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 2.15 describes the process for preparing and participating in an audit (including internal, sponsor, IRB or FDA) 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

Audit: A systematic and independent examination of study-related activities and documents to determine whether the evaluated study-related activities were conducted and that the data were recorded, analyzed and accurately reported according to the protocol, Sponsor's SOPs, GCP and the applicable regulatory requirements.

Audit Certificate: A written statement, signed by an auditor, which documents that an audit was performed.

Audit Report: A written evaluation by the auditor of the results of the audit.

Audit Trail: The documentation ("paper trail") that allows reconstruction of the course of events.

Certified Copy: A copy of original information that has been verified, as indicated by dated signature, as an exact copy having all of the same attributes and information as the original.

Direct Access: Permission to examine, analyze, verify and reproduce any records and reports that are important to evaluation of a clinical study. Any party (e.g., domestic and foreign regulatory authorities, Sponsors, monitors and auditors) with direct access should take all reasonable precautions within the constraints of the applicable regulatory requirement(s) to maintain the confidentiality of subjects' identities and Sponsors' proprietary information.

Essential Documents: All the documents that individually and collectively permit evaluation of the conduct of a study and the quality of the data produced.

Inspection: The act by a regulatory authority of conducting an official review of documents, facilities, records and any other resources that are deemed by the authority to be related to the clinical study and that may be located at the site of the study, at a Sponsor's and/or CRO's facilities or at other establishments deemed appropriate by the regulatory authority.

Regulatory Authority: 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.

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

4. PROCEDURES

A. Preparing for an Audit

The PI and delegated research team members will permit monitoring and auditing by the sponsor, the IRB, and all appropriate regulatory authorities, including the FDA. The PI and delegated research team members will maintain a list of appropriately qualified persons to whom the PI has delegated significant clinical research study-related duties. The investigational site will work with the auditor or inspector to arrange a mutually agreed upon date and time to conduct the audit.

If the investigational site is notified of an audit, the PI or delegated research team member should obtain, at a minimum, the following information:

- Name and contact information of the auditor(s)/inspector(s)
- Number of auditors/inspectors expected
- Dates the auditor(s)/inspector(s) is expected to be on site
- Why the audit/inspection is being done
- The study to be audited, if a particular study
- The subject records to be reviewed, if known
- Whether the auditor(s)/inspector(s) plan to tour the facility

The investigational site will schedule an appropriate room for the audit that is away from clinical activity and in a private setting. They will also schedule any meetings with key personnel requested by the auditor.

The primary research team member assigned to the clinical research study should be the main point of contact for scheduling and organizing the audit and will notify all appropriate members of the study team immediately (e.g., PI, Sub-investigators, other research team members engaged in the study, Department Head, the IRB of record, LSUHSC IRB if not the IRB of record,

Study sponsor, investigational pharmacy, and non-LSUHSC study site officials).

The PI and delegated research team members will prepare for the scheduled auditing visit by ensuring all clinical research study related documents are current, organized, complete and accurate prior to the visit. They will also ensure all original, relevant source documents and all clinical research study related documents are requested and available to the auditor during the visit.

If an auditor requests to review source documents directly in the electronic medical record, the PI or delegated research team member should contact the appropriate office at the study site to identify the appropriate way for the auditor to view the source documents. Acceptable, suggested methods for allowing auditors direct access include allowing the auditor over the shoulder access to the electronic medical record with a research team member; or a research team member sharing their screen showing the electronic medical record. If direct viewing is not requested, copies of the electronic source documents may be made available to the auditor. These requests will be reviewed and approved at the discretion of the study team.

The PI and delegated research team members will be prepared for the auditor to review and verify all of the following:

General Site Review

- The PI has adequate qualifications and resources and these remain adequate throughout the clinical research study period.
- The staff and facilities, including laboratories and equipment, are adequate to safely and properly conduct the clinical research study and these remain adequate throughout the clinical research study period.
- The PI and delegated research team members are adequately informed about the clinical research study.
- The PI and the delegated research team members are performing the specified clinical research study functions in accordance with the protocol and any other written agreement between the sponsor and the investigator/institution, and the PI has not delegated these functions to unauthorized individuals.
- The investigator and delegated research team members follow the approved protocol and all approved amendments, if any.

