How the Past Influenced Human Research Protection Regulations

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Outline

- Overview of Regulated Research
- Overview of OHRP
- A Few Historical Events and their Effect on Human Research Protections
U.S. Regulated Human Subject Research
U.S. Regulated Research

- Research utilizing an FDA regulated product (drugs, biologics or devices)
- Research supported or conducted by a “Common Rule” Department or Agency of the Federal Government
Signatories to the Federal Policy for the Protection of Human Subjects

- "The Common Rule"
- Adopted June 18, 1991

HHS Regulated Human Subject Research
Research Supported or Conducted by HHS

- National Institutes of Health (NIH)
- Centers for Disease Control & Prevention (CDC)
- Agency for Healthcare Research & Quality (AHRQ)
- Health Resources & Services Administration (HRSA)
- Food & Drug Administration (FDA)
- Administration on Aging (AoA)
- Administration for Children & Families (ACF)
- Centers for Medicare & Medicaid Services (CMS)
- Indian Health Services (IHS)
HHS Regulations

- Title 45 Code of Federal Regulations Part 46 (45 CFR 46)
  Basic Policy for the Protection of Human Research Subjects – Subpart A
  - Originally adopted May, 1974
  - Latest Revision June 23, 2005
Additional Protections Included in 45 CFR 46

- **Subpart B** - Additional DHHS Protections for Pregnant Women, Human Fetuses and Neonates Involved in Research (revised November 13, 2001)

- **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
Department of Health and Human Services Organizational Chart
(Selected Portion)

- The Secretary
  - Deputy Secretary
- Assistant Secretary for Health
  - Office of Public Health & Science
  - U.S. Public Health Service Commissioned Corp
  - Office for Human Research Protections
OHRP Organization Chart

Office of the Director
Bernard Schwetz, Director
Melody Lin, Deputy Director
Michael Carome, Associate Director, Regulatory Affairs

Secy's Advisory Committee (SACHRP)
Kathy Slatinshek
Executive Director

International Activities
Melody Lin, Activity Director

Division of Compliance Oversight
Kristina Borror, Director

Division of Education & Development
Shirley Hicks, Director

Division of Policy and Assurances
Irene Stith-Coleman, Director
Historical Events and Human Research Protections
1946 Nuremberg Trial

During the Nuremberg War Crimes Trials, 23 German doctors were charged with crimes against humanity for “performing medical experiments upon concentration camp inmates and other living human subjects, without their consent, in the course of which experiments the defendants committed the murders, brutalities, cruelties, tortures, atrocities, and other inhuman acts.”
The Nuremberg Code

As part of the verdict, the Court enumerated some rules for "Permissible Medical Experiments", now known as the “Nuremberg Code”. These rules include:

- voluntary consent
- benefits outweigh risks
- ability of the subject to terminate participation
Thalidomide Tragedy

- Thousands of birth defects in Europe
- FDA’s Medical Officer, Dr. Frances Kelsey, avoided approving the drug
- Following the tragedy in 1962, Congress passed the Kefaufer-Harris Amendments, requiring all drugs to prove efficacy and safety before approval.
1964- Declaration of Helsinki

Recommendations Guiding Medical Doctors in Biomedical Research Involving Human Subjects

Adopted by the 18th World Medical Assembly, Helsinki, Finland, 1964.
Subsequently revised over the years

“Concern for the interests of the subject must always prevail over the interests of science and society.”
1966 - Henry Beecher's Article

“Ethics and Clinical Research”
Henry K. Beecher

- 22 published medical studies presenting risk to subjects without their knowledge or approval
- Published in some of the most prestigious journals and conducted at some of the most prestigious institutions
Examples of Unethical Research

- Willowbrook School, NY – deliberately infected mentally retarded children with hepatitis virus
- Jewish Chronic Disease Hospital, NY - Injected live cancer cells into non-consenting elderly patients
- Milgram Study, Yale University - "Behavioral study of obedience"
- Tea Room Trade Study, St. Louis – Homosexual encounters in men’s rooms in public places
Public Health Service Policy

In 1966 the Department of Health Education and Welfare (DHEW), Public Health Service (PHS), National Institutes of Health (NIH) issued policies for the protection of human subjects in research.
Requirements for Public Health Service Grantee Institutions

- Three topics to be addressed by prior committee review for all PHS-supported human subject research:
  - Protection of the rights and welfare of the subjects
  - Assure appropriate methods of informed consent
  - Determine acceptable balance of risks and benefits
- Beginnings of the Institutional Review Board (IRB)
1972 - Report of U.S. Public Health Service Syphilis Study

Public Health Service (PHS) study conducted from 1932 to 1972, in Macon Co., Alabama. Examined the natural course of untreated syphilis in African-American men. The subjects were unknowing participants in the study; they were not told that they had syphilis, nor were they offered effective treatment.
National Research Act

- 1973 Kennedy Hearings “Quality of Health Care - Human Experimentation”
- 1974 National Research Act
  - Established the “National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research”
  - Required IRBs at institutions receiving DHEW support for human subjects research
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

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
1974 - Regulations for the Protection of Human Subjects

HHS (formerly DHEW) issues Title 45 Code of Federal Regulations Part 46 (45 CFR 46) the Basic Policy for the Protection of Human Research Subjects
Basic Protections

The regulations contain three basic protections for human subjects:

- Institutional Assurances
- IRB Review
- Informed Consent
An OHRP-Approved Assurance

- Institutions that “engage” in human subjects research conducted or supported by HHS must sign a written Assurance (Federalwide Assurance)
- This documents the institution’s commitment to compliance with the Terms of Assurance & HHS regulations
Institutional Review Boards

Institutional Review Board (IRB): A committee charged with the review of human subject research to assure that the subjects’ rights and welfare are adequately protected.
Required IRB Review

- Initial Review & Approval - prior to the initiation of any research activity
- Prior to initiating any changes to previously approved research
- Continuing Review – interval appropriate to degree of risk, but not less than once per year
Informed Consent

Key principles of obtaining informed consent

- Full disclosure of the nature of the research and the subject's participation
- Adequate comprehension on part of potential subjects
- Voluntary participation
Remember

Protecting Human Research Subjects is a Shared Responsibility
OHRP Contact Information

- Website: [www.hhs.gov/ohrp](http://www.hhs.gov/ohrp)
  Regulations, Guidance Documents, Frequently Asked Questions (FAQs)
- Email: OHRP@HHS.GOV
- Toll-free phone #: 1-866-447-4777
- Main phone #: 240-453-6900
- Join Listserv: