# Monitoring, Auditing and Compliance

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# What is Monitoring?

Monitoring is an **ongoing process** of overseeing the progress of a clinical trial, **from start to finish**.

Monitoring is a quality control tool for verifying that study activities are being carried out as planned, so that deficiencies can be identified and corrected.

# What is Auditing?

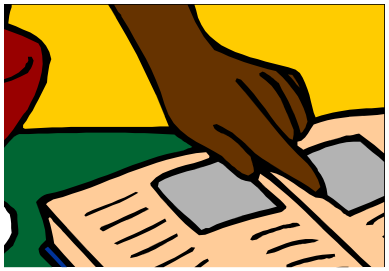
Auditing is a systematic and independent review of a clinical trial to determine if activities were conducted according to protocol and regulations.

Auditing is a quality assurance tool for providing assurance that study activities were carried out as planned.

# Monitoring v. Auditing

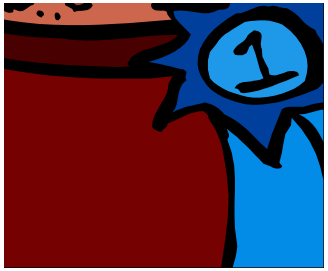
## Monitoring

- **ongoing process** of overseeing the progress of a clinical trial
- review of trial conduct from **start to finish**



## Auditing

- an **independent, systematic** review of a clinical trial
- a compliance **snapshot**



# Monitoring v. Auditing

Both processes assess compliance with federal regulations, the scientific protocol, sponsor requirements, and institutional policies.

Effective monitoring is critical to human subject protection, conduct of high-quality studies and data Integrity.

Audits provide assurance that studies are conducted according to appropriate regulations and guidance, in order to provide accurate data.

# Monitoring & Auditing at Emory

## Monitoring

- Sponsor monitoring
- Winship Cancer Institute internal monitoring
- Self-monitoring

## Auditing

- Clinical Trials Audit and Compliance (CTAC)
- Office of Compliance
- IRB

# What's required?

FDA regulations obligate sponsors to oversee their clinical trials.

21 CFR 312.50 and 812.40

Emory IRB requires a monitoring plan for studies which are more than minimal risk & may also be required in minimal risk studies .

Emory IRB P&P 51

# Data Safety Monitoring Plan

A data safety monitoring plan (DSMP) describes how the Principal Investigator plans to oversee the human subjects' safety and welfare during the conduct of the trial.

# Data Safety Monitoring Plan

## Monitoring Plan Components

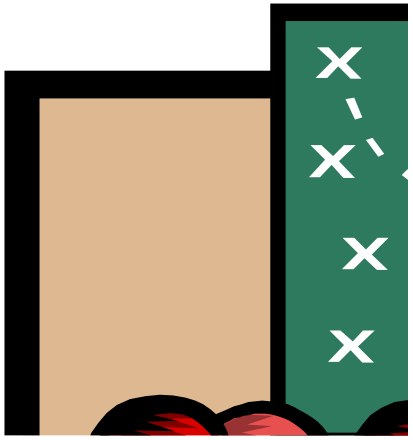
- **Data Safety Monitoring Plan** – How is safety information collected from sites and from other sources (e.g., other studies, other countries where drug is approved, etc.); evaluated; and results disseminated to investigators?
  - Data Safety Monitoring Board (DSMB) – Who will review safety data, consider stopping rules, etc.?

- **Site Monitoring Plan** – How is information being collected about protocol compliance at each site and the quality of the data being collected?

# Site Monitoring Plan

Plan must define how data accuracy and protocol compliance will be ensured and validated.

Plan must define reporting obligations for protocol deviations/violations and noncompliance.



# Site Monitoring plan

Should describe the monitoring methods, responsibilities, and requirements for the trial.

Required elements include:

- the frequency of the monitoring
- who will conduct the monitoring
- what data will be monitored
- how the data will be evaluated for problems
- what actions will be taken upon the occurrence of specific events or end points
- how/when communication to the IRB will occur

# Site Monitoring Plan

The plan should specify the following elements:

**Frequency of reviews**.

Example : Review after the first three subjects are enrolled. At a minimum, review is required annually.

**Identity of site monitor**.

Example: Specify position of person who will monitor or name CRO to which monitoring has been delegated.

**Scope of site monitoring**.

Example: Informed consent process, eligibility, CRFs, AE reporting

**Number of records reviewed**.

Example: 10% or 2 of the first 5 subjects enrolled

**Plan for evaluating and documenting findings/observations**.

Example: a monitoring report will be provided to the S-I within 5 days of review.

**Follow-up process**.

Example: PI will document receipt & review of the monitoring report, resolutions and/or corrective actions to findings on the Site Monitoring Log; PI will notify IRB according to P&P

# Monitoring

FDA Draft Guidance makes clear that sponsors can use a variety of approaches to fulfill monitoring responsibilities.

Types of monitoring

- On-Site Monitoring
- Centralized Monitoring
- Self Monitoring

# Self Monitoring

A process for self-assessment of protocol compliance and data integrity

Can be part of an overall DSMP depending on the degree of risks to subjects

Includes review of essential documentation, subject records, adverse events, etc.

Should be completed regularly once subjects have been enrolled.

# Self-Monitoring

Customize the Emory University Self-Monitoring Tool for your study activities

Modify to include review of the specific human subject protection and data integrity risks of the trial

Tool is located on these websites

IRB
http://www.irb.emory.edu/forms/clinical.html
OC
http://compliance.emory.edu/FDA-regulated-studies/resources/index.html
CTAC
http://www.ctac.emory.edu/clinical_trial_resources/Clinical%20Trial%20Tools.html

# Resources

The Office of Compliance (OC) and Clinical Trial Audit and Compliance (CTAC) work with study teams and are available for consultation and review of monitoring plans.

Additional tools for Emory sponsors and sponsor-investigators are available at compliance.emory.edu

# Auditing and Compliance @ CHOA

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# Why do we audit studies?

- To preserve subject welfare and integrity of research data.

- Types of audits performed at Children's
  - **Study Start-up**
  - **For Cause** (i.e., noncompliance, patient safety, etc.)
  - **Not-For-Cause** (quality assurance purposes)

# The Auditors are coming!

## Suggested Ways to Organize Documents

- All files should be kept in one designated area
- All documents should be maintained in chronological order
- IRB approvals, which can be subdivided as follows:
  - Initial Approval
  - Modification Forms
  - Continuing Review
  - Adverse Event Reports
  - Approved Consent forms
  - Patient facing material

# Other items needed in regulatory files

- Master Protocol and each revision of the protocol
- Shipment receipts
- Correspondence
- Logs
  - Delegation of Authority
  - Subject Enrollment
  - Drug Dispense/Return
  - Monitor Visit
  - Protocol training

# Top clinical trial audit findings

1. **Failure to adhere to the protocol**
   - If it's not documented, it did not happen.

2. **Inaccurate and incomplete study records**
   - Questionnaires
   - Fill in all check boxes and lines

# Top clinical trial audit findings

3. **Lack of documentation that a copy of the consent form was given to the participant.**
   - How do you do this? Create a consent note explaining everything that happened during the consent process.
4. **Improper documentation that eligibility criteria are satisfied.**
   - Create an inclusion/exclusion criteria CRF. This should list all criteria needed for a participant to enter the study, whether they fit the criteria, and have a signature line for the PI (or designee).

# Top clinical trial audit findings

5. **Difference in procedures**
   - We have found that the protocol and consent forms do not always match. This usually happens when the study is an investigator initiated study.
   - As you read both documents please be mindful that there could be inconsistencies that need correction.

# Top clinical trial audit findings

6. **The use of white out is not acceptable.**
   - If it's in your desk…throw it away! When you use white out, you're obstructing the original text.
   - Federal regulation CFR812.140 specifies that an investigator must maintain accurate, complete and current records.
   - ICH GCP E6 Part 4.9.3 recommends that any change or correction to a CRF should be dated, initialed, and explained (if necessary) and should not obscure the original entry.

# Questions

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