Bioresearch Monitoring

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Topics

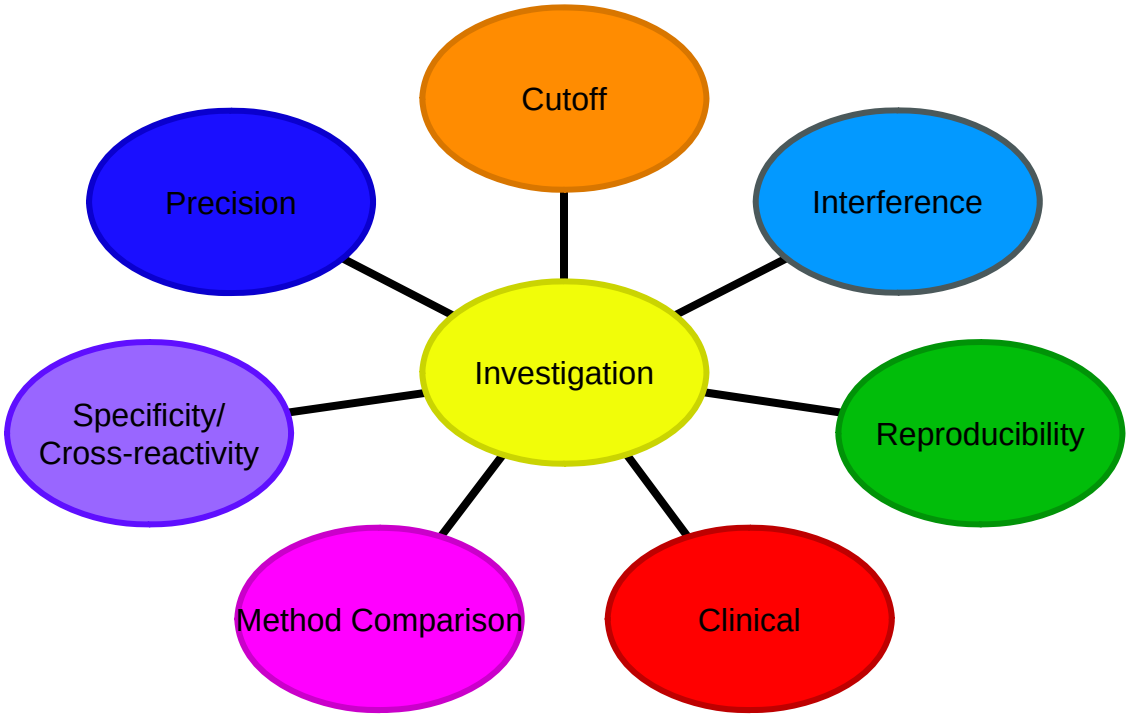
- General Responsibilities
- Sponsor Inspections & Audits
- Compliance Decisions
- Compliance Metrics

“Device Bioresearch”

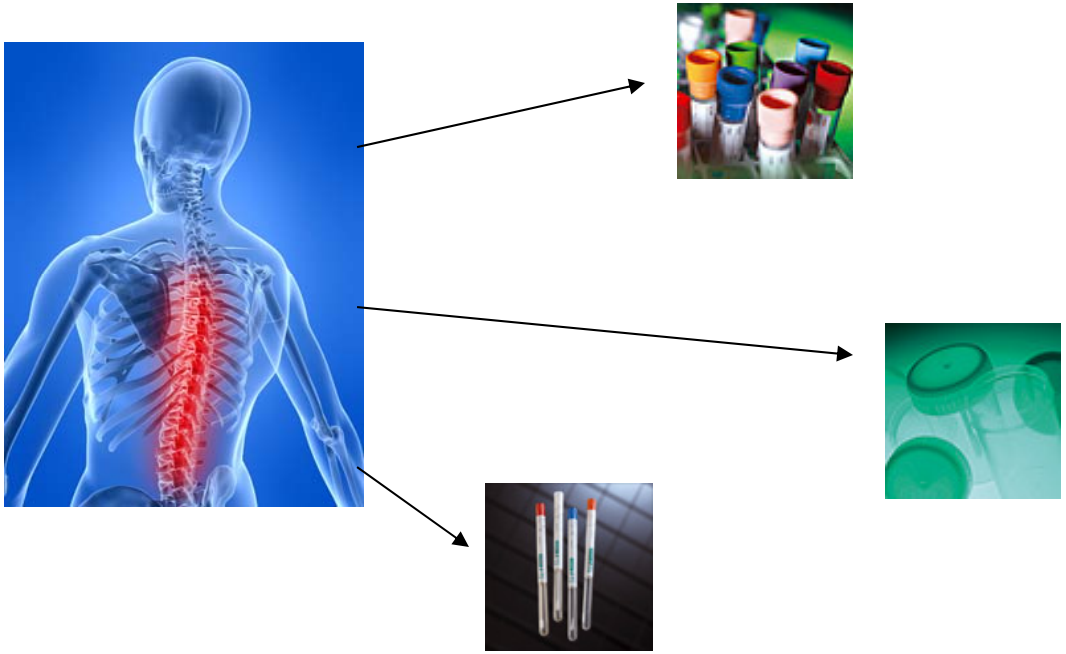
- A clinical investigation or research involving one or more subjects to determine the safety or effectiveness of a device

