Overview of OHRP's Compliance Oversight Activities

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Presentation Overview

- OHRP's jurisdiction and authority
- OHRP compliance oversight activities
- Common areas of noncompliance identified by OHRP
- Underlying causes of noncompliance
- Solutions to correct/prevent noncompliance

OHRP's Jurisdiction and Authority

Title 45
Code of Federal Regulations
Part 46

Protection of Human Subjects

(Last revised November 13, 2001)

Ethical Framework for 45 CFR Part 46 The Belmont Report

- Respect for Persons
- Beneficience
- Justice

Fundamental Provisions of 45 CFR Part 46

- IRB review
- Legally effective informed consent
- Assurance of Compliance

OHRP's Jurisdiction

- Research conducted or supported by the Department of Health and Human Services (HHS)
- Research conducted at an institution holding an applicable Assurance of Compliance

OHRP Compliance Oversight Activities

OHRP Compliance Oversight Activities

- For-cause compliance oversight investigations (over 750 since January 1990)
- Not-for-cause compliance oversight evaluations (a few prior to 9/01; 5 since 9/01)

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

OHRP Compliance Oversight Site Visit

- Duration: 2-3 days
- Site visit team: 3-4 OHRP staff and 3-4 outside expert consultants
- Record review
- Interviews
- Presentation of findings at exit briefing

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 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- Noncompliance identified, and OHRP approval of Assurance withdrawn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.

Level of Noncompliance

- Investigator
- Institutional review board
- Senior institutional officials

Common Areas of Noncompliance Identified by OHRP

Common Areas of Noncompliance (1)

- OHRP Compliance Activities: Common Findings and Guidance – 7/10/02 http://ohrp.osophs.dhhs.gov/references/findings.pdf

- http://ohrp.osophs.dhhs.gov/detrm_letrs/lindex.htm

Common Areas of Noncompliance

- Initial and continuing IRB review
- Expedited IRB review procedures
- Reporting of unanticipated problems
- IRB review of protocol changes
- Informed consent
- IRB membership, expertise, staff, support, and workload
- Documentation of IRB procedures, activities, and findings

Analysis of data on OHRP's findings of noncompliance

Analysis of data on OHRP's findings of noncompliance (1)

- Compliance oversight letters issued between 10/01/98 and 6/30/02
- 269 determination letters to 155 institutions
- 18 institutions site-visited
- 1,120 citations of noncompliance or deficiencies
- 142 institutions (92%) had at least one finding (range 0-53, median 4)

Cited Deficiency	All Institutions (N = 155)	Site-Visited Institutions (N = 18)
Research conducted without IRB review	17%	22%
Deficiency in IRB initial review process	55%	94%
Deficiency in IRB continuing review process	45%	72%
Deficiency in use of expedited IRB review procedure	17%	61%
Deficiency in satisfying reporting requirements	17%	39%
Deficiency in IRB review of protocol changes	25%	39%
Deficiency in application of exempt categories of research	6%	28%
Failure to obtain informed consent of subjects	16%	11%
Deficiency in documentation of informed consent	8%	6%
Deficiency in IRB-approved informed consent docs/process	51%	78%
Deficiency in IRB membership	11%	61%
IRB members lack sufficient understanding of regulations	7%	44%
Indequate IRB meeting space, staff, and resources	8%	50%
Overburdened IRB	5%	28%
Deficiency in IRB records, including IRB minutes	37%	78%
Deficiency in written IRB policies and procedures	55%	72%

OHRP Compliance Oversight Data - 10/1998 to 6/2002

Distribution of Noncompliance Findings (269 Letters)

Table 2: Distribution of OHRP-Cited Deficiencies for All Institutions

Category of Deficiency	Number of Citations	Percent of Citations
Deficiency in IRB initial review process	277	25%
Deficiency in IRB-approved informed consent documents/process	304	27%
Deficiency in IRB continuing review process	109	10%
Deficiency in written IRB policies and procedures	88	8%
Deficiency in IRB records, including IRB minutes	70	6%
Deficiency in IRB membership/training/support/workload	49	4%
Deficiency in IRB review of protocol changes	45	4%
Deficiency in use of IRB expedited review procedure	46	4%
Deficiency in satisfying reporting requirements	35	3%
Research conducted without IRB approval	25	2%
Failure to obtain informed consent of subjects	26	2%
Other miscellaneous deficiencies	46	4%
Total	1120	100%

OHRP Compliance Oversight Data - 10/1998 to 6/2002

Distribution of Noncompliance Findings (269 Letters)

Table 3: Distribution of OHRP-Cited Deficiencies Related to Initial IRB Review

Category of Deficiency in IRB Initial Review	Number of Citations	Percent of Citations
Deficiency related to criteria required for IRB approval	88	32%
Deficiency related to findings for research involving children	39	14%
Contingent approval with substantive changes/clarifications without further review by convened IRB	33	12%
Deficiency related to findings for waiver of informed consent requireme	30	11%
IRB review without quorum	25	9%
Failure to review federal grant applications	16	6%
Deficiency related to findings for research involving prisoners	14	5%
Other miscellaneous deficiencies	32	12%
Total	277	100%

OHRP Compliance Oversight Data - 10/1998 to 6/2002

Distribution of Noncompliance Findings (269 Letters)

Table 4: Distribution of OHRP-Cited Deficiencies Related to Informed Consent

Category of Deficiency Related to Informed Consent	Number of Citations	Percent of Citations
Deficiency in description of purpose, procedures, and duration	63	19%
Deficiency in description of risks and discomforts	56	17%
Deficiency in description of benefits	20	6%
Deficiency in description of alternatives	20	6%
Deficiency in description of other elements of informed consent	61	18%
Language too complex	31	9%
Use of exculpatory language	7	2%
Failure to obtain informed consent of subjects	26	8%
Deficiency in documentation of informed consent	12	4%
Other miscellaneous deficiencies	34	10%
Total	330	100%

Underlying Causes of Noncompliance

- Inadequate education and training of IRB members, IRB staff, and investigators
- Inadequate staff and resources for the IRB
- Overburdened IRBs

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