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BLOOMBERG
SCHOOL *of* PUBLIC HEALTH

Cases and Codes

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Cases and Codes

- ◆ Topics to be covered
 - Cases
 - Codes, guidelines, and regulations



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Section A

History of Research Ethics

Cases and Codes

- ◆ Themes
 - Lessons from history
 - Policymaking in response to tragedy



Nuremberg Trials of Nazi Germany

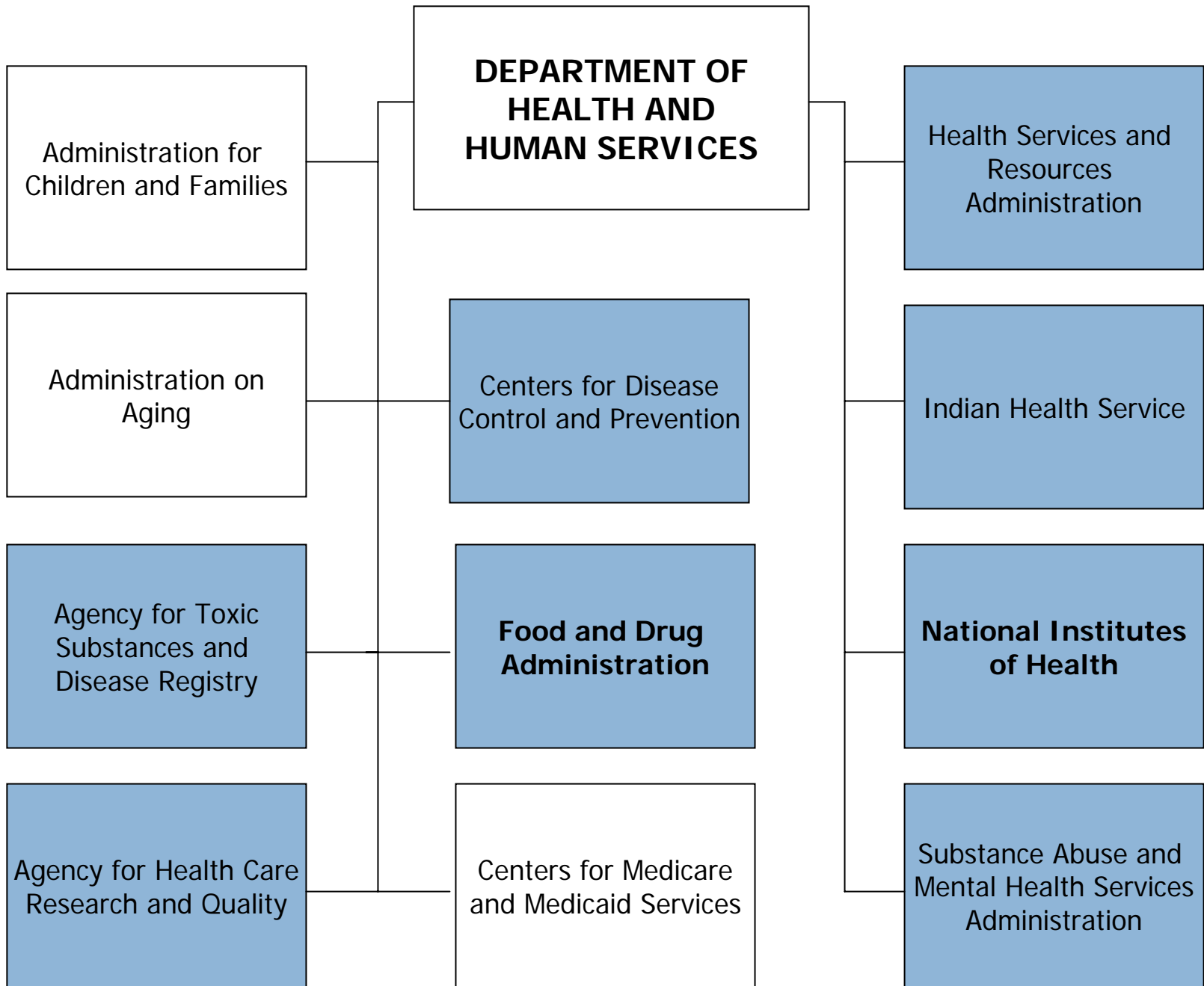
- ◆ Physicians
- ◆ Projects carried out . . .
 - Improving survival and rescue of German troops
 - Testing of medical procedures and pharmaceuticals
 - Experiments to confirm Nazi racial ideology

