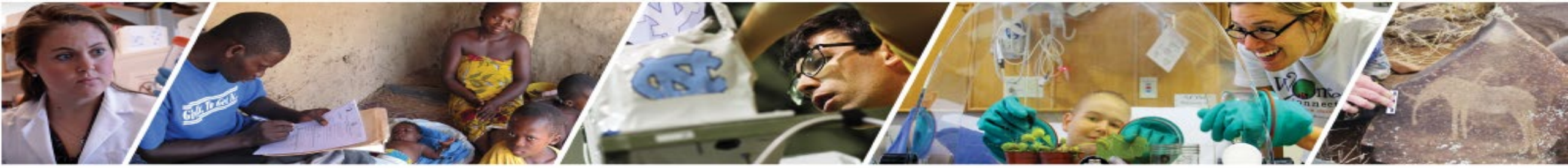
Audits & Inspections
A Deeper Dive



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UNC RESEARCH

Objectives

- List common triggers for clinical trial audits or inspections.
- Describe the inspection process from the PI point of view.
- List practical approaches to avoid inspection observations.
- Describe how to respond to inspection observations.

Triggers for Sponsor Audits

- Preparation for filing a New Drug Application/Premarket Approval application with the FDA
- Follow up on monitoring reports
- Ensure monitoring activities are compliant with the quality management plan – are the monitors doing their job?

Outcome Goal: Sponsor

Ensures source documentation is accurate/complete

Ensures site is prepared/organized for potential FDA inspection

Ensures proper monitoring of the study was accomplished

Triggers for FDA Inspections

- Routine - submission of data to FDA in support of a Marketing Application or Amendment to an Existing Application

Triggers for Inspections

For Cause – investigate a specific problem that has come to FDAs attention

- Subject or Sponsor Complaint(s)
- Reports of UPIRSO(s)
- Reports of Serious and/or Continuing Non-Compliance

Outcome Goal: FDA

Ensure the rights safety & welfare of human subjects have been protected

Ensure the data submitted is accurate, reliable and verifiable

Ensure compliance with FDAs regulations governing the conduct of the trial

FDA Regulations Governing Clinical Trials

21CFR312.60 – Drugs and Biologics – Investigator Responsibilities

21CFR812.100 – Devices – Investigator Responsibilities

21CFR50 – Protection of Human Subjects

- Informed Consent
- Safeguards for Children

21CFR54 – Financial Disclosure by Clinical Investigators

21CFR56 – Institutional Review Boards

Outcome Goal: Site

Demonstrate that:

- Patient safety a priority
- Commitment to data integrity
- Compliance with regulations

Inspection Timeline

- Verbal Notification of Inspection
- Opening Meeting
- Inspection Begins
  - Document Review
  - Daily Meetings

Types of Information to be Reviewed

- Specific requirements from the Center associated with the inspection (CDER, CDRH, etc)
- Facility & equipment
- Regulatory Documents (Essential Documents)
- Test article accountability records
- Subject case histories & case report forms

Facilities & Equipment

Inspector may want to physically see:

- Where study visits occurred (clinic space, CTRC)
- Where lab specimens were processed
- Where the investigational product was stored

Regulatory Documents

1572/Investigator Agreement

Financial Disclosure forms

Protocols/Amendments

ICFs

Recruitment materials – IRB approval

Sponsor correspondence – email communications, newsletter

Monitoring reports (if sponsor provided)

Delegation Records

Study Staff CVs/resumes

Training records

Test Article – Investigational Product

- Shipping/Receipt records
- Dispensing/Return Records
- Drug accountability documentation
- Device documentation

Case Histories & Case Report Forms (CRFs)

- Complete and accurate case histories – source documents
  - must have documentation that informed consent was obtained prior to conduct of procedures related to the study
  - compliance with eligibility criteria
  - compliance with protocol
  - adverse events collection and reporting

- CRFs – does the data in the CRF match the source?
  - FDA has a set of data submitted by sponsor & verify that data against the source

Inspection Timeline

Wrap Up Meeting

Debrief

Response to Observations

15 days to respond

Corrective and Preventive Action Plans

Available support

Ensuring Compliance Apriori

- Hold regularly scheduled meeting with research staff & DOCUMENT minutes
- Ensure ALL study staff are trained on the protocol, IP, specimen handling, etc & DOCUMENT
- Ensure tasks are delegated appropriately
- Follow up on items noted during monitoring visits

Resources

OCT Website - Audits and Inspections

FDA Guidance: Investigators Responsibilities

Walkthrough of an FDA Clinical Investigator Site Inspection - August 6, 2020