IRB 101: An Introduction to IRB

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Today’s Agenda

- What is the IRB?
- Human Subject Research Defined
- What IS Informed Consent?
- Communicating with the IRB
- Submitting a Study
- Timeframes and Timetables
- What to Expect during Review
- Post–Approval – Now What?
- Question and Answer
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
- Per Federal regulations (45CFR46) IRBs are mandated to maintain a specific composition
  - 5 Members, Scientists, Non–Scientists, Community Members, Non–Affiliated party
The birth of the Institutional Review Board resulted from an unfortunate history of crimes against humanity in the name of science and research
Nazi Medical Experiments with Cold Water
Nuremberg Trials: 1946–1947

- Forced prisoners to participate in research without informed consent

- Many defendants argued that the experiments were morally justified since the participants were going to die anyway, and their sacrifice would provide scientific knowledge benefiting many

- 15 of the 25 defendants (20 MDs) were found guilty and 7 were sentenced to death

- The judgment included a set of standards known as the Nuremberg Code, an ethical yardstick
Nuremberg 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

- Adapted from a section of the August 1947 verdict called “Permissible Medical Experiments”

- 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
Tuskegee Syphilis Study: 1932–1972


- Subjects were disadvantaged, rural African-American men: 399 chosen who were infected and 201 who were not
  - Provided with free medical exams, free meals, and burial insurance, but were not told about their disease

- Men were denied treatment, although penicillin was accepted treatment in 1943, and PCN was available for syphilis treatment in 1952
1963 – 1966, studies were carried out at the Willowbrook State School, a New York State institution for "mentally defective persons"

Designed to gain an understanding of the natural history of infectious hepatitis and subsequently to test the effects of gamma globulin in preventing or ameliorating the disease

The subjects, all children, 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
Investigators defended their actions by pointing out that the vast majority of children acquired the infection anyway while at Willowbrook, and perhaps it would be better for them to be infected under carefully controlled research conditions.

During the studies, Willowbrook closed its doors to new patients, claiming overcrowded conditions. The hepatitis program, which occupied its own space at the institution, continued to admit new patients. Parents were unable to admit their child to Willowbrook unless agreed to his/her participation in the studies.

Public outcry over the perception that parents and their children were given little choice about whether or not to participate in research.
The Jewish Chronic Disease Hospital Study – 1960s

- 1963 at New York City's Jewish Chronic Disease Hospital to develop information on the nature of the human transplant rejection process

- Involved the injection of live cancer cells into patients who were hospitalized with various chronic debilitating diseases

- Researchers claim oral consent was given but not documented. Patients were not told that they would receive cancer cells because the investigators believed this would frighten the patients unnecessarily

- Investigators defended the conduct of the study on the basis that they had good cause to predict that the cancer cells were going to be rejected
Outcomes

- Tuskegee Lead to the National Research Act of 1974, requiring regulatory protection for human subjects

- The National Research Act also created the National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research
  - This commission wrote the “Belmont Report” in 1979, which is the cornerstone statement of ethical principles for treatment of research subjects

- In 1981 the DHHS & FDA published convergent regulations that were based on the Belmont Principles

- In 1991, after 10 years of negotiation, 17 federal departments and agencies agreed to adopt the basic human subjects protections. This is referred to as the “Common Rule”
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
Belmont Report

- 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

Respect for Persons

Beneficence

Justice
Respect for Persons

- The freedom and capacity of subjects must be protected
- Each subject is an autonomous agent
- 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
Researchers have the obligation to secure the well-being of subjects

Possible benefits must be maximized and possible harms must be minimized
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.
Per Federal regulations (45CFR46.102(d)), research is defined as the **systematic investigation**, including research development, testing and evaluation, *designed to develop or contribute to generalizable knowledge*. 
Per Federal regulations (45CFR46.102(f)), a human subject is defined as:

- A living individual about whom an investigator (whether professional or student) conducting research obtains
  - Data through intervention or interaction with the individual, or
  - Identifiable private information
If your project meets the criteria described, then it may be research with human subjects

**BUT**

- The IRB can make this determination for you
Review Types

- **Exempt**
  - Must meet certain criteria
  - Differs from “Not Human Subjects Research” (designation made by IRB)

- **Expedited**
  - Must meet certain criteria
  - Does not mean “fast”
  - Reviewed by Chair and/or Designee

- **Full Board**
  - Reviewed by fully convened Board
What IS Informed Consent?

- 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 (ICD).
- 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
- The Belmont Report states that an autonomous agent is “an individual capable of deliberation about personal goals and of acting under the direction of such deliberation”
- 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
Required Elements of ICD

- Per 45CFR46.166(a), the list of required elements includes:
  - A statement that the study involves research, an explanation of the purposes, the expected duration, a description of the procedures, and identification of any experimental procedures
  - A description of foreseeable risks/benefits
  - Disclosure of appropriate alternatives
  - A statement on the extent to which confidentiality will be maintained
ICD Elements, Cont.

- Discussion of compensation and explanation regarding availability of medical treatments for research-related injury (minimal risk research only)

- Contact information for questions about research subject rights and research-related injury

- A statement that participation is voluntary, refusal to participate will involve no penalty or loss of benefits, and the subject is free to withdraw at any time

- Other additional elements as appropriate (i.e., HIPAA Authorization for research performed by covered entities)
The IRB has created several templates to ensure that researchers’ ICDs include all of the required elements.

There are Tip Sheets located on the IRB website at: http://www.research.usf.edu/cs/irb_Tips.htm
The IRB mandates that all investigators complete a comprehensive course on Human Subject Protections

- The list of available courses is available on the IRB website
- The recommended course is delivered via Collaborative Institutional Training Initiative (CITI Program – www.citiprogram.org)
- The IRB policy (HRPP Policy 711) on investigator education may be found on the IRB website: http://www.research.usf.edu/cs/irb_policies.htm
The USF IRB has recently converted to an electronic system, eIRB

*Account Activation Takes Approximately 48 hours*
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
  - 5 Biomedical/1 Social & Behavioral per month
Important Notes on Timeframes

- It is important to note that the review process requires careful collaboration with multiple parties.

- Not all studies are approved on first submission.
  - **Allow at least 30–45 days to ensure adequate time for review.**
Once the approval letter has been issued, the research may commence.

All protocol amendments and/or revisions MUST be submitted to the IRB BEFORE implementation.

Expedited and Full-board studies require annual review.

Exempt studies are approved for 5 years.

Once the study is complete, a final report MUST be submitted to the IRB to officially close the study.
Questions??