Informed Consent

- Each subject has consented to direct access to his/her original medical records for clinical research study-related monitoring, audit, IRB review, and regulatory inspection.
- Informed consent was obtained and details of the informed consent discussion are adequately documented in the study records before each subject's participation in the clinical research study.
- The correct version of the consent was used to obtain consent.
- The PI is enrolling only eligible subjects.

Clinical Research Data/Documents

- Source documentation, case histories, CRF entries and other clinical research study records are accurate, complete, current, and maintained.
- The PI provides all required reports, notifications, applications, and submissions, and

these documents are accurate, complete, timely, legible, dated, and identify the clinical research study.
- Adverse events (AEs) are appropriately reported within the time periods required by the protocol, IRB, and applicable regulatory requirements.
- The PI and delegated research team members are maintaining the essential documents as outlined in the Essential Documents SOP.

Investigational Product

- The investigational product storage conditions are acceptable and supplies are sufficient throughout the clinical research study.
- The investigational products are supplied only to eligible subjects and at the protocol specified doses.
- Subjects are provided with necessary instruction on the proper use, handling, storing, and returning of the investigational products.
- The receipt, use, and return of the investigational products at the clinical research study site are controlled and documented adequately.
- The disposition of unused investigational products complies with applicable regulatory requirement and is in accordance with the sponsor's authorized procedures.

B. During the Audit

When the auditor arrives, the delegated research team member **will request identification** and orient them to the investigational site facilities. Sponsor auditors should sign the monitoring visit log, as applicable.

The research team member assigned to that clinical research study may be the main point of contact for the auditing visit. The research team member should provide the auditor with all clinical research study documents requested for review and check in with the auditors throughout the day to address any questions or arrange any requested meetings with key personnel.

If copies of source documents or CRFs are requested, the primary coordinator or delegated research team members will make a copy for the auditor or FDA investigator, ensuring it is marked or stamped "Confidential," and make a copy for the investigational site records, which will be maintained with all other relevant audit documents. An auditor or investigator may take their copies with them when the audit is complete.

C. Audit Exit Interview

The PI, delegated research team members, and a member of the IRB staff, at a minimum, will be present for the audit exit interview. Sub-investigators, CTO supervisor and other research representatives may be present, if requested. The investigational site should be prepared for the auditor to discuss:

- Any deviations from the protocol
- Applicable regulatory requirements
- Signed Investigator Agreement
- SOPs and investigational site processes
- Case histories
- Record keeping or management of regulatory documents

- Inaccurate data entry or invalid data
- Inadequate accountability and management of investigational product
- Inadequate protection of human subjects
- Inadequate PI oversight or delegation of responsibilities, and recommendations to secure compliance

The auditor should provide the investigational site with a certificate of audit or formal audit summary that includes details on what the auditors reviewed and any significant findings, deviations, and deficiencies noted. Audit findings discussed in detail should also be documented by the investigational site.

The PI and delegated research team members will address all findings, deviations and deficiencies presented by the auditor within a specified timeline in a formal response to the audit report. Responses should be based on the requirements of the auditing body. The formal response will include a cover letter, a statement of acknowledgement of each audit finding, any additional supportive source documentation, and detailed summary of corrective actions that will be implemented to eliminate future deficiencies such as departmental SOPs, training and education initiatives, revised protocol and new policies. All corrective actions will be documented, filed appropriately, and implemented within the timeline specified in the audit response letter.

Audit findings and corrective actions implemented will be communicated to key entities notified of the initial audit.

D. Additional Information Regarding FDA Inspections

In addition to the processes in sections A, B and C above, the following information applies to FDA inspections.

