Protecting Human Research Participants

NIH Office of Extramural Research

(Excerpt)

Introduction

Research with human subjects can occasionally result in a dilemma for investigators. When the goals of the research are designed to make major contributions to a field, such as improving the understanding of a disease process or determining the efficacy of an intervention, investigators may perceive the outcomes of their studies to be more important than providing protections for individual participants in the research.

Although it is understandable to focus on goals, our society values the rights and welfare of individuals. It is not considered ethical behavior to use individuals solely as means to an end.

The importance of demonstrating respect for research participants is reflected in the principles used to define ethical research and the regulations, policies, and guidance that describe the implementation of those principles.

History

What This Module Covers:

Before discussing the current system for the protection of human subjects in research, it is important to review some of the significant historical events that have influenced current ethical guidelines and HHS regulations.

Historical Events

- Outcomes of the Syphilis Study at Tuskegee

The first accounts of this study appeared in the national press in 1972. The resulting public outrage led to the appointment of an ad hoc advisory panel by the Department of Health, Education and Welfare (which later was split into the Department of Education and the Department of Health and Human Services [HHS]) to review the study and develop recommendations to ensure that such experiments would never again be conducted.

Outcomes included:

1. National Research Act of 1974

2. Basic HHS Policy for Protection of Human Research Subjects

3. National Commission for the Protection of Human Subjects of Biomedical and

- Behavioral Research

Timeline of Events

--1932-1972: Syphilis Study at Tuskegee

More information may be found in: Brandt, AM. 1978. Racism and Research: The Case of the Tuskegee Syphilis Study. Hastings Center Report 8(6): 21-29, and in Jones, JH. 1993. Bad Blood: Tuskegee Syphilis Experiment. Rev. ed. New York: Free Press.

--1939-1945: Nazi Medical War Crimes

More information may be found in: Annas, GJ, and Grodin, MA. 1992. The Nazi Doctors and the

Nuremburg Code, Human Rights in Human Experimentation. New York: Oxford University Press.

--1944-1974: Cold War Human Radiation Experiments

The U.S. Government conducted more than 400 experiments to determine the effects of exposure to ionizing radiation on human health or to calibrate instruments designed to detect radiation. Most studies involved minimal risks and most of those involving greater than minimal risks included appropriate informed consent.

There were, however, cases where human subjects suffered physical injuries as a result of participating in studies that offered no prospect of direct benefit, or from interventions that were considered controversial at the time that were presented as standard practice.

See https://www.atomicheritage.org/history/human-radiation-experiments for more

--1991: Publication of the Common Rule

The Federal Policy for the Protection of Human Subjects or the "Common Rule" was published in 1991 and codified in separate regulations by 15 Federal departments and agencies

See: http://www.hhs.gov/ohrp/humansubjects/commonrule/index.html for more information.

--1993-1994: Revelation of Human Radiation Experiments

President Clinton established the Advisory Committee on Human Radiation Experiments to investigate human radiation experiments during the period 1944 to 1974; examine cases in which radiation was intentionally released into the environment for research purposes; identify ethical and scientific standards for evaluating these events; and deliver recommendations to the Human Radiation Interagency Working Group. The Committee recommended government apologies and financial compensation in cases where:

Efforts were made by the government to keep information secret from these individuals, their families or the public to avoid embarrassment or potential legal liability, and where this secrecy had the effect of denying individuals the opportunity to pursue potential grievances

There was no prospect of direct medical benefit to the subjects, or interventions considered controversial at the time were presented as standard practice, and physical injury attributable to the experiment resulted

See https://ehss.energy.gov/ohre/road

--2000: The Office of Human Research Protections

The Office of Human Research Protections (OHRP) was elevated to the level of the U.S.

Department of Health and Human Services, replacing the NIH Office for Protection from Research Risks (OPRR). The OHRP provides leadership for all 17 Federal agencies that carry out research involving humans under the Common Rule regulations. The Office has regulatory authority for the protection of human subjects in research and policies and procedures for Institutional Review Boards.

