Historical Perspectives on Human Subject Research
Why do we have IRBs?

- To protect the rights and welfare of human research participants
- To help investigators recognize and address human subjects’ issues in their research
- To advocate for justice
- To advocate for autonomy
- To be a public watchdog
- To guard against scandal
- To act as an arbiter of scientific merit (*to a limited extent*)
Research Ethics Milestones*

Trigger Events

- Syphilis Study Begins 1932
- The Nazi Experiments
- Human Radiation Experiments
- The Thalidomide Tragedy
- Milgram Study

Ethics Milestones

- 1947 Nuremberg Code
- 1962 Amendments to the Food, Drug & Cosmetic Act
- 1964 Declaration of Helsinki

*From “Protecting Study Volunteers in Research” Dunn & Chadwick
Research Ethics Milestones

Trigger Events
- The Beecher Article: 1966
- The Syphilis Study Expose: 1972

Ethics Milestones
- The Belmont Report: 1979
- Consolidated HHS/FDA Regulations: 1981
- CIOMS Guidelines: 1982
- Common Rule: 1991
- National Bio-Ethics Advisory Committee: 1995
The Nuremberg Doctors Trial of 1946

- The Nazi regime exploited human beings by forcing them to participate in research without consent.
- The 23 defendants were charged with murder, torture, and other atrocities committed under the guise of medical science.
- 15 were found guilty and 7 were sentenced to death.
The Nuremberg Code

- “When is research criminal?”
- Only addresses research on normal subjects

The beginning of codification of research regulations

- Need for Scientific Merit
- Informed Consent
- Right to Withdraw
- Risk/Benefit Balance
The Milgram Obedience Study, 1963

- 60% of the “teachers” were persuaded to give shocks up to the highest level, even after the “learner” appeared to lose consciousness.

- At the study debriefing many of the “teachers” justified their actions by saying they were only following instructions.

- The role of deception in human subject research continues to be debated even today.

- The federal regulations allow deception in research, but only in limited conditions and only with IRB approval.
The Study of Untreated Syphilis in the Negro Male, the Tuskegee Study

Macon County, Alabama, 1932-1972

Penicillin was accepted as the treatment for syphilis in 1943 and was widely available for syphilis treatment by 1952 but was withheld from the study subjects.

Public outrage over this study lead to the National Research Act of 1974, requiring regulatory protection for human subjects.
Ethics Milestones as reaction to the Syphilis Study

- The National Research Act
- The National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research
- The “Belmont Report” (the cornerstone statement of ethical principles for treatment of research subjects)
- Federal Regulations based on the Belmont Principles
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 Principals:

- **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

Additional protections for vulnerable populations in Subparts B-D

Federal Regulations and Policy

Additional Protections Included in 45 CFR 46:

- Subpart B - Additional DHHS Protections Pertaining to Research, Development, and Related Activities Involving Fetuses, Pregnant Women, and Human In Vitro Fertilization

- 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
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.
Applicability

- Federally supported or conducted research
- Research which is not federally supported or conducted, if the research is carried out in accord with a Multiple Project Assurance (MPA) approved by OHRP
Basic Protections

The federal regulations contain three basic protections for human subjects:

- Institutional Assurances
- IRB Review
- Informed Consent
IRB Decision Matrix

**BENEFICIENCE**
- Risk/Benefit Analysis
- Experimental Design
- Qualifications of PI

**JUSTICE**
- Subject selection
- Inclusion/exclusion
- Recruitment

**RESPECT FOR PERSONS**
- Informed consent
- Surrogate consent
- Assent
- Protection of subjects (especially vulnerable populations)