IRB Inspections

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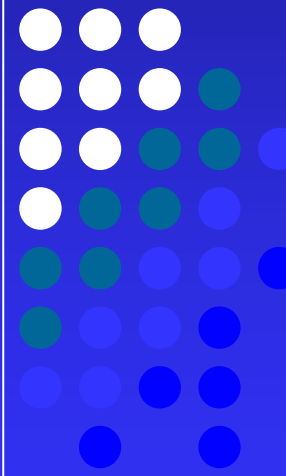

Objectives

- Inspections Program
  - OHRP
  - FDA
- Tips for Preparation
- Behavioral Guidelines

Jurisdiction

- OHRP
  - 45 CFR 46
  - OHRP approved assurance
- FDA
  - 21 CFR 56
  - 21 CFR 50

Inspections Program

- OHRP
  - For cause site visit
  - Not for cause site visit
- FDA
  - Routine surveillance inspection
  - Directed inspection

OHRP Compliance Oversight Investigation

- Receive allegation of noncompliance
- Determine OHRP jurisdiction
- Written inquiry to appropriate institutional officials
- Review of institution's report and relevant IRB documents
- Additional correspondence/telephone interview/site visit as needed
- Issue final determinations

OHRP For-Cause Site Visits

- When does OHRP conduct a site visit?
- Base on:
  - Nature and severity of the allegations
  - Evidence of systemic problems
  - Appropriateness of any corrective actions taken
  - Perceived need for more in-depth discussions with institution staff

OHRP For-Cause Site Visits

- Interview with:
  - Institutional administrator(s)
  - IRB Chairperson(s)
  - IRB members
  - IRB staff
  - Investigators who conduct human subjects research
  - Others as appropriate

OHRP For-Cause Site Visits

- Record Reviews
  - Select 50-75 active protocols for review of entire IRB record on-site
  - Last 25 protocols approved by the IRB under an expedited review procedures
  - Last 25 amendments approved by the IRB under an expedited review procedure
  - Protocols determined to be exempt during the past 6 months
  - Minutes for all IRB meetings for last 4 years

OHRP For-Cause Site Visits

- Findings
  - Meet with the signatory officials on the Assurance, or their designees on last day to describe OHRP's findings

OHRP Not-For-Cause Compliance Oversight Evaluations

Purpose of OHRP Not-for Cause Evaluations

- To assess institutional compliance with 45 CFR 46
- In absence of specific allegations
- Somewhat proactive
- Some evaluations are partially "for cause" – previous compliance problems

Status of OHRP Not-for-Cause Evaluations

- Ten institutions have been evaluated
- Two evaluations were not on-site (teleconference and paper review)
- Institutions have praised the process and felt it was a valuable learning experience

OHRP Compliance Oversight Investigation Possible Determinations/Outcomes (1)

- Protections under an institution's Assurance are
  - in compliance
  - in compliance, but recommended improvements have been identified
- Noncompliance identified, and
  - corrective actions required
  - Assurance restricted pending required corrective actions
  - OHRP approval of Assurance withdrawn

OHRP Compliance Oversight Investigation Possible Determinations/Outcomes (2)

- OHRP may recommend that HHS Officials
  - suspend
  - terminate

Compliance Oversight Investigation Possible Determinations/Outcomes (3)

- OHRP may recommend:
  - Debarment of
    - Institutions
    - Investigations

      (ineligible for HHS research support)

FDA IRB Inspections

- Selection Criteria
  - Past inspection history
    - Frequency
    - Compliance status
  - Activity of IRB
  - New IRBs
  - Complaints

FDA IRB Inspections

- Routine
  - Inspections assigned on cyclic basis for surveillance
- Directed
  - Complaints to FDA
    - FDA, other agencies
    - Sponsor/monitor
    - Subjects/Public

FDA IRB Inspections

- Inspections are announced and scheduled in advance
  - Consist of interviews with responsible IRB staff
  - In-depth review of SOPs , files and records
  - Active FDA regulated studies

Scope of FDA IRB Inspections

- IRB membership
- Written procedures
- Initial review and approval of studies
- Continuing review of research
- IRB reporting to investigator and institution

