Overview

- OHRP Overview
- Top 10 Human Research Protection Compliance Risks
- OHRP Compliance Data
- Common Findings
- How to Protect Your Institution
OHRP Overview

What is the Office for Human Research Protections (OHRP)?

- Provides leadership in protection of rights, welfare, and wellbeing of subjects involved in research conducted or supported by US Department of Health and Human Services
- Provides clarification and guidance
- Develops educational programs and materials
- Maintains regulatory oversight
- Provides advice on ethical and regulatory issues pertaining to biomedical and behavioral research
Federal Regulation and Policy

- HHS regulations: Title 45 CFR part 46
- Subpart A – basic HHS Policy
  - IRB & informed consent requirements
    “The Common Rule” - Federal Policy
  - Other Federal Departments & Agencies have adopted

Additional HHS Protections

- Subpart B - Pregnant Women, Human Fetuses, and Neonates
- Subpart C - Prisoners
- Subpart D – Children
- Subpart E – IRB Registration
Determining Applicability of Regulations

Prerequisite:

- Research involving human subjects conducted or supported by HHS (or other Federal Departments or Agencies) that is not otherwise exempt
- Non-exempt human subject research covered by Assurance of Compliance

Top 10 Compliance Risks
Top 10 Compliance Risks

- Inadequate IRB staff and resources
- Inadequate IRB documentation
- Failure to conduct auditing
- Inadequate written procedures
- Inappropriate IRB reporting lines
- Inadequate communication
- Inadequate resources for researchers
- Insufficient support from leadership
- Inadequate education
- Failure to utilize regulatory flexibility

Inadequate IRB staff and resources
Inadequate IRB staff and resources-findings

- “OHRP found that X institution does not have sufficient staff to ensure that all IRB review and recordkeeping duties are completed.”
- “OHRP finds that the X IRB administrative staff lacks sufficient space to conduct IRB duties.”

What Kind of Resources Do IRBs Need?

- Sufficient number of professional and administrative staff to handle workload
- Sufficient meeting and file storage space
Inadequate IRB documentation

Examples

• “IRB-like records maintained by X institution are limited to copies of IRB minutes and ‘protocol notebooks’ containing only the most current copies of IRB approved protocol-related documents…”

• “The IRB files…failed to document a complete history of protocol activities.”

• “Minutes of IRB meetings fail to include all required information”
Recording-Keeping Requirements

- Copies of
  - research proposals reviewed
  - scientific evaluations, if any
  - approved sample consent documents
  - progress reports submitted by investigator
  - reports of injuries to subjects

§46.115(a)(1)

IRB Records (cont’d)

- IRB meeting minutes
- Records of continuing review activities
- Correspondence between IRB and PIs
- List of IRB members
- Written IRB procedures
- Statement of significant new findings provided to subjects

§46.115(a)(2-7)
Failure to conduct auditing

Regulatory Requirement

- The procedures which the IRB will follow for determining which projects need verification from sources other than the investigators that no material changes have occurred since previous IRB review.

§46.103(b)(4)
Some Criteria for Auditing

- Randomly selected projects;
- Complex projects involving unusual levels or types of risk to subjects;
- Projects conducted by investigators who previously have failed to comply with the requirements of the HHS regulations or the IRB;
- Projects where concerns have been raised based upon information provided in continuing review reports or from other sources).

Types of Auditing to Consider

- Audit research studies (Is the protocol being followed? Are subjects given adequate information during consent?)
- Audit IRB operations (Are IRB determination appropriate? Are protocols reviewed in a timely manner?)
Inadequate written procedures

Regulatory Requirements for Written Procedures

Procedures IRB will follow for:

- Conducting initial and continuing review of research
- Reporting its findings and actions to the investigator and the institution
- Determining which projects:
  - require review more often than annually
  - need verification that no material changes have occurred

§46.103(b)(4)
Regulatory Requirements for Written Procedures (cont’d)

Procedures IRB will follow for:

- Ensuring prompt reporting to the IRB of proposed changes in a research activity and ensuring that such changes in approved research may not be initiated without IRB review and approval except when necessary to eliminate apparent immediate hazards to the subject

§46.103(b)(4)

Regulatory Requirements for Written Procedures (cont’d)

Procedures IRB will follow for:

Ensuring prompt reporting to the IRB, appropriate institutional officials, the Dep’t or Agency head, and OHRP of any

- unanticipated problems involving risks to subjects or others
- any serious or continuing noncompliance
- any suspension or termination of IRB approval

