Procedure Name: FDA Audits Procedure	**Number:** SOP 14 v3.0
Subject: Clinical Research	**Effective Date:** June 02, 2017
Linked Policy: Clinical Research Operations & Compliance Policy	**Revised Date:** February 23, 2023

PURPOSE:

This Standard Operating Procedure (SOP) outlines the procedure for preparing for a FDA audit/inspection. An audit/inspection is designed to assess the research teams' extent of compliance with the protocol, SOPs, GCPs, and applicable Federal Regulations.

SCOPE:

This SOP applies to all research team members involved in preparing for, and participating in, FDA audits of clinical research conducted at GWU MFA.

RESPONSIBILITY:

The Principal Investigator (PI) is responsible for preparing for, and participating in FDA audits unless the PI has delegated one or more of these responsibilities to a designated research team member as documented on the Delegation of Responsibilities Form. Despite a delegation of responsibilities for preparation for a FDA audit, the Principle Investigator is still the sole party responsible for research compliance, and the repercussions of non-compliance.

PROCEDURES:

Notification of Audit

1. Notify the Office of Clinical Research as soon as the notification of a FDA audit is received
2. Following notification of a FDA audit, cooperate with inspector in determining a date for the audit. NOTE: Often the FDA gives a one day notice and comes the next day after the notification for audit is received.
3. Try to determine reason for the audit.
4. Confirm the date and time of the audit and the exit interview.
5. Notify the appropriate IRB of the impending FDA audit.
6. Notify the CRO/Sponsor of the audit date.
7. Additional parties to notify include, but are not limited to: The PI, the research coordinator, the full study team, Investigational Drug Services (if applicable), the Associate & Assistant Director of Clinical Research, and MFA Legal Counsel in the Compliance Office.

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8. Discuss with the Sponsor the appropriate preparation procedures for the audit. The Sponsor may want to be involved in the preparation for the audit.

Audit Preparation

1. Designate one person to be the audit liaison.
2. PI notifies/organizes the research team and assigns roles for audit preparation and conduct.
3. Notify other personnel and departments that the inspector may wish to meet (e.g., sub-investigators, research staff, pharmacist, lab personnel, etc.) and coordinate interview appointments.
4. Find the auditor a HIPAA complaint workspace that does not compromise the confidentiality of other research studies.
5. Source Document Verification
    a. Retrieve and review source documents, medical records, and CRFs for each subject.
    b. Ensure all source documents are available and complete for the auditor to review.
6. Consent/Research Subject Authorization Form (ICF) Review
    a. Verify that subjects signed the current, IRB approved ICF prior to treatment administration.
    b. Verify that revisions of the informed consent were issued and that each subject signed them accordingly.
7. Protocol Exceptions / Violations and Patient Non-compliance
    a. Ensure availability of clear documentation and Sponsor approval of protocol exceptions that were requested during the course of the study.
    b. Ensure availability of any reports submitted to the IRB, or overseeing entity
8. Equipment Verification
    a. Verify all equipment used in the conduct of a study was present and in good working condition.
    b. Provide calibrations and other maintenance records as required by the auditor.
    c. Provide verification that the facilities are adequate for each study.
9. CRF Comparison to Source Document
    a. Verify all CRFs are available and complete.
    b. Review must demonstrate that source documents support all CRF entries and adherence to the protocol.
    c. Conduct a 100% pre-audit to verify that all subjects enrolled met inclusion/exclusion criteria.

d. Verify that the Investigator's signature is on completed CRFs where required.
e. Ensure that all dates on CRFs are valid and correct.

10. Regulatory Binder Audit
    a. Ensure that all regulatory documentation and correspondence is available, complete and current (protocol, investigator brochure, protocol amendments, form FDA 1572).
    b. Review all IRB files for:
        - Initial approval letters;
        - Amendment approval letters;
        - Informed consent/research subject authorization forms;
        - Correspondence; and
        - Status reports for: 1) continuing review approval; 2) adverse and serious adverse event reporting, particularly death; 3) protocol deviations/violations; 4) study termination and summary report; and 5) all other correspondence with the IRB
11. Meet with the IRB staff for review and documentation of complete IRB/regulatory files.
12. Protocol Exceptions/Violations and Patient Non-compliance.
    - Verify documentation, and Sponsor approval, of protocol exceptions that have been requested during the course of the study.
13. Investigational Product Accountability Verification
    a. Verify adequate investigational product accountability, consisting of the following:
        - Quantity of drug/device shipped;
        - Date of arrival;
        - Condition at receipt;
        - Proper storage;
        - Any Temperature deviations
        - Quantity of drug/device dispensed and returned by each individual subject;
        - Quantity of drug/device returned to the Sponsor; and
        - Quantity of drug/device lost due to lost-to-follow-up subjects; consider the drug used.
    b. Verify that drug/device storage area and refrigerator temperatures have been completely and accurately documented and that the drug has been properly stored.

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Note: According to FDA, the drug accountability error margin is 0%. All sites must be able to account for all study drugs/devices with no discrepancies.

14. Overall Conduct of the Study
    - Via the Delegation of Authority Log, verify research responsibilities documentation. Documentation of research responsibilities is very important to FDA and should therefore be made very clear.

Day of Audit

1. Verify the credentials of the auditor.
2. Request a copy of the FDA Form 482, Notice to Inspect.
3. Sign the FDA Form 482.
4. Provide the auditor with a HIPAA compliant workspace.
    - Ensure that the workspace does not compromise the confidentiality of other research studies.
5. Provide study materials to the auditor upon request.
6. Make required copies of requested documents and maintain a copy for the site.
7. Be available to answer questions throughout the audit upon request.

