When the Feds Come A-Knockin': How to Prepare for an OHRP Evaluation of Your Program

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Presentation Overview

- Background and OHRP compliance oversight procedures
- Preparing for an OHRP evaluation
- Common findings
- Test your knowledge
- Conclusions and resources

OHRP's Jurisdiction

- Research involving human subjects conducted or supported by HHS that is not otherwise exempt

and

- Non-exempt human subject research covered by Assurance of Compliance

Compliance Oversight Investigation

- Receive allegation or indication of noncompliance
- Determine OHRP jurisdiction
- Send written inquiry to appropriate institutional officials
- Review institution report and relevant IRB documents
- Communicate with institution as needed (correspondence/telephone interviews/site visit)
- Issue final determinations

Poll

- Compliance Oversight Interactions

A. My institution has been the subject of a for-cause OHRP evaluation

B. My institution has been the subject of a not-for-cause OHRP evaluation

C. My institution has been blessedly free of compliance oversight intervention from OHRP

May Refer Complaint

- FDA
- Other Common Rule agency
- Other HHS agency

Preparing for an OHRP evaluation

Suggestions on Preparing for an Inquiry

- Review "OHRP Recent Compliance Oversight Determinations" 02-04-2009

http://www.hhs.gov/ohrp/compliance/findings/index.html

- Re-review regulations, particularly the subparts
- Review OHRP guidance documents
- Review your institution's SOPs and update as necessary
- Ensure clear and consistent documentation of IRB activities
- Designate one contact person for the compliance oversight coordinator who will coordinate requests, questions, etc.

For-Cause vs. Not-For-Cause

- For-Cause: Responds to substantive allegations or indications of noncompliance in HHS-supported research or under an applicable assurance; usually through correspondence (>90%)
- Not-for-Cause: Assesses institutional compliance with 45 CFR 46 in absence of specific allegations; can be partially "for-cause" (previous compliance problems or vague allegations); often through site visit (~1/3)

For-Cause Site Visit

- Decision to conduct a for-cause site visit is based on
  - Nature and severity of allegations
  - Evidence of systemic problems
  - Appropriateness of any corrective actions
  - Perceived need for more in-depth discussions with institution staff

Site Visits Differ

For-cause:

- Triggered by open compliance case
- Site visit team includes OHRP lawyer,
  2-5 OHRP staff,
  2-4 outside consultants
- 3-4 days
- Dual focus on allegations and systemic protections

Not-for-cause:

- No open compliance case
- Site visit team consists of 1-3 OHRP compliance staff plus 1-3 outside consultants
- 2-3 days
- Focus on systemic protections

Record Reviews for Site Visits

- Prior to visit, OHRP selects 25 to 75 active protocols for on-site review of entire IRB record
- Institution must also have available:
  - Last 25 protocols and amendments approved by IRB under expedited review procedures
  - Protocols determined to be exempt during the past 6 months
  - Minutes for all IRB meetings for past 4 years

Interviews at Site Visits

- Institutional administrator(s)
- IRB chairperson(s)
- IRB members
- IRB staff
- Investigators research related to allegations (for-cause only)
- Investigators who conduct human subjects research (chosen by institution)
- Others as appropriate

Institutional/IRB Preparation for OHRP Site Visit: Location

- Requested files should be easily accessible to OHRP team
  - In room where record review happening, or
  - Transportable between rooms
- Make available staff to retrieve additional requested items
- Ensure adequate space for OHRP site visit team to conduct record review

Institutional/IRB Preparation for OHRP Site Visit: Records

- Are files in order? Easy to follow chronologically?
- Does institution have an electronic filing system? OHRP access to electronic files? Easy to follow?
- Are excerpts from minutes in each IRB file? If not, are minutes easily available?

