Human Subjects Committee Protecting Human Research Subjects

Objective

- Familiarity with Human Subject research requirements
- Understanding of need for protection of research subjects

Glossary of Key Terms:

- **Assent:** Agreement by an individual who is not competent to give legally valid informed consent (e.g., a child or decisionally impaired person) to participate in research.
- **Assurance:** A formal written commitment that is submitted to a federal agency in which an institution promises to comply with applicable regulations governing research with human subjects and stipulates the procedures through which compliance will be achieved.
- **DHHS:** U.S. Department of Health and Human Services, a federal agency.

- **FDA**: Food and Drug Administration, an agency of the federal government and part of DHHS.
- **Human Subjects**: Living individual(s) about whom an investigator conducting research obtains 1) data through intervention or interaction with the individual; 2) or identifiable private information.

- **Informed consent:** A person's voluntary agreement based upon adequate knowledge and understanding of relevant information to participate in research or to undergo a diagnostic, therapeutic, or preventative procedure. In giving consent, subjects may not waive or appear to waive any of their legal rights, or release or appear to release the institution or agent from liability for negligence.
- **Institution**: Any public or private entity or agency.
- **Institutional Review Board:** A specially constituted review body established or designated by an entity to protect the welfare of the human subjects recruited to participate in biomedical or behavioral research. Also known as the "IRB" or Human Subjects Committee.

- **Investigator/ Principal Investigator**: The scientist or scholar with primary responsibility for the design and conduct of a research project.
- **Minimal risk:** A risk is minimal where the probability and magnitude of harm or discomfort anticipated in the proposed research are not greater, in and of themselves, than those ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests.
- **OHRP:** Office for Human Research Protection, an agency of the federal government and part of DHHS.

- **Protocol:** The formal design or plan of an experiment or research activity; specifically the plan submitted to an IRB for review and to the agency for research support. The protocol includes a description of the research design or methodology to be employed, the eligibility requirements for prospective subjects and controls, the treatment regimen, and the proposed methods of analysis that will be performed on the collected data.
- **Research**: A systematic investigation (i.e. the gathering and analysis of information) designed to develop or contribute to generalizeable knowledge.

- **Review (of research):** The concurrent oversight of research on a periodic basis by an IRB. In addition to the at least annual reviews mandated by the federal regulations, reviews may, if deemed appropriate, also be conducted on a continuous or periodic basis.
- **Risk:** The probability of harm or injury (physical, psychological, social, or economic) occurring as a result of participation in a research study.
- **Vulnerable population:** Those subjects that require special protections, i.e. children, decisionally impaired, pregnant women and fetuses, and prisoners.

Research on Human Subjects is Regulated by
45 CFR 46 (DHHS)
21 CFR 50, 21 CFR 56 (FDA)

WHY?

Historical Perspective

Nazi Experiments – War Crimes and Crimes Against Humanity (1946)

- Freezing Experiments
- Infectious Diseases
- High and Low Altitude Experiments
- Pharmacological Experiments
- Surgical Experiments
- Traumatic Injuries

Thalidomide Tragedy (1961)

- Approved sedative in Europe in late 1950s
- Not approved by FDA, but the manufacturer gave samples to US physicians and paid them to study its safety and efficacy.
- By 1961, evidence of damage to fetus if given to pregnant mother during the first trimester.

NEJM Reported in 1966:

- Acute strep infection study. Control group receives no treatment, rheumatic fever develops in more than 70 subjects.
- Live cancer cells injected into subjects without informed consent to study immunity.

U.S. Government Funded Syphilis Study in African American Men (1932-1972). "Tuskegee"

- 400 Syphilitic men and 200 control group recruited in 1932-33, to study "bad blood".
- Subjects offered free exams, medical care, and "therapeutic" spinal taps.
- 1943 Penicillin is established as treatment for syphilis.
- 1951 Penicillin is widely available for treatment – continued to withhold from study subjects because of "never again" scientific opportunity.
- 1972 Exposed in Media
- 1973 Surviving subjects treated with penicillin
- 1974 National Research Act is implemented

1974 National Research Act

- Commission for the Protection of Human Subjects in Biomedical and Behavioral Research
- OPRR – now OHRP developed to protect human research subjects
- Required IRB review of federally funded research

- The Nuremberg Code
- The Declaration of Helsinki
- The Belmont Report

The Belmont Report – Ethical Principles

- Respect for Persons
  - -Individual Autonomy
  - -Protection of individuals with reduced autonomy
- Beneficence
  - -Maximize benefits and minimize harms
- Justice
  - -Equitable distribution of research costs and benefits

Federal Regulation Requirements (The Common Rule):

- Review of research by an IRB
- Informed consent of subjects
- Institutional assurance of compliance

IRB Membership and Qualifications

Qualifications and Requirements

- At least five members with varying backgrounds for complete and adequate review of research
- One scientific member
- One nonscientific member
- One member not otherwise affiliated with the Institution
- Inclusion of one or more individuals who are knowledgeable re vulnerable subjects – prisoner advocate
- No member may participate in the review of any project in which the member has a conflicting interest
- Expert consulting as needed, expert may not vote

Voting process for IRB

- Except when an expedited review procedure is used, the IRB must review research at convened IRB meetings at which a majority of the IRB members are present. