Ensuring that the rights and welfare of participants in research are protected.
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UC Human Research Protection Program (HRPP) and Institutional Review Board (IRB)
Scope, Purpose, and Process

- Describe the ethical principles for the protection of human subjects of research
- Identify human subjects research projects that require oversight by the UC IRB
- Outline the UC HRPP protocol review process
- Recommend ways to improve interactions with the HRPP and IRB
History of Human Subject Abuse

Timeline of Events

Explore the Timeline by clicking on an event.

1939-1945 Nazi Medical War Crimes
1946 Nuremberg Doctors’ Trial
1947 American Psychological
1948 UN adopted Universal Declaration of Human Rights
1947 Nuremberg Code
1944-1974 Cold War Human Radiation Experiments
1932-1972 Syphilis Study at Tuskegee
1953 First U.S. Federal Policy for Protection of Human Subjects
1956 Willowbrook Study
1963 Jewish Chronic Disease Hospital Study
1966 Henry Beecher’s Publication
1964 Declaration of Helsinki
1974 Federal Protection for Human Subjects
1979 The Belmont Report
1980 Publication of FDA Regulations
1982 CIOMS Guidelines
1991 Publication of the Common Rule
1993-1994 Advisory Committee on Human Radiation Experiments
1995 Establishment of the National Bioethics Advisory Commission
1996 HIPAA Privacy Rule
1999 The Death of Jesse Gelsinger
2004 OHRP
2000 SACHRP

https://phrp.nihtraining.com/history/07_history.php
The Nazi-era Abuses

Experiments on non-consenting prisoners

- Injecting dye into the eyes
- Surgeries without anesthesia
- Induction of head injuries
- Exposure to extreme temperatures
- Infecting of individuals with malaria
The Nuremberg Code


The basic principles governing the ethical conduct of research involving human subjects
THE NUREMBERG CODE

1. The voluntary consent of the human subject is absolutely essential. This means that the person involved should have legal capacity to give consent; should be so situated as to be able to exercise free power of choice, without the intervention of any element of force, fraud, deceit, duress, over-reaching, or other ulterior form of constraint or coercion; and should have sufficient knowledge and comprehension of the elements of the subject matter involved, as to enable him to make an understanding and enlightened decision. This latter element requires that, before the acceptance of an affirmative decision by the experimental subject, there should be made known to him the nature, duration, and purpose of the experiment; the method and means by which it is to be conducted; all inconveniences and hazards reasonably to be expected; and the effects upon him of his health or person, which may possibly come from his participation in the experiment.

   The duty and responsibility for ascertaining the quality of the consent rests upon each individual who initiates, directs or engages in the experiment. It is a personal duty and responsibility which may not be delegated to another with impunity.

2. The experiment should be such as to yield fruitful results for the good of society, unprocurable by other methods or means of study, and not random and unnecessary in nature.

3. The experiment should be so designed and based on the results of animal experimentation and a knowledge of the natural history of the disease or other problem under study, that the anticipated results will justify the performance of the experiment.

4. The experiment should be so conducted as to avoid all unnecessary physical and mental suffering and injury.

5. No experiment should be conducted, where there is an a priori reason to believe that death or disabling injury will occur, except, perhaps, in those experiments where the experimental physicians also serve as subjects.

6. The degree of risk to be taken should never exceed that determined by the humanitarian importance of the problem to be solved by the experiment.

7. Proper preparations should be made and adequate facilities provided to protect the experimental subject against even remote possibilities of injury, disability, or death.

8. The experiment should be conducted only by scientifically qualified persons. The highest degree of skill and care should be required through all stages of the experiment of those who conduct or engage in the experiment.

9. During the course of the experiment, the human subject should be at liberty to bring the experiment to an end, if he has reached the physical or mental state, where continuation of the experiment seemed to him to be impossible.