FDA IRB Inspections

- Discuss IRB administration and procedures
  - Individual responsibility and authority
  - Membership
  - Operations
  - Record keeping requirements
  - Review and approval of informed consent

FDA IRB Inspections

- Record Review
  - SOPs
    - Must have written procedures as required by 21 CFR 58.108
    - Should agree with procedures described during interview

FDA IRB Inspections

- Inspection of IRB files-FDA regulated study files
  - Minutes of meetings
  - List of IRB members
  - Documents submitted to IRB to obtain study approval
  - Correspondence between IRB and investigator
  - Records of continuing review
  - Any other records

Conclusion of FDA IRB Inspection

- Exit interview with management
  - Discussion of inspection findings
  - Issuance of an FDA 483

Post FDA IRB Inspection

- Detailed Narrative Report Prepared
- Submitted to HQ BIMO Staff for Evaluation

FDA Compliance Inspection Classification (1)

- NAI – No Action Indicated
- VAI – Voluntary Action Indicate
  - Objectionable conditions or practices were found, but FDA is not prepared to take or recommend any administrative of regulatory action

FDA Compliance Inspection Classification (2)

- OAI – Official Action Indicated
  - Regulatory and/or Administrative actions will be recommended due to significant objectionable observations

Post FDA IRB Inspection

- Correspondence
  - Sent to IRB Chair
  - Describes which practices or conditions, were determined to be objectionable
  - Letters are sent for serious noncompliance and require a response

Tips Prior to Inspection (1)

- Know what the regulatory requirements are for your operations
  - 21 CFR 50 and 56 IRBs and informed consent
  - 21 CFR 312 Clinical Investigators and Sponsors of Drugs and biologics
  - 21 CFR 812 Clinical Investigators of Medical Devices

Tips Prior to Inspection (2)

- Obtain and be familiar with the Compliance Program covering your operation
- Retain all records necessary to completely reconstruct activities and findings

Tips During the Inspection (1)

- Have the most responsible personnel available
  - IRB Chair
  - IRB administrator/Exec. Sec.
  - Institutional official

Tips During the Inspection (2)

- Have all records readily available and organized
- Be available throughout the inspection to answer questions

Tips During Inspection (3)

- Update records, organized and be available
  - Inventory of ongoing research and current status
  - IRB SOPs covering current practices
  - IRB membership rosters, current and past
  - IRB meeting minutes
  - Records of tracked studies
    - Protocol, consent forms, IRB correspondence, etc.

Behavioral Guidelines

Rules to Follow During Inspection

- Know the contents of your job description
- Be aware of your body language
- Never remain in the room to chat with a inspector after you have answered all inspection related questions.

More to do's…

- Be yourself
- Remain focused
- Answer only the question asked

More to do's…

- Think before you answer. There are no bonus points for being fast
- Remain calm, remember you do your job every day, and no one knows your job as well as you

What is Redacting?

- Redacting is the act of selecting or adapting for publication or release
- Remove all information that the inspector is not legally entitled to see

Use Caution During Inspection

- Don't fill in the silences
- Don't allow yourself to become irritated. Maintain a professional demeanor at all times

More cautions…

- Answer all "yes" or "no" questions with "yes" or "no"
- Do not editorialize or volunteer information

More cautions…

- Never hand a document directly to a inspector - - - always pass documents to the inspection team leaders

More cautions…

- Never volunteer information on any subject
- Never refer to another topic, area, or procedure when answering a question

Body Language

- Do not sit on the edge of your chair,
- Make eye contact
- Do not play with your hair, twirl your thumbs, click your ink pin, or tap your fingers

Body Language

- Do not watch the door
- Never cross your arms over your chest or slouch in your chair

Statement to Avoid…

- "It's supposed to do (fill in the blank)."
- "Wow, it usually never does it right the first time!"
- "Do you want to know how it is supposed to happen or how it really happens?"

Statement to Avoid…

- "I didn't even know we had an SOP for that!"
- "I didn't even know the SOP said that."
- "I don't know (with no follow-up)."

Statement to Avoid…

- "Let me show you what we do for Pfizer (or any other client)."
- "Would you like to see all our metrics?"
- "Well, I can try to do that for you, but I've never really been trained."