Exit Interview

1. Study specific staff, a Research Team representative and PI are to attend the Exit Interview.
2. Document notes of comments, issues and areas of concern for prompt follow-up.
3. If a Form FDA 483 is issued, the PI will review the content of the FDA 483 for any inaccuracies and negotiate any needed corrections with the inspector.

Unavailable for FDA Review

The following is a general list of materials that the FDA does NOT have access to:

- Financial data (ie. Contract);
- Pricing data;
- Personnel data other than information establishing the qualifications of technical and professional personnel;
- Research data except to the extent such information may be required to be made available for inspection or submitted directly to the agency; and

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- Pharmacist's and Physician's records unless the individuals are engaged in clinical trials as leading to applications for product approvals from the FDA

Post Audit

1. If a FDA Form 483 is issued to the PI, Research Team in conjunction with the Sponsor and IRB will assist with the preparation of a prompt, formal written response to the FDA.
2. If a FDA Form 483 is issued, send a copy of the Form and the response to the IRB and the Sponsor. Retain a copy in your regulatory binder for reference.
3. The Research team, along with the IRB, will monitor when corrective action(s) are implemented.

Review and Revision

The SOP Review Committee shall review this SOP every 2 years. This SOP may be reviewed more frequently if it does not reflect current operations.

Attachments

FDA Compliance Checklist
Site Preparation Checklist

REFERENCES:

21 CFR 312.60	General responsibilities of investigators.
21 CFR 312.62	Investigator recordkeeping and record retention.
21 CFR 312.64	Investigator reports.
21 CFR 312.66	Assurance of IRB review.
21 CFR 312.68	Inspection of investigator's records and reports.
21 CFR 812.40	General responsibilities of sponsors.

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21 CFR 812.43	Selecting investigators and monitors.
21 CFR 812.100	General responsibilities of investigators.
21 CFR 812.110	Specific responsibilities of investigators.
21 CFR 812.140	Records.
21 CFR 812.145	Inspections.
21 CFR 812.150	Reports.
Aug2013	FDA Guidance for Industry: Oversight of Clinical Investigations- A Risk-Based Approach to Monitoring
June 2010	Information Sheet Guidance for IRBs, Clinical Investigators, and Sponsors: FDA Inspections of Clinical Investigators
ICH E6 (R2)	Integrated Addendum to International Council for Harmonization (ICH) E6 (R1): Guideline for Good Clinical Practice E6 (R2)
Oct 2015	MFA Investigational Drug Service Policies and Procedures
June 2017	GWU MFA Clinical Research SOPs
	SOP 02: Research Team Responsibilities
	SOP 03: Regulatory Binder and Study File Maintenance

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	SOP 04: Research Team Communications/Interactions with IRB
	SOP 05: Case Report Form Completion and Query Resolution
	SOP 06: Source Documentation
	SOP 07: Maintenance of Equipment
	SOP 11: Drug Accountability, Dispensation and Return

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FDA Compliance Checklist

1. How does the Principal Investigator retain control of the conduct of the study?
2. What authority and to whom has the following been delegated? Is it documented and how is such delegation supervised?

    - Subject contact and procedures
    - Consenting processes
    - Drug dispensation/ accountability
    - Laboratory tests/results
    - Concomitant medications
    - Adverse events
    - Serious adverse events
    - Administrative issues: correspondence, IND safety reports, amendments, etc

3. What laboratories were utilized during the study, and how were they deemed qualified to perform such tests?
4. Where is the raw data stored? Were multiple locations used?
5. What, if any, other physicians and study staff are associated with the study?
6. Who controls the storage, dispensing, and the return of the study medications? (And how is it supervised?)
7. How were subject's made aware of new information, which may have affected their willingness to continue study participation?
8. How are patients who are considered for and/or enrolled in the study kept track of?

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Site Preparation Checklist For FDA Audits

IRB Number:

Protocol Number:

Protocol Title:

Notification **Notify All Parties Involved with the Study**	**YES**	**N/A**	**Notes**
Sponsor			
IRB			
Sub-investigator(s)			
Pharmacy/MFA IDS			
Laboratories			
Medical Records			
Research Administration			
Legal Counsel			
Space reservation, phone, copier, conference room			
Organization **General Overview of Study**	**YES**	**N/A**	**Notes**
Prepare General Overview of Study			

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List involved personnel and their delegated responsibilities. Refer to Delegation of Responsibilities Form			
List all screened subjects			
List all enrolled subjects including name, address and/or phone number, date enrolled/completed, medical record number			
Files Management **Organize regulatory files by general heading arranged in chronological order**	**YES**	**N/A**	**Notes**
Protocol (all versions)			
Investigator's Brochure (all versions)			
Protocol amendments			
Form FDA 1572 (all versions)			
Curriculum Vitae for all investigators on FDA 1572			
Initial IRB Approval letter for study			
IRB approval(s) for amendments with approved ICF changes (if applicable)			
ICF (originals) for all enrolled subjects			
ICFs for screened subjects			
Status reports for:			
a. Yearly renewal			
b. Adverse events			
c. Deaths			

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d. Study termination			
e. Final summary			
Sponsor/CRO/IRB correspondence/communication			
Monitoring Log			
Lab certification and normal ranges			
Drug log including:			
a. Receipt of drug			
b. Disbursement			
c. Return			
Completed CRF for each subject enrolled			
Source documents for each subject enrolled			
Review **Collect and review data for each enrolled subject**	**YES**	**N/A**	**Notes**
CRFs completed for each subject enrolled			
Data Correction Forms for each CRF (if applicable)			
Condition of subject at time of entry into study (i.e., that all eligibility criteria are met):			
a. Clinical assessments of the subject during the course of the study			
b. Lab reports			
c. Diagnostic tests/Procedures			

d. Dose modifications			
e. Adverse events			
f. Protocol exemptions			
g. Early termination/death			