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

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OHRP

# Presentation Overview

- DCO Procedures
- Preparing for an OHRP evaluation
- Common Findings

# OHRP's Jurisdiction

- Research involving human subjects conducted or supported by HHS (or other Federal Department or Agency that has adopted the federal policy) 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
- Written inquiry to appropriate institutional officials
- Review of institution report and relevant IRB documents
- Additional correspondence/telephone interviews/site visit as needed
- Issue final determinations

# Opening a compliance case

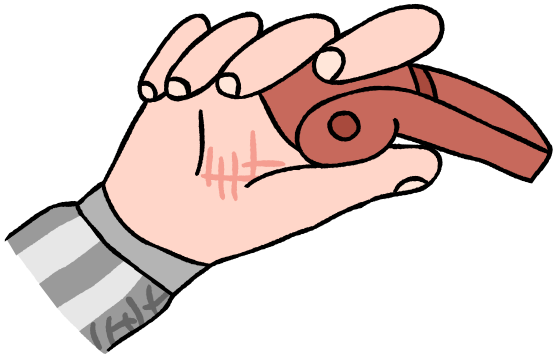
- OHRP's possible responses to initial institutional response:
  - Send another letter, asking additional questions and expressing concerns
  - Conduct phone interviews
  - Conduct an on-site evaluation of human subject protections

# Poll

A. My institution has been the subject of a for-cause OHRP evaluation
B. My institution has been the subject of a for-cause OHRP evaluation
C. My institution has been blessedly free of compliance oversight intervention from OHRP

# May refer case to others

- FDA
- Other Common Rule Agency
- Other HHS Agency



# For-Cause vs Not-for-Cause

- For-Cause- substantive allegations or indications of noncompliance in HHS-supported research or under an applicable assurance; usually through correspondence (>90%)
- Not-for-Cause- To assess 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 (~2/3)

# For-Cause Site Visit

- When does OHRP conduct a for-cause site visit? Decision 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

# Difference between FC and NFC Site visits

**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 on 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 of human subjects

# Record Reviews for Site Visits

- Prior to site visit, OHRP selects between 25 and 75 active protocols for review of entire IRB record on-site
- Records institution must 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 last 4 years

# Interviews at Site Visits

- Institutional administrator(s)
- IRB Chairperson(s)
- IRB members
- IRB staff
- Investigators in research complained about (for-cause only)
- Investigators who conduct human subjects research
- Others as appropriate

# Institutional/IRB preparation for OHRP site visit – space issues

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

# Institutional/IRB preparation for OHRP site visit – records/files

- Are files in order? Easy to follow chronologically?
- Access to electronic files? Easy to follow interface between electronic files and paper files?
- 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
  - Variety of investigators
- If IRB members or investigators will be teleconferencing, ensure technological facilities/capabilities

# After site visit

- OHRP will send a letter with official findings (of noncompliance) 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, and corrective actions required
- Noncompliance identified, and Assurance restricted/suspended pending required corrective actions

