

CRA Special Session on Regulatory Affairs, Part II

SWOG Spring 2010 Group Meeting

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Outline

- A little background and context
- Assurances
- Compliance
- OHRP Activities Update

Office for Human Research Protections (OHRP)

(Formerly Office for Protection from Research Risks)
Department of Health and Human Services
Office of Public Health and Science

Ethical Principles

- Nuremberg Code
- Declaration of Helsinki
- The Belmont Report

The Belmont Report

Ethical Principles and Guidelines for the Protection of Human Subjects of Research



The National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research
April 18, 1979

The Belmont Report

Three Basic Ethical Principles:

- Respect for Persons
 - Individual autonomy
 - Protection of individuals with reduced autonomy
- Beneficence
 - Maximize benefits and minimize harms
- Justice
 - Equitable distribution of research costs and benefits

Federal Regulations and Policy

45 CFR 46 - Basic DHHS Policy for Protection of Human Research Subjects - Subpart A

Originally adopted January 13, 1981
Revised June 18, 1991

"The Common Rule" - Federal Policy for the Protection of Human Subjects June 18, 1991

Departments of Agriculture, Energy, Commerce, HUD, Justice, Defense, Education, Veterans Affairs, Transportation, and HHS. NSF, NASA, EPA, AID, Social Security Administration, CIA, and the Consumer Product Safety Commission.

Federal Regulations and Policy

Additional Protections Included in 45 CFR 46:

- **Subpart B** - Additional DHHS Protections Pertaining to Research, Development, and Related Activities Involving Pregnant Women and Fetuses
- **Subpart C** - Additional DHHS Protections Pertaining to Biomedical and Behavioral Research Involving Prisoners as Subjects
- **Subpart D** - Additional DHHS Protections for Children Involved as Subjects in Research

Food and Drug Administration



Regulations:

- IRB - 21 CFR 56
- Informed Consent - 21 CFR 50

HHS vs. FDA Regulations

- Basic requirements for IRBs and Informed Consent are congruent
- Differences center on differences in applicability
 - HHS regulations based on federal funding of research
 - FDA regulations based on use of FDA regulated product: drugs, devices, or biologics

Definitions

- **Research** - a systematic investigation designed to develop or contribute to generalizable knowledge.
- **Human Subject** - a living individual about whom an investigator conducting research obtains
 - data through intervention or interaction with the individual, or
 - identifiable private information

Assurances

HHS Regulations (45 CFR part 46)

HHS will conduct or support non-exempt human subject research only if:

- the institution has an OHRP-approved assurance, and
- the institution has certified to HHS
 - research was reviewed and approved by IRB, and
 - the research will be subject to continuing review §46.103(b) & (f)

Institutional Responsibilities

Protect Human Subjects in Research

Responsibilities shared by
Institutional Officials, IRBs, and Investigators

Institutional Assurance

- Documentation of institution's commitment to comply with applicable regulations §46.103(b) & (f)
- Generally recognized by other federal departments & agencies
- Method of compliance oversight for OHRP
- Federalwide Assurance (FWA) – only assurance option

Terms of the FWA

- Ethical principles
- Applicability
- Compliance with Federal policy and other applicable laws, regulations, policies
- Written procedures
- IRB responsibilities
- Informed consent requirements
- Collaborating institutions

Terms of the FWA, cont'd

- Independent investigators
- Institutional support for IRBs
- Compliance with terms of FWA
- Assurance training
- Educational training
- FWA renewal and update

Assurance Applications – Extending FWA

- Individual Investigator Agreement
 - independent investigators
 - investigators at another institution
- Assured institution responsible for oversight of research
- Sample agreement and guidance available at the OHRP website

Assurance Applications - Relying on External IRB

Institution responsibility

- Written agreement
 - IRB authorization agreement
- <http://www.hhs.gov/ohrp/humansubjects/assurance/iprotsup.rtf>
- Ensure research conducted per IRB approved plan
- Procedures for reporting to OHRP

Assurances and IRB Registration

- Active Federalwide Assurances: 10,700+
- Active IRB Organizations: 6,000+
- ...and counting



COMPLIANCE

COMPLIANCE OVERSIGHT JURISDICTION

- 45 CFR 46
- OHRP APPROVED ASSURANCE

Compliance Investigations, For Cause

HOW AN INVESTIGATION GETS STARTED

- COMPLAINTS
- SELF-REPORTING
- MEDIA
- OTHER INCIDENT REPORTS

Compliance Investigations, For Cause, cont'd.