The FDA conducts both announced and unannounced inspections of clinical investigator sites. Reasons for inspections include but are not limited to the following:

- To verify the accuracy and reliability of data submitted to the agency (e.g., Data Integrity Audit, Sponsor Submission for FDA Approval of Drug or Device).
- As a result of a complaint to the agency about the conduct of a study at a particular investigational site (including concerns or complaints of a sponsor).
- Upon termination of the clinical site (e.g., high volume of protocol deviations, adverse events, etc).
- To verify the conduct of a clinical research study and protection of human subjects during an active study (e.g., Inspection for Safety and Efficacy Events).
- At the request of an FDA review division.
- In relation to specific classes of investigational products that the FDA has identified as products of special interest in its current work plan (e.g., targeted inspections based on current public health concerns).

Announced Inspections

An inspector will contact the PI to schedule an inspection. After the PI or research team member schedules the inspection, they must contact the IRB of record (and the LSUHSC IRB, if Reliance), study sponsor and any non-LSUHSC study sites with details of the inspection. When the inspector arrives on site, he or she will present their credentials, identification and a copy of the

FDA Form 482: Notice of Inspection for signature. The PI or research team member should *request the documents if not presented.*

Unannounced Inspections
If a FDA inspector arrives unannounced, the PI and delegated research team members must accommodate the request and follow the processes described above.

Inspection Outcomes
If deficiencies are found during an FDA inspection, the inspector will outline the issues in a written FDA Form 483: Inspectional Observations. These observations are typically based on FDA regulations 21 CFR 50, 54, 56, 312 and/or 812. If an FDA 483 form is issued, the PI is responsible for writing a formal response addressing how the deficiencies will be corrected and prevented from occurring in the future. The response may be in collaboration with key clinical research stakeholders (e.g., IRB of Record, non-LSUHSC study sites), if needed. This response will be sent to the appropriate FDA District Office within 15 business days of receiving the inspection results, with copies to the IRB of Record.

5. APPLICABLE REGULATIONS AND GUIDANCE

LSU Health Guidance/Policy	Title
LSUHSC Institutional Review Board	LSUHSC HRP Policies & Procedures
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 Office of Compliance Programs	Compliance Training Policy
LSU System	LSU PM #36 Information Security Plan
LSUHSC Policy	Records Retention and Disposition Policy
Louisiana Secretary of State	Records Retention Schedule

Federal/International Regulation/Guidance/Policy	Title
21 CFR 11	Electronic Records; Electronic Signature
21 CFR 312.56(a)(b)	Responsibilities of Sponsors & Investigators: Review of Ongoing Investigations
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 812.45(e)	Investigational Device Exemption: Informing Investigators
21 CFR 812.46(a)	Responsibilities of Sponsors: Monitoring Investigations
HHS Office of Human Research Protections	Compliance Oversight Procedures for Evaluating Institutions
ICH E6(R2)	Guideline for Good Clinical Practices E6 Integrated Addendum
FDA BIMO Compliance Programs	7348.809 Institutional Review Board
FDA BIMO Compliance Programs	7348.810 Sponsors and Contract Research Organizations
FDA BIMO Compliance Programs	7348.811 Clinical Investigators and Sponsor-Investigators
FDA Guidance for Industry	Frequently Asked Questions – Statement of Investigator Form FDA 1572
FDA Guidance for Industry	Clinical Investigator Administrative Actions - Disqualification
FDA Guidance for Industry	Circumstances that Constitute Delaying, Denying, Limiting, or Refusing a Drug Inspection
FDA Guidance for Industry	Gifts to FDA: Evaluation & Acceptance

6. MATERIALS

6.1. HSC IRB FDA Audit Preparation Guidance

6.2. FDA Inspection Intake Form

6.3. FDA Inspection Checklist

6.4. Post-Approval Monitoring and Education Self-Evaluation

6.5. Self-Audit Tool: Informed Consent Review Worksheet

6.6. Self-Audit Tool: Subject Record Review

Approved by:

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