# Compliance Oversight Investigation
## Possible Determinations/Outcomes (2)

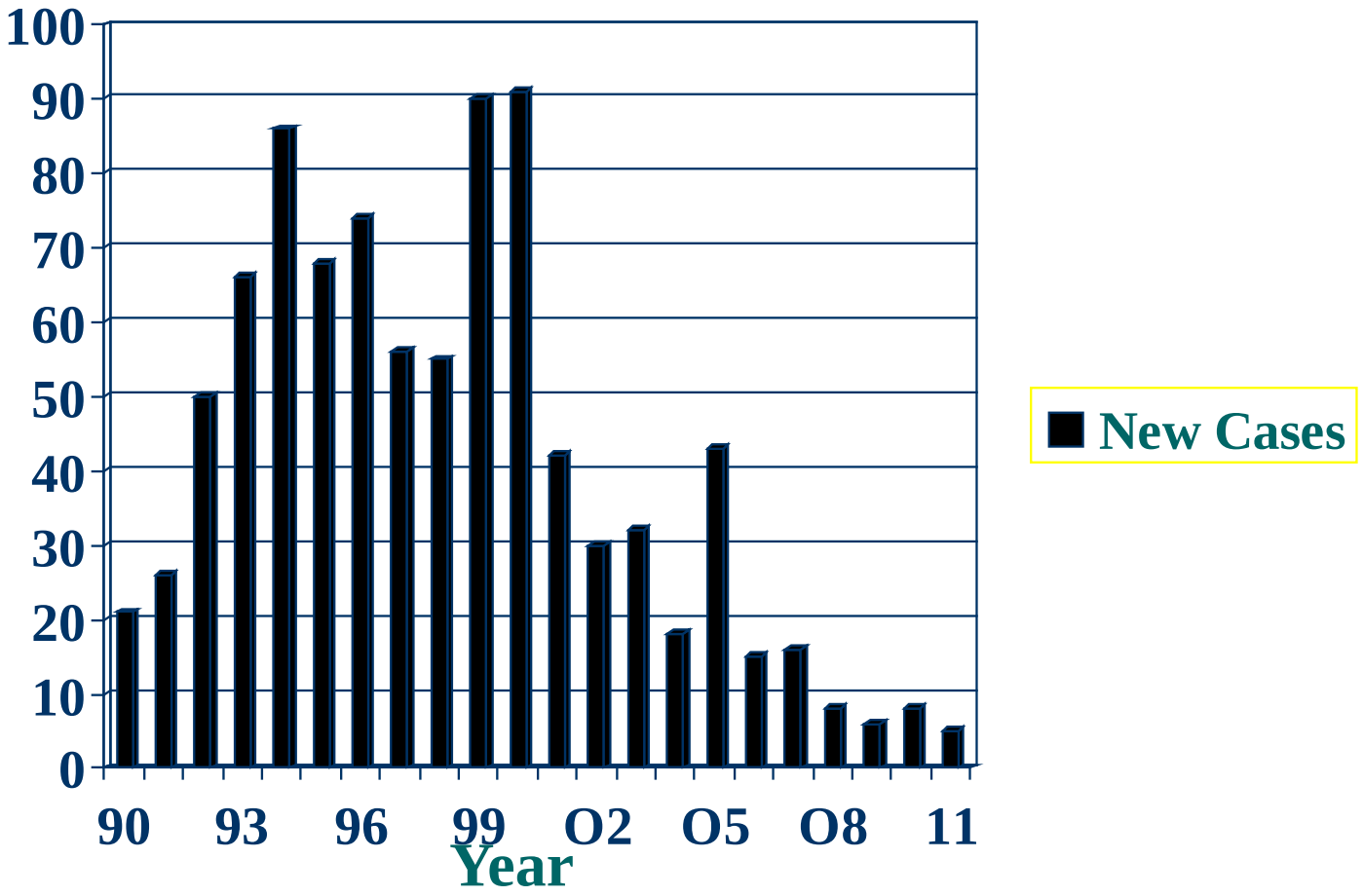
- Noncompliance identified, and OHRP approval of Assurance withdrawn
- OHRP may recommend to appropriate HHS Officials or PHS agency heads that:
  - **an institution or investigator be temporarily suspended or permanently removed from participation in specific project**
  - **peer review groups be notified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

