Bioresearch Monitoring

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Disclaimer

- The contents of this presentation are my own and do not necessarily reflect the views and/or policies of the Food and Drug Administration or its staff as per 21 CFR 10.85.

Topics

- BIMO Program
- Regulations
- Good Clinical Practices
- Inspections

FDA BIMO Program

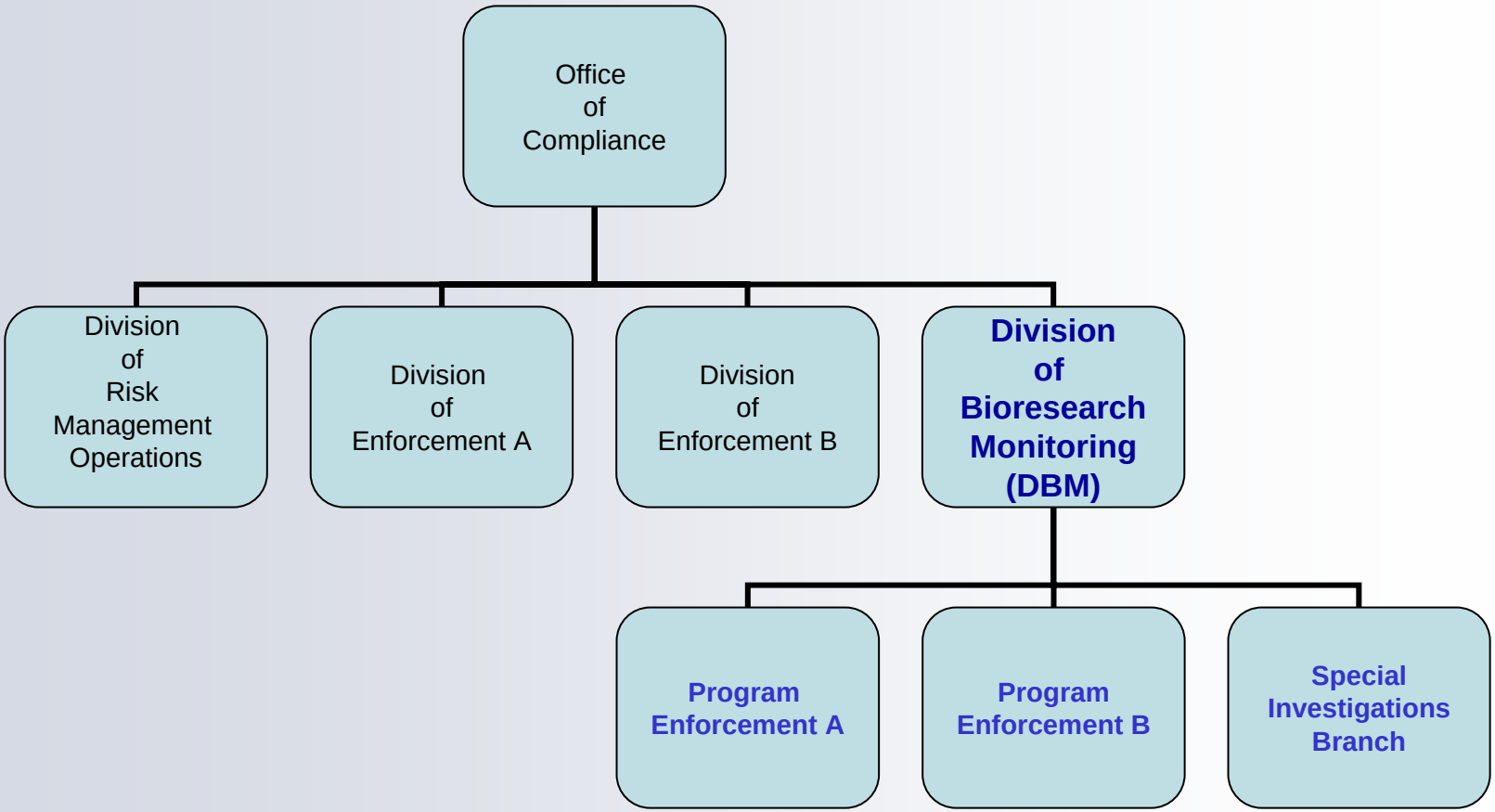
- On-site inspections
- Data audits

Monitor FDA-regulated research

Program Objectives

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