10. During the course of the experiment, the scientist in charge must be prepared to terminate the experiment at any stage, if he has probable cause to believe, in the exercise of the good faith, superior skill and careful judgement required of him, that a continuation of the experiment is likely to result in injury, disability, or death to the experimental subject.

US Public Health Service Tuskegee Syphilis Study 1932-1972

"Tuskegee Study of Untreated Syphilis in the Negro Male"

- 600 African-American men from rural Alabama
- Determine from autopsies what the disease does to the human body.
- No successful treatments for syphilis at the time
US Public Health Service Tuskegee Syphilis Study 1932-1972

"Tuskegee Study of Untreated Syphilis in the Negro Male"

- Promised free transportation to and from hospitals, free hot lunches, free medicine for any disease other than syphilis and free burial after autopsies were performed
US Public Health Service Tuskegee Syphilis Study 1932-1972

"Tuskegee Study of Untreated Syphilis in the Negro Male"

- Penicillin became the treatment of choice for the disease in the late 1940s
- The “Patients were not denied drugs, rather, they were not offered drugs.”
- 15 scientific reports were published in the medical literature
HOUSE COMMITTEE BACKS AMENDMENT SEEKING WARS END

Foreign Affairs Panel Votes 10 to 11, in a Move to Get Blow to White House

Group Ears Strongly Upholds Vietnam Policy—Takes Conditions Softer

By JOHN W. FISKE Special to The New York Times
WASHINGTON, July 25—The House Foreign Affairs Committee, once an ardent booster of the Vietnam war, voted today for legislation that would end a termination of American involvement in the war, subject to a limited cease-fire with North Vietnam and removal of American prisoners.

By a vote of 16 to 11, the committee attached the antiwar amendment to a $15 billion foreign aid and assistance bill. A corresponding bill in the Senate was voted down yesterday after a similar but stronger antiwar amendment was

Dean at Columbia Is Shot; Suspended Student Sought

College Official, at Work in Hamilton Hall Office, Struck by 3 Bullets

By RICHARD M. GANS

Dean Henry S. Coleman of Columbia College was shot three times and mortally wounded yesterday afternoon, and police officials said they were seeking a suspended undergraduate for questioning.

Mr. Coleman, the dean of students, and one of the most popular figures on the Columbia campus, was shot in the chest, jaw and wrist while working in his office at Hamilton Hall. He was reported in good condition and "doing fine" last night after undergoing chest surgery at St. Luke's Hospital.

The undergraduate being sought was identified as Eugene McKinney, a 20-year-old Chicagoan. The Police Department's chief spokesmen, Det. John D. Galanos, declined to say explicitly whether Mr. McKinney was a suspect, but he observed that "Eugene McKinney is currently being sought for questions in connection with this crime." And he added that "something further I say at this time could affect the investigation."
WASHINGTON, July 25—For 40 years the United States Public Health Service has conducted a study in which human beings with syphilis, who were induced to serve as guinea pigs, have gone without medical treatment for the disease and a few have died of its late effects, even though an effective therapy was eventually discovered.

The study was conducted to determine from autopsies what the disease does to the human body.

Officials of the health service who initiated the experiment have long since retired. Current officials, who say they have serious doubts about the morality of the study, also say that it is too late to treat the syphilis in any surviving participants.

Doctors in the service say they are now rendering whatever other medical services they can give to the survivors while the study of the disease's effects continues.

Dr. Merlin K. DuVal, Assistant Secretary of Health, Education and Welfare for Health and Scientific Affairs, expressed shock on learning of the study. He said that he was making an immediate investigation.

The experiment, called the Tuskegee Study, began in 1932 with about 600 black men.
President Clinton apologized for the emotional, medical, research and psychological damage of the study in 1996.
In 1972, the public became aware of the Tuskegee study, which took place in the southern United States from 1932 to 1972.

In 1974 the National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research was established.


