LSU HEALTH COORDINATOR COMPETENCIES

PREPARING FOR AN FDA INSPECTION

Objectives

- Discuss the purpose of an FDA Inspection
- Identify the types of inspections the FDA conducts
- Walk through the Inspection process from initial notification to responding to deficiencies.

What is the Purpose of an FDA Inspection?

- Ensure the protection of the rights, safety, and welfare of human subjects involved in FDA-regulated clinical trials
- Verify the accuracy and reliability of the clinical data submitted to FDA in support of research or marketing applications
- Assess compliance with statutory requirements and FDA's regulations governing the conduct of clinical trials

What Types of Inspections Does the FDA Conduct?

- Pre-Approval Inspection
- Routine Inspection
- Compliance Follow-up Inspection
- For-Cause Inspections

Inspection procedures vary slightly depending upon the product type (e.g., drug, biologic, medical device) and the type of inspection; however, the FDA conducts both announced and unannounced inspections of clinical investigator sites

Notification of Inspection

How Will the FDA Notify Me of an Inspection?

FDA usually contacts the PI to schedule an audit.

- Usually, 5 days notice

Remember that a notification of the inspection is a courtesy, not a necessity.

When the FDA Calls…

Ask for the following information:

- The name and contact information of the Auditor/Inspector;
- The number of auditors expected;
- The dates the inspector(s) expects to be on site;
- Why the inspection is being done;
- The study to be audited, if a particular study;
- The subjects to be reviewed, if known; and,
- Whether they plan to tour the facility

Refer to CTO Audit/Inspection Intake Form

AUDIT/INSPECTION INTAKE FORM

Date of Call: Click or tap to enter a date.

Person Taking the Call: Click or tap here to enter text.

AUDITOR/INSPECTOR INFORMATION

Number of Auditors/Inspectors Expected: Click or tap here to enter text.

Name(s): Click or tap here to enter text.

Title(s): Click or tap here to enter text.

Contact Information: Click or tap here to enter text.

AUDIT/INSPECTION VISIT INFORMATION *(Wait for answers. Do not make suggestions)*

Anticipated Start Date: Click or tap to enter a date.

Expected Duration: Click or tap here to enter text.

Purpose of the Inspection:

- ☐ Pre-Approval (NDA/ANDA)
- ☐ Routine (IND, Manufacturer)
- ☐ Follow-Up (483, warning letter)
- ☐ Directed/For-Cause
- ☐ Other

Who/What is Being Inspected:

Clinical Trial(s): Click or tap here to enter text.
PI/Co-I(s): Click or tap here to enter text.
Site: Click or tap here to enter text.
Other: Click or tap here to enter text.

ADDITIONAL INFORMATION *(Ask the auditor/inspector. Do not make suggestions)*

Does the auditor/inspector want/need to tour the facility? ☐ Yes ☐ No

Does the auditor/inspector want specific personnel available? ☐ Yes ☐ No

***If Yes*, Who:**
Click or tap here to enter text.

When:
Click or tap here to enter text.

Does the auditor/inspector want specific documents available? ☐ Yes ☐ No

***If Yes*, What Documents**: *(Ask for confirmation of requested documents in writing)*
Click or tap here to enter text.

This document has been created by the LSUHSC-NO IRB and CTO as guidance to help investigators and research staff throughout the process of a Food and Drug Administration (FDA) inspection. It is important to take detailed notes during all communication and interaction with the inspector/auditor. Once you have been notified of an audit/inspection, please send a copy of this form to IRBOffice@lsuhsc.edu and CTO@lsuhsc.edu

CTO-1160 Audit/Inspection Intake Form

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What Should I Do Once Notified?

PI or person taking the call should notify:

- Principal Investigator (if he/she is not the person who took the call);
- PI's Department Head;
- The entire study team;
- The local Human Research Protection Program/Office of Research/IRB;
- IRB of Record, if applicable;
- Study Sponsor;
- Investigational Pharmacy, if involved; and,
- Institutional administrative official(s) if the research is being conducted at any external collaborative site

How Should I Prepare for an Audit?

