Bioresearch Monitoring Program
Enforcing Good Clinical Practice Regulations

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Specific Learning Objectives

- You will learn which entities of government evaluate the integrity of data collected on unapproved regulated products.
- You will increase your understanding of the regulatory environment through an introduction to the surveillance of clinical and non-clinical trials of regulated products.
- You will increase your knowledge of the product approval process through the discussion of the place of the BIMO Inspection in the approval process.

- IND Regs 1963
- BIMO Program established in 1977 by a task force including industry
- Regulations for CIs and Sponsors/Monitors in 1987 (312, 314, 511, 514)
- Regulations promulgated for CIs of device studies in 1980 (812)

Who gets a BIMO inspection?
Who decides who gets a BIMO inspection?
What gets inspected?
How does it get inspected?
Why does it get inspected?
Who gets a BIMO inspection?
- Clinical Investigators
- Sponsors of Clinical Research
- Reviewers of Clinical Research (IRBs)

Who decides who gets a BIMO inspection?
- CDER- DSI (Division of Scientific Investigation) in the Office of Medical Policy
- CDRH- DBM (Division of Bioresearch Monitoring) in the Office of Compliance
- CBER- Office of Biologics Quality/Division of Inspections and Surveillance
- CVM- Center for Veterinary Medicine

What gets inspected?
- Clinical Research on products regulated by the FD&C Act
- Investigational products
- New indications for previously approved products

How does it get inspected?
- On-site inspection of records required by the FD&C Act
- Investigators in the field
- National Experts
Why does it get inspected?

- Verification of documentation provided to FDA in support of an application for approval
- Surveillance of clinical trials in vulnerable populations and/or of novel therapies
- Follow-up on complaints

How do we inspect a clinical trial?

- Assignments come from the Center that regulates the product
- Specific instructions come with the Assignment

Compliance Programs

- CPGM 7348.809, Institutional Review Board

- CPGM 7348.808, Good Laboratory Practice (Nonclinical Laboratories)
  [http://www.fda.gov/ora/compliance_ref/bimo/7348_808/default.htm](http://www.fda.gov/ora/compliance_ref/bimo/7348_808/default.htm)

- IOM (Investigations Operations Manual)
How we inspect a study at a CI.

- Make an appointment
- Open the inspection with a 482, Notice of Inspection
- Inventory the records
- Verify all subjects’ records present

- Verify Informed Consent, 100%
- Verify required reports
- Verify required IRB approvals
- Verify Investigator Agreements, 1572s, CVs, Financial Disclosures

- Verify documentation of investigator and staff training
- Perform audit of some (or all) of the data in the CRFs compared to the source documents
- Perform data listing audit against the source

Review the following files:
- IRB correspondence
- Sponsor correspondence
- Reconcile drug or device accountability records
Address the following:

- investigator control of the study
- investigator compliance with the protocol
- investigator adherence to the regulations

- deficiencies in documentation
- discrepancies in documentation
- adequacy of monitoring
- accuracy of the data

Inspection Closeout

- Inspectional findings
- Response
- Form 483, Inspectional Observations

PITFALLS

- Informed consent process
- Adverse event reporting
- Inclusion/exclusion criteria documentation
- Scheduling of study-related testing
After the inspection

- EIR
- Classification of the inspection
- NAI, VAI, OAI

Top 5 BIMO Observations:

- Conduct per IP
- Case Hx
- Drug Acnt
- No IC
- IRB Rpt

Next 5 BIMO Observations:

- IRB Minutes
- nonclin IP
- IRB SOP
- IC issues
- IRB Review

CI Inspections
Classifications, FY’03 (All Centers)

- NAI: 8%
- VAI: 5%
- OAI: 5%
- Pending: 36%
- n= 624
Clinical Investigator Inspections
All Centers - FY’04

- NAI: 12%
- VAI: 13%
- OAI: 33%
- Pending: 42%
- Total: n = 589

IRB Classifications
All Centers - FY’03

- NAI: 63%
- VAI: 4%
- OAI: 4%
- Pending: 29%
- Total: n = 317

Sponsor/Monitor/CRO Inspections All Centers - FY 03

- NAI: 17%
- VAI: 12%
- OAI: 36%
- Pending: 35%
- Total: n = 127

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- RESEARCH is the systematic testing of a hypothesis.
- RESEARCH is not Clinical Practice
Examples of Inspectional Observations

REFERENCES

- Compliance Programs
  http://www.fda.gov/ora/cpgm/default.htm
  http://www.fda.gov/ora/compliance_ref/bimo/7348_811/default.htm
  http://www.fda.gov/ora/compliance_ref/bimo/7348_810/default.htm
  http://www.fda.gov/ora/compliance_ref/bimo/7348_808/default.htm
  http://www.fdanews.com/wbi/bookstore/106-1.html ($253.00) or
  http://www.fda.gov/ora/inspect_ref/iom/ (free)