To learn more about OHRP, visit http://www.hhs.gov/ohrp/

--2004: The Secretary's Advisory Committee on Human Research Protections

The Secretary's Advisory Committee on Human Research Protections (SACHRP) was established to provide expert advice and recommendations to the Secretary of Health and Human Services and the Assistant Secretary for Health on issues and topics pertaining to or associated with the protection of human research subjects. See http://www.hhs.gov/ohrp/sachrp.

Regulations

The Belmont Report summarizes the three basic ethical principles of clinical research as:

1. Respect for persons

    a. Individuals should be treated as autonomous agents

    b. Persons with diminished autonomy are entitled to additional protections

2. Beneficence

    a. Do no harm

    b. Maximize possible benefits and minimize possible harms

3. Justice

a. Requires that individuals and groups be treated fairly and equitably in terms of bearing the burdens and receiving the benefits of research

Justice requires:

- Fair procedures and outcomes in the selection of research participants, and
- Distribution of benefits and burdens among the populations participating in research.

Individual justice requires that:

- Benefits of participation in research are offered to a diverse eligible population, and
- Risks of participation in research are shared by a diverse population

Social justice requires that consideration is given to classes of subjects that ought, and ought not, to participate in research. Considerations are based on:

- The ability of members of that class to bear burdens and
- The appropriateness of placing further burdens on already burdened persons.

Informed Consent

The HHS regulations (45 CFR 46.116) require that investigators obtain legally effective informed consent from prospective participants in a way that allows them to consider whether or not to participate and that minimizes the possibility for coercion or undue influence.

Potential participants must understand that enrolling in the research is voluntary and that they may withdraw from the study at any time without penalty or loss of benefits (45 CFR 46.116(a)).

In order for participation in research to be voluntary, the potential for coercion and undue influence must be minimized.

Informed consent should be understood as an on-going process rather than a level of legal protection for an institution. It is not intended to be a one-time act of having a participant sign a form.

Informed consent is designed to inform research subjects about the purpose, risks, potential benefits and alternatives to the research that allows people to make a decision about whether or not to participate based on their own goals and values. This exchange of such information should occur at enrollment and throughout the study.

Investigators are responsible for providing information during the informed consent process in a manner that is understandable to the potential participants. Investigators should not enroll anyone in a study unless the investigator is confident that the individual comprehends all information disclosed and agrees

to procedures described during the informed consent process.

Respect for Persons:

During the informed consent process, the principle of respect for persons is applied by requiring that all human subjects provide voluntary informed consent to participate in the research.

Practical application of this principle means that potential study participants must:

- Give their consent freely and voluntarily
- Have the decisional capacity to understand the information presented to them
- Be provided complete information about the study in order to make an informed decision

Institutional Review Boards

Institutional Review Boards (IRBs) are specialized committees required by HHS regulations that safeguard the rights and welfare of human subjects. IRBs determine "the acceptability of proposed research in terms of institutional commitments and regulations, applicable law, and standards of professional conduct and practice" (45 CFR 46.107).

The major roles of IRBs in the oversight of research are:

1. Initial review and approval or disapproval of the proposed research activity
2. Ensuring that the proposed informed consent process meets all of the requirements of 45 CFR 46.116
3. Providing continuing oversight for progress reports and protocols for ongoing research Studies

Criteria for IRB Approval of Research (45 CFR 46.111)

- Risks to human subjects are minimized
- Risks to human subjects are reasonable in relation to anticipated benefits, if any, to human subjects and the importance of the knowledge that may reasonably be expected to result from the research
- Selection of human subjects is equitable

• Informed consent will be sought from each prospective research participant or the prospective research participant's legally authorized representative in accordance with and to the extent required by the HHS regulations (45 CFR 46.116)

• Informed consent will be appropriately documented in accordance with and to the extent required by the HHS regulations (45 CFR 46.117)

• When appropriate, the research plan makes adequate provision for monitoring the data collected to ensure the safety of the human subjects, and when appropriate there are adequate provisions to protect the privacy of human subjects and to maintain the confidentiality of data