Ethical Considerations in Conducting Human Subjects Research

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What is an IRB?

• IRB is an acronym for Institutional Review Board

• The IRB is responsible for the review and approval of all research involving human subjects
  ▪ Scientific validity
  ▪ Ethical review

• Function of the IRB: Protecting the rights, welfare and safety of human subjects through
  ▪ review
  ▪ approval
  ▪ continuing oversight

IRB Jurisdiction

Jurisdiction of the IRB - All research activities involving human subjects

Per Federal Regulations:

• Research is defined as a systematic investigation, including research development, testing and evaluation, designed to develop or contribute to generalizable knowledge.

• A Human Subject is defined as a living individual about whom an investigator conducting research obtains data through intervention or interaction with the individual or identifiable private information

For a project to include human subjects research under the purview of the USF IRB, both of the definitions outlined above must be met.
Why Were IRBs Formed?

The birth of the Institutional Review Board resulted from an unfortunate history of crimes against humanity in the name of science and research.

Research Ethics: Historical Events

Monster Study: 1939

- Termed the "Monster Study" by peers of the PI, Wendell Johnson from University of Iowa
- 22 orphaned children selected for this study on stuttering. Some who actually stuttered and some who did not.
- The investigators provided positive feedback to some of the subjects and negative feedback to others, depending upon whether they were included in the control or experimental group
- Many of the children with normal speech patterns suffered negative psychological effects, and some developed lifetime speech problems
Nuremburg Trials: 1946 - 1947

- Trials at Nuremburg – series of military tribunals in response to WWII atrocities in the concentration camps
  - “Researchers” conducted cruel experiments on children & adults held in the camps with no informed consent
- Many defendants argued that the experiments were morally justified
  - Participants were going to die anyway
  - Sacrifice would provide scientific knowledge benefiting many
- 15 of the 25 defendants (20 MDs) were found guilty and 7 were sentenced to death

Nuremburg Code: 1947

- Developed as a direct result of the Nazi medical experiment atrocities committed during World War II that were revealed at the Nuremberg Trials.
  - Makes clear that
    - The welfare and rights of human subjects must be protected
    - The research conducted must be sound and beneficial
    - The freedom of human subjects to participate or not is inviolable

Nuremburg Photographs

- Children at Auschwitz exposed to medical experiments during the Nazi regime
  - Cold Water experiments
  - Medical personnel experiment on a prisoner at the Buchenwald concentration camp.
Willowbrook State School: 1963-1966

- Designed to gain an understanding of the natural history of infectious hepatitis and to test the effects of gamma globulin in preventing or ameliorating the disease
- Children subjects were deliberately infected with the hepatitis virus
  - Early subjects were fed extracts of stools from infected individuals and later subjects received injections of more purified virus preparations
  - Only children whose parents gave permission to participate in the research were admitted
- Investigators stated that the vast majority acquired hepatitis while at Willowbrook, and it would be better for them to be infected under carefully controlled research conditions

Milgram Experiments: 1960s

- Measured the willingness of subjects to obey an authority figure who instructed them to complete a task that conflicted with their conscience
  - Subject (T) instructed by the researcher (E) to give what subject believes are painful shocks to the learner-actor (L) when an incorrect answer is given
  - Subjects believed actual shocks were being given for incorrect responses
- Many subjects realized they were capable of committing acts of extreme violence against others
- Ethical questions raised due to the associated extreme emotional stress and insight into personal flaws inflicted upon the subjects

The Tearoom Study: 1965-1970

- Conducted by Laud Humphreys, a Ph.D. student studying stereotypical beliefs about men who committed impersonal sexual acts with one another in public restrooms.
- He gained the trust of individuals by posing as a voyeur and lookout.
- He secretly followed some men and recorded license numbers of their vehicles.
- A year later, Humphreys showed up at their private homes disguised and claiming to be a health service interviewer. He asked questions about their sexual orientation, marital status, race, job and other personal information.
The Tearoom Study, cont.

- The report had enough detail that the identities of some participants were obvious to them and their families.

- Issues:
  - Subjects were never consented
  - Invasion of privacy
  - Failure to protect against deductive disclosure of identity
  - Deception was used with no debriefing
  - There was a risk of societal harm and risk of civil or criminal liability (many of the men were married and these at the time, arrests for this behavior in public was more prevalent)

Tuskegee Syphilis Study: 1932 – 1972


- Subjects were disadvantaged, rural African-American men, several who were already infected and some who were not
  - Provided with free medical exams, free meals, and burial insurance, but were not told about their disease

- Infected men were denied treatment, although penicillin was accepted treatment in 1943, and PCN was available for syphilis treatment in 1952

The Havasupai: 2010

- As part of a partnership with the tribe, Arizona State University (ASU) collected specimens for diabetes research in 1989.

