

Policy Number: 1

Title: Human Subjects Research Overview

Date of Last Revision: July 5, 2007

I. Introduction

In accordance with the UCLA Federalwide Assurance (FWA) maintained with the Department of Health and Human Services (DHHS), Office for Human Research Protections (OHRP), all human subjects research conducted by or under the auspices of UCLA will be performed in accordance with Title 45 Code of Federal Regulations, Part 46 (45 CFR 46). Human subjects of clinical investigations regulated by the Food and Drug Administration (FDA) are also protected under 21 CFR 50 and 21 CFR 56. In addition, the actions of UCLA will also conform to all applicable federal, State and local laws and regulations.

University policy requires that researchers respect and protect the rights and welfare of individuals recruited for, or participating in, research conducted by or under the auspices of UCLA. In the review and conduct of research, actions by UCLA will be guided by the principles set forth in the Belmont Report, i.e., respect for persons, beneficence, and justice.

As federally mandated, UCLA designates and impanels the Institutional Review Boards (IRBs) to protect the rights and welfare of human research subjects. The Office for Protection of Research Subjects (OPRS) at UCLA was created to support investigators and to staff the IRBs. The IRBs are required by federal regulations to review all University affiliated human subject research conducted by or under the auspices of UCLA, regardless of funding, to ensure the rights, welfare, and protection of all subjects.

II. Brief History of Research Ethics

Nuremberg Code: On December 9, 1946, an American military tribunal opened criminal proceedings against 23 leading German physicians and administrators for their willing participation in war crimes and crimes against humanity. German physicians were charged for conducting medical experiments on thousands of concentration camp prisoners without their consent. Many of the subjects of these experiments died or were permanently crippled. The Nuremberg Code was established in 1948 as a direct result of this trial, becoming the *first international document which advocated voluntary participation and informed consent in research.*

Declaration of Helsinki: In 1964, the World Medical Association developed the Declaration of Helsinki as a statement of ethical principles to provide guidance to physicians and other

participants in medical research involving human subjects. The Declaration *governs international research ethics and is the basis for Good Clinical Practices used today.*

National Research Act: Between 1932 and 1972, the US Public Health Service conducted a research project involving low-income African-American males infected with syphilis. Subjects were not told about their disease, and although a proven cure (penicillin) became available in 1950s, the study continued until 1972 with participants being denied treatment. Many subjects died of syphilis during the study. The study was stopped in 1973. As a result of the Tuskegee Syphilis Study, the National Research Act of 1974 was passed.

The National Research Act created the **National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research**, which was *charged to identify the basic ethical principles that should underlie the conduct of biomedical and behavioral research involving human subjects and to develop guidelines which should be followed to assure that such research is conducted in accordance with those principles.* The Commission drafted The Belmont Report, a foundational document for the ethics of human subjects research in the United States.

The Belmont Report: In 1974, the passage of the National Research Act established the National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research. The Commission published the Belmont Report - Ethical Principles and Guidelines for the Protection of Human Subjects of Research, which *articulates the basic ethical principles that guide the conduct of research with human subjects and form the foundation of 45 CFR 46.* Three principles were defined in the report as basic to the protection of human subjects: 1) respect for persons, 2) beneficence, and 3) justice.

1. In consideration of **respect for persons**, investigators are required to seek voluntary, written informed consent from potential subjects. Voluntary informed consent means that subjects are given explicit assurances of the voluntary nature of their participation in terms that are easy to understand and are not under duress. The consent form also includes adequate information about the study that will assist subjects in intelligently deciding whether to participate in research. In addition, respect means honoring the privacy of individuals and maintaining their confidentiality. Respect for minors and mentally disabled persons requires taking extra precautions to protect those individuals who are immature or incapacitated, perhaps even to the extent of excluding them from participation in certain research. The extent of protection depends on the risks and benefits of the research to the participants.
2. The principle of **beneficence** requires that researchers maximize the potential benefits to the subjects and minimize the potential risks of harm. Benefits to the subjects, or in the form of generalized knowledge gained from the research, should always outweigh the risks. Finally, if there are any risks resulting from participation in the research, then there must be benefits, either to the subject, or to humanity or society in general.
3. The principle of **justice** means that subjects are selected fairly and that the risks and benefits of research are distributed equitably. Investigators should take precautions not to systematically select subjects simply because of the subjects' easy availability, their

compromised position, or because of social, racial, sexual, economic, or cultural biases institutionalized in society. Investigators should base inclusion criteria on those factors that most effectively and soundly address the research problem.

Investigators and the IRBs are responsible for ensuring that the review and conduct of research conducted by or under the auspices of UCLA is guided by the principles set forth in the Belmont Report.

III. Definitions

A. **Research** is defined by 45 CFR 46.102(d) as a systematic investigation, including research development, testing and evaluation, designed to develop or contribute to generalizable knowledge. Activities which meet this definition constitute research for purposes of this policy, whether or not they are conducted or supported under a program which is considered research for other purposes. For example, some demonstration and service programs may include research activities.

B. **Human subject** is defined by 45 CFR 46.102(f) as a living individual about whom an investigator (whether professional or student) conducting research obtains: (1) data through intervention or interaction with the individual, or (2) identifiable private information.

1. **Intervention** includes both physical procedures by which data are gathered (for example, venipuncture) and manipulations of the subject or the subject's environment that are performed for research purposes.

2. **Interaction** includes communication or interpersonal contact between investigator (or his/her research staff) and subject (or the subject's identifiable private information).