21 CFR 812.3(h)

Investigation



Subject



21 CFR 812.3(p)

Sponsor Responsibilities

- General Duties
- Selection of investigators
- Monitoring
- Controlling distribution & disposition of devices
- Prohibition of promotion & other practices
- Supplemental applications
- Maintaining records
- Submitting reports
- Following Good Clinical Practices

FDA Responsibilities

- Monitoring FDA-regulated research
  - Conducting on-site inspections
  - Auditing data
  - Determining compliance
  - Initiating regulatory actions

FDA Objectives

- Protecting human research subjects
- Ensuring quality and integrity of data

Inspection of Sponsors

- Selecting Qualified Investigators

Inspection of Sponsors

- Signed investigator agreements +
- Clinical investigator training

Inspection of Sponsors

- IRB information
- Informed consent information
- Monitoring information

Monitoring

- Caution: Monitoring only → Quality
- Monitoring is critical!
  - Oversight of Clinical Investigations – A Risk-Based Approach to Monitoring

    http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM269919.pdf

Inspection of Sponsors

- Data management systems and procedures

- Subject records and case report forms

Inspection of Sponsors

- Adverse events information
- Device accountability records
- Other

Inspections

- Review & collect records
- Interview relevant staff
- Discuss findings
- Issue 483, if needed

483 Response

Submit within 15 working days!

- Root cause and extent of the problem
- Corrective and preventative actions
- Timelines for implementation
- Supporting documentation

Determining Compliance

- Establishment Inspection Report (EIR)
- 483 response
- Compliance history
- Number and significance of the deviations
- Impact on human subjects
- Impact on data quality

Data Quality and Reliability

- Protocol deviations?
- Sloppiness?
- Investigator compliance issues?
- Inaccurate data? Omissions of relevant data? Changed data?
- Untrue statements?
- Pattern of errors?