CDRH BIMO


Office of Compliance
Division of Risk Management Operations
Division of Enforcement A
Division of Enforcement B
Division of Bioresearch Monitoring (DBM)
Program Enforcement A
Program Enforcement B
Special Investigations Branch

DBM's Roles

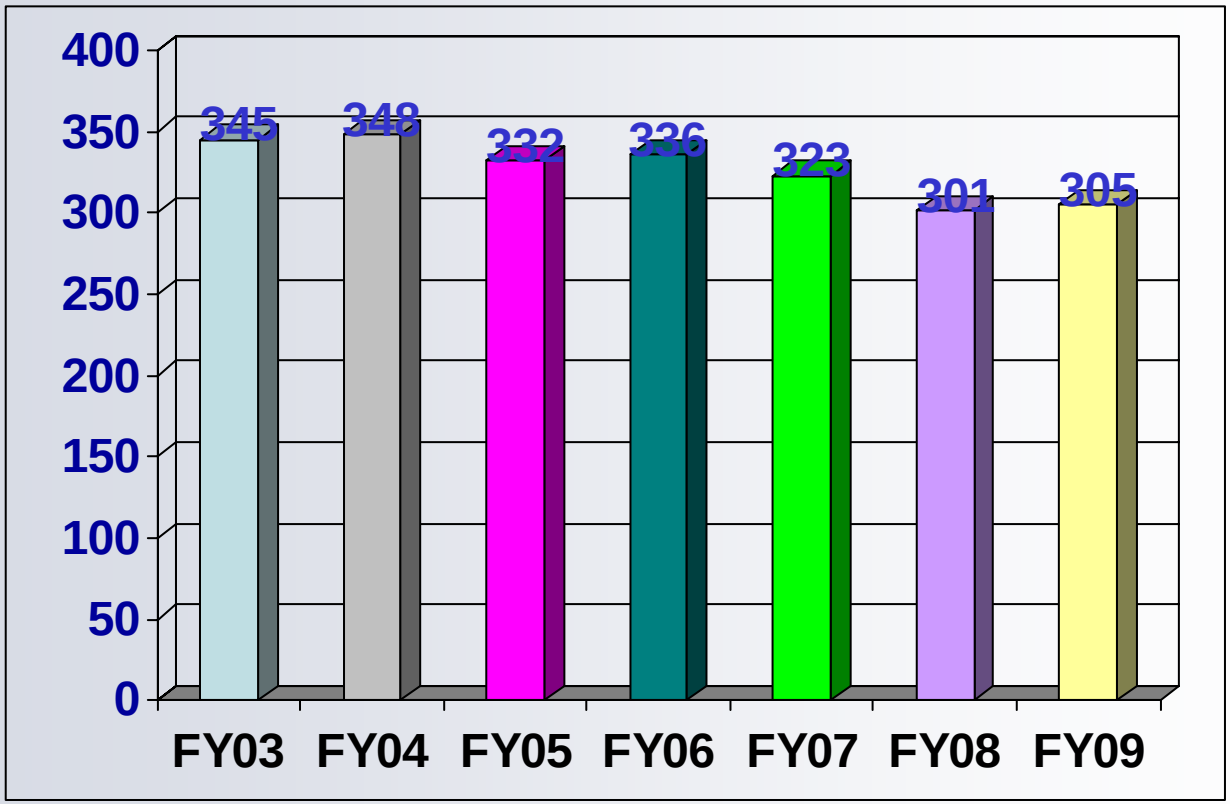
- Audits clinical and nonclinical data
- Coordinates inspections/investigations
- Coordinates application integrity cases
- Reviews promotion and advertising claims
- Initiates regulatory actions
- Conducts educational outreach

