West Virginia Clinical and Translational Science Institute
Clinical Trials Center of Excellence

STANDARD OPERATING PROCEDURE

Title:		No.: COE-102.00	
External Audit Management		Page 1 of 5	
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Purpose:

This standard operating procedure (SOP) describes the operations followed at West Virginia University Health Sciences Center campuses when a routine/not-for-cause or for-cause external audit (sponsor/CRO, Food and Drug Administration (FDA) or other regulatory agencies) occurs to assess the site's extent of compliance with regulatory requirements designed to insure the safe and effective conduct of clinical research.

Scope:

This SOP describes procedural pathways to prepare for an audit of all clinical studies conducted at the site. It describes the steps followed by the site from the time that the audit is scheduled through all follow-up activities associated with the audit responses to the findings. This SOP excludes external audits directed at Institutional Review Board (IRB) compliance reviews.

Definitions:

Audit: A systematic and independent examination of trial-related activities and documents to determine whether the evaluated trial-related activities were conducted, and the data were recorded, analyzed, and accurately reported according to the protocol, sponsor's standard operating procedures (SOPs), good clinical practice (GCP), and the applicable regulatory requirement(s). [ICH E6]

Inspection: The act by a regulatory authority(ies) of conducting an official review of documents, facilities, records, and any other resources that are deemed by the authority(ies) to be related to the clinical trial and that may be located at the site of the trial, at the sponsor's and/or contract research organization's (CROs) facilities, or at other establishments deemed appropriate by the regulatory authority(ies). [ICH E6]

Form 482: FDA Notice of Inspection Form.

Form 483: FDA Notification of objectionable conditions.

Inspector/Auditor: The representative of the Regulatory Agency (Inspector) or Sponsor (Auditor) performing the audit.

Materials:
Attachment 1- Audit Checklist
Attachment 2- Employee Guidelines during the Audit Process

Responsibility:

This SOP applies to the clinical departments and HSC institutions actively engaged in clinical research involving human subjects.

Procedure:

A. Preparing for the External Audit

Note: For unannounced regulatory agency audits, the inspectors should be placed in a private area such as a conference room upon arrival and the Clinical Trials Center of Excellence (COE) contacted immediately. The steps below will then be followed as applicable.

1. Notification of appropriate parties will be performed in a timely manner according to the type of external audit:
    a. Regulatory Agency Audit:

When notified of a Regulatory Agency audit, such as the FDA, immediately contact the Clinical Trials Center of Excellence. A COE Representative will assist to establish the name(s) and credentials of the inspector(s), the scope of the inspection (routine or for-cause) and agree on all dates/availability in advance. The COE representative will help coordinate the visit and will distribute the information as soon as possible to:

i. The Sponsor
ii. The WVU Institutional Review Board (IRB)
iii. The IRB of record, if not WVU IRB
iv. The Office of Sponsored Programs (OSP) Office
v. WVU Internal Audit Team, Legal Counsel
vi. WVU HSC Leadership (ie. AVP, Clinical and Translational Research or designee), the Chair of the department/institution, Principal Investigator (PI) and Research team, including Laboratory, Pharmacy and any other personnel/departments involved with the conduct of the trial(s) identified.

b. Sponsor/Cooperative Group Audit

If notified of a Sponsor/Cooperative group audit, a designated clinical trials team representative will coordinate the visit and will inform:

i. Clinical Trials Center of Excellence who will provide assistance as needed and oversight of the audit process

ii. WVU Internal Audit Team

iii. The WVU Institutional Review Board (IRB)

iv. The IRB of record, if not under local oversight

v. The Office of Sponsored Programs (OSP) Office

vi. The PI and Research team, including Laboratory, Pharmacy and any other personnel/departments involved with the conduct of the trials.

2. Ensure that all documentation, including informed consent forms, source documents, Case Report Forms (CRF)s, and the regulatory binder for the trial identified as the focus of the audit are accurate, complete and available for review by the auditor. The Audit Checklist should be used as a guide.

3. Ensure that the study drug / device accountability records are accurate, complete and available for review. If there were any instances in which emergency breaking of the blind was required, the documentation should be available.

