Brief History of the Protection of Human Subjects in Research

Photo credit: Main Commission for the Investigation of CrimesAagainst the Polish Nation-Institute of National Memory, Warsaw, Poland. http://www.ushmm.org/research/doctors/two.htm

- Physical and mental suffering and injury should be avoided
- There should be no expectation that death or disabling injury will occur from the experiment
- Risk vs. benefit
- Protect subjects against injury, disability, or death
- Only scientifically qualified individuals should conduct human experimentation
- Subject can terminate her/his involvement

- The "Modern" era of human subject protection is considered to have started with the promulgation of the Nuremberg Code.

Declaration of Helsinki

Recommendations Guiding Medical Doctors in Biomedical Research Involving Human Subjects

- 1953: World Medical Association
- 1964: Guide of ethical principles issued
- Amended: 1975, 1983, 1989, 1996, 2000

1947: Nuremberg Code

10 key points

- Voluntary informed consent
- Experiment should be for the good of society, results not obtainable by other means
- Experiment should be based upon prior animal studies

Picture credit: U.S. Holocaust Memorial Museum, Washington, D.C. http://www.ushmm.org/research/doctors/howen.htm

Issues addressed:

- Research w/humans should be based on laboratory and animal experimentation
- Experimental protocol should be reviewed by independent committee
- Informed consent
- Research conducted by medically/scientifically qualified individuals
- Risks/benefits
- Privacy of the subject
- Publication of research results

1966: Henry Beecher NEJM article

"Ethics and Clinical Research"

- 22 human research investigations of dubious ethicity
- Discussed:
  - Study design
  - Informed consent
- Some subjects did not know that they were involved in an experiment
- Standard of care treatments withheld
- Patients were harmed by the studies

- Applications
  - Informed Consent
    - Information
    - Comprehension
    - Voluntariness
  - Assessment of Risks and Benefits
    - Many kinds of harms and benefits: physical, psychological, legal, social, economic
    - Justification of risk
    - Vulnerable populations
  - Selection of Subjects
    - Individual: Researchers exhibit fairness
    - Social: Distinction between classes able to bear the burden of research participation

1974: Congresses Passes the National Research Act

- Informed consent
- IRBs
- Creates the National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research
  - 1979: Ethical Principles and Guidelines for the Protection of Human Subjects in Research (Belmont Report)

Council for the International Organization of Medical Sciences (CIOMS)

- 1982: *Proposed International Guidelines for Biomedical Research Involving Human Subjects*
- 1991: *International Guidelines for Ethical Review of Epidemiological Studies*
- 1993: *Guidelines* revised to address issues raised by vaccines and drugs trials, transnational research, and studies with vulnerable populations

1979: Belmont Report

- Research vs. Practice
- Basic Ethical Principles
  - Respect for persons
    - Individuals should be treated as autonomous agents
    - Those with diminished autonomy are entitled to protection
  - Beneficence
    - Do no harm
    - Maximize possible benefits and minimize possible harms
  - Justice
    - "Fairness in distribution"- Who ought to receive the benefits of research and bear its burdens?

- **1991:** 17 Federal agencies that conduct, support or regulate human subjects research adopt the **Federal Policy for the Protection of Human Subjects**

  - "Common Rule" -

  Federal Register (6/18/91); 56: 28002-28032

  - 3 Basic Protective Mechanisms for Human Subjects

    (1) IRB Review of Research

    (2) Informed Consent by Subjects

    (3) Institutional Assurances of Compliance

"The most important continuing protection for human subjects is the presence of well-trained and sensitized investigators and IRB members"

Protecting Human Subjects:
Status of Recommendations
OIG, DHHS (2000)