Regulations

- 21 CFR Part 812
  - Investigational Device Exemptions
- 21 CFR Part 50
  - Protection of Human Subjects
- 21 CFR Part 56
  - Institutional Review Boards
- 21 CFR Part 58*
  - Good Laboratory Practice for Nonclinical Laboratory Studies

*not applicable to IVD studies

CDRH BIMO Inspections



Inspection Sites

- Sponsors/Monitors (S/M), Contract Research Organizations (CROs) or Other Third Parties
- Clinical Investigators (CIs)
- Institutional Review Boards (IRBs)
- Nonclinical Laboratories*

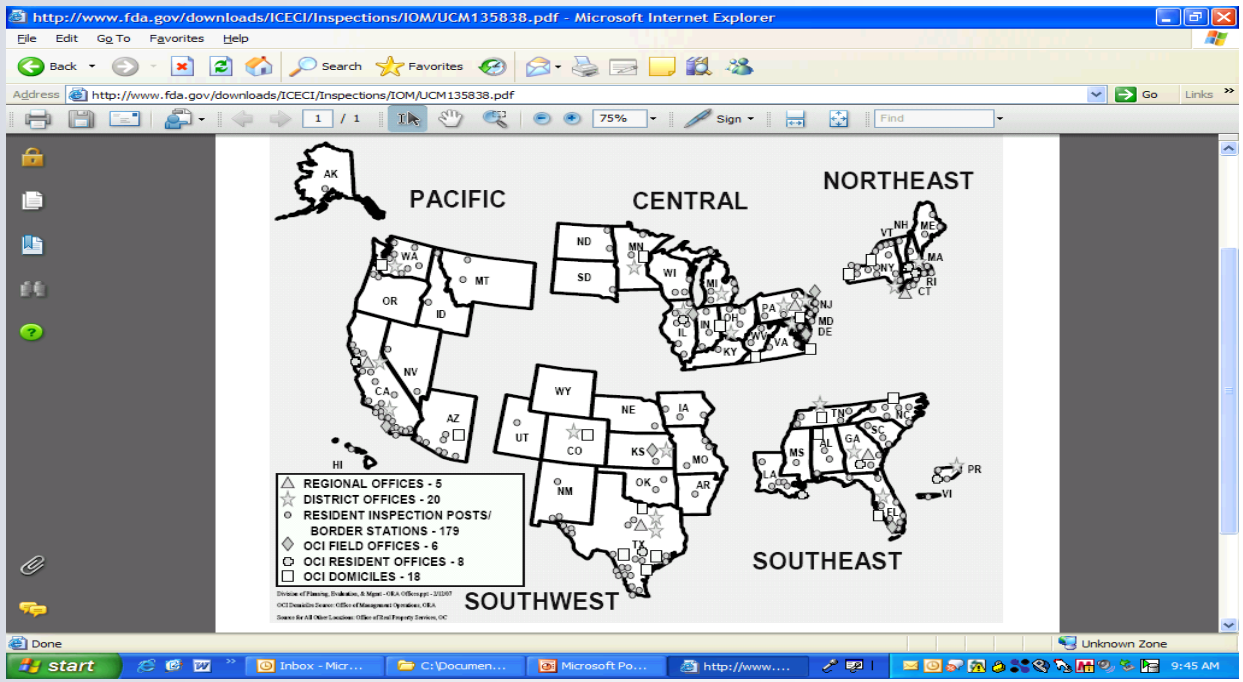
*described in Part 58

Inspection Triggers

- Marketing application
- Novel technology
- Vulnerable population
- Surveillance
- Complaint
- Previous violative inspection

Inspection Assignment

- DBM creates memo → ORA Headquarters



Inspection Focus

- Monitor compliance
  - Human subject protection (Parts 50 & 56)
  - Study conduct (Part 812)
- Assess data quality
- Address special issues or problems