Inspection Classifications

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

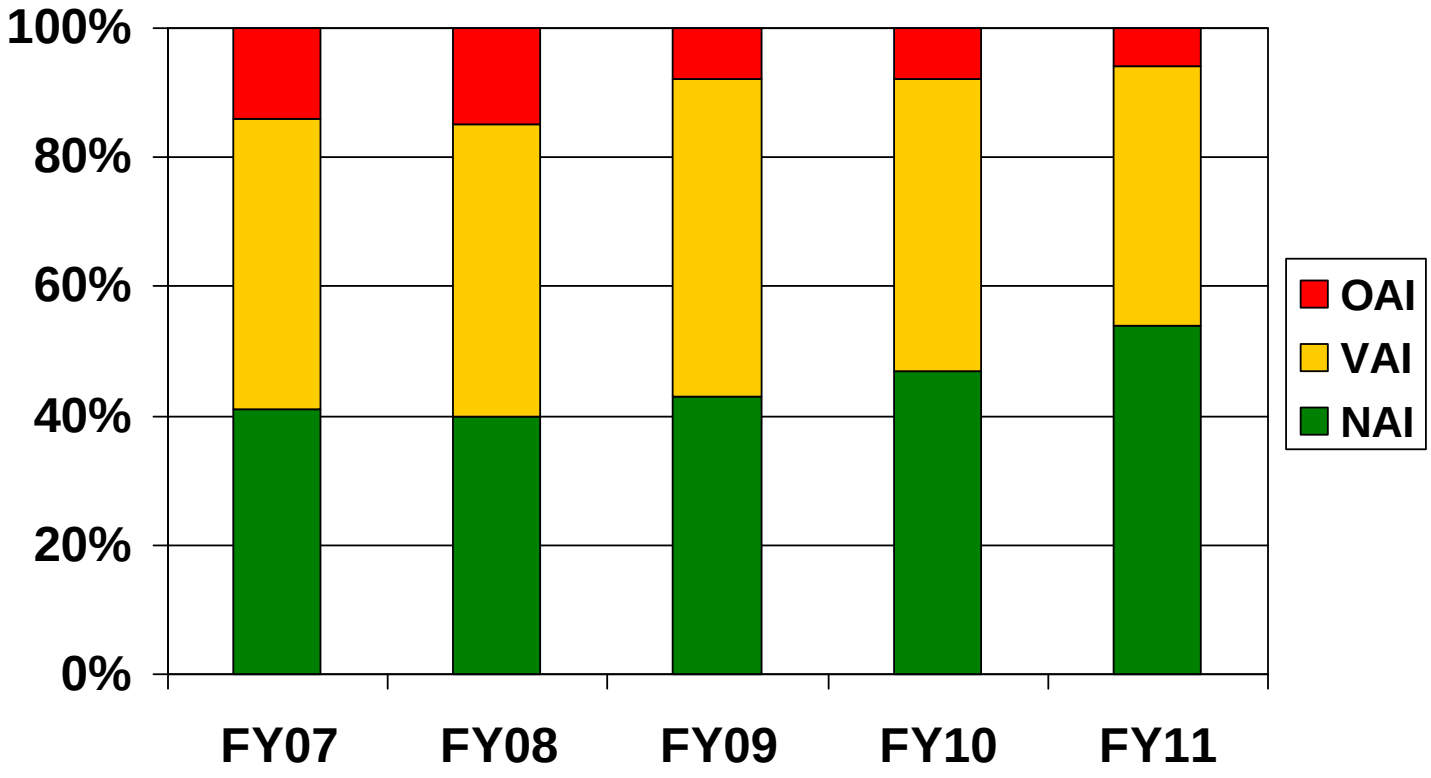
Correspondence

- Firm in Compliance Letter
- Information Letter
- Untitled Letter
- Warning Letter
- Regulatory Follow-up Letter
- Application Integrity Policy (AIP) Letter