Summary Counts, Past 5 Years

- Not as many as you might think
- Down from 66 active cases in 2006 to 8 currently active

Compliance Investigations, Not-For-Cause

- Since 2006, 15 conducted (3 on-site, 12 “paper” visits)
- Not based on a complaint or problem

Compliance Oversight FY 2009

- New For-Cause Cases Opened (six)
- New Not-for-Cause Evaluations (four)
- Determination Letters (34)
- Processed and Closed Incident Reports (more than 1100)

OHRP Compliance Procedures

HUMAN SUBJECTS
COMPLIANCE OVERSIGHT PROCEDURES

www.hhs.gov/ohrp/compliance/ohrpcomp.pdf

OHRP COMPLIANCE PROCEDURES

- WRITTEN COMPLAINTS
- OHRP INITIATES INQUIRY
- OHRP EVALUATION

<http://www.hhs.gov/ohrp/compliance/ohrpcomp.pdf>

OHRP COMPLIANCE SITE VISIT

- SITE VISIT TEAM
 - 2-4 OHRP STAFF
 - 2-3 CONSULTANTS (e.g., IRB CHAIR, SCIENTIFIC SPECIALTY)
- SPECIFIC COMPLAINT
- SYSTEMIC PROTECTIONS

Compliance, cont'd.

“GREATEST HITS”
COMMON FINDINGS AND GUIDANCE

NOW PLAYING AT:
www.hhs.gov/ohrp/compliance/findings/pdf

Compliance--GREATEST HITS

- DEFICIENCIES IN INFORMED CONSENT
 - PROCESS
 - DOCUMENTSee,
www.hhs.gov/ohrp/ohrp/policy/index.html#informed

Compliance--GREATEST HITS, Cont'd

- DEFICIENT CONTINUING REVIEW
 - UNTIMELYSee,
<http://www.hhs.gov/ohrp/policy/index.html#continuing>

Compliance-GREATEST HITS, cont'd

- INADEQUATE MINUTES
 - FAILURE TO DOCUMENT
REQUIRED FINDINGS FOR
WAIVER OF CONSENT

Compliance-GREATEST HITS, cont'd

- FAILURE TO NOTIFY OHRP OF
 - UNANTICIPATED PROBLEMS
 - NONCOMPLIANCE
 - SUSPENSIONS
 - TERMINATIONSSee,
<http://www.hhs.gov/ohrp/humansubjects/guidance/irbgd702.htm>

Compliance-GREATEST HITS, cont'd

- DEFICIENT IRB PROCEDURES
 - INADEQUATE WRITTEN IRB POLICIES

Compliance Actions

ACTIONS DESIGNED TO ENSURE PROTECTION OF HUMAN RESEARCH SUBJECTS

- TERMINATION
- SUSPENSION
- CORRECTIVE ACTIONS
 - REWRITE/INSTITUTE NEW PROCEDURES
 - EDUCATION
 - INCREASED IRB STAFFING, OTHER RESOURCES

What's Going On?

Education and Development Fiscal Years 2010-11

- Research Community Fora (RCFs) – 2010
 - Seattle, WA – February 4, 2010
 - Chicago, IL – May 21, 2010
 - Cleveland, OH – September 16, 2010
- 2011 RCFs
 - Houston, TX – January 24, 2011
 - ?? Spring 2011 – *any reasonable offer will be entertained...*
 - St. Louis, MO – September 2011

Education and Development Fiscal Year 2010

Quality Improvement Program

- QA/QI Consultations
- QI "SOP" Workshops

Education and Development Fiscal Year 2010

Quality Improvement Workshops

- Up to seven anticipated, across country:
e.g., Gettysburg, PA; Las Vegas NV; San Antonio, TX; Indianapolis, IN (April 28-29); Miami, FL (June 22-23); New England; New Jersey (August)
- Exact locations and dates TBD

Policy and Assurances: Regulation and Guidance (FY 2009)

- IRB Organization Registration Rule (Published 1/15/09; Effective 7/14/09)
- Significant Findings and Concerns of Noncompliance (Revised 2/13/09)
- Request for information and comments on IRB accountability (3/5/2009; Due 6/3/2009)
- Guidance on the Genetic Information Nondiscrimination Act: Implications for Investigators and Institutional Review Boards (4/7/2009)