Institutional/IRB Preparation for OHRP Site Visit: Interviews

- Confirm that parties to be interviewed by OHRP will be available at the specified times
  - Allow adequate time to contact investigators prior to site visit
  - Ensure availability of a variety of investigators
- If IRB members or investigators will teleconference, ensure technological facilities/capabilities

After Site Visit

- OHRP will send a letter with official findings and additional questions/concerns within a few weeks
- Institution will be asked to respond with corrective action plans within about 6 weeks
- OHRP will evaluate adequacy of corrective action plans

Compliance Oversight Investigation
Possible Determinations/Outcomes (1)

- Protections under an institution's Assurance are in compliance
- Protections under an institution's Assurance are in compliance, but recommended improvements have been identified
- Noncompliance identified, corrective actions required
- Noncompliance identified, Assurance restricted/suspended pending required corrective actions

Compliance Oversight Investigation
Possible Determinations/Outcomes (2)

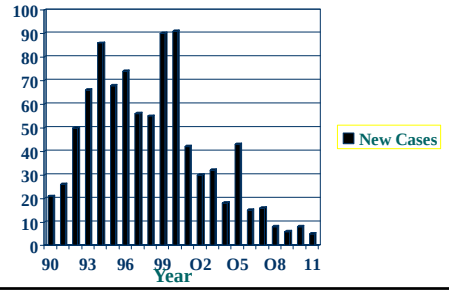
- Noncompliance identified, OHRP approval of Assurance withdrawn
- OHRP may recommend to appropriate HHS officials or PHS agency heads that
  - **an institution or investigator be temporarily suspended or permanently removed from participation in specific project**
  - **peer review groups be notified of an institution's or an investigator's past noncompliance prior to review of new projects**

Compliance Oversight Investigation
Possible Determinations/Outcomes (3)

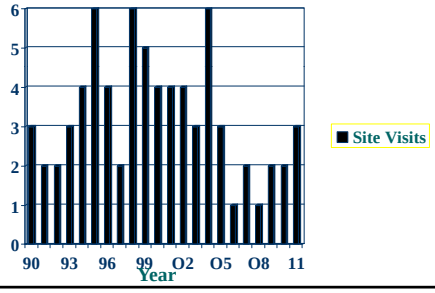
- OHRP may recommend that institutions or investigators be declared ineligible to participate in HHS-supported research (debarment). Debarment initiated in accordance with procedures specified at 45 CFR Part 76.

OHRP Compliance Data

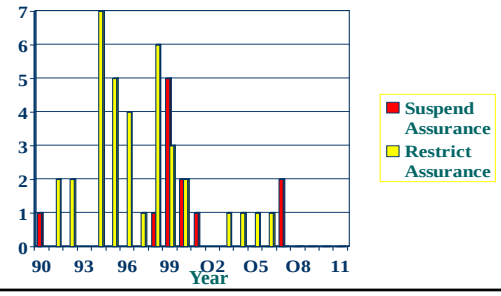
OHRP Compliance Oversight
New Cases Initiated – 1990-2011



OHRP Compliance Oversight
Site Visits – 1990-2011



OHRP Compliance Oversight
Suspend/Restrict Assurance – 1990-2011



Common Findings

- Determination letters: http://www.hhs.gov/ohrp/compliance/letters/index.html
- Significant findings: http://www.hhs.gov/ohrp/compliance/findings.pdf
- Borror et al., "A Review of OHRP Compliance Oversight Letters." *IRB: Ethics and Human Research*. Sept-Oct 2003; Vol. 25 No 5: 1-4.
- Weil et al., "OHRP Compliance Oversight Letters: *An Update" IRB: Ethics and Human Research*. March-April 2010; Vol. 32 No 2: 1-6.

Most Common Findings (1)

- **Informed consent documents deficient with respect to risks and discomfort, other elements** [45 CFR 46.116(a)(2)]
- **Insufficient information to make determinations required for approval** [45 CFR 46.111]
- **Inadequate written procedures** [45 CFR 46.103(a) and 46 103(b)(4)(5)]

Most Common Findings (2)

- **Failure to obtain legally effective informed consent** [45 CFR 46.116]
- **Protocol changes without IRB review** [45 CFR 46.103(b)(4)(iii)]
- **Failure to conduct continuing review at least annually** [45 CFR 46.109(e)]
- **Inadequate IRB minutes** [45 CFR 46.115(a)(2)]

Most Common Findings (3)

- **Failure to report noncompliance, etc.** [45 CFR 46.103(a) and 46 103(b)(5)]
- **Expedited review conducted by someone other than an experienced IRB member** [45 CFR 46.110(b)]
- **Failure of IRB to make and document required findings for waiver of informed consent** [45 CFR 46.117(c)]

Test Your Knowledge

Consent Document Deficient with Respect to Risks and Discomfort

- **§46.116(a)(2)** states that in seeking informed consent the following information shall be provided to each subject … A description of any reasonably foreseeable risks or discomforts to the subject

Risks and discomforts- Need to be in Informed Consent Document?