History of Research Ethics

- ◆ 1931—regulations on new therapy and experimentation
 - Based on 1900 Ministry of Health regulations

History of Research Ethics

- ◆ 1949—Nuremberg Code
 - Response to medical experimentation conducted by Nazi physicians
 - Voluntary consent is essential
 - Subject can terminate participation at any time
 - Conducted as to avoid all unnecessary physical and mental suffering and injury



**DEPARTMENT OF
HEALTH AND
HUMAN SERVICES**

Administration for
Children and Families

Administration on
Aging

Agency for Toxic
Substances and
Disease Registry

Agency for Health Care
Research and Quality

Centers for Disease
Control and Prevention

**Food and Drug
Administration**

Centers for Medicare
and Medicaid Services

Health Services and
Resources
Administration

Indian Health Service

**National Institutes
of Health**

Substance Abuse and
Mental Health Services
Administration

History of Research Ethics

- ◆ 1953¹
 - All research to be reviewed by a committee
 - Voluntary agreement required

History of Research Ethics

- ◆ 1962—Kefauver-Harris amendments to Food, Drug, and Cosmetic Act
 - Response to Thalidomide disaster
 - Required Phase I, II, III, and IV testing of drugs
 - Imposed informed consent requirements on researchers during three phases of testing

History of Research Ethics

- ◆ 1964—Declaration of Helsinki
(revised—1975, 1983, 1989, 1996, 2000)
 - Developed by medical professionals
 - Based on Nuremberg principles
 - Independent review
 - Reports should not be published if research not in accordance with Declaration of Helsinki

History of Research Ethics

1. 1966—U.S. Federal Agency Policies
2. Statement of policy on clinical investigations using human subjects
3. Group consideration and **informed consent** in clinical research (NIH)
4. Statement on policy concerning consent for use of investigational drugs on humans

History of Research Ethics

- ◆ 1966—Henry Beecher article in NEJM
 - Willowbrook
 - Jewish Chronic Disease Hospital

Willowbrook Concerns

- ◆ Vulnerable subjects
- ◆ How informed was the informed consent
- ◆ Potential for coercion

Jewish Chronic Disease Hospital



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<http://www.stanford.edu/dept/DoR/hs/History/his06.html>*

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Jewish Chronic Disease Hospital Concerns

- ◆ Vulnerable population
- ◆ No internal review
- ◆ Absence of physician permission
- ◆ No consent or poor consent

History of Research Ethics

- ◆ 1972—Tuskegee Syphilis Study
 - Ad Hoc Advisory Committee

Tuskegee Syphilis Study

- ◆ 1973—Congressional hearings and Ad Hoc Advisory Committee
- ◆ Committee recommends establishment of National Human Investigation Board
- ◆ Congress passed National Research Act

History of Research Ethics

- ◆ 1974—National Research Act
 - National commission for the protection of human subjects of biomedical and behavioral research

History of Research Ethics

- ◆ 1978—the Belmont Report
 - Ethical principles and guidelines for the protection of human subjects in research
 - Beneficence
 - Respect for persons
 - Justice

History of Research Ethics

- ◆ 1981—Federal Policy for the Protection of Human Subjects
 - Codified work of National Commission
 - Institutional Review Boards required and defined
 - Applies to research conducted by U.S. investigators at home and abroad