3. **Private information** includes information about behavior that occurs in a context in which an individual can reasonably expect that no observation or recording is taking place, and information which has been provided for specific purposes by an individual and which the individual can reasonably expect will not be made public (for example, a medical record). Private information must be individually **identifiable** (i.e., the identity of the subject is or may readily be ascertained by the investigator or associated with the information) in order for obtaining the information to constitute research involving human subjects. Identifiable private information obtained from a primary participant about a third party may constitute research involving human subjects.

C. **Human subject** is defined by the FDA in 21 CFR 50.3(g) and 56.102 (e) as an individual who is or becomes a participant in research, either as a recipient of the test article or as a control. A subject may be either a healthy human or a patient. For device research, a subject is also an individual on whose specimen a device is used (21 CFR 812.3(p)).

D. **Clinical Investigation** is defined by the FDA in 21 CFR 50.3(c) and 56.102(c) as any experiment that involves a test article and one or more human subjects and that is subject to FDA regulations.

1. **Test article** is defined by the FDA in 21 CFR 50.3(j) and 56.102(l) as any drug (including a biological product for human use), medical device for human use, human food additive, color additive, electronic product, or any other article subject to FDA regulations.

E. **Human Subject Research:** Any research that involves humans as defined in 45 CFR 46.102(f) or any clinical investigation that involves humans as defined by the FDA.

Please refer to [*OPRS/IRB Policy 3: Human Subjects Research Determinations*](#) for details of OPRS/IRB responsibility for determining what activities constitute human subjects research and require IRB review and approval or Certification of Exemption from IRB review.

V. **Shared Responsibility for the Ethical Conduct of Research with Human Subjects**

The dignity and welfare of individuals who participate in research is a central concern of everyone involved with the protection of human subjects. The university, investigators and their research staff, and the IRBs/OPRS, share the collective responsibility for the ethical conduct of research. This collaboration must exist in a culture of trust, complete openness, and honesty by upholding the highest ethical principles in the conduct of research. By upholding the highest standards, we build public support for the pursuit of greater knowledge in a safe research environment.

VI. **Institutional Review Board (IRB) Responsibility**

The review of research involving human subjects performed by faculty, students, or employees of UCLA is conducted by five IRBs:

1. **North General Institutional Review Board (NGIRB)** reviews social-behavioral research, including anthropology, psychology, sociology, education, linguistics, AGSM and economics.
2. **South General Institutional Review Board (SGIRB)** reviews social-behavioral research related to public health, including health services, quality of care, quality of life, health prevention and education, psycho-social drug abuse research, etc.
3. **Medical Institutional Review Board 1 (MIRB1)** reviews general biomedical research excluding oncology, infectious diseases and neuroscience research.

4. **Medical Institutional Review Board 2 (MIRB2)** reviews biomedical research in oncology, HIV-AIDS and infectious diseases.
5. **Medical Institutional Review Board 3 (MIRB3)** reviews biomedical research in the neurosciences and general biomedical research.

The IRBs are comprised of faculty representatives from various academic disciplines at UCLA, clinicians, researchers, non-scientific members, and community subject representatives who are not affiliated with the university. The Committees operate within the federal guidelines with respect to the review and approval of research protocols involving human subjects.

The IRBs are charged with a twofold mission: 1) to determine and certify that all projects reviewed by the Committees conform to the federal and state regulations and institutional policies regarding the health, welfare, safety, rights, and privileges of human subjects; and 2) assist investigators in conducting ethical research which complies with all regulations and policies in a way that permits accomplishment of the research activity.

The mission is accomplished through the conduct of ethically responsible and scientifically valid research, continuous education of the investigators, IRB staff and members, ongoing review of research activities, including new findings, and compliance with federal and state regulations and institutional policies.

The process of Committee review of protocols involves Committee review, negotiations between investigators and the IRBs for approval of research, and IRB/OPRS outreach to the research community. The process serves to ensure safe and ethical conduct of research that ultimately will protect the rights and welfare of human subjects.

Please refer to [*OPRS/IRB Policy 2: Activities Subject to UCLA OPRS/IRB Jurisdiction*](#) for details of IRB authority and responsibility.

VIII. Human Research Policy Board

The Human Research Policy Board (HRPB) is an administrative board advisory to and appointed by the Executive Vice Chancellor. The HRPB is a standing committee of senior administrators, IRB chairs, senior faculty from the biomedical, social, and behavioral sciences, and an Academic Senate observer. The Board addresses institutional human research related policy issues but does not assess research proposals or serve as an additional IRB. The HRPB is not authorized to accept or consider appeals of IRB decisions.

Regulations:

45 CFR 46
21 CFR 50, 56
21 CFR 312, 600
21 CFR 361
21 CFR 812

References:

The National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research, The Belmont Report - Ethical Principles and Guidelines for the Protection of Human Subjects of Research, April 18, 1979.

<http://hhs.gov/ohrp/humansubjects/guidance/belmont.htm>

Attached:

- ORPS-1 UCLA Assurance Policies
<http://oprs.ucla.edu/human/documents/pdf/UCLA-Assurance-Policies.pdf>
- OPRS-6 UCLA OPRS Human Research News, "Vice Chancellor Roberto Peccei on the responsibilities of faculty, staff, administration, the IRBs, ARC, and OPRS," November 11, 2004.
http://oprs.ucla.edu/human/news/item?item_id=127272