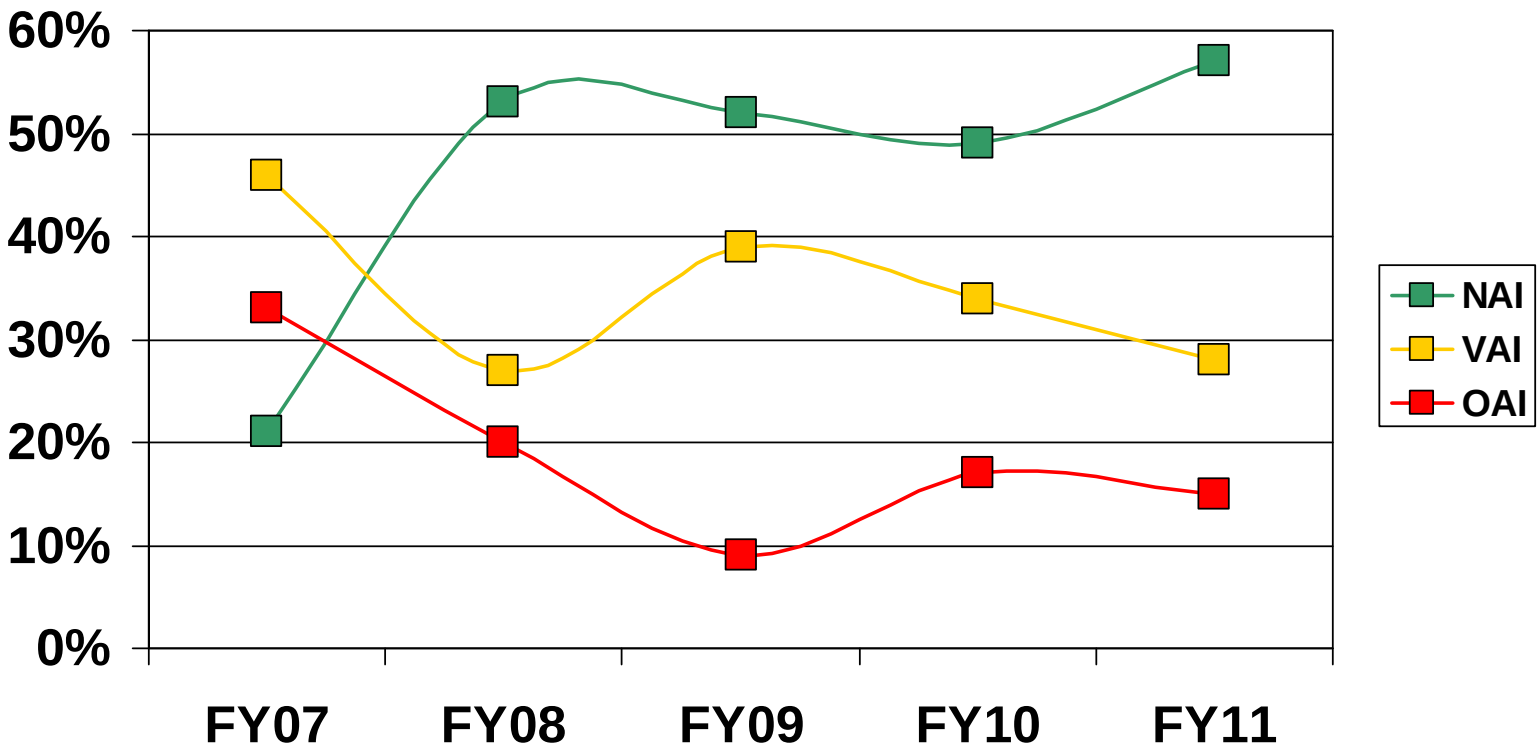
FDA Regulatory Actions

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

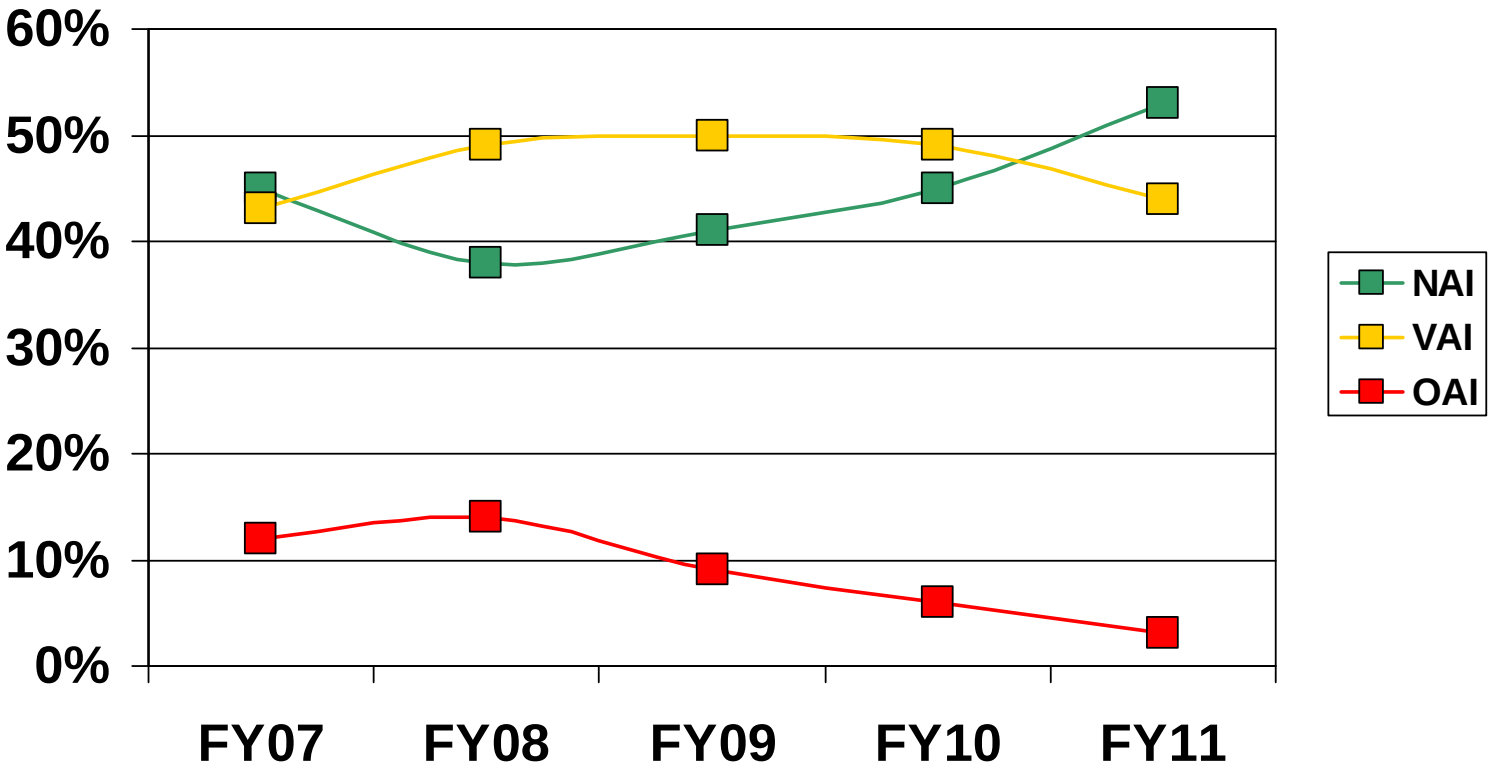
CDRH BIMO Compliance Rates



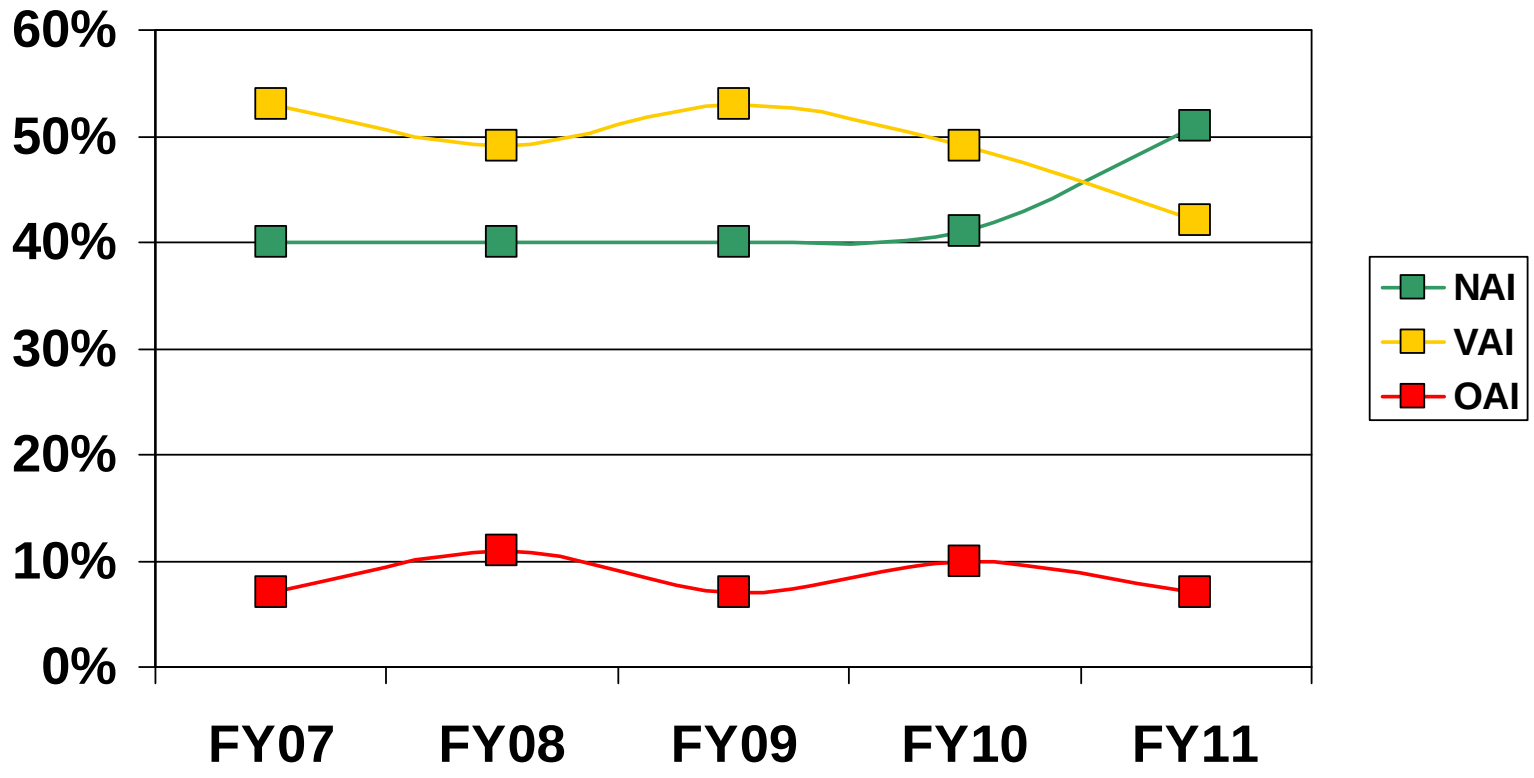
CDRH Sponsor Compliance Rate



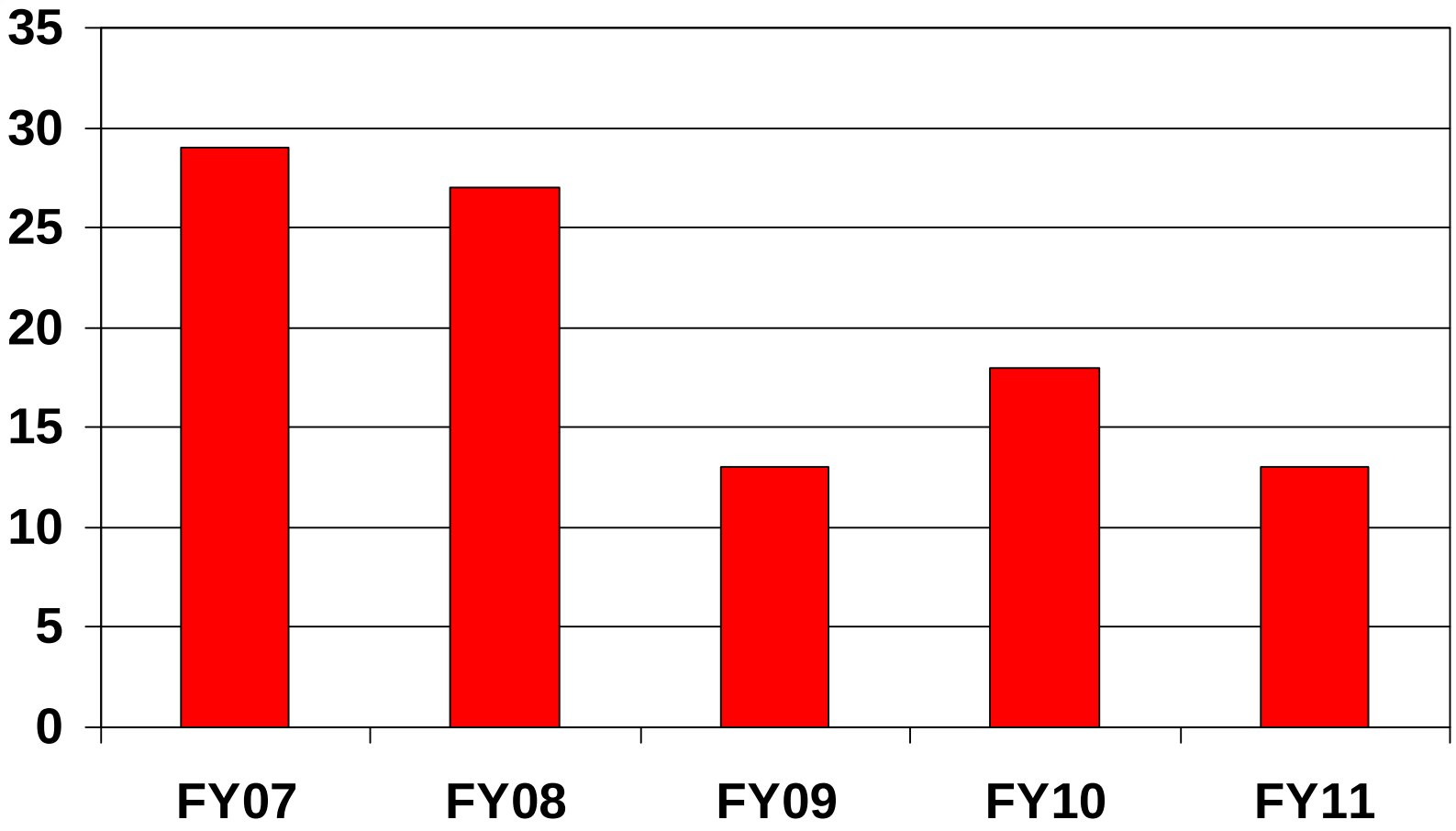