History of Research Ethics

- ◆ 1982—International Guidelines for Biomedical Research Involving Human Subjects (revised—1993, 2002)
 - Drafted by Council for International Organizations of Medical Sciences (CIOMS)

History of Research Ethics

- ◆ 1982—International Guidelines for Biomedical Research Involving Human Subjects (revised—1993, 2002)
 - First code to consider less developed communities
 - Consent of individuals/communities
 - Local review procedures
 - Obligations of sponsors



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Section B

Current Issues in Research Ethics

Current Issues in Research Ethics

- ◆ 1994—Advisory Committee on Human Radiation Experiments
 - Review of past experiments
 - Contemporary projects

Advisory Committee on Human Radiation Experiments (1994)

- ◆ Recommendations
 1. Apologies and compensation
 2. Revisions of Radiation Exposure Compensation Act (1950)
 3. Improvements in protections for human subjects

Current Issues in Research Ethics

- ◆ 1994—NIH inclusion guidelines
 - Women and minorities
 - Improving access
 - Harms of exclusion

Current Issues in Research Ethics

- ◆ 1995—National Bioethics Advisory Commission Reports
 - Incompetent adults
 - Human biological materials
 - Conduct of research in developing countries
 - Conduct of research in U.S.

Current Issues in Research Ethics

- ◆ 1998—NIH Inclusion Guidelines
 - Children

Current Issues in Research Ethics

- ◆ 1998—Institutional Review Board closures
 - Suspension/deactivation of Multiple Project Assurances (MPAs)
 - Temporary suspension
 - MPA restriction

Current Issues in Research Ethics

- ◆ 2001—Death of a healthy volunteer
 - Ellen Roche

The Johns Hopkins Hospital



Current Issues in Research Ethics

- ◆ 1999—Gene Therapy Trials
 - Jesse Gelsinger Case

Current Issues in Research Ethics

- ◆ 1999—Gene Therapy Trials
 - FDA/NIH response

Current Issues in Research Ethics

- ◆ 2000—National Human Research Protections Advisory Committee
 - Advisory to DHHS
 - Companion effort to establishing OHRP

Current Issues in Research Ethics

- ◆ 2002—Secretary's Advisory Committee on Human Research Protections
 - Advisory to DHHS

Current Issues in Research Ethics

- ◆ 2000—Declaration of Helsinki
 - Short-course AZT trials

Current Issues in Research Ethics

- ◆ 2000—Declaration of Helsinki
 - 1996—“The potential benefits, hazards, and discomforts of a new method should be weighed against the advantages of the **best current** diagnostic and therapeutic methods . . .”

Current Issues in Research Ethics

- ◆ 2000—Declaration of Helsinki
 - 1996—“. . . in any medical study, every patient—including those in the control group, if any—should be assured of the **best proven** diagnostic and therapeutic methods. This does not exclude the use of an inert placebo in studies where **no proven** diagnostic or therapeutic method exists.”

Current Issues in Research Ethics

- ◆ 2000—Declaration of Helsinki
 - 2000—“The benefits, risks and burdens, and effectiveness of a new method should be tested against those of the **best current** prophylactic, diagnostic, and therapeutic methods . . .”

Current Issues in Research Ethics

- ◆ 2000—Declaration of Helsinki
 - 2000—". . . this does not exclude the use of placebo or no treatment in studies where **no proven** prophylactic, diagnostic, and therapeutic method exists. At the conclusion of the study, every patient entered into the study should be assured of access to the **best proven** prophylactic, diagnostic, and therapeutic methods identified by the study."

Current Issues in Research Ethics

- ◆ 2001—WMA clarification
 - Placebo-controlled trials are acceptable when there is . . .
 - A scientifically sound, methodologic reason
 - A minor condition—little or no harm

Summary

- ◆ Lessons from history
- ◆ Ongoing efforts