



Preparing for a FDA Medical Device Clinical Investigator Inspection

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FDA Is Coming!





FDA 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 clinical investigator inspections
- Describe inspection procedures
- Discuss common inspectional observations and how to respond to them
- Provide points to consider



Topics

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



Medical Device CI Inspections

- A type of FDA inspection designed to determine compliance with FDA regulations and statutory requirements
- Inspections conducted at CI sites
- Inspections typically involve:
 - Interviewing
 - Comparing site data with Sponsor or FDA data
 - Evaluating systems
 - Determining adherence to the investigational plan
 - Touring the research site
 - Copying study records



Pre-Inspection Process

- Inspection assignments
 - 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
 - Most responsible clinical investigator/designee 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.) present his or her credentials
- Issuance of Form FDA 482, Notice of Inspection
- Request that a summary of any inspectional findings be provided at the end of each day
- Inspection is conducted during normal business hours



What Do We Inspect?

- Protocol (original & revisions)
- Investigator agreements & financial disclosures
- Case report forms
- Inclusion/Exclusion criteria
- Informed consent forms
- Adverse events including unanticipated adverse device effects (UADEs)
- Other required reports
- Electronic records
- Other study subject records



What Do We Inspect? (cont.)

- Qualification records for Clinical Investigators
- Training records
- Study delegation sheet
- Correspondence
- Device accountability records
- Standard operating procedures for conduct of study



Inspection Conclusion

- FDA Investigator conducts a close out meeting with clinical investigator
- 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 CI Deficiencies

- Failure to follow the investigational plan
- Failure to maintain case histories
- Inadequate device accountability
- Failure to obtain adequate informed consent
- Inadequate UADE reporting
- Failure to submit progress reports
- Failure to follow conditions of approval imposed by an IRB



Post Inspection Process

- The FDA investigator completes Establishment Inspection Report (EIR)
- The EIR, FDA 483 (if issued), supporting documentation, and the preliminary district classification is forwarded to CDRH
- CDRH evaluates the report and determines the final classification for the inspection
- Inspection findings and preliminary recommendations are reported to the appropriate CDRH review division
- Consult with other FDA Centers such as CBER or CDER



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
clinical investigators
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
- Time frame for training
- Supporting documentation



Written Response (cont.)

The FDA 483 cited the following: *An unexpected adverse device effect for study ABC was not reported to the Sponsor and IRB within 10 working days after receiving knowledge of the event.*

The clinical investigator provided the following response:

- “Due to an oversight, a UADE for this study was not reported to the sponsor and the IRB within 10 working days of receiving knowledge of the event. As a corrective and preventive action, we have implemented a written procedure to ensure that all UADEs will be reported within 10 working days. All study staff have already been trained on this new procedure. Copies of this procedure and associated training records are attached. We have also reviewed adverse events for our other studies and concluded that this issue was an isolated event. Within 6 months, we will conduct an audit of all adverse events to determine if this corrective action was effective.”



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
- Oversee delegation of duties
- Know your IRB's requirements
- Understand requirements of the protocol



Points to Consider (cont.)

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





Summary

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