§46.103(a) and §46.103(b)(5)
Inappropriate IRB reporting lines

Potential Conflict of Interest

- IRB reports to Director of Sponsored Research
- SO interference with IRB’s proper execution of responsibilities
- SO not authorized to act for institution in matters re HSP
- SO fails to assume obligations imposed by regs re HSP
Inadequate communication

Communication Lines

- Between IRB and investigator
- Between IRB and institutional officials
- Between IRB staff and IRB members
- Between institution and funding agency
- Between institution and federal regulatory agency
Improving Communication

- Make SOPs and forms user-friendly
- Automatic reminders for deadlines
- Have regular meetings between offices/departments
- Cross-pollination
- Formal training in negotiation skills and conflict resolution
- Always be respectful

Inadequate resources for researchers
What Resources to Researchers Need?

• Adequate
  – Time
  – Space
  – Staff
  – Money
  – Equipment
  – Training

To conduct human subjects research

Insufficient support from leadership
Culture of Responsibility

- Human subjects protections is a shared responsibility:
  - IRBs
  - Investigators
  - Subjects
  - Sponsors
  - Institutional officials

All have a role in ensuring subjects are protected and risks are minimized.

Inadequate education
Education Necessary For:

- IRB members and staff
- Investigators
- Subjects
- Institutional officials
- Others?

Failure to utilize regulatory flexibility
What are some sources of flexibility in the regulations?

- Extent of Federalwide Assurance
- Required review of human subjects research
- Exemptions
- Expedited review
- Waiver or alteration of informed consent
- Waiver of documentation of informed consent
- Cooperative research review arrangements

What’s the Risk of Not Utilizing Flexibility?

- IRBs and investigators get bogged down in unnecessary procedures
- Everyone is overworked
- Real problems can “slip through the cracks”
- Problems more likely to be overlooked
OHRP Compliance Data

OHRP Compliance Oversight
New Cases Initiated – 1990-2014
OHRP Compliance Oversight
Site Visits – 1990-2013

Common OHRP Findings of Noncompliance
Common Areas of Noncompliance

- Recent Compliance Oversight Determinations -- 2-4-2009
  http://www.hhs.gov/ohrp/compliance/findings/index.html
- Determination letters:
  http://www.hhs.gov/ohrp/compliance/letters/index.html

Most Common Findings (1)

- ICDs deficient with respect to basic elements [45 CFR 46.116(a)]
- Inadequate written procedures [45 CFR 46.103(a) and 46 103(b)(4)(5)]
- Research conducted without IRB approval [45 CFR 46.103(b) and 46.109(a)]
- Insufficient info to make determinations required for approval [45 CFR 46.111]
- Failure to document informed consent [45 CFR 46.117(a)]
- Failure of IRB to make and document required findings for waiver of informed consent [45 CFR 46.117(c)]
Most Common Findings (2)

- 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)]
- Inappropriate application of exempt categories of research [45 CFR 46.101(b)]
- Failure to obtain legally effective informed consent [45 CFR 46.116]
- Enrollment procedures did not minimize possibility of coercion or undue influence [45 CFR 46.116]

Most Common Findings (3)

- Failure of IRB to Determine That Criteria for IRB Approval Are Satisfied [45 CFR 46.111]
- Failure of IRB to Document Consideration of Additional Safeguards for Vulnerable Subjects
- Failure of IRB to Make Required Findings When Reviewing Research Involving Prisoners [45 CFR 46.305]
- Inadequate IRB meeting minutes and retention of IRB records [45 CFR 46.115(a)]
- IRB meeting convened without quorum (lack of a majority) [45 CFR 46.108]
How to Protect Your Institution

Solutions to Correct/Prevent Noncompliance

- Education
- Adequate IRB staff and resources
- Adequate IRB documentation (in particular, adequate minutes of IRB meetings)
- Periodic self-assessment of institutional system for protecting human subjects
- Adequate written procedures
- Utilize the flexibility in the regulations
- “Culture of conscience”
OHRP Education Resources

- Research Community Fora
- 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_ded_qatool.html
- QI Consultation
- QA Workshops
OHRP Contact Information

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

Key Points

• Document everything
• Education is paramount
• Communicate early and often (and respectfully)
• Audit/monitor IRB procedures and worrisome investigators/research
• Utilize the flexibility at your disposal
Office for Human Research Protections

THANK YOU for protecting Human Subjects!