IRB Registration Rule

- Subpart E to 45 CFR part 46
 - Requires IRBs to register with HHS
 - Compatible with the IRB Registration Requirements of the FDA, Allowing the Operation of a Single HHS IRB Registration System
- Effective July 14, 2009...Register Within 60 Days of the Effective Date-by September 14, 2009
- Register Electronically Via the OHRP Website

Revised Compilation of Recent Determinations of Noncompliance

- OHRP has revised its 2005 document "Significant Findings and Concerns of Noncompliance," to delete determinations that have not been made recently, add new determinations that have been made since 2005, and provide additional regulatory citations
- Can be found at:
<http://www.hhs.gov/ohrp/compliance/findings.html>

Request for Information and Comments (ANPRM) on IRB Accountability

- Pursue a notice of proposed rulemaking?
- Would hold IRBs and the institutions or organizations operating the IRBs directly accountable for meeting certain regulatory requirements of 45 CFR part 46
- Hopes to encourage institutions to rely on external IRBs
- Reduce administrative burdens without diminishing HSP

Cooperative Research

In the conduct of cooperative research projects, each institution is responsible for safeguarding the rights and welfare of human subjects and for complying with this policy. ...[A]n institution participating in a cooperative project may enter into a joint review arrangement, rely upon the review of another qualified IRB, or make similar arrangements for avoiding duplication of effort. (45 CFR 46.114)

Guidance on the Genetic Information Nondiscrimination Act (GINA)

- Provides background on protections provided by the GINA and discusses some of the implications of GINA for investigators who conduct, and IRBs that review, genetic research, particularly with respect to the criteria for IRB approval of research and the requirements for obtaining informed consent
- <http://www.hhs.gov/ohrp/humansubjects/guidance/gina.html>

OHRP Guidance--Sample Informed Consent Language:

- A new Federal law, called the Genetic Information Nondiscrimination Act (GINA), generally makes it illegal for health insurance companies, group health plans, and most employers to discriminate against you based on your genetic information. This law generally will protect you in the following ways:
 - Health insurance companies and group health plans may not request your genetic information that we get from this research.
 - Health insurance companies and group health plans may not use your genetic information when making decisions regarding your eligibility or premiums.
 - Employers with 15 or more employees may not use your genetic information that we get from this research when making a decision to hire, promote, or fire you or when setting the terms of your employment.All health insurance companies and group health plans must follow this law by May 21, 2010. All employers with 15 or more employees must follow this law as of November 21, 2009.
Be aware that this new Federal law does not protect you against genetic discrimination by companies that sell life insurance, disability insurance, or long-term care insurance.

New Draft Guidances (FY 2010)

- Draft Guidance on IRB Continuing Review of Research
- Draft Guidance on IRB Approval of Research with Conditions
- Both released for public comment on November 6, 2009; comment period closed on January 5, 2010

Draft Guidance on Continuing Review of Research (FY 2010)

- Responsive to SACHRP recommendations regarding clarity, efficiency, flexibility and use of examples (though does not accept every SACHRP recommendation)
- When finalized will supersede January 2007 OHRP Guidance on Continuing Review

Draft Guidance on IRB Approval of Research with Conditions (FY 2010)

- Responsive to SACHRP recommendations regarding clarity, efficiency, flexibility and use of examples
- Brings coordinated focus to both issues of continuing review and conditional approval

Frequently Asked Questions (FAQs)

New and Newish FAQs

- Questions and Answers on Quality Improvement Activities – December 30, 2008
- Exempt Research Determinations – October 15, 2009

OHRP FAQs Answers on Quality Improvement Activities

- **Question 1:** How does HHS view quality improvement activities in relation to the regulations for human research subject protections?
- **Question 2:** Do the HHS regulations for the protection of human subjects in research (45 CFR part 46) apply to quality improvement activities conducted by one or more institutions whose purposes are limited to: (a) implementing a practice to improve the quality of patient care, and (b) collecting patient or provider data regarding the implementation of the practice for clinical, practical, or administrative purposes?

OHRP Electronic Access

- **Web Site:** <http://www.hhs.gov/ohrp>
IRB Registration & Assurance Filing
Quality Improvement Program
Policy Guidance
Compliance Oversight
Educational Materials/Workshops
SACHRP
- **Listserv**
- **Email:** ohrp@hhs.gov

Contact Information

- Main Phone Number: 240-453-6900
- Toll Free Phone Number: 1-866-447-4777
(1-866-HHS-HRPP)
- New Staff Phone Numbers—check website