Preparing for an FDA Medical Device Sponsor Inspection

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FDA Is Coming!

Bioresearch Monitoring (BIMO) Program

- FDA Bioresearch Monitoring (“BIMO”) program
  - To protect human research subjects from undue hazard or risk
  - To ensure the quality and integrity of data submitted in support of device applications
- BIMO inspections

Objectives

- Describe FDA medical device sponsor inspections
- Describe the inspection process
- Discuss common inspectional observations and how to respond to them
- Provide points to consider

Topics

- Device Sponsor Inspections
- Pre Inspection Process
- FDA Inspection Preparation
- Inspection Day
- What do we inspect?
- Inspection Conclusion
- Common Sponsor Deficiencies
- Post Inspection Process
- Inspection Classification
- Written Response
- Points to Consider
- Summary

Medical Device Sponsor Inspections

- A type of FDA inspection designed to monitor and review various aspects of the conduct/reporting of FDA-regulated research
- Inspections conducted on-site at sponsors, monitors, and contract research organizations
- Inspections typically involves interviews, review or inspection of documents, evaluation of systems, facility tours, and compliance with regulations

Pre-Inspection Process

- Inspection assignments are issued by FDA Center to district office
- FDA investigator may pre-announce inspection
- Types of FDA inspections:

  -Routine/Surveillance

  -For Cause

Inspection Preparation

- Have available
  - Top management official available for inspection day
  - Personnel knowledgeable about all aspects of the study
  - A quiet area to conduct inspection with access to a photocopier
- Have available and organized
  - All study documents including electronic records if applicable.
  - Standard Operating Procedures (SOPs)

Inspection Day

- FDA personnel (Field Investigators, Center personnel, etc.) will present his or her credentials
- Issuance of Form FDA 482, Notice of Inspection
- If not provided, ask for a review of findings at the end of each inspection day
- Inspection is conducted during normal business hours

What Do We Inspect?

- Protocol (original & revisions)
- Investigator agreements & financial disclosures
- Organizational charts
- Correspondence
- CRO or vendor agreements
- Device accountability records
- Monitoring plan & reports

What Do We Inspect? (cont.)

- Qualification records for Monitors and Clinical Investigators
- Training records
- Study subject records (CRFs, diaries, etc.)
- Unanticipated Adverse Device Effects (UADEs) or adverse event reports
- Clinical Databases/Data line listings
- Standard Operating Procedures for conduct of study

Inspection Conclusion

- FDA Investigator conducts a close out meeting with management
- FDA Investigator issues a Form FDA 483, Inspectional Observations for significant deviations from the regulations
- Form FDA 483 does not represent a final Agency determination
- Opportunity to respond to observations

Common Sponsor Deficiencies

- Inadequate monitoring
- Failure to secure investigator compliance
- Failure to submit Progress Reports
- Inadequate UADE analysis and reporting
- Failure to notify FDA, investigators or IRBs
- Inadequate device accountability
- Failure to obtain signed Investigator Agreement
- Failure to obtain FDA or IRB approval
- Unqualified monitors

Post Inspection Process

- The FDA investigator completes Establishment Inspection Report (EIR)
- The EIR, FDA 483 (if issued), supporting documentation, and the preliminary district classification of the inspection is forwarded to FDA Center for review
- The FDA Center evaluates the report and determines the final classification for the inspection
- The inspection findings and preliminary recommendation are then reported to the review division as part of the application review

Inspection Classification

- No Action Indicated (NAI)
  - No objectionable conditions or findings
- Voluntary Action Indicated (VAI)
  - Objectionable conditions or findings
  - But not at threshold to take or recommend administrative or regulatory action
- Official Action Indicated (OAI)
  - Serious objectionable conditions found
  - Regulatory action recommended

Written Response

FDA recommends that sponsors provide a written response to the FDA 483

Written Response (cont.)

- An evaluation of the extent of the problem
- Assessment of the root cause of the problem
- Any corrective actions
  - Not just a statement that you will correct or plan to correct the problem
  - What was corrected?
  - When was it completed?
  - Is the problem systemic?
- Preventive actions to prevent recurrence of the problem in future studies
- Timeframe for training
- Supporting documentation

Written Response (cont.)

The FDA 483 cited the following: *Investigator Agreements were not obtained from Dr. Smith and Dr. Doe.*

The sponsor provided the following response:

- "A formal procedure for obtaining investigator agreements (IA's) was not in place at the time of this study. We recently obtained these IA's from Drs. Smith and Doe. We developed and implemented an SOP requiring the IA's to be obtained prior to shipping the device to the clinical site. We attached copies of these two Dr's signed IA's and the SOP. We trained all study personnel on this new SOP. See attached copy of the training material and training log. After 6 months, we will conduct an audit of all IA's to determine if this preventive action assists with ensuring adequate IA's."

Points to Consider

- Be courteous and responsive to FDA personnel
- Keep study files organized at all times.
- Maintain ALL correspondence

  -letters, faxes, e-mails, memos, phone contacts
- Maintain written procedures:
  - Operations, Device Safety, Monitoring, Regulatory, Quality Assurance, Device Accountability, and Training
  - Non compliance

Points to Consider (cont.)

If it is not documented, it didn't occur!

Summary

- Described device sponsor inspections
- Described the inspection process
- Discussed common inspectional observations and how to respond to them
- Provided points to consider