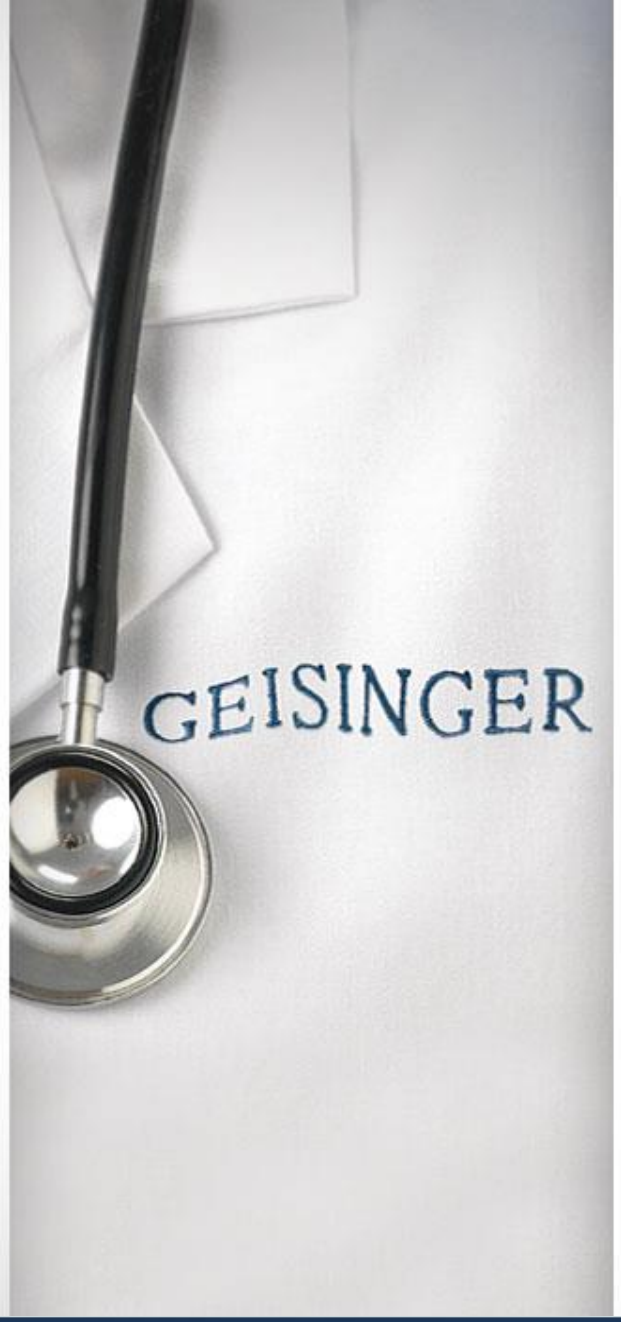

What to Expect During an FDA Audit

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Disclaimer

- This is an educational session
- This presentation represents the views of the presenters
- This session is not intended to provide legal advice. Please consult with your leadership for advice tailored to your individual/institutional needs when facing an audit.

Roundtable Objectives

- Understand the FDA BIMO program
- Preparing for an FDA Inspection
- Undergoing an FDA Inspection
- Preventative Actions
- Geisinger Experience

What is the FDA BIMO Program?

- Comprehensive program of on-site inspections and data units designed to monitor ALL aspects of the conduct and reporting of FDA-regulated research.

Reference: Information Sheet Guidance for Institutional Review Boards, Clinical Investigators, and Sponsors
http://www.fda.gov/ScienceResearch/SpecialTopics/RunningClinicalTrials/GuidancesInformationSheetsandNotices/default.htm

Goals of the FDA BIMO Program

- Protect the rights, safety, and welfare of subjects involved in FDA-regulated clinical trials
- Verify the accuracy/quality, integrity and reliability of clinical trial data submitted to the FDA in support of research or marketing applications (IDEs, INDs, 510(k)s or PMAs)
- Assess compliance with FDA regulations, IRB Policies and Procedures and Institutional/Unit requirements (SOPs/practices)

ORA Offices and Divisions

Do you know where our closet FDA office is?

Why is a site Chosen for Inspection?

- Routine
- Directed/ “For Cause”

Why is a Site Chosen for Inspection?

