI or delegated research study team member will also promptly

provide written reports to the sponsor and IRB, where required by the applicable regulatory requirements, on any changes significantly affecting the conduct of the study and/or increasing the risk to subjects. This may include any changes to:

- Protocol
- Informed Consent Form
- Safety of the investigational product (including IND safety reports)

The PI or delegated research team members will ensure that the study regulatory files are organized, complete and accurate. Any additional documentation created or received over the course of the study will be filed appropriately. All original documents will be maintained and revised documents will be added to the study regulatory file (See Attachment B: Regulatory Documents Checklist).

The investigator should maintain adequate and accurate source documents and trial records that include all pertinent observations on each of the site's trial subjects. Source data should meet ALCOA-C criteria:

- Attributable
- Legible
- Contemporaneous
- Original
- Accurate
- Complete

Changes to source documentation should be traceable, should not obscure the original entry, and should be explained if necessary (e.g., via an audit trail). When corrections are necessary, the original entry should be struck through by a single line and indicate the date, reason for correction, and the initials as found on the Delegation of Authority Log of the individual making the correction.

When working with hospitals and clinics, follow their site-specific SOPs. For non-electronic records, official documents should be documented as a "Certified Copy" with a signature and date.

C. Termination (Closure) of the Study

To prepare for a study termination/close-out visit with the sponsor, the PI or delegated research team member will:

- Review all study regulatory files for accuracy and completeness.
- Resolve all outstanding sponsor queries.
- Reconcile all investigational study product accountability and shipment records.
- Evaluate requirements for data storage and prepare for a potential sponsor quality assurance review or FDA inspection (See Attachment D: Study Termination Checklist).
- Update ClinicalTrials.gov status and report results (if applicable).

The PI or delegated research team member will notify the IRB of record, the LSUHSC IRB, and

Sponsored Projects Accounting when the study has been closed. The notification to the IRB, at a minimum, will include the number of subjects enrolled, notice that all Serious Adverse Events have been reported (if required), subject withdrawals from study, and deaths on study, if any, have occurred. The sponsor will also receive a copy of this report from the site. The investigational site will ensure the return or destruction of all study-related materials.

If the study is terminated prematurely or suspended for any reason, the PI or delegated research team member will promptly inform the study subjects, ensure appropriate therapy and follow-up for the subjects receiving intervention/treatment, and, inform the regulatory authorities including the IRB of record and the FDA (if applicable).

If the PI terminates or suspends a study without prior agreement from the sponsor, the investigator will inform the sponsor and the IRB and provide a detailed explanation of the termination or suspension.

If the sponsor terminates or suspends a study, the PI will promptly submit to the IRB as an amendment or closure request and provide the IRB a detailed written explanation of the termination or suspension.

If the IRB terminates or suspends its approval of a study, the PI will promptly notify the sponsor and provide the sponsor with a detailed written explanation of the termination or suspension.

Upon closure of the study the PI will provide the sponsor with all required reports, the IRB with a summary of the study outcome, and any regulatory authority that may require a report.

D. Essential Document Retention

The LSU Health policy states all research-related records need to be maintained for at least 10 years after the research has ended unless longer as required by other entities (sponsor, contractual requirement, patent requirements, publication, FDA, etc.).

For an FDA regulated study:
Drugs/Biologics: An investigator shall retain records for a period of 2 years following the date a marketing application is approved for the drug indication being investigated; or, if no application is to be filed or if the application is not approved for such indication, until 2 years after the investigation is discontinued and FDA is notified. If there are space limitations, these records can be maintained in off-site storage.

Device: An investigator or sponsor shall maintain the records for a period of 2 years after the latter of the following two dates:

1. The date on which the investigation is terminated or completed, or
2. The date that the records are no longer required for purposes of supporting a premarket approval application or a notice of completion of a product development protocol.

If there are space limitations, these records can be maintained in off-site storage.

5. APPLICABLE REGULATIONS AND GUIDANCE

LSU Health Guidance/Policies	Title
LSUHSC HRP Policies & Procedures	2.05 IRB Records
LSUHSC HRP Policies & Procedures	5.02 Record Keeping by Investigators
LSUHSC Office of Compliance Programs	Electronic Data Interchange Requirements
LSUHSC Office of Compliance Programs	Privacy Requirements
LSUHSC Office of Compliance Programs	Information Security Requirements
LSUHSC Policy	Records Retention and Disposition Policy
Louisiana Secretary of State	Records Retention Schedule
LSUHSC Clinical & Translational Research Center (CTRC)	PM 204 SOP for Regulatory Files and Subject's Records

Federal/International Regulation/Guidance/Policy	Title
21 CFR 11	Electronic Records; Electronic Signatures
21 CFR 50	Protection of Human Subjects
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 312.68	Investigational New Drug Application: Inspection of Investigator's Records and Reports
21 CFR 812.140	Investigational Device Exemptions: Records and Reports
ICH E6(R2)	Guideline for Good Clinical Practices E6 Integrated Addendum
FDA Guidance for Industry	Electronic Source Data in Clinical Investigations

6. MATERIALS

6.1. Essential Document Checklist

6.2. Regulatory Document Checklist

6.3. IRB Submission Checklist

6.4. Study Termination Checklist

Approved by:

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