



# Bioresearch Monitoring

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# Topics

- BIMO Program
- Inspections
- Regulatory Actions
- Examples of Noncompliance
- Tips for Success

# BIMO Program Description

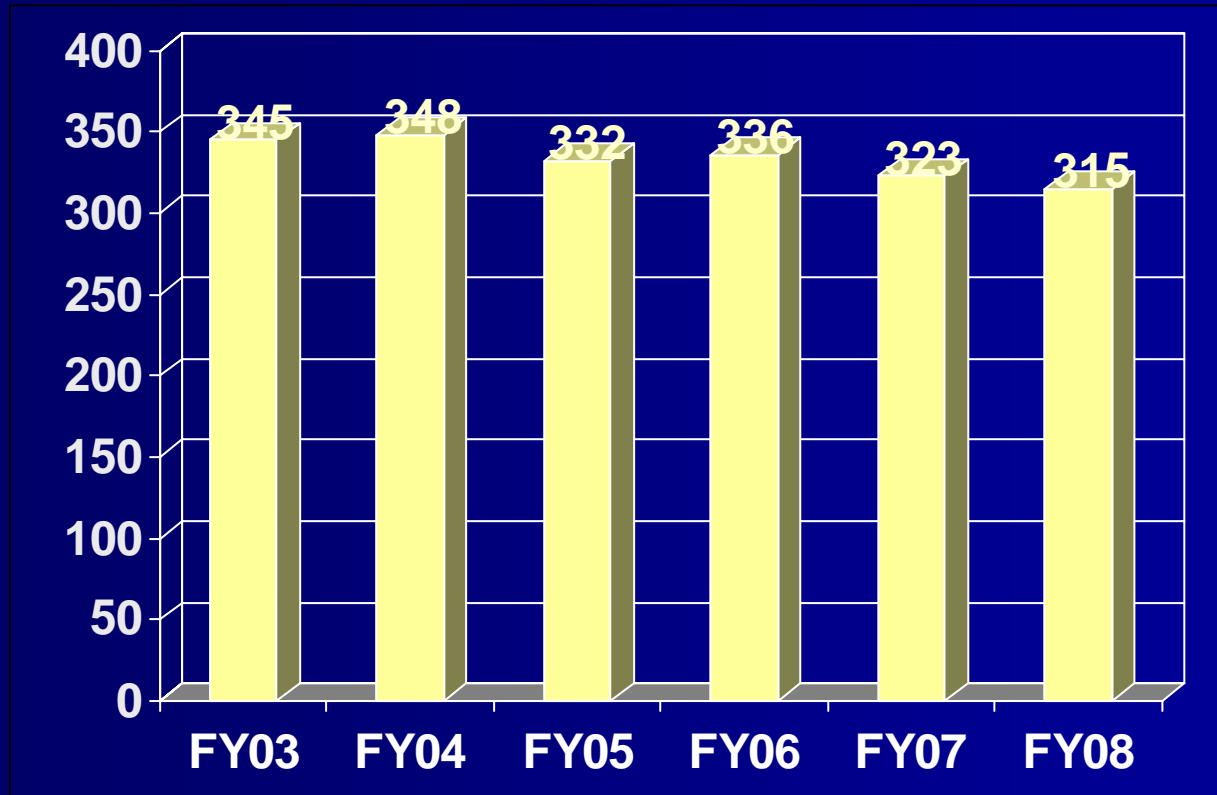
- A comprehensive, Agency-wide program of on-site inspections and data audits designed to monitor all aspects of the conduct and reporting of FDA-regulated research.