POLL

1. Risks associated with add'l PET scans
2. Risks of standard care if dictated by protocol
3. New findings of risks in a study arm
4. Risks of violation of confidentiality -could damage a subject's reputation
5. None of the above

Insufficient Information to Make Determinations

- **§46.111** In order to approve research covered by this policy the IRB shall determine that all of the following requirements are satisfied:
  - Risks to subjects are minimized and reasonable in relation to anticipated benefits
  - Selection of subjects is equitable
  - Informed consent will be sought and documented
  - Study has adequate provision for monitoring
  - Study has adequate provisions to protect privacy
  - Study has additional appropriate safeguards for vulnerable subjects

The IRB May Approve Research with the Following Questions/ Conditions without Re-review by Convened IRB

POLL

1. Concern about supervisors encouraging their employees to participate in research.
2. Info on where biopsies were taken from.
3. Precise language changes to protocol or ICDs.
4. Substantive changes with clearly stated parameters that the changes must satisfy.

Inadequate Written Procedures

- §46.103(a)&(b)(4) & (5) requires that institutions have written procedures that the IRB will follow:
  - Initial and continuing review
  - Reporting findings
  - which projects need verification of no changes
  - prompt reporting to the IRB of proposed changes
  - Reporting of
    - Unanticipated problems
    - Suspension/termination of IRB approval
    - Serious or continuing noncompliance

Do the Regulations Require the following Written Procedures?

POLL

1. The procedures for determining when to audit research.
2. Procedures for determining exemptions.
3. Procedures for reporting suspension by DSMB.
4. Procedures for approving research involving prisoners.
5. None of the above.

Which of the Following Need to be Reported to OHRP?

POLL

1. Subjects' confidential contact information was used inappropriately by study staff.
2. Non-exempt human subjects research conducted without IRB review/approval.
3. Suspension/Terminations of sponsor approval.
4. Study drug dosing errors.
5. None of the above.

Protocol Changes without IRB Review

- §46.103(b)(4) requires that IRBs ensure prompt reporting to the IRB of proposed changes in a research activity, and for ensuring that such changes in approved research, during the period for which IRB approval has already been given, may not be initiated without IRB review and approval except when necessary to eliminate apparent immediate hazards to the subject.

The Regs require IRB review of which of the following protocol changes?

POLL

1. Enrolling ineligible subjects.
2. Added lab to test for emergent risk.
3. Increase enrollment limits.
4. New recruitment ads.
5. None of the above.

Required Findings for Waiver of Informed Consent

- 45 CFR 116. (d) An IRB may approve a consent procedure which does not include, or which alters, some or all of the elements of informed consent set forth in this section, or waive the requirements to obtain informed consent provided the IRB finds and documents [four specific findings]

Waive Informed Consent for the Following Studies?

POLL

1. Record review study.
2. Research involving couple therapy in alcohol treatment.
3. Study on teaching vascular surgery interns vascular surgery skills.
4. Deception research.
5. None of the above.

Conclusions and Resources

Solutions to Correct/Prevent Noncompliance

- **Education**
- **Adequate IRB staff and resources**
- **Adequate number of IRBs**
- **Adequate IRB documentation (in particular, adequate minutes of IRB meetings)**
- **Periodic self-assessment of institutional system for protecting human subjects**
- **Adequate written procedures**

OHRP Education Resources

- Research Community Forums
- Speaking invitations
- OHRP website --http://www.hhs.gov/ohrp/
- OHRP Email Box -- ohrp@hhs.gov
- Quality Assessment Program
- Training videos and other materials

http://www.hhs.gov/ohrp/education/training/ded_video.html

OHRP Quality Improvement (QI) Resources

- Quality Assurance (QA) Self-Assessment Tool http://www.hhs.gov/ohrp/education/qip/ohrp_dedd_qatool.html
- QI Consultation
- QI/Standard Operating procedures workshops

OHRP Contact Information

- OHRP website: http://www.hhs.gov/ohrp/
- OHRP telephone: 1-866-447-4777
- OHRP e-mail: ohrp@hhs.gov

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