Human Subject Protection

- Informed consent (IC) requirements
- IC elements - §50.25
- IC documentation - §50.27
- Leftover specimen documentation*
- IRB review and approval

Using Leftover Specimens

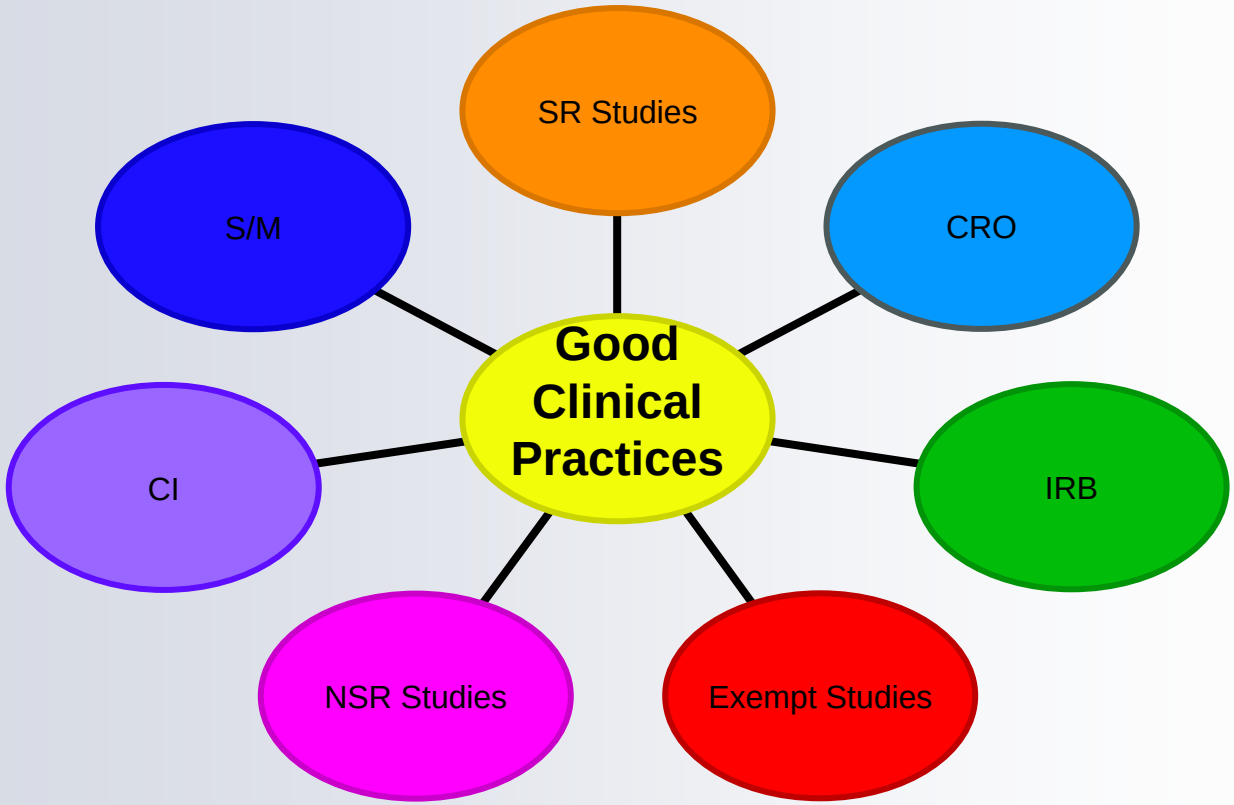
- Sponsor Responsibilities
  - Maintain written documentation
    - 7 Factors supporting use of leftover specimens
    - Specimen provider's policies and procedures to ensure that the subject cannot be identified
  - Provide documentation to IRB

www.fda.gov/downloads/RegulatoryInformation/Guidances/ucm127033.pdf

Study Conduct

- Significant Risk studies
  - Responsibilities of Sponsors (Subpart C)
  - Records and Reports (Subpart G)
- Non-Significant Risk studies
- Exempt studies

