Coordination of External Regulatory Audits/Inspections		
VCU/VCU Health CLINICAL RESEARCH STANDARD OPERATING PROCEDURES		
SOP No.: CR-RE-305.3a	Status: Final	Version Date: 02/11/2025 Effective Date: 03/14/2025

PURPOSE

This Standard Operating Procedure outlines the procedures to facilitate an audit/inspection of a clinical research study by an external regulatory agency including, but not limited to, the Food and Drug Administration (FDA) and Office for Civil Rights. External audits may be conducted by federal or state agencies that have oversight of research.

REQUIREMENTS

This policy applies to all key study personnel involved in arranging, managing, or participating in an audit/inspection of a research study at any VCU/VCU Health facility by an external regulatory agency.

In accordance with VCU Research Compliance Notice 17-002 Notice of External Audit or Inspection, it is the responsibility of the Principal Investigator (PI) and research team to both manage the external audit process and inform responsible parties, including the VCU Office of the Vice President for Research and Innovation (OVPRI) of the impending audit within 24 hours of receipt of notification. The IRB of record should be notified of becoming aware of an audit, inspection, or inquiry by a federal agency according to the timeline and procedures of the respective IRB policies. For an inspection from an external regulatory agency other than the FDA, follow OVPRI guidance as directed. Additional guidance regarding external inspections is located in OVPRI's FDA program manual.

Note: This policy does not apply to routine monitoring visits or routine audits conducted by the Sponsor.

The remainder of this SOP is specific for FDA inspections.

DEFINITIONS

Audit- A systematic and independent examination of trial-related activities and records performed by the sponsor, service provider (including contract research organization (CRO)) or institution to determine whether the evaluated trial-related activities were

conducted and the data were recorded, analyzed, and accurately reported according to the protocol, applicable standard operating procedures (SOPs), Good Clinical Practice (GCP) and the applicable regulatory requirement(s).

FDA Form 482 – "Notification of Inspection" – The FDA Form 482 is the official FDA document that an investigator presents to a facility/site when they arrive to conduct an inspection. The form gives the FDA the authority to access, inspect and copy any relevant records. The 482 should be made out to the most responsible person at the inspection (typically the principal investigator).

FDA Form 483 – "Inspectional Observations" – The purpose of the FDA Form 483 notifies the most responsible person (e.g.: principal investigator at the site) of objectionable conditions. An FDA Form 483 is issued to the most responsible person at the conclusion of an inspection when an FDA investigator(s) has observed any conditions that in their judgment may constitute violations of the Food Drug and Cosmetic (FD&C) Act and related Acts. The FDA Form 483 is a report that does not include observations of questionable or unknown significance at the time of the inspection. There may be other objectionable conditions that exist at the firm that are not cited on the FDA Form 483.

FDA inspection actions:

- No action indicated (NAI): no objectionable conditions or practices were found during the inspection.
- Voluntary action indicated (VAI): objectionable conditions or practices were found, but the agency is not prepared to take or recommend any administrative or regulatory action.
- Official action indicated (OAI): regulatory and/or administrative actions are recommended.

PROCESS

All studies subject to federal, state, or local regulations or that receive federal, state, or local funding are subject to inspection. The PI is responsible for following the applicable regulations listed in the reference section.

FDA may conduct an inspection of a clinical site for a variety of reasons such as, but not limited to, surveillance, for-cause or application-based inspections..

Upon notification of an impending audit or inspection, the process outlined in the VCU Research Compliance Notice 17-002 Notification Requirement for Research Subject to External Audit or Inspection, must be followed to notify the applicable parties. In the event that the inspection is unannounced, notification according to the compliance

notice should be followed at that time. Specific guidance for research teams is also included in this document. OVPRI's Regulatory Affairs Program assists with external audits prior, during and after notification of inspection. Prior to the arrival of the inspectors, the study team should determine who will be the primary day-to-day point of contact throughout the inspection (e.g.,: lead coordinator).

During the inspection, OVPRI's Regulatory Affairs Program will be available to provide as much assistance and support to the study team(s) as needed. The PI should be available throughout the inspection including at the opening and closing meetings. The inspection should occur in a private room that will be undisturbed and is clear of any other materials (other study binders). Only individuals relevant to the inspection should be introduced or involved in the inspection. At the end of the inspection, a closing meeting will be conducted which provides the inspector's observations and the issuance of a FDA Form 483 if applicable. The team present at the closing meeting will have the opportunity to respond to the observations verbally.

After the inspection, an inspection report will be provided to the most responsible person at the site. The report will list the inspection outcome as NAI, VAI or OAI. If a FDA 483 is issued, the study team will work with the assistance of OVPRI to formally respond to the FDA 483 within 15 business days.

REFERENCES

A. Code of Federal Regulations
   - 21 CFR 312.60- 21 CFR 312.69 – Investigator responsibilities at a site for studies being conducted under an IND
   - 21 CFR 812.100- 21 CFR 812.140 – Investigator responsibilities at a site for studies being conducted under an IDE

B. FDA
   - Chapter 48 of Bioresearch Monitoring Program Manual: Clinical Investigators and Sponsor-Investigators

C. VCU
   - Compliance Notice 17-002 Notification Requirement for Research Subject to External Audit or Inspection

D. When VCU is the IRB of record: HRPP Policies and Guidance; HRPP Toolkit
   - HRP-103; Investigator Manual
   - HRP-103p; pSite Investigator Manual

Review/Revision History CR-RE-305		
Version No.	**Effective Date**	**Description**
CR-RE-305.3a	03-14-2025	● Updated to ICH E6(R3)
CR-RE-305.3	03-01-2025	● Clarified when the IRB of record should be notified ● Revised Form 482 – "Notification of Inspection" definition ● Revised FDA Form 483 – "Inspectional Observations" definition ● Clarified FDA inspection actions ● Updated IRB policies to align with the HRPP Policies and Guidance; HRPP Toolkit ● Minor formatting edits ● Reference links updated
CR-RE-305.2a	07-01-2020	● Links updated
CR-RE-305.2	07-01-2020	Biennial review performed Minor formatting edits Reference links updated
CR-ST-305.1	11-01-2017	● Original