4. Ensure that records of staff qualifications and training are available for review by the auditor.

5. As time allows, prepare staff for the audit using the Employee Guidelines during the Audit Process.

6. For a Regulatory Agency audit, reserve at least 2 conference rooms, as possible, one for the inspector and one for material preparation for the estimated duration of audit.

B. <u>During the audit:</u>

1. An audit lead/host will be designated by HSC Research Leadership and will meet with the auditor/inspector and request to see identification to confirm name and credentials.
2. If this is an FDA audit, request Form FDA 482 (Notification of Inspection). For Regulatory Agency audits, a COE representative will participate in tours, interviews and preparation of documents for audit.
3. Provide an SOP index, organizational charts, and other documents as deemed appropriate, orientation and access to the study records and tour of requested departments/areas, as applicable to the auditor/inspector.
4. Provide copies of requested study-related documents. A Quality Control review will be performed by a quality assurance representative and/or members of the research team for all documentation to ensure it is complete prior to being provided to the auditor/inspector as possible.
5. For a regulatory agency audit, copies will be made of every document provided and kept as part of the audit documents and conversations will be documented by a scribe, as possible.
6. Regulatory agency inspectors will not be given access to the Electronic Medical Records (EMR), however printouts will be provided. If direct access is specifically requested, then WVU personnel will navigate the system for the inspector.

7. Ensure that questions posed by the auditor/inspector are answered by appropriate study personnel.

8. Written daily summaries will be provided by the host of the audit to key personnel/management and will include:
   - Documents/tours provided
   - Any issues found
   - Tasks to be completed prior to next scheduled audit date

C. Post-Audit Follow Up

1. The Principal Investigator, audit lead and HSC Research Leadership will participate in the exit meeting with the auditor/inspector. A representative from WVU Internal audit and WVU IRB should also attend for Regulatory Agency audits.

   If this was an FDA audit, request Form FDA 483, if issued. Form 483 will be distributed to the Sponsor, the IRB, the PI and the OSP, and HSC Research leadership redacted as needed.

2. A lead person for the response will be designated by HSC Research Leadership and will direct efforts to generate the response to the audit report/Form 483 as soon as possible after its receipt, within the expected deadline. Reply to each item in the report, providing clarification or steps that will be taken to institute corrective and preventive actions based on the identified root cause(s) of the issues.

   In the case of a Regulatory Agency audit, generally the lead person for the response will be a COE representative. The clinical research team will provide clear and objective responses on each regulatory audit finding to the COE representative to include in the response. For an FDA Form 483, a response must be provided within 15 working days.

   Sufficient time should be planned for review of the response by designated reviewers from HSC Research Leadership.

3. Send the final response to internal personnel and departments as needed.
   For Regulatory Agency audits, the response will be distributed to the Sponsor, the IRB, the PI, WVU Internal Audit office and the OSP. A COE representative will send the initial response to the Regulatory Agency and any subsequent response until all findings are closed.

   In the case a warning letter is issued by the FDA, notification will be provided to the groups identified in section A.1.a. Steps C.2 and C.3 above will be repeated.

   For Sponsor/Cooperative group audits, the response will be prepared by the clinical research team and provided to the Center of Excellence once finalized. A COE representative can assist with the response as needed.

4. The COE will perform periodic verifications that all audit findings and corrective/preventive actions have been closed out in a timely manner.

History of Revisions to SOP

Effective Date	Nature of Revision
16 APR 2021	New SOP

COE-102.00
Attachment 1 – Audit Checklist

PREPARING FOR AN AUDIT CHECKLIST

1. ORGANIZATION		YES	N/A	COMMENTS
Notify all parties	Sponsor(s) (if an FDA audit)			
	WVU IRB IRB of Record (if not local oversight)			
	Principal Investigator/ Sub - Investigators			
	Investigational Pharmacy			
	Laboratories			
	Medical records			
	Administration: -Office of Sponsored Programs (OSP) -Internal Audit Office			
	Legal counsel			
	Clinical Trials Center of Excellence			
	Reserve work space for the auditor			
General overview of the study	Prepare a general overview of the study			
	Ensure applicable SOPs are readily available			
	List all personnel and responsibilities delegated and provide evidence of study related training for all study personnel.			