Those principles respect for persons, beneficence and justice are accepted as the 3 fundamental principles for the ethical conduct of research involving human participants.
The Belmont Report
Basic Ethical Principles

1. Respect for Persons
   – individuals should be treated as autonomous agents

“To respect autonomy is to give weight to the autonomous person’s considered opinions and choices while refraining from obstructing his or her actions...”

– Belmont Report
The Belmont Report
Basic Ethical Principles

2. Beneficence
   – maximize benefits and minimize harms

"Persons are treated in an ethical manner not only by respecting their decisions and protecting them from harm, but also by making efforts to secure their well-being. Such treatment falls under the principle of beneficence. The term beneficence is often understood to cover acts of kindness or charity that go beyond strict obligation. In this document, beneficence is understood in a stronger sense, as an obligation."

– Belmont Report
3. Justice

– fairness in selection of research participants

"Just as the principle of respect for persons finds expression in the requirements for consent, and the principle of beneficence in risk/benefit assessment, the principle of justice gives rise to moral requirements that there be fair procedures and outcomes in the selection of research subjects."

– Belmont Report
• US Federal Regulations on Human Subjects Research
  – HHS
  – FDA
45CFR46

• Title 45--Public Welfare

• PART 46-PROTECTION OF HUMAN SUBJECTS
  – Subpart A “The Common Rule” 1991
SUBPART A—
Basic HHS Policy for Protection of Human Research Subjects

Sec.
46.101 To what does this policy apply?
46.102 Definitions.

46.103 Assuring compliance with this policy—research conducted or supported by any Federal Department or Agency.

46.104. [Reserved]
46.106

46.107 IRB membership.
46.108 IRB functions and operations.
46.109 IRB review of research.

46.110 Expedited review procedures for certain kinds of research involving no more than minimal risk, and for minor changes in approved research.

46.111 Criteria for IRB approval of research.

46.112 Review by institution.

46.113 Suspension or termination of IRB approval of research.

46.114 Cooperative research.

46.115 IRB records.

46.116 General requirements for informed consent.

46.117 Documentation of informed consent.

46.118 Applications and proposals lacking definite plans for involvement of human subjects.

46.119 Research undertaken without the intention of involving human subjects.

46.120 Evaluation and disposition of applications and proposals for research to be conducted or supported by a Federal Department or Agency.

46.121 [Reserved]

46.122 Use of Federal funds.

46.123 Early termination of research support. Evaluation of applications and proposals.

46.124 Conditions.
45CFR46

• Title 45--Public Welfare

• PART 46-PROTECTION OF HUMAN SUBJECTS
  – Subpart B    Prisoners
  – Subpart C    Pregnant women and fetuses
  – Subpart D    Minors
  – Subpart E    Registration of IRBs
Common Rule & Other Changes

01/17/2018: The U.S. Department of Health and Human Services (HHS) issued an Interim Final Rule delaying the implementation of the final revisions to the Federal Policy for the Protection of Human Subjects (a.k.a. the "Common Rule") until July 19, 2018.

NIH policy changes (e.g., single IRB of Record) remain scheduled to go into effect on January 25, 2018.

Major Regulation Changes

- **Continuing Review** - No longer required for some minimal risk research, including studies where the only remaining activity is the analysis of identifiable data/biospecimens or activity to obtain follow-up clinical data.

- **Exemptions** - New categories and clarification of existing categories. Some exemptions may require "limited IRB review" (similar to an expedited review process), while others may qualify for "self-determination".

- **Informed Consent** - A new "Key Elements" section and a rearrangement of content is designed to facilitate a potential subject’s decision to participate or not.
Regulations: Non-Federally Supported Studies Involving Human Subjects

21 CFR 50: Protection of Human Subjects

- Requirement for informed consent
  - Elements of informed consent
  - Documentation of informed consent

21 CFR 56: Institutional Review Boards

- Requirements for IRB review
  - Membership, functions, review procedures, etc.
  - Criteria for IRB approval

Applies to all clinical investigators regulated by FDA
Role of the IRB

• Assures that:
  – conducted in accordance with
    • the principles of the Belmont Report
    • federal, state, and local laws and regulations
    • UC HRPP Policies and Procedures
Does your project need IRB review?
Does your research need IRB review?