Study Conduct



Good Clinical Practices

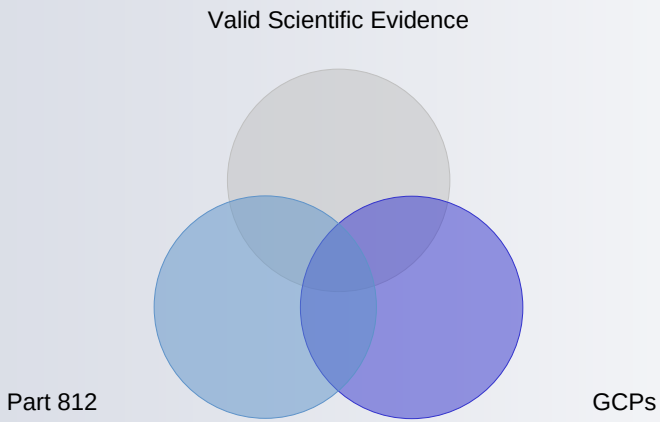
- Ensure human subject protection
- Follow investigational plan
- Select appropriate sites/qualified researchers
- Maintain records
- Submit reports

Good Clinical Practices

- Implement procedures that assure quality and reliability of data
- Follow SOPs
- Monitor the study

Other Responsibility

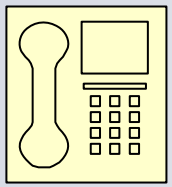
- Ensure studies are based on valid scientific evidence (21 CFR 860.7)



Certifications

- Truthful and Accuracy Statement
- Financial Disclosure

Scheduling Inspection



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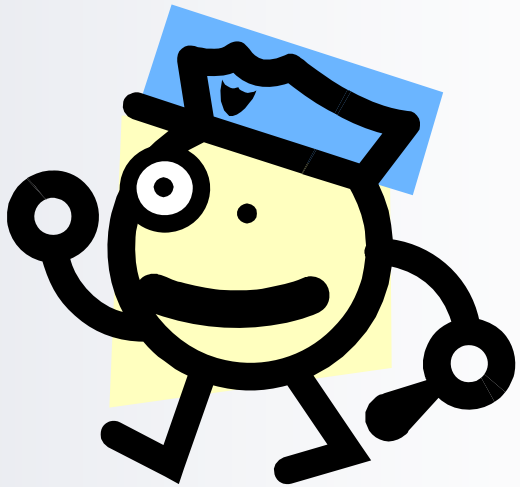
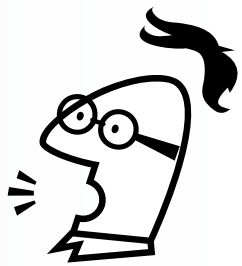
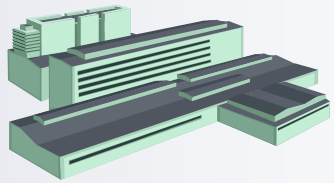




Inspection Process

- Show credentials
- Issue Form FDA 482
- Discuss general nature of the inspection
- Tour facilities



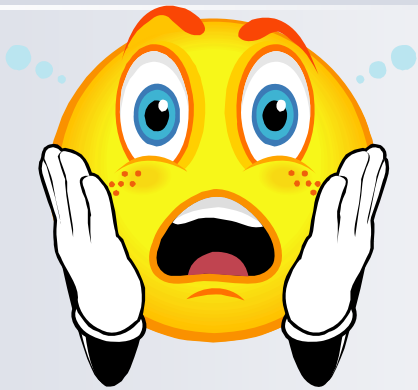
Inspection Process

- Review various records
- Collect records
- Interview relevant staff
- Discuss inspection proceedings and findings

Inspection Closeout

- Discuss final observations
- Issue Form FDA 483 “Inspectional Observations,” if needed

If you receive a 483 . . .