- Researchers then used the samples, without complete consent, for unrelated studies on schizophrenia, migration and inbreeding- all taboo topics for the tribe

- In 2004, the Havasupai Tribe filed a lawsuit against Arizona Board of Regents and ASU researchers

- A settlement was reached in 2010:
  - $700,000
  - Medical care & educational services
  - Return of known remaining specimens

Guatemala Inoculation Studies: 1946-1948

- US Public Health Service Sexually Transmitted Diseases Study of 1946-1948
  - Conducted by the same PI as the syphilis studies in Tuskegee

- Intent was to discover new ways to prevent STDs
  - First experiments involved infecting female commercial sex workers with gonorrhea or syphilis, and then allowing them to have unprotected sex with soldiers or inmates
  - When few men became infected, research approach was changed to intentional infection of soldiers, prisoners and mental health patients

- ~1500 subjects involved
  - Governmental & Institutional officials were aware, but no subject consent obtained
  - Most, but not all, were treated for their infections

National Research Act of 1974

- Created the National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research

- Charge to the Commission:
  - Identify the basic ethical principles that should underlie the conduct of biomedical and behavioral research involving human subjects
  - Develop guidelines which should be followed to assure that such research is conducted in accordance with those principles

The Belmont Report: 1979

- Issued April 1979 by the National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research

- Made necessary due to a long history of various questions, concerns, difficulties and problems that arose in medical experimentation and other forms of research efforts involving the enrollment of human subjects

- Distinguished between medical practice (treatment) and research

- Established the responsibility of the investigator to submit research activity for review by an Institutional Review Board
The Three Pillars of Belmont

Respect for Persons

• The freedom and capacity of subjects must be protected

• Each subject is an autonomous agent, capable of making their own decisions, and not to be used as a means to an end

• Special measures must be taken to protect the rights and welfare of persons with diminished autonomy

• Informed consent is central to protecting the autonomy of human subjects

Beneficence

• Researchers have the obligation to secure the well-being of subjects

• Possible benefits must be maximized and possible harms must be minimized

Justice
Justice

- Researchers question who receives the benefits of research and who bears its burdens
- There must be fairness in the distribution of the risks and benefits of the research
- Each person must equally share in the distribution of risks/benefits according to individual need, individual effort, societal contribution, and merit

Review Types

Exempt –
Minimal risk research, which is reviewed by the Chairperson or Designee. Study approval for five years and then automatically closed.
Examples:
- Anonymous Surveys
- Data that is “already on the shelf”
- Research comparing standard practice methodology in an educational setting
- No radically new instructional strategy or use of random assignment of subjects
- Common practice in elementary, secondary, or post-secondary settings

18 HIPAA Identifiers
These identifiers must be removed for a study to be considered de-identified:

1. Name
2. All geographical subdivisions smaller than a state (street address, city, county, precinct). Note: Zip codes or the equivalent must be removed, but the first three digits of the zip code is not considered a “direct identifier” if geographical units formed by combining all zip codes with the same three digits contain more than 20,000 individuals.
3. All elements of dates except year, for dates directly related to an individual, e.g., date of birth, admission date, discharge date, date of death.
4. Telephone numbers
5. Facsimile numbers
6. Electronic mail addresses
7. Social Security numbers
8. Medical Records numbers, prescription numbers
9. Health Plan numbers
10. Account Numbers
11. Certificate/license numbers
12. Vehicle identification/serial numbers/license plate numbers
13. Device identifiers/serial numbers
14. Universal Resource Location (URLs) for Web sites
15. Internet Protocol (IP) Address
16. Biometric identifiers, e.g. fingerprints, voice prints
17. Full face or comparable photographic images
18. Any other unique number, characteristic, or code that could be used to identify the individual. (If you abstract any unique identifiers, please specify)
Review Types, cont.

**Expedited**
Minimal risk research, which is reviewed by the Chairperson or Designee. Study approval for one year. Continuing review application must be submitted to continue study activities.

Examples:
- Surveys that include identifiable information
- Interviews
- Analysis of data collected (or that will be collected) for non-research purposes
- Secondary data analysis
- Video or audio recordings
- Focus Groups

**Full Board**
Reviewed by fully convened Board. Study approval for one year. Continuing review application must be submitted to continue study activities.

Examples:
- Greater than minimal risk research
- Studies involving prisoners or data about prisoners
- Novel therapeutic interventions
- Other vulnerable populations
- Collecting information that could place the participant at risk of civil or criminal liability or may cause other societal harms (stigma, ostracism, excommunication, etc.)

What Is Informed Consent?

*(HRPP Policy #601)*

- Informed consent is central to the protection of human subjects. It is both a process and a procedure
  - The process is the exchange of information that takes place between the prospective subject, and the investigator and study staff, before, during and sometimes after the study
  - The procedure includes the shaping and signing of an informed consent document
  - There are also times the IRB can waive consent
Informed Consent & Belmont

• IC is founded on the principle of Respect for Persons
• Requires that individuals be treated as autonomous agents, and that the rights and welfare of persons with diminished autonomy be appropriately protected
• Respect for persons requires that prospective research subjects “be given the opportunity to choose what shall or shall not happen to them” and thus necessitates adequate standards for informed consent

What to Expect during Review

• Once your study has been fully submitted through eIRB, a Research Compliance Administrator (RCA) will review the application
  - He/she will contact you if there are questions or necessary revisions needed

• The study will be reviewed per its “category”
  - Exempt & Expedited review studies are reviewed by the Chair and/or Designee
    • Most Social & Behavioral fall into these categories
  - Full-board studies are reviewed at the convened meetings
    • 3 Biomedical/1 Social & Behavioral per month

Useful Links and Resources


ARC (Online submission system) Help Desk Contact: rsrch-arc@usf.edu or 813-974-2880

ARC Home Page: https://ARC.research.usf.edu/prod/ (ARC training materials can be found in the menu on the left side of the page)

IRB (HRPP) Web Site: http://www.research.usf.edu/dric/hrpp/default.asp

CITI Education: https://www.citiprogram.org/

IRB Manager: Brandy Hutchinson bhutchin@usf.edu

IRB Education Coordinator: Olivia@usf.edu (also contact for guidance on need for IRB oversight of Social & Behavioral studies)
Questions?