Center for Clinical and Translational Research Standard Operating Procedure

Section **Clinical Research Center** Date Created**:** **November 1, 2010**

Title: **Audits and Inspections** Date Reviewed/Modified: **July 7, 2021**

SOP Number: **SOP- 3** Version Number: **6**

PURPOSE: This standard operating procedure (SOP) describes the operations followed at this site when an audit occurs including FDA inspections/audits conducted under FDA's Bioresearch Monitoring (BIMO) program.

SCOPE: This SOP applies to the procedures to prepare for an audit conducted at this site. It describes the steps the site follows from the time the site is notified of the audit until all follow-up activities associated with the audit are completed.

PERSONNEL RESPONSIBLE: This SOP applies to members of the clinical research team involved in arranging, managing, or participating in the audit at this research site. This includes the following: Sponsor, Sponsor-Investigator, Principal Investigator, Sub-Investigators, Director of Clinical Research Operations, Research Nurse Coordinators, Regulatory Designee, Investigational Pharmacists, and/or other pertinent staff.

DEFINITIONS:

- **Audit:** A systematic and independent examination of trial-related activities and documents by the Food and Drug Administration (FDA), sponsor, or other regulatory agency. An audit is to determine whether the trial-related activities were conducted, and the data were recorded, analyzed, and accurately reported according to the protocol, site's standard operating procedures (SOPs), good clinical practice (GCP), and the applicable regulatory requirements(s).
- **Audit Trail:** Documentation that allows reconstruction of the course of events.
- **Bioresearch Monitoring (BIMO) Program** – The objectives of the bioresearch monitoring program are twofold: (1) to ensure the quality and integrity of data and information submitted in support of investigational and marketing clearance applications or submissions [IDEs, PMAs, and 510(k)s]; and (2) to ensure that human subjects taking part in investigations are protected from undue hazard or risk. The Division is also charged with the implementation of the FDA's Application Integrity Policy (AIP) for medical devices and radiological health products.
- **Compliance:** Adherence to all the trial-related requirements, good clinical practice (GCP) requirements, and the applicable regulatory requirements.
- **Direct Access:** Permission granted to any party (e.g., domestic and foreign regulatory authorities, sponsors, monitors, and auditors) to examine, analyze, verify, and reproduce any records and reports that are important to evaluation of a clinical trial.
- **Documentation:** All records, in any form (including, but not limited to: written, electronic, magnetic, and optical records; and scans, x-rays, and electrocardiograms) that describe or record the methods, conduct, and/or results of a trial, the factors affecting research, and the actions taken.

- **Food and Drug Administration (FDA or USFDA)** – Is a federal agency of the United States Department of Health and Human Services, one of the United States federal executive departments. The FDA is responsible for protecting and promoting public health through the control and supervision of food safety, tobacco products, dietary supplements, prescription and over-the-counter pharmaceutical drugs (medications), vaccines, biopharmaceuticals, blood transfusions, medical devices, electromagnetic radiation emitting devices (ERED), cosmetics, animal foods & feed and veterinary products.
- **Essential Documents:** Documents that individually and collectively permit evaluation of the conduct of a study and the quality of the data produced.
- **Good Clinical Practice (GCP):** A standard for the design, conduct, performance, monitoring, auditing, recording, analysis, and reporting of clinical trials that provides assurance that the data and reported results are credible and accurate, and that the rights, integrity, and confidentiality of trial subjects are protected.
- **Source Documents:** Original documents, data, and records (e.g., hospital records, laboratory results, memoranda, subjects' diaries or evaluation checklists, pharmacy dispensing records) that contain the first recording of pertinent information.
- **Standard Operating Procedures (SOPs):** Detailed, written instructions which describe department specific activities, clarify expectations for staff performances, provide supporting documentation for auditors and facilitate critical evaluation of department practices.

PROCEDURES:

Notification of Audit:

1. Obtain the following information:
    a. Contact information if we need to call back
    b. Date and time we can expect the auditor
    c. Name of the auditor(s)
    d. Name of the study they are auditing
    e. Type of audit

Preparing for the audit

Responsible Team Members	***Tasks to Implement:***
• PI • Research Lead • Research nurse/coordinator • Support staff • Regulatory assistant	Ensure that all documentation, including informed consent forms, source documents, CRFs, and the regulatory binder for the study are identified as the focus of the audit are accurate, complete, and available for review by the auditor. (Attachment A, Audit Preparation Checklist).
• Research nurse/coordinator • Study pharmacist	Ensure that the study drug/device dispensing records are accurate, complete and available for review. If there were any instances in which emergency breaking of the blind was required, have that documentation available. (Attachment A Audit Preparation Checklist)
• Study pharmacist	Ensure that drug accountability records are accurate, complete and available for review.
FOR FDA AUDIT ONLY	If notified of an FDA audit, the PI is responsible to ensure the following are immediately notified: • Research Staff involved with the trial • Sponsor / Clinical Research Organization (CRO) • Section Chair • IRB (and Scientific Review Committee Chair if applicable) • Investigational Pharmacy • UNMC, NM, IRB compliance officers, Legal Counsel

