

Brief History of the Protection of Human Subjects in Research

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

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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/charges.htm>
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- 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

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

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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

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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

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1966: Henry Beecher NEJM article

“Ethics and Clinical Research”

- 22 human research investigations of dubious ethnicity
- 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

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1974: Congress 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)

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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?

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- 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

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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

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- 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

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“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)

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