- ✓ Designate a person to oversee the inspection
- ✓ Designate a "scribe" to take minutes
- ✓ Reserve meeting room(s)
  - Auditor workspace
  - Audit support room/office
- ✓ Review the Protocol with everyone on the study team
- ✓ Review the regulatory files/binders and any other study records

TIP: *Study files and subject records should be audit-ready at all times throughout the life of the trial.*

FDA INSPECTION CHECKLIST

Before a scheduled visit, the Research Team should complete the following activities:

Task	Items	Complete	N/A	Notes
Audit Notification				
Notify all parties of impending audit	Principal Investigator (PI)	☐	☐	
	Department Head	☐	☐	
	Entire Study Team	☐	☐	
	LSUHSC IRB	☐	☐	
	IRB Of Record, if not LSUHSC	☐	☐	
	Study Sponsor	☐	☐	
	Investigational Pharmacy	☐	☐	
	Administrative Official at Research Sites	☐	☐	
Reserve space for inspector(s)	Workspace	☐	☐	
	Phone	☐	☐	
	Copier	☐	☐	
	Table	☐	☐	
Organization				
Study Overview	Prepare general overview of study	☐	☐	
	List of personnel and delegated responsibilities	☐	☐	
Subject List	List of all subjects including name, contact info, enrollment & completion dates, and MRN	☐	☐	
	List of all subjects screened with enrollment or reason for not enrolled	☐	☐	
PI Current Studies	List of PI's current active studies	☐	☐	
File Management				
Organize Files	Protocol (all versions)	☐	☐	
	Investigator's Brochure (all versions)	☐	☐	
	Protocol amendments	☐	☐	
	Form FDA 1572 or Declaration of Investigator (all versions)	☐	☐	
	CVs for PI, Sub-Investigators listed on 1572 or DOI	☐	☐	
	Copies of up-to-date training certificates for all research personnel	☐	☐	
IRB Files	Initial Approval Letter and original informed consent	☐	☐	
	Amendment approvals with approved informed consent	☐	☐	
	Renewal approvals	☐	☐	
	Event Tracking Log	☐	☐	
	Resolution of Reportable Events	☐	☐	
Communication	Sponsor Correspondence	☐	☐	

CTO-1161 FDA Inspection Checklist

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PERFORMANCE SITES AND STUDY POPULATION

Please list all sites where research activities are taking place:	Click or tap here to enter text.
Were all external institutional approvals secured prior to initiation of the study? (*check all that apply*)	☐ UMC RRC ☐ Children's Hospital ☐ Tulane ☐ Ochsner ☐ Woman's Hospital ☐ Our Lady of the Lake ☐ West Jefferson ☐ Other: Click or tap here to enter text.
Please indicate if any of the following study populations are represented by participants you have enrolled:	☐ Children ☐ Pregnant Women, Fetuses, or Neonates ☐ Prisoners ☐ LSUHSC Faculty/Staff or Students ☐ Individuals with impaired decision making capacity ☐ Economically or educationally disadvantaged individuals ☐ Institutionalized Individuals ☐ Undocumented Immigrants ☐ None of the Above

REGULATORY DOCUMENTATION

Protocol		Yes	No
1	Is the most recent version of the protocol saved in a study binder (paper, electronic, or both)?	☐	☐
2	Are there previous versions of the protocol? *If no, skip to* ***FDA-Regulated…***	☐	☐
3	Are the previous versions saved in a study binder (paper, electronic, or both)?	☐	☐
4	Is the version # and version date included on each document?	☐	☐

FDA-Regulated Research		Yes	No
1	Is this an FDA-regulated study? *If no, skip to* ***Federally Funded Research***	☐	☐
2	Is there a signed 1572 saved in a study binder (paper, electronic, or both)?	☐	☐
3	Has a copy of the 1572 been provided to the IRB?	☐	☐
4	Is the Clinical Investigator Financial Disclosure form (FDA 3455 or 3454) for each investigator saved in a study binder (paper, electronic, or both)?	☐	☐

Post-Approval Monitoring Self- Assessment Tool

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This document has been created by the LSUHSC-NO IRB and CTO as guidance to help investigators and research staff throughout the process of a Food and Drug Administration (FDA) inspection. This tool could also be used by the research team for investigator-initiated studies to conduct their own quality assurance reviews.

This tool is to be used as guidance. Some of the items included on this worksheet may not be applicable to all studies. Refer to the Appendix for details of which regulations, policies or guidance may be referenced for further clarification.

PROTOCOL INFORMATION

PI Name:Click or tap here to enter text. **Site Number**: Click or tap here to enter text.

Protocol: Click or tap here to enter text.

SUBJECT RECORD REVIEW

Subject ID Number: Click or tap here to enter text.

