

How the Past Influenced Human Research Protection Regulations

Shirley J. Hicks

**Director, Division of Education and Development
Office for Human Research Protections
U.S. Department of Health and Human Services**

February 14, 2007



OHRP

OFFICE FOR HUMAN RESEARCH PROTECTIONS

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

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

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)

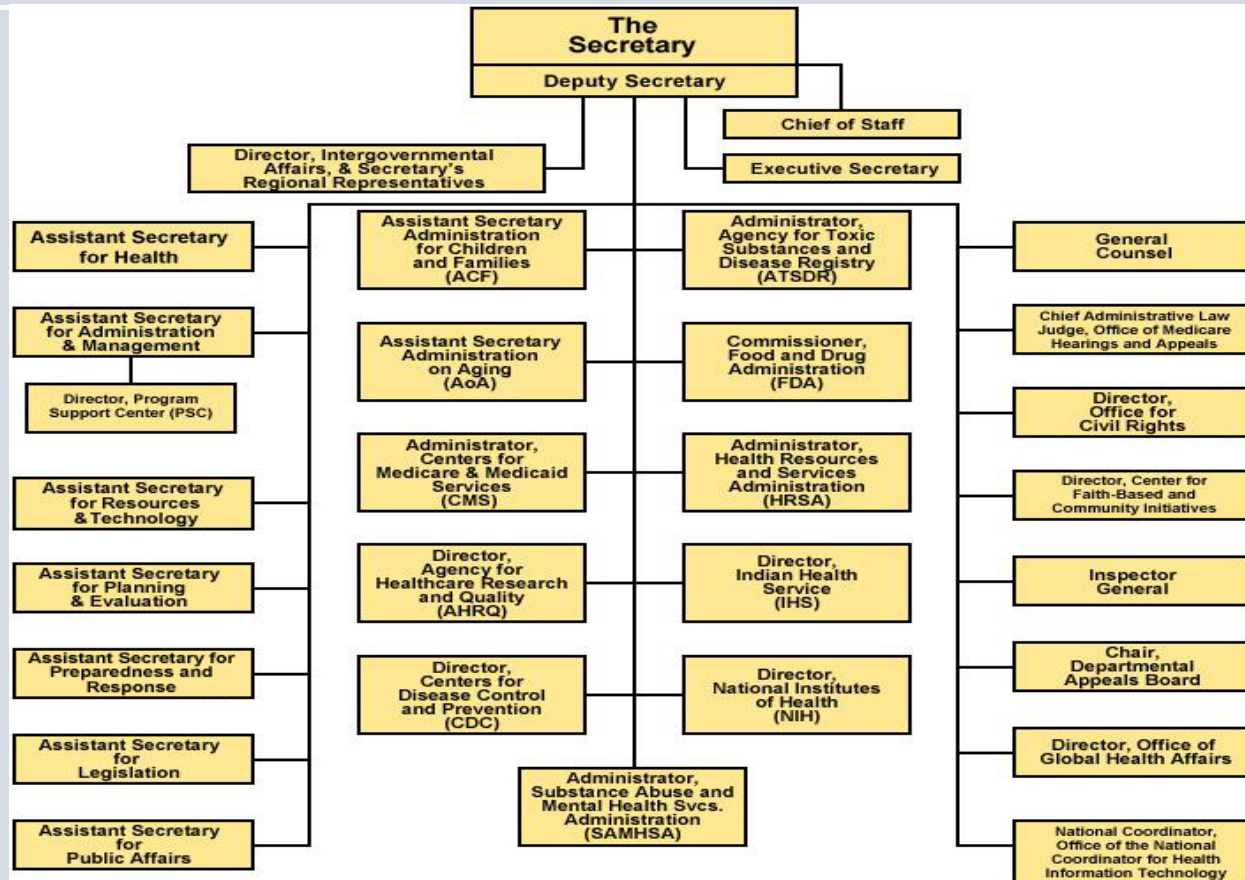
HHS Regulations

- **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

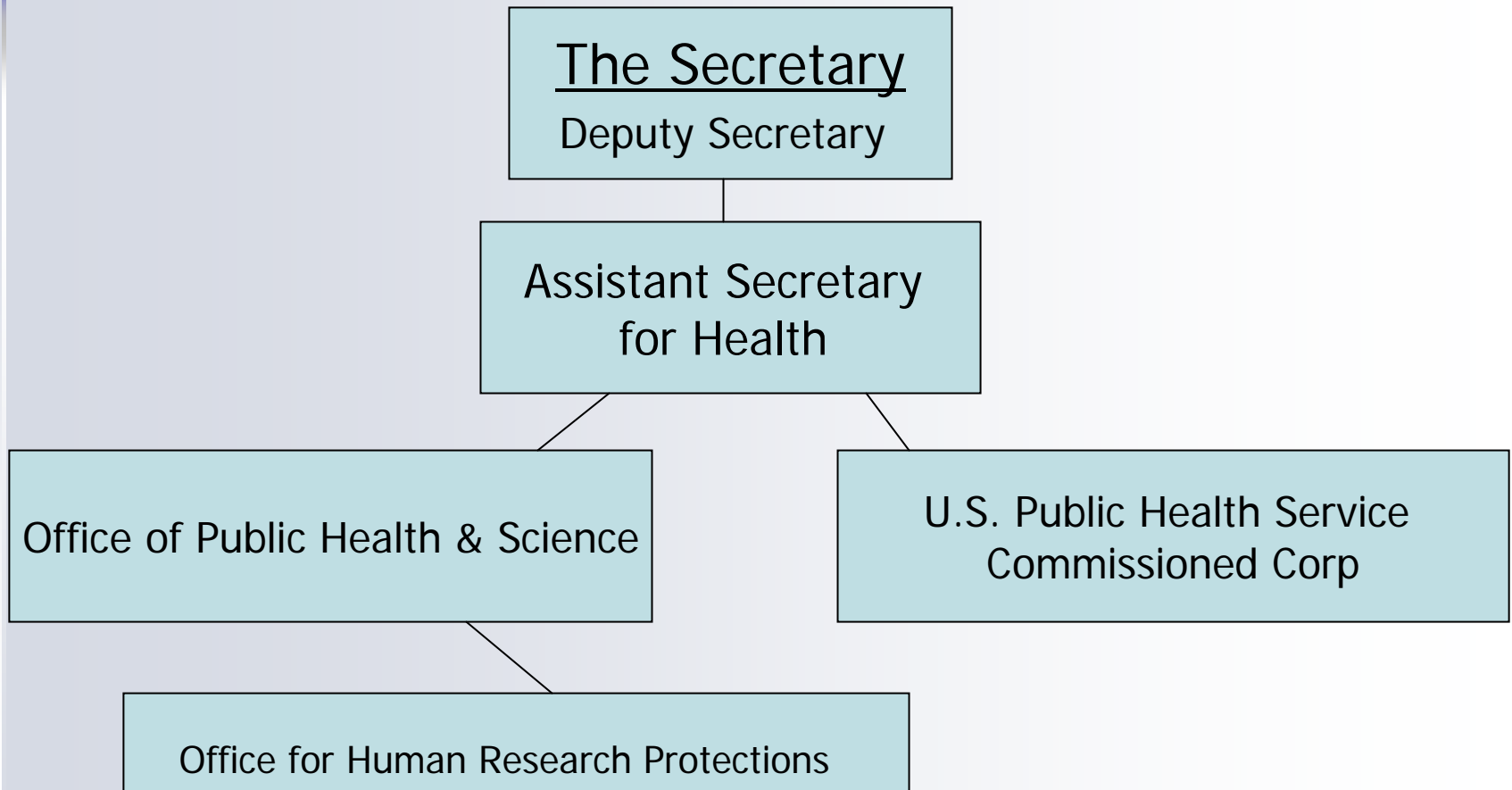
Additional Protections Included in 45 CFR 46