Research + Human Subject = IRB
45CFR46 Definitions

• Research
  – “a systematic investigation…designed to develop or contribute to generalizable knowledge.”
45CFR46 Definitions

• Human subject
  – a living individual about whom an investigator conducting research obtains
  – data through intervention or interaction with the individual
  – identifiable private information.
RESEARCH
Systematic investigation and designed to develop or contribute to generalizable knowledge

HUMAN SUBJECT
Research about a living individual either through intervention/interaction or identifiable private information

IRB Review
Is your research subject to the FDA regulations?
Definitions-FDA

• Clinical investigation
  – Any experiment that involves a test article and one or more human subjects, meets the requirements for prior submission to the Food and Drug Administration under section 505(i) or 520(g) of the act, or
  – The results of which are intended to be used as part of an application for a research or marketing permit.
Definitions-FDA

• Human subject
  – individual who is or becomes a participant in research
  – recipient of the test article or as a control
  – either a healthy individual or a patient
Definitions-FDA

• **Test article**

  Any article subject to regulation under the act or under the Public Health Service Act
  - drugs
  - biological product
  - medical device
  - human food additive
  - color additive
  - electronic product
Levels of IRB Review

**Full Board**
- More than “minimal risk” to subjects
- Not covered under other review categories
- Example: interventions involving physical or emotional discomfort or sensitive data

**Expedited**
- Not greater than minimal risk
- Fits one of the 9 Expedited Review Categories*
- Examples: Collection of biospecimens by noninvasive means, Research with existing documents/record collected for non-research purposes in which subjects are identifiable

**Exempt**
- Less than “minimal risk”
- Fits one of the 6 Exempt Categories*
- Example: Research with de-identified records, anonymous surveys

*Defined by federal regulation (45 CFR 46)
Tara Knipp, CIP

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Board Member, University of Cincinnati Institutional Review Board

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Overview of HRPP & IRB

- UC HRPP/IRB responsibilities
  - Administration of IRB activities,
  - SBR and Medical research
  - Central/Single IRB review of multisite research,
  - Quality assurance audits,
  - Support for FDA regulated research
  - Researcher training
  - Support contract review, data requests, reliance agreements

- Weekly full Board meetings

- 4,433 determinations in 2017
Submission & Review Process

• Send request for ePas account with name, email address, UC ID, department affiliation and last four digits of SSN (non employees need to self register via CPD prior to sending request)

• Access ePas account and open new study application or applicable submission type (amendment, continuing review, or reportable event). Complete smartform, upload applicable documents and submit.
Submission & Review Process

• HPA performs regulatory category, reviews submission documents and assigns IRB reviewer(s). May send submission back to the research team or send it on to the IRB reviewer(s). Two week window.
• IRB member(s) review submission. May send submission back to the HPA with approval or changes requested. Two week window.
• Once approved, HPA issues approval letter and documents.
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Improving Your Experience and Outcomes

Remember that the process is a partnership
Improving Your Experience and Outcomes

• Complete the research protocol prior to starting the ePAs study application.
• Verify that the information in the research protocol, informed consent form, ePAs study application as well as other documents is consistent prior to submission.
• Remember that each study record can only have one submission under review at a time.
Improving Your Experience and Outcomes

• Get to know the regulations, guidelines, policies, procedures and standard practices for the type of research you are conducting.

• Be considerate and respectful of the HRPP/IRB person with whom you are interacting.

• Call for help when you are doing something new (e.g., remuneration, enrolling vulnerable populations, international research, etc.).
Institutional Review Board

Ensuring that the rights and welfare of participants in research are protected.