- Routine selection based on a % of all clinical data submitted with New Drug Application (NDA)

OR

- Site with notably high or fast enrollment
- Site conducting multiple studies or large pivotal trials
- Site conducting a study supporting a switch to “over-the-counter” status
- Site conducting study supporting a submission to FDA for NDA, marketing, license, etc.
- Site had an important product crucial study for key decision for approval

* Sponsors can often predict which sites will be selected

Why is a Site Chosen for Inspection?

Directed or “For Cause”

- Problem noted at the IND/IDE stage
- Complaints made to the FDA from Sponsor/CRO/Institution/IRB/Sub-Investigator or former PI/Study Team Personnel/Subject
- Site has previously undergone an FDA inspection for related or unrelated study
- Unusually larger number of subjects for a given location
- Data look better than it should
- Follow-up to a prior inspection

Why is a PI Chosen for Inspection?

- PI conducts many FDA-regulated studies
- PI conducts study outside his/her specialty
- PI conducts pivotal study for new drug application (NDA)
- PI submits safety and efficacy data that is inconsistent with other studies under and IND/IDE
- Rapid enrollment
- Sponsor or IRB notifies the FDA of problems/allegation or misconduct or noncompliance
- FDA received a complaint related to PI or the study
- Unexpected number of subjects w/ specific diagnosis for a given area

FDA Notification and Authority

21 CFR 312 (Drugs)

“ An investigator shall upon request from any properly authorized officer or employee of FDA, at reasonable times, permit such an officer or employee to have access to, and copy and verify any records or reports made by the investigator pursuant to 21 CFR 312.62”

The Phone Call…

First and foremost- DON’T PANIC!

Ask (politely):

- Why?
- Who?
- What?
- Who will be coming?
- When?
- How long?
- Any specific requests?

Who to Call Next

- Sub-investigators
- Past study coordinators, if applicable and available
- Division/Department Administration
- IRB
- Research Compliance
- Other units supporting the conduct of the studies or interest (i.e. pharmacy, lab medicine, etc.)
- Sponsor

Next Steps Before the FDA Arrives

- Schedule Pre-audit review meeting with internal team to discuss strategies
- Determine inspection accommodations
- Develop audit contact sheet for quick reference
- Review study documentation and organization
- Prepare to welcome the investigator

Organization and Review of Documents

- Retrieve ALL study related material
- Recall study records (study protocols, protocol amendments, IRB approvals and reports, study device accountability records, monitoring logs, site personnel logs, study subject enrollment logs, etc.)
- Review all regulatory binders and records to refresh memory and be familiar with organization of documents.

What to know about the Study Team Before the FDA Arrives

- Review who is currently responsible for each step of the study process
- Review who was historically responsible
- Ensure staff understands on-going responsibilities
- Ensure pertinent staff are available

Do you have everything?

- All required documents (organized, complete and current?)
- Review study team documentation (qualifications, training and delegations?)
- Review pertinent dates
- Review pertinent study team members
- Review findings of recent monitors visits
- List and shortcomings for further discussion before the inspection

They’re Here!

Day 1 – Entrance Interview begins…

- FDA investigator(s) should present credentials; if not, you may ask to view them
- FDA Form 482 – Notice of Inspection
- Entrance Interview with PI and study team

Inspection- Questions and Requests

- Facility Tour by FDA Inspector(s)
- Requested document copies by FDA Inspector(s)
  - Only give what is requested – only provide copies of documentation indicated by “Copy” stamp and keep a record of all documentation provided to the FDA in the inspection file.
  - Not disclosable during an audit
    - Personnel records
    - Financial Data
    - Internal Memos
    - Sales Data
    - Quality Assurance Records
- PI Availability during the Inspection

Exit Interview

- Schedule to ensure PI availability and invite other crucial departments as needed (i.e. Research Compliance, Department Leadership, etc.)
- FDA Inspector will discuss oral “suggestions” or “discussion items.” If there are significant, serious findings, the FDA may issue a Form 483
- Be sure to ask for clarification as needed
- Correct significant factual errors in discussion items during the exit conference since there is still the opportunity to keep them out of the Inspector’s report.
- LISTEN, LISTEN, LISTEN

Preventative Actions

- Organization is Key
- Develop strong communication with the team
- Monitor and Audit Studies Frequently
  - Internal study audits and reviews
- Document, Document, Document
  - Understand and document who does What, When and How
  - SOP Development and Maintenance

Geisinger Experiences…..

Remember:

- If it is not documented, it did not happen!
- Quality cannot be added or fixed at the end of a study – it must be built in at the beginning and is a continual process developed throughout the course of the study.

Questions?