- **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

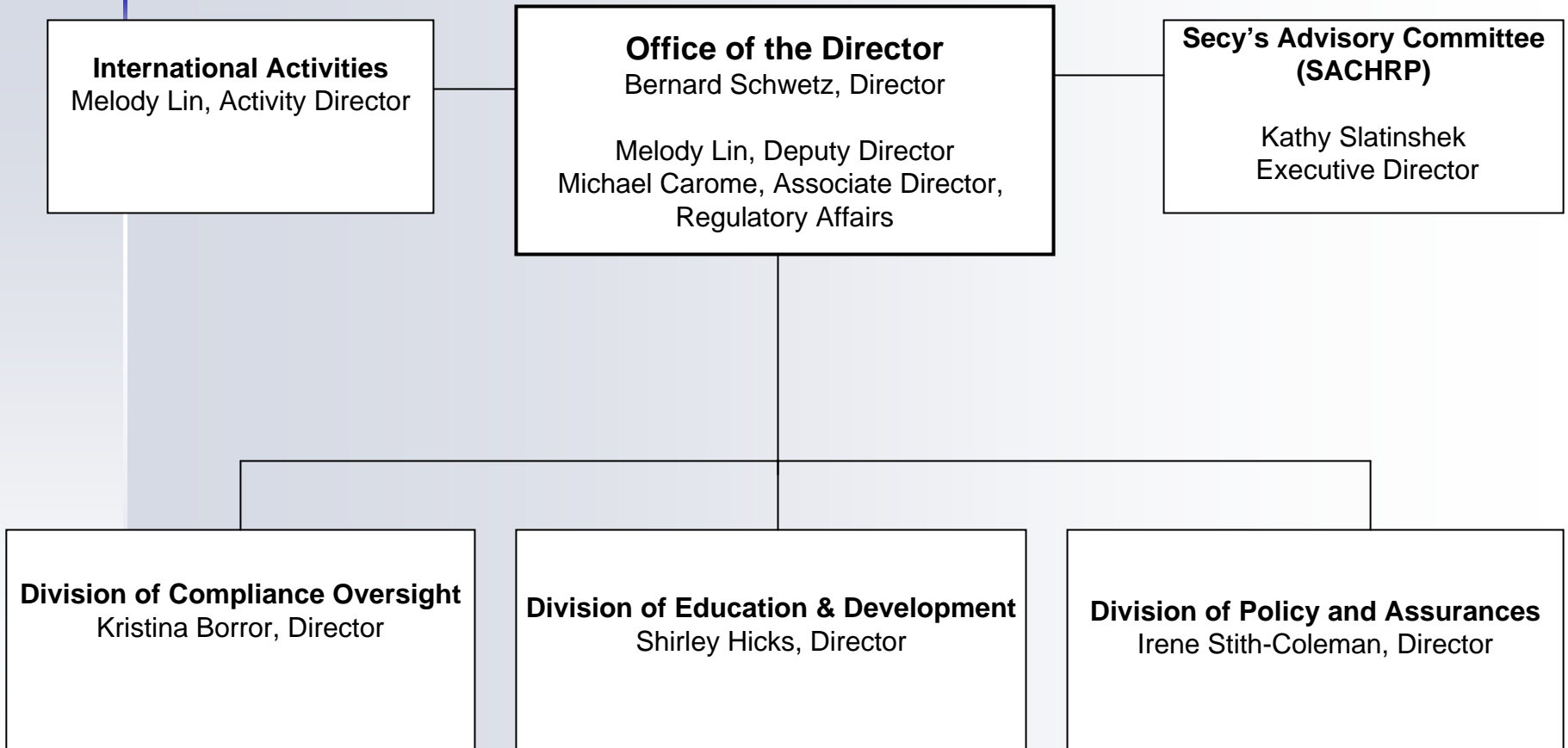
Department of Health & Human Services Organizational Chart



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



OHRP Organization Chart



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 Kefauver-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

New England Journal of Medicine (1966)

- 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)
- 1971 - Institutional Guide to DHEW Policy on the Protection of Human Subjects

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

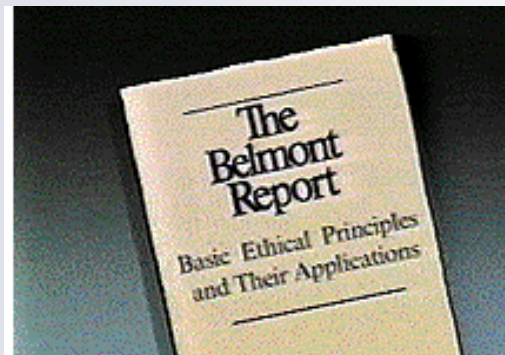


National Research Act

- 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

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:

<http://www.hhs.gov/ohrp/news/index.html>