

# Basics of Monitoring

UW Bioen 599

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# What is Monitoring

- Monitoring is the review of the Principal Investigator's compliance with the regulations and the requirements of the protocol
- Monitoring is the systematic review of
  - The Regulatory Binder
  - The Case Report Forms and source documents
  - The Informed Consent Forms
  - The Investigational Supplies accountability

# Monitoring vs. Auditing

- Monitoring is an ongoing review of the investigator, staff, labs, documents, and all data points. It is conducted by an employee or a representative of the company, such as a CRO's monitor to assess the site's performance.
- Auditing is a point in time inspection of the investigator, staff, labs, documents and a pre-determined selection of a percentage data points (usually the clinical endpoints and safety data) by a company employee or a third party to assess the performance of the site AND of the monitor.

# Ways of Monitoring

## ■ On-site

- As required by the January 1988 Guidance Document

## ■ Remotely

- In addition to, not in lieu of, on site monitoring
- Can be telephone calls, e-mails, FAXes or letters

# When to Monitor

- Pre-study
- Initiation Visit
- Routine, ongoing visits
- End of Study or Close-Out Visit
- “For Cause” Visit

# Monitoring Reports

- Audiences for the report
  - Supervisor, senior management
  - FDA investigators
- Contents
  - Attendees
  - Findings and Observations
  - Recommendations for improvement
- Deficiency List
- Action Item list

# Monitoring visits

Early visits: Pre-study and initiation  
Routing monitoring visits  
Close-out visits  
“For cause” visits  
Monitoring “tools”

# Pre-Study Site Visit

## ■ Purpose

- visit the site to determine the adequacy of the facility and equipment;
- meet the investigator and staff;
- discuss the number of possible candidates for the study;
- review the protocol and regulatory obligations

## ■ Report:

- Write and submit monitoring report

# Initiation Visit

## ■ Purpose:

- To assess investigator's performance and compliance after one to two patients have been enrolled
- To check Regulatory Binder
- To verify consent forms are signed appropriately
- To check CRFs against source documents for first few patients
- To check investigational supplies accountability
- To examine adverse event reports, if any
- To check on any protocol deviations and ensure they were properly documented

# Routine Monitoring Visit

## ■ Purpose:

- To assess investigator's ongoing performance and compliance
- To follow-up on action items from last visit
- To check Regulatory Binder
- To verify consent forms are signed appropriately
- To check CRFs against source documents
- To assist site in resolving queries
- To check investigational supplies accountability
- To examine adverse event reports, if any
- To check on any protocol deviations and ensure they were properly documented

# Close-Out Visit

## ■ Purpose:

- To assess investigator's overall compliance
- To follow-up on action items from all visits
- To check Regulatory Binder
- To verify consent forms were signed appropriately
- To check final CRFs against source documents
- To ensure all queries have been resolved
- To check investigational supplies accountability
- To examine adverse event reports, if any
- To check on any protocol deviations and ensure they were properly documented
- To prepare Investigator Site files for storage and retrieval, if need be for an FDA inspection

# “For Cause” Monitoring Visit

- Possible reasons for this type of visit
  - Enrollment too high or too low
  - More adverse events at that site than at any other
  - Poor compliance with protocol, i.e., many protocol deviations, ineligible subjects enrolled
  - Continually incorrect investigation supplies accountability
  - Suspicion that data may not be substantiated

# “For Cause” Visit

- Make appointment for at least two monitors, or a monitor and a supervisor, to visit site
- If the problem is considered to be compliance-related, send letter indicating the problem and suggestions to correct and prevent in the future
- If the problem may be related to fraud, seek advice from the company attorney.
- **DOCUMENT EVERYTHING!**
- Send follow-up letter to site indicating findings and corrective actions.

# Monitoring Tools

- Monitoring supplies
- Make a list for each site of where the source documents can be found, e.g., in the subject's study chart, in the hospital charts, etc.
- Develop checklist for activities at the site
  - Deficiencies from last visit
  - Table of CRFs completely reviewed, partially reviewed, and those that the site has finished that have not yet been reviewed
  - Inventory: shipped, received, used, repaired, returned, replaced