List of subjects	To be kept as a reference for site research staff to facilitate retrieval of information during the audit: List all subjects screened, consented, including name, address, and/or phone number, date enrolled and/or randomized and completed, medical record number			

2. FILES MANAGEMENT		YES	N/A	COMMENTS
Organize all regulatory files by general heading arranged in chronological order	Signed, dated and approved Protocol (all versions) and amendments			
	Investigator's Brochure (all versions)			
	Form FDA 1572 or Investigator Agreement (all versions)			
	CVs for PI and Sub - Investigators listed on all versions of Form FDA 1572/Investigator Agreement			
IRB files	Approval letter (initial) for initial protocol with original Informed Consent Form			
	Amendment approval(s) with approved informed consent (if applicable)			
	Informed consent forms (originals) for enrolled subjects			
	Informed consents for screened subjects			
	Status reports for:			
	· Yearly renewal(s)			
	· Serious Adverse Events (SAE) and Adverse Events (AE)			
	· Deaths			
	· Study Hold or Termination			
	· Final summary			

Communications	Sponsor correspondence			
	CRO correspondence			
	IRB Correspondence			
	Monitoring log			
Laboratory	Laboratory certification and normal ranges			
	Logs to include:			
IP accountability	· Receipt			
	· Dispensing			
	· Return			
Subject documents	Completed CRFs for each subject enrolled			
	Source documents for each subject enrolled			

3. REVIEW		YES	N/A	COMMENTS
Collect and review for each subject enrolled	CRFs completed for each subject enrolled			
	Data correction forms for CRFs			
Medical records and/or study files	Source documents for each subject enrolled that document the following:			
	· Medical History of subjects at time of entry into the study (i.e., all inclusion/exclusion criteria are met)			
	· Eligibility Determination and sign off			
	· Concomitant medications			
	· Clinical assessments of the subject during the course of the study			
	· Laboratory reports			
	· Diagnostic tests			
	· Dose modifications			
	· SAEs or AEs/death			
	· Protocol and Subject Deviations			
	· Early termination			
	· Patients lost to Follow ups/ Patients still in study			

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Attachment 2 – Employee Guidelines during the Audit Process

Do:

1. Become familiar with the process and purpose of the audit.
2. Ensure your training records are current and complete.
3. Make yourself, or a qualified designate, readily available upon the request of the auditor.
4. Remain available during the entire time of the visit in case additional questions or information is needed.
5. Be cooperative and polite; make precise, concise and honest statements. Be sure that you understand the question posed by the auditor prior to replying; ask for clarification if needed.
6. Be cooperative but do not volunteer information.
7. Discuss only those items or trials identified on the audit agenda.
8. Allow the auditor time to take notes during conversation.
9. Answer only the question asked and only questions relevant to your Job Description/study involvement. If you do not know the answer, say so and defer to another employee, if applicable, or provide an answer at a later time during the audit.
10. Be professional at all times (i.e. NO chewing gum, NO inappropriate conversation, NO interrupting or arguing with the inspector). Assure that appearance is clean and professional at all times.
11. Keep confidential information filed away and office areas neat.
12. Provide documentation as requested by the auditor to the audit lead or designate in a timely manner.
13. For Regulatory Agency audits, interview or meet with the auditor only if the audit lead or designate is present.
14. Answer all questions truthfully to the best of your ability.

Do not:

1. Do not keep the auditor waiting.
2. Do not provide confidential records (i.e. Personnel, salary records).
3. Do not interrupt the auditor when they are talking or asking a question.
4. Do not be defensive, do not withhold information, do not argue or complain about any involved party (e.g., Sponsor/IRB).
5. Do not use your personal cell phone during interactions with the auditor, they should be muted or placed on vibration mode.
6. Do not provide any gifts to the auditors; as such action may be interpreted as coercive. Do not offer refreshments or lunch.
7. Do not provide documentation directly to the auditor(s) without prior permission from the audit lead or designate.