# BIMO Program Objectives

- Protect the rights, safety, and welfare of human research subjects
- Ensure the quality and integrity of research data

# CDRH BIMO Inspections



# CDRH BIMO Inspections (IVDs)

- *Who?* Sponsors/Monitors (S/M), Contract Research Organizations (CROs), Clinical Investigators (CIs), and Institutional Review Boards (IRBs)
- *What?* Primarily PMAs and 510(k)s
- *Where?* U.S. and foreign countries

# Inspection Triggers

- Marketing application
- Novel technology
- Vulnerable population
- Surveillance
- Complaint

# BIMO Inspection Focus

- Monitor compliance with . . .
  - human subject protection requirements
  - study conduct procedures
- Assess data quality by verifying the accuracy of data in the submission
- Address special issues or problems

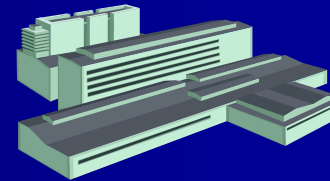
# Inspection Process

- Telephone call – short notice
- Arrival
  - FDA investigator will . . .
    - show credentials
    - issue a written notice of inspection to most senior person (Form FDA 482)
    - discuss the general nature of the inspection



# Inspection Process

- Tour facilities
- Review various records
- Collect records to substantiate observations/facts
- Collect sworn affidavits, if needed
- Discuss inspection proceedings and findings



# Specific Questions

- Does 510(k) data match source documents?
- Was IRB approval obtained?
- Was informed consent obtained (if applicable)?
- Was the device labeled appropriately?
- Was the study protocol followed?
- Was the study monitored (if applicable)?
- What activities were undertaken to assure the quality and reliability of the data?
- Are device records accurate and complete?

# Inspection Closeout Meeting

- Discuss final observations
- FDA investigator may issue a Form FDA 483 "Inspectional Observations"



# If you receive a 483 . . .



- Respond verbally at the closeout meeting
- Send a written response to the FDA District Office

# Actual Response

- CRO: "The study was not properly conducted because all of the study coordinators' techniques in performing the testing were poor despite the fact that they were provided with written instructions, verbal guidance, and a demonstration of how to use the kit."

# Actual Response

- Monitor: "Site coordinators often were not available while I was on-site. Therefore, if I saw errors, I made corrections. I just didn't initial, date, or document a reason for each change."

# Actual Response

- Sponsor: "We had nothing to do with the 510(k) submission. The correspondent incorrectly identified samples as duplicate numbers. The correspondent inadvertently omitted test results."

# Written Responses

Include . . .

- Assessment of the root cause of the problem
- An evaluation of the extent of the problem
- Any immediate corrective actions
- Any preventative actions to avoid recurrence
- Supporting documentation
- Timelines for implementation

# Post-Inspection

- FDA Field Office
  - Prepares Establishment Inspection Report (EIR)
  - Submits EIR & supporting documentation to CDRH
- CDRH/BIMO
  - Reviews EIR, 483 (if issued), any responses
  - Determines final classification
  - Issues correspondence
  - Initiates follow-up actions

# Compliance Classifications

- **No Action Indicated (NAI)**
  - No objectionable conditions or practices
- **Voluntary Action Indicated (VAI)**
  - Objectionable conditions or practices but not at threshold for regulatory action
- **Official Action Indicated (OAI)**
  - Serious objectionable conditions found
  - Regulatory action recommended