INFORMED CONSENT	Yes	No	N/A	☐ Not Reviewed	Notes
1. Are the signed, original consent(s)/assent(s) documents present in the study records?	☐	☐	☐		Click or tap here to enter text.
2. Are the signed, original HIPAA documents present in the study records?	☐	☐	☐		Click or tap here to enter text.
3. Has the subject signed and dated the correct version(s) of the informed consent/assent document(s)?	☐	☐	☐		Click or tap here to enter text.
TIP: Determine if the signed consent(s)/assent(s) the appropriate version based on the most recently IRB approved document when informed consent/assent was obtained.					
4. Has the legally authorized representative and/or impartial witness signed and dated the correct version(s) of the consent/assent form document(s) as applicable?	☐	☐	☐		Click or tap here to enter text.
5. Are all consents complete (full signatures and dates by both parties, all checkboxes include responses, are pages initialed if necessary)?	☐	☐	☐		Click or tap here to enter text.
TIP: If the consent form documents are not complete, is there documentation to explain why the dates do not match?					
6. Do the signatures and dates for the subject & person obtaining informed consent/HIPAA match?	☐	☐	☐		Click or tap here to enter text.
TIP: If the signature dates do not match, is there documentation to explain why the dates do not match?					

CTO-1162 Subject Record Review Worksheet

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CTO-1163 Informed Consent Review Worksheet

LSUHSC-NO CTO
DOC ID: CTO-1163
VERSION DATE: 08.02.2022

INFORMED CONSENT REVIEW WORKSHEET

PI Name: Click or tap here to enter text. **Protocol:** Click or tap here to enter text. **Site Number:** Click or tap here to enter text.

Subject Study ID	Subject Initials	Version Date	Approval Date	Date Subject Signed	Subject Signature Confirmed	Date Consenter Signed	Consenter Signature Confirmed	Signature Dates Match	Consent Form Fields Completed	Original Signed ICF Available	Consent Process Documented	Subject Re-Consented
					Y / N		Y / N	Y / N	Y / N / NA	Y / N	Y / N	Y / N / NA
					Y / N		Y / N	Y / N	Y / N / NA	Y / N	Y / N	Y / N / NA
					Y / N		Y / N	Y / N	Y / N / NA	Y / N	Y / N	Y / N / NA
					Y / N		Y / N	Y / N	Y / N / NA	Y / N	Y / N	Y / N / NA
					Y / N		Y / N	Y / N	Y / N / NA	Y / N	Y / N	Y / N / NA
					Y / N		Y / N	Y / N	Y / N / NA	Y / N	Y / N	Y / N / NA
					Y / N		Y / N	Y / N	Y / N / NA	Y / N	Y / N	Y / N / NA
					Y / N		Y / N	Y / N	Y / N / NA	Y / N	Y / N	Y / N / NA
					Y / N		Y / N	Y / N	Y / N / NA	Y / N	Y / N	Y / N / NA
					Y / N		Y / N	Y / N	Y / N / NA	Y / N	Y / N	Y / N / NA
					Y / N		Y / N	Y / N	Y / N / NA	Y / N	Y / N	Y / N / NA
					Y / N		Y / N	Y / N	Y / N / NA	Y / N	Y / N	Y / N / NA
					Y / N		Y / N	Y / N	Y / N / NA	Y / N	Y / N	Y / N / NA
					Y / N		Y / N	Y / N	Y / N / NA	Y / N	Y / N	Y / N / NA
					Y / N		Y / N	Y / N	Y / N / NA	Y / N	Y / N	Y / N / NA
					Y / N		Y / N	Y / N	Y / N / NA	Y / N	Y / N	Y / N / NA
					Y / N		Y / N	Y / N	Y / N / NA	Y / N	Y / N	Y / N / NA

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Is the Sponsor Involved in the Audit?

Before the Inspection

The sponsor may send representatives to assist you in preparing for the audit.

- The study sponsor will frequently offer assistance in organizing the study records if time permits, as they are sometimes aware of a possible upcoming audit prior to actual contact by the FDA inspector.

During the Inspection

If the sponsor representative wishes to be present during the inspection, notify the FDA auditor and invite the sponsor representative to observe and take notes

- Ask that they not communicate with the auditor unless asked specific questions

FDA Inspection Visit

Inspector Arrival

1. Escort Inspector to designated inspection space
2. Inspector should provide the team with a Form 482, Notification of Inspection
3. Inspector should present their badge
   - If not presented, ask to see their badge
4. Provide the Inspector with all clinical research study documents requested for review
5. The FDA Inspector will request:
   - List of the PI's currently active studies
   - The PI to summarize and discuss the study identified for inspection
   - The PI to summarize his/her responsibilities with respect to the study.

First Day of Inspection

- A brief introductory presentation showing the organizational chart, headcount, hours of operation and facility layout may be made on the first day.
- The inspection probably will include a facility tour, generally on the first day.
  - Provide the inspector a copy of the facility diagram plainly depicting the equipment flow and the personnel.
  - If the inspector requests to take photographs ensure management representative or scribe, take similar photographs.

