TOPICS

• FDA Notification: Immediate Next Steps

• Inspection Overview

• Inspection Preparation
FDA NOTIFICATION:
The FDA makes contact – immediate next steps

E-mail MedicalQAInspectionMgmt@pfizer.com with the following:

- Protocol Number
- Site Information (Principal Investigator Name, Site No., Contact Details such as phone number and e-mail, and Address)
- Name of Inspector [if known]
- Dates of Inspection

ENSURE AVAILABILITY

- All subjects’ medical records
- Source documents
- Investigator Site Files

COORDINATE LOGISTICS

- Identify all relevant personnel
- Reserve an inspection room for at least a week’s duration
- Coordinate preparation activities
## INSPECTION OVERVIEW:
**FDA’s Bioresearch Monitoring (BIMO) Program**

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<th>BIMO PROGRAM OBJECTIVES</th>
<th>TYPES OF INSPECTIONS</th>
<th>POTENTIAL OUTCOMES</th>
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| 1. Protect the rights, safety, and welfare of subjects in FDA-regulated trials. | 1. Routine
- New Drug Applications |
| 2. Determine the accuracy and reliability of clinical trial data submitted to FDA in support of research or marketing applications; and | 2. Directed
- Investigate problems that have been identified at the Investigational new Drug (IND) stage (e.g., data audits) |
| 3. Assess compliance with FDA’s regulations governing the conduct of clinical trials, including those for informed consent and ethical review. | 3. For Cause
- Investigate complaints (e.g., allegations of falsification, lack of oversight, inadequate monitoring)
- Compliance follow-up for previous deficiencies |
| | 1. No observations with or without discussion points. |
| | 2. Warning Letter |
| | 3. Disqualification of clinical investigators [21 CFR 312.70] |
| | - Repeated and deliberate failure to comply with the requirements. |
| | - Repeated or deliberate submission of false information to the FDA or to the sponsor in any required report, |
| | - FDA provides notice of matter to investigator and provides opportunity to explain (Notice of Initiation of Disqualification Proceedings and Opportunity to Explain – NIDPOE). |
| | - May result in ineligibility to receive investigational drugs. |
INSPECTION OVERVIEW: General Inspection Steps

1. Pre-Inspection
   - Inspectors receive inspection assignments from the FDA Center
   - FDA Center selects sites

2. Opening Meeting
   - Form FDA 482 “Notice of Inspection” is issued to the most responsible person.
   - Explains why the FDA is there and what records and documents will be reviewed.

3. Inspection Conduct
   - Review of Records
     - Source Documents & Medical Records
     - Case Report Forms
     - Data Listing Submitted
     - Primary Efficacy
     - AEs/SAEs
     - Safety: Labs, etc.
   - Copying and collection of exhibits
   - Facility Tour
   - Interviews

4. Closing Meeting
   - If applicable, Inspector issues Form FDA 483, which are:
     - Significant deviations from Regulations.
     - Observations are based only on the FDA Investigator’s review of available records and information.
     - Observations do not represent final Agency determination regarding compliance.
     - If a Form FDA 483 is issued, assistance is available:
       - Findings should be responded to within 15 business days.
       - Corrective actions should be taken for deficiencies, AND preventative actions to prevent recurrence.
       - Documentation of completion of actions should be provided with the response (e.g., updated SOP).

5. Post-Inspection
   - Inspector prepares Establishment Inspection Report (EIR) and recommends classification.
   - FDA Center reviews and classifies findings:
     - NAI: No Action Indicated [no objectionable conditions or practices found (or the objectionable conditions do not justify further regulatory action)]
     - VAI: Voluntary Action Indicated [objectionable conditions or practices found, but agency is not prepared to take or recommend any administrative or regulatory action]
     - OAI: Official Action Indicated [regulatory and/or administrative actions recommended]
   - Inspected entity will receive a copy of the EIR. Please forward to MedicalQAInspectionMgt@pfizer.com.
INSPECTION PREPARATION:
Primary Commitments in Form FDA 1572

- Obtain informed consent
- Follow the approved protocol
- Personally conduct and supervise the study
- Administer test article only to subjects under the control of the Investigator
- Timely report adverse events to sponsor
- Maintain adequate and accurate records

Derived from the following sections of Title 21, Code of Federal Regulations: General responsibilities (21 CFR 312.60); Control of investigational drug (21 CFR 312.61); Record keeping and retention (21 CFR 312.62); Investigator reports (21 CFR 312.64)
Common BIMO Observations for Clinical Investigators

• Failure to follow the investigational plan and/or regulations
• Protocol Deviations
• Inadequate record-keeping
• Inadequate accountability for the investigational product
• Inadequate communication with the IRB
• Inadequate subject protection – failure to report AEs and informed consent issues
INSPECTION PREPARATION: Common Preparation Areas

**Discussion Points**
- Site Organizational Structure
- Subject Recruitment
- Protocol & Protocol Amendments
- Processes: Informed Consent, IRB Reporting, SAE Reporting, Delegation, Training, Oversight, IP
- Data Handling & Responsibilities
- Monitoring

**Facilities & Equipment**
- Suitability to meet protocol requirements
- Maintenance and proper use

**Documentation**
- Available, organized, and complete
- Evidence that all data are aligned
- Evidence of proper informed consent process
- Evidence that IP handling and dispensing are appropriate
- Evidence of adequate communications with the IRB
- Evidence of monitoring and follow-up to and by the sponsor

**Interview**
- Understand the question and seek clarification – do not interpret
- Answer only the question as asked
- Answer honestly – do not be evasive or give false/misleading info
- Answer succinctly
- Refer to SMEs, when appropriate
- Be comfortable with silence

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If you remember nothing else, when the FDA calls...

IMMEDIATELY NOTIFY

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- Protocol Number
- Site Information (Principal Investigator Name, Site No., Contact Details such as phone number and e-mail, and Address)
- Name of Inspector [if known]
- Dates of Inspection
Thank You