- Address concerns at closeout meeting
- Respond in writing within 15 working days

Written Responses

- Root cause of the problem
- Extent of the problem
- Corrective actions
- Preventative actions
- Timelines for implementation
- Supporting documentation

Post-Inspection

- Establishment Inspection Report (EIR)
- Reviews
- Classification
- Correspondence
- Follow-up actions

Inspection Classifications

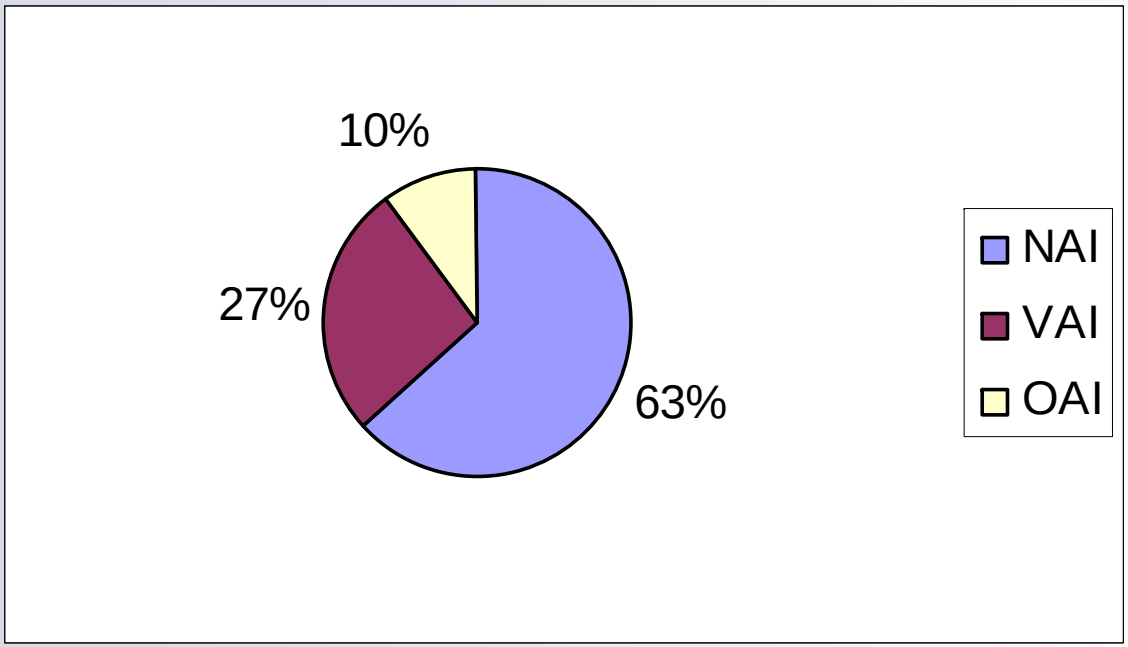
- No Action Indicated (NAI)
- Voluntary Action Indicated (VAI)
- Official Action Indicated (OAI)

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

Compliance Rate

- 2009 IVD EIRs



Top Sponsor Deficiencies

- Ensuring proper monitoring
- Securing investigator compliance
- Maintaining correspondence

Top CI Deficiencies

- Following investigational plan and FDA regulations
- Maintaining records showing reasons for protocol deviations
- Reporting deviations to sponsor and IRB

Top IRB Deficiencies

- Conducting continuing review
- Preparing and maintaining minutes

Summary

- Know your responsibilities and comply with the regulations
- Follow good research/clinical practices
- Ensure studies are based on valid scientific evidence

Resources

- IVD Studies – Frequently Asked Questions

  http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm078309.htm

- BIMO

  http://www.fda.gov/Training/CDRHLearn/ucm162015.htm#bimo

Proposed Rule

- Reporting Information Regarding Falsification of Data

Comments due 5/20/2010

http://edocket.access.gpo.gov/2010/pdf/2010-3123.pdf

THANK YOU

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