# Compliance Oversight Investigation
## Possible Determinations/Outcomes (3)

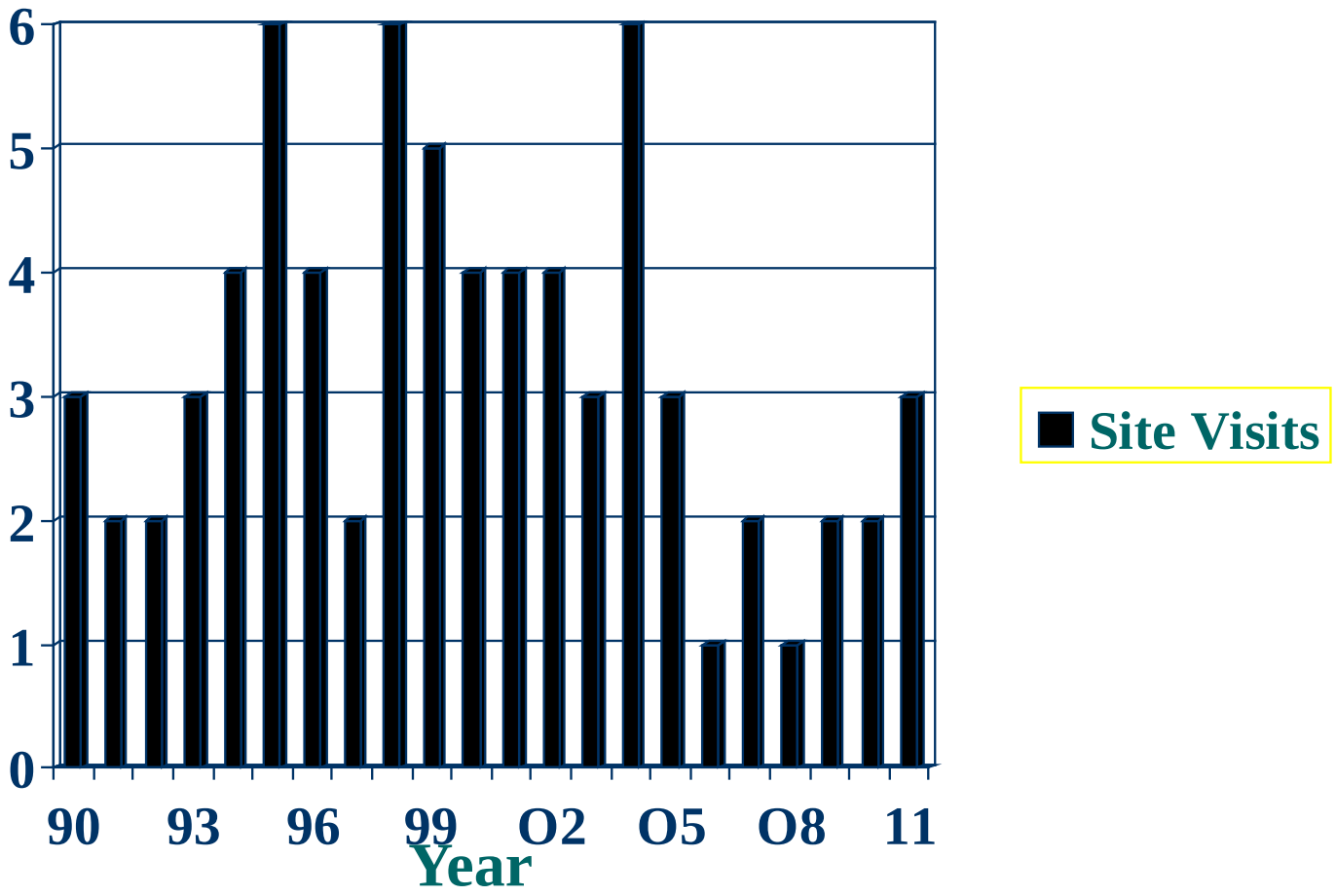
- OHRP may recommend that institutions or investigators be declared ineligible to participate in HHS-supported research (Debarment). Debarment will be initiated in accordance with procedures specified at 45 CFR Part 76.

# OHRP Compliance Data

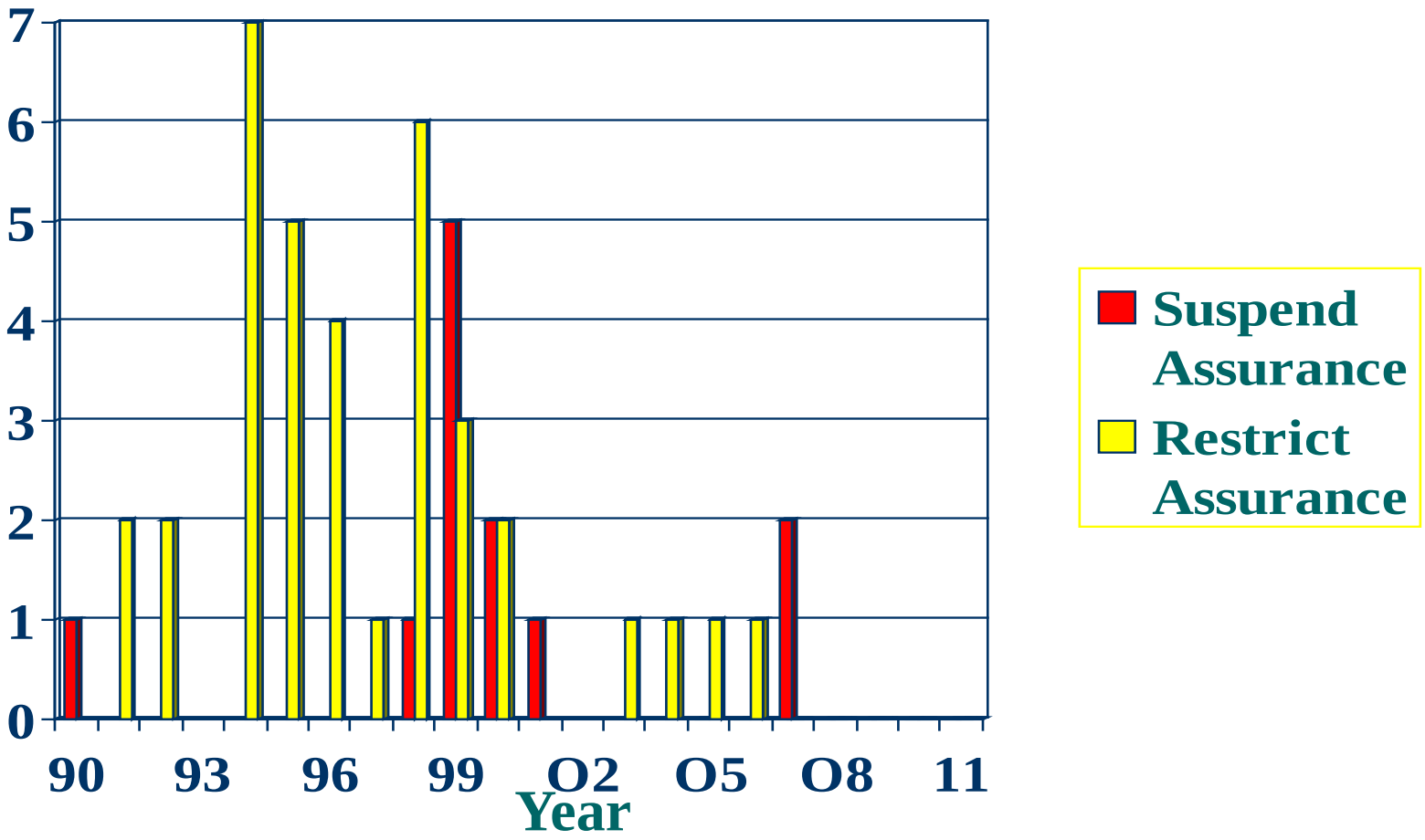
# OHRP Compliance Oversight
## New Cases Initiated – 1990-2011