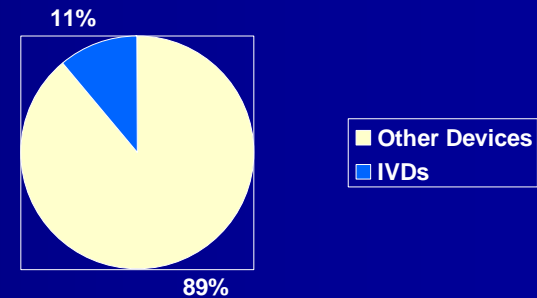
# FDA Regulatory Actions



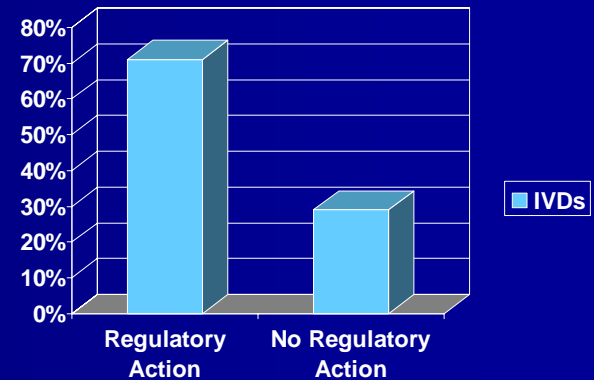
- Rejection of data
- Deficiency letter
- Withdrawal of submission
- Untitled letters
- Warning letters
- Consent Agreement
- Disqualification
  - CI, IRB, GLP
- IRB restrictions
  - No new studies/subjects
- Application Integrity Policy (AIP)
- Civil Money Penalties
- Seizure / Detention
- Injunction
- Criminal Prosecution

# Complaint Investigations

- Active Cases in FY08



- Of the IVD cases, 71% included a regulatory action



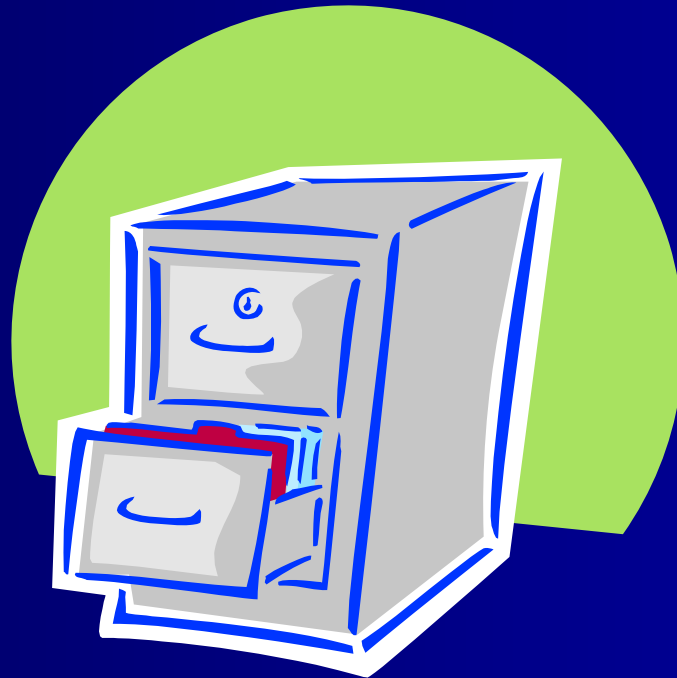
# Confusion



- IDE-exempt IVD studies do not require IRB review and approval.
- IRB review is not required when leftover human specimens are used.
- IVD nonclinical studies using leftover human specimens are not subject to IRB review.

**FALSE!**

# Case Studies



# Tips



- Know your responsibilities and applicable regulations, *including QSR*
- Ensure studies are based on valid scientific evidence (21 CFR 860.7)
- Follow good research practices/good clinical practices (GCPs)

# GCPs

- Ensure the rights, safety, and well-being of subjects
- Have a detailed study protocol & ensure it is followed
- Select appropriate sites & use qualified individuals to conduct the trial
- Maintain accurate, complete, and current records

# GCPs

- Submit complete, accurate, and timely reports
- Implement procedures that assure quality and reliability of data
- Have written SOPs and follow them
- Monitor the study



# Resources



- Device Advice
  - [www.fda.gov/cdrh/devadvice](http://www.fda.gov/cdrh/devadvice)
- Good Clinical Practice
  - [www.fda.gov/oc/gcp/default.htm](http://www.fda.gov/oc/gcp/default.htm)
- Informed Consent for IVD Studies
  - [www.fda.gov/cdrh/oivd/guidance/1588.html](http://www.fda.gov/cdrh/oivd/guidance/1588.html)
- IVD Studies – Frequently Asked Questions
  - [www.fda.gov/cdrh/oivd/guidance/1587.pdf](http://www.fda.gov/cdrh/oivd/guidance/1587.pdf)
- Office of In Vitro Diagnostics
  - [www.fda.gov/cdrh/oivd](http://www.fda.gov/cdrh/oivd)

THANK YOU!