Protection of Human Subjects in Research Funded or Regulated by U.S. Government: How today's rules prohibit ethical abuses in human subjects research

Federal regulations for the protection of human subjects in research have evolved over time in response to increasing awareness of ethical issues. Today, a researcher who is compliant with current Federal regulations would not be able to conduct a study, domestically or in another country, with the ethical violations present in the Sexually Transmitted Disease (STD) Inoculation Study.

The history of biomedical research in the U.S., 1940-1970's:

There was tremendous growth in research around World War II. Human subjects research entered what some scholars have described as an "unashamedly utilitarian phase." Subjects were often institutionalized individuals who were not always fully informed of the risks of the study or asked for consent.

Infectious disease research, particularly venereal diseases, was a focus of the U.S. government because of the toll diseases like syphilis and gonorrhea were taking on the armed services. One method for studying infectious disease was by intentionally infecting subjects with the disease-causing pathogen. Prisoners were commonly used because they were easily monitored in a highly controlled environment. Dr. Cutler was a researcher on two such studies: infection of prisoners with gonorrhea at the United States Penitentiary at Terre Haute (1943) and with syphilis at Sing Sing Correctional Facility (1953).

Abuses began to emerge into public awareness in the 1960s and 70s. Henry Beecher outlined 22 studies that violated basic standards of ethical research. His manuscript included the infamous Willowbrook hepatitis studies (1956-1970). In addition, the USPHS Tuskegee Syphilis Study (1932-1972) received significant attention from the media and lawmakers in the early 1970s.

The history and evolution of human subjects protections:

Prior to World War II there were no specific codes of ethics, laws, or regulations governing the conduct of human subjects research. In 1949 The Nuremberg Code was developed in response to the medical experiments from the Nazi doctor's trial. It outlined ten principles for ethical research, including the importance of voluntary consent of research subjects.

In 1964 the Declaration of Helsinki was issued by the World Medical Association as a guide for physicians conducting research. In 1966 the Public Health Service issued a policy requiring informed consent. As a response to the abuses in the Tuskegee study the U.S. Congress passed the National Research Act in 1974, which established the National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research. This Commission drafted a set of guidelines (the Belmont Report) for the ethical conduct of research including three key principles: respect for persons, beneficence, and justice.

Current human subjects protections:

The Belmont report was subsequently adopted by the U.S. Department of Health and Human Services as regulations governing all research involving human subjects supported or conducted by the Department. These rules, referred to as the Common Rule (45 CFR 46), were later adopted by other federal agencies that conduct or support research. All U.S. government funded human subjects research, domestic and

international, is governed by the Common Rule. The Common Rule sets forth requirements for: review by an Institutional Review Board (IRB), informed consent, and additional protections for vulnerable populations.

The National Institutes of Health (NIH) requires that NIH-supported projects must meet the current human subjects protections requirements. In addition, grant applications for research conducted in the U.S. or internationally must describe the following: the risks to any human subjects enrolled in the study, the protections the researchers will provide against those risks, and the potential benefits of the proposed research to the subjects and others.

This could not happen today

When Dr. Cutler and his colleagues were conducting their studies in Guatemala in 1946, there were no formalized regulations regarding the protection of human subjects in research. Today the regulations that govern research funded by the United States Government, whether it is conducted domestically or internationally, would prohibit this type of study.

Protections for vulnerable populations: Current Federal regulations provide additional protections and special requirements for research involving children and prisoners and instruct IRBs to be cognizant of the special problems of research involving vulnerable populations. Groups considered to be vulnerable are: children, prisoners, pregnant women, mentally disabled persons, and economically or educationally disadvantaged persons. Studies seeking to enroll vulnerable subjects must provide additional safeguards to protect the rights and welfare of these subjects.

Informed consent: Dr. Cutler and his colleagues used deception to infect vulnerable captive individuals in Guatemala. This is prohibited today. Researchers must fully explain the risks associated with their study to all research participants. Participants must indicate their informed consent.

Review by an Institutional Review Board: Human subject research is reviewed and approved by an IRB using the following criteria: 1) risks to subjects must be minimized and reasonable in relation to anticipated benefits; 2) the selection of subjects must be equitable, with attention to the special problems of research involving vulnerable populations; 3) additional safeguards must be included if the research involves vulnerable populations; 4) informed consent must be sought and appropriately documented if the risk is greater than minimal; 5) researchers must continually monitor the data collected to ensure safety of subjects; and 6) the privacy of subjects must be maintained.