CDRH Investigator Compliance Rate



CDRH IRB Compliance Rate

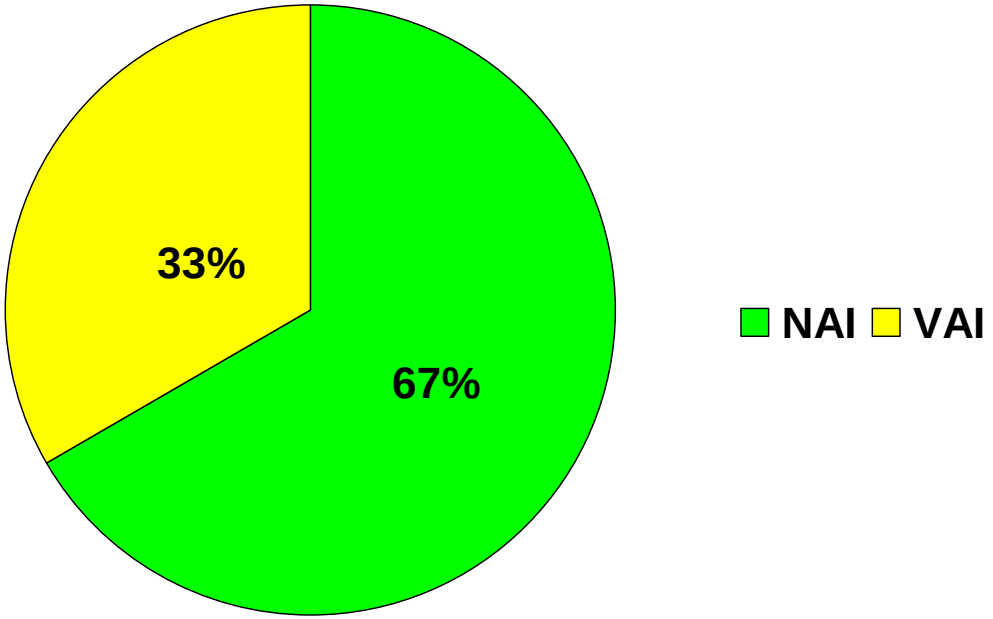


CDRH BIMO Warning Letters



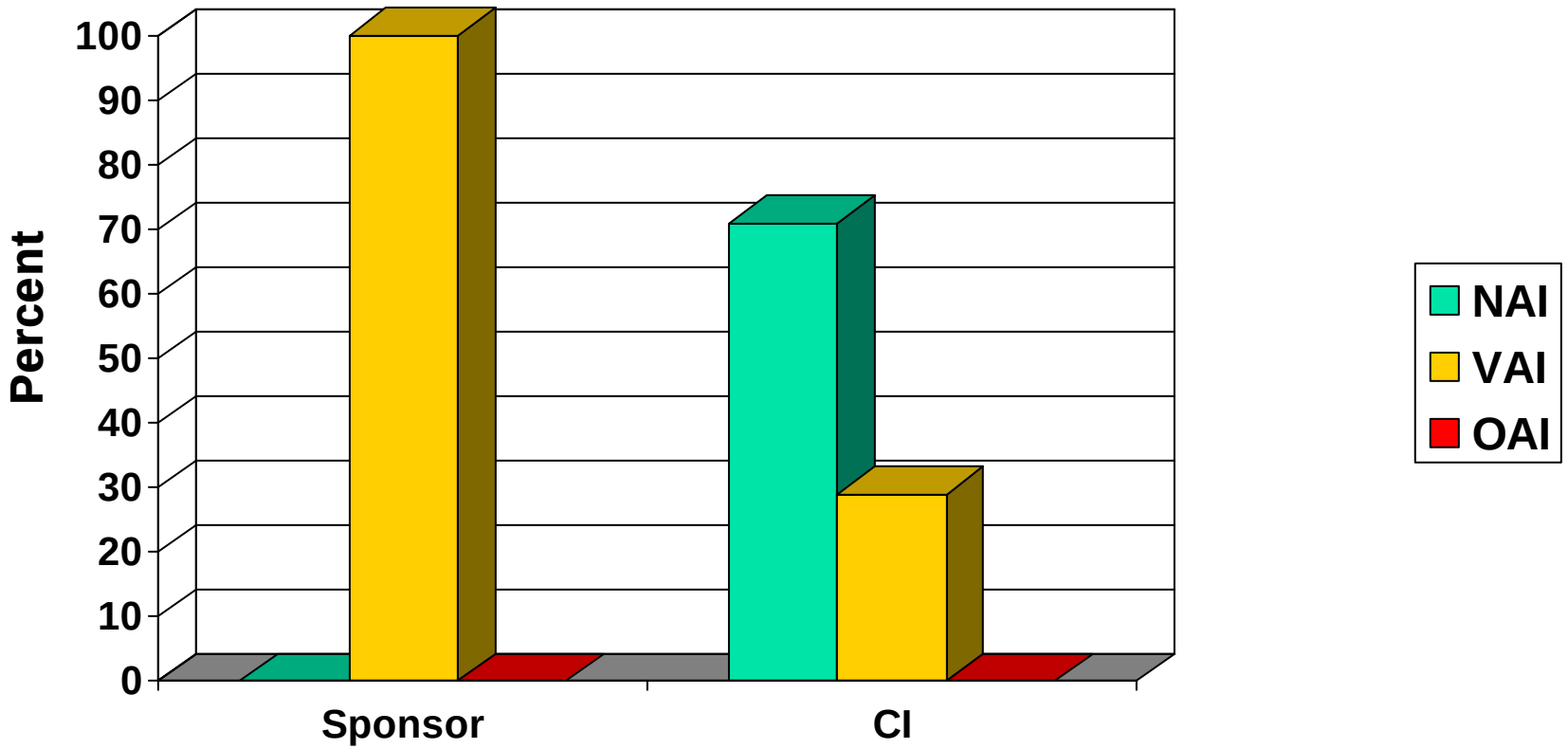
IVD BIMO Compliance Rate

FY11



9% increase in VAIs

IVD Sponsor v. CI Compliance Rate
FY11



FY11 IVD Sponsor Deficiencies

- Failure to ensure proper monitoring
- Failure to ensure IRB review & approval
- Failure to maintain accurate & complete device accountability records

FY11 IVD Investigator Deficiencies

- Failure to follow investigational plan & signed agreement
- Failure to obtain informed consent & IRB approval before allowing subject to participate
- Failure to maintain accurate & complete device accountability records

Ensuring Trial Quality & Integrity

- Protocol
- Training
- Monitoring

Don't forget to seek 

from FDA.

Updates

- Inspections of post-approval studies
- Inspections of Accredited Persons
- New informed consent element

Resources

- IVD Studies – Frequently Asked Questions

  http://www.fda.gov/downloads/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm071230.pdf

- BIMO

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

THANK YOU

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