Providing Documents for Review

Provide all materials requested by the inspector

- "General" study materials including the regulatory documents binders, all signed informed consent forms, a sampling of specific patient records.
- Study finances (budget, contract, etc.) and personnel records are not included in the standard inspection, and should be excluded from the files shared with the inspector

TIP: *When documents are copied for Inspectors, make an extra copy for the site's FDA inspection file.*

TIP: *Only documents specifically requested by the inspector should be provided for review.*

End of Each Day

- You may ask about the progress of the audit
- Take this opportunity to ask questions or to clarify misunderstandings
- On the final day, verify all documents are returned to you

PI Responsibilities

- The Principal Investigator should set aside some time each day to talk with the Inspector.
- In the event that the Inspector does not initiate an end of day summary and discussion, the PI should request the meeting

TIP: *The buck stops with the Principal Investigator*

Answering FDA Inspector Questions

Answer questions as if you were in a deposition.

- Listen to the question carefully.
- Be truthful.
- Be concise.
- DO NOT speculate or guess.
- DO NOT argue.

TIP: *During the inspection, the person coordinating the inspection should keep an exhibit log that includes a list of ALL questions asked by the Inspector*

TIP: What Inspectors are Looking At

- Who performed various aspects of the protocol for the study (i.e. who verified inclusion and exclusion criteria, who obtained informed consent, who collected adverse event data);
- Whether the IRB approved the protocol, informed consent form, and any amendments to the protocol prior to implementation;
- Whether the condition under study was in fact diagnosed;
- Whether the clinical investigator and study staff adhered to the sponsor's protocol and investigational plan and whether protocol deviations were documented and reported appropriately;
- Whether the subject, or the subjects' legally authorized representative, signed informed consent documents prior to entry into the study;
- Whether study eligibility criteria were met

TIP: What Inspectors are Looking At

- Whether the subject received any potentially interfering medication prohibited by the protocol;
- Whether authority to conduct aspects of the study was delegated, and if so, how the conduct of the study was supervised by the clinical investigator;
- Where specific aspects of the investigation were performed;
- How the study data were obtained and where the study data were recorded
- Accountability for the investigational product, including shipping records and disposition of unused investigational product;
- Whether the clinical investigator submitted all reportable adverse events;
- Whether the subject received proper follow-up, as outlined in the protocol, after completion of the study-related activities

TIP: What Inspectors are Looking At

- The monitor's communications with the clinical investigator/study team;
- The monitor's evaluations of the progress of the investigation; and,
- Corrective actions in response to previous FDA inspections, if any, and regulatory correspondence or sponsor and/or monitor correspondence.

Exit Interview

The FDA Inspector will usually hold an exit interview, or "close-out," at the conclusion of the inspection

- During this meeting with the PI the Inspector will review audit findings and clarify any issues found during the inspection.

Document the exit interview, specifically noting observations, recommendations, comments, and any commitments discussed.

- Clarify and seek to correct any errors in the findings.

After the Inspection

After the Inspection

- A detailed report, summarizing the inspection should be written (by the PI or the person designated to coordinate the inspection) from the inspection notes immediately (*aka* Inspection Summary Report)
- After the inspection has been completed, the FDA investigator submits a written report of findings to FDA headquarters.
- Upon review and consideration of the report provided, FDA Headquarters will send the investigator a communication based on the reports

FDA Post-Inspection Communications

- **No significant deviations**: The FDA investigator observed basic compliance with pertinent regulations.
- **Informational or Untitled letter**: The informational letter identifies deviations from the statutes and regulations that do not meet the threshold of regulatory significance for a Warning Letter.
- **Warning letter** (*aka FDA Form 483*): This warning letter identifies serious deviations from statutes and regulations and is issued for violations of regulatory significance.
- **A Notice of Disqualification Proceeding and Opportunity to Explain (NIDPOE) Letter**: Investigator has repeatedly or deliberately failed to comply with applicable regulatory requirements, or has deliberately or repeatedly submitted false information

Common Deficiencies

- Failure to follow the investigational plan/protocol
- Failure to maintain case histories
- Inadequate drug/device accountability
- Failure to obtain adequate informed consent
- Inadequate SAE reporting
- Failure to submit progress reports
- Failure to follow IRB approval requirements

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What Happens If I Receive a 483 or NIDPOE?

- FDA will expect responses usually within 15 calendar days.
- The Sponsor, LSUHSC HRPP and/or the Clinical Trials Office, and possibly Legal should work with the PI in preparing responses to FDA warning letters and NIDPOE, however the P.I. is ultimately responsible.
- The FDA inspector will file an EIR within approximately 30 days.

Resources

- HRP-2680 FDA Audit Preparations Guidance
- CTO SOP 2.15 Clinical Research Audits
- CTO Audit/Inspection Tools