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?
- PI-Initiated Studies & PI Responsibility
- Submitting a Study
- What to Expect during Review
- Timeframes and Timetables
- 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
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.
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.
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”
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
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.
What is Research?

- 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.
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)
ICD Templates & Tip Sheets

- 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
Where to Begin

- 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
Special Considerations for PI-Initiated Studies

- Does your study require FDA approval?
  - If you are researching a novel drug or device, or are experimenting with an off-label use of an approved drug or device, you may need to consult with the FDA.

- Is your study going to be implemented at multiple sites?
  - Multi-center studies may require additional documentation from the participating centers in order for final IRB approval to be issued.

- Are there any COIs that need to be managed? (e.g. patents, ownership rights, investments, etc.)
The Principal Investigator ultimately shoulders the responsibility for the conduct of the study, including the actions or inactions of the study team, support staff, pharmaceutical staff, etc.
Submitting a Study

- The USF IRB has recently converted to an electronic system, eIRB

*Account Activation Takes Approximately 48 hours
The staff on the eIRB help desk have created several tutorials for working in eIRB, including submitting new studies and converting paper studies into the eIRB system.
The eIRB system is a “Smart Form” driven system

As you or your study team answer questions on the application, the forms will be customized to ensure that only those questions that are likely to apply to your research will appear

- TIP: It’s a good idea to answer BOTH the required questions (*) AND the optional questions to ensure a more seamless 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
- Full-board studies are reviewed at the convened meetings (5 Biomedical/1 Social & Behavioral per mo)
  - Some boards may request that the PI be present at the convened meeting in order to answer questions about the study.
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, after which they are closed.

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