# OHRP Compliance Oversight
## Site Visits – 1990-2011



# OHRP Compliance Oversight
## Suspend/Restrict Assurance – 1990-2011



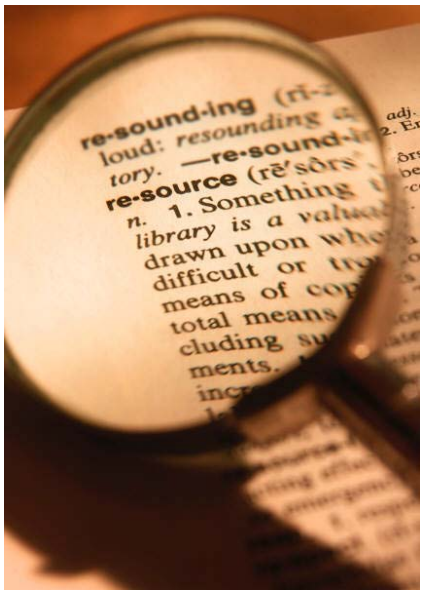
# OHRP Education Resources

- 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 QI Resources

- QA Self-Assessment Tool-- http://www.hhs.gov/ohrp/education/qip/ohrp_ded_qatool.html
- QI Consultation
- QI/SOP workshops



# 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

# 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 46.116(a)(2): risks and discomfort; and other elements
- Insufficient info 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)]

# ICD deficient with respect to risks and discomfort-Regulations

- **§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 ICD?

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

A. 1 and 3

B. 1, 3, & 4

C. 1 and 4

D. All of the above

# Insufficient info to make determinations- Regulations

- **§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 doc'd
  - adequate provision for monitoring
  - adequate provisions to protect privacy
  - additional safeguards for vulnerable subjects

# The IRB may approve research with the following questions/ conditions without re-review by convened IRB-

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

A. 1 and 2

B. 1 and 3

C. 3 and 4

D. None of the above

# Inadequate written procedures-Regulations

- §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 regs require the following written procedures?

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.

A. 1

B. 1 and 2

C. 1, 3, and 4

D. None of the above

# Which of the following need to be reported to OHRP?

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 DSMB approval
4. Study drug dosing errors

A. 1 and 2

B. 1, 2, and 3

C. 1, 2 and 4

D. All of the above

# Protocol changes without IRB review- Regulations

- §46.103(b)(4) requires 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?

1. Enrolling ineligible subjects
2. Added lab to test for emergent risk
3. Increase enrollment limits
4. New recruitment ads

A. 1 and 2
B. 1, 3, and 4
C. 1, 2, and 3
D. All of the above

# Required findings for waiver of informed consent-Regulations

- 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?

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

A. 1
B. 1 and 4
C. 1, 2, and 3
D. All of the above

# 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 Contact Information

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