	• Associate Vice-Chancellor for Clinical Research at UNMC, Vice President for Research at Nebraska Medicine and the Director of Clinical Research Operations

During the audit

• PI • Director of Clinical Research Operations • Research Lead • Research nurse/coordinator • Regulatory assistant • Support staff	Meet with the auditor or inspector. Request to see identification, and if this is an FDA audit, request Form FDA 482. Provide orientation and access to the study records and files. Provide copies of requested study-related documents. Ensure that questions posed by the auditor or inspector are answered by appropriate study personnel. If you do not know the answer to the question, do not guess. Answer only what is asked. Put the auditor in a room without other records/study documents. (See Attachment A)
FOR FDA AUDIT ONLY	An individual listed on the IRB for the study will be identified to log into Electronic Medical Record production version and navigate patient charts on behalf of the FDA auditor.

Following up after the audit

• PI • Director of Clinical Research Operations • Research lead • Research nurse/coordinator	Participate in the exit interview with the auditor or inspector. **NOTE**: if an FDA 483 is issued it must be responded to within 15 days of receipt. The sponsor should be provided

• Legal counsel	with an opportunity to assist in the response. The reply should be routed through VCR Office, Legal Counsel, IRB, & SRC if applicable prior to submitting to FDA.
• PI • Director of Clinical Research Operations • Research lead • Research nurse/coordinator	PI will respond to the audit report as soon as possible after its receipt. Reply to each item in the report, providing clarification or steps that will be taken to institute corrective action. When responding to an FDA audit, PI will prepare a written response(s) after collaboration with the VCR office and IRB. All FDA audit response(s) will be communicated with UNMC and NM leadership by the PI in collaboration with VCR office.

ASSOCIATED FORMS:

Attachment A – Audit Preparation Checklist

SOP-3 Attachment A audit_prep_checkl

RESOURCES:

- Compliance Program 7348.810 Bioresearch Monitoring: Sponsors, Contract Research Organizations and Monitors https://www.fda.gov/inspections-compliance-enforcement-and-criminal-investigations/fda-bioresearch-monitoring-information/compliance-program-7348810-bioresearch-monitoring
- Compliance Program 7348.811 Bioresearch Monitoring: Clinical Investigators https://www.fda.gov/inspections-compliance-enforcement-and-criminal-investigations/fda-bioresearch-monitoring-information/compliance-program-guidance-manual-fda-staff
- *Information Sheet Guidance for IRBs, Clinical Investigators and Sponsors – FDA Inspections of Clinical Investigators (*Rep.*).* (June 2010). US Department of Health and Human Services FDA.
- International Conference on Harmonization (ICH) https://www.ich.org/home.html

- Perelman. (2014, March 27) *How to Survive an FDA Inspection.* Presented at School of Medicine Office of Research.
- *What You Need to Know to Prepare for a FDA Audit.* Presented at Forte Research Systems Webinar.
- UNMC: #6109 Investigations by Government Officials, Regulatory Agencies, and Other Third Parties.
- Nebraska Medicine:
    - LD03 Government Investigations Response Guide
    - MS40 Vendor Interactions

Staff Accountability:

Developed By: Director of Clinical Research Operations, Clinical Research Center
Associate Vice Chancellor for Clinical Research, Clinical Research Center
Reviewed By: Director of Clinical Research Operations, Clinical Research Center

Department Approval

Signed LuAnn Larson Date: Jul 7, 2021
Director of Clinical Research Operations

Signed Matt Lunning Date: Aug 2, 2021
Medical Director of Clinical Research Center

SOP-3 Audit and Inspections_AUG2019- FInal

Final Audit Report 2021-08-02

Created:	2021-07-07
By:	Charles Miller (charles.miller@unmc.edu)
Status:	Signed
Transaction ID:	CBJCHBCAABAAVUobCAT4oLI3DsIT9TOEJml6o1IAOOpN

"SOP-3 Audit and Inspections_AUG2019- FInal" History

Document created by Charles Miller (charles.miller@unmc.edu)
2021-07-07 - 8:20:13 PM GMT- IP address: 192.94.102.5

Document emailed to LuAnn Larson (llarson@unmc.edu) for signature
2021-07-07 - 8:21:09 PM GMT

Email viewed by LuAnn Larson (llarson@unmc.edu)
2021-07-07 - 9:12:00 PM GMT- IP address: 35.230.12.88

Document e-signed by LuAnn Larson (llarson@unmc.edu)
Signature Date: 2021-07-07 - 9:12:49 PM GMT - Time Source: server- IP address: 35.230.12.88

Document emailed to Matt Lunning (mlunning@unmc.edu) for signature
2021-07-07 - 9:12:51 PM GMT

Email viewed by Matt Lunning (mlunning@unmc.edu)
2021-07-07 - 9:46:52 PM GMT- IP address: 184.97.174.53

Document e-signed by Matt Lunning (mlunning@unmc.edu)
Signature Date: 2021-08-02 - 4:10:13 PM GMT - Time Source: server- IP address: 35.230.6.182

Agreement completed.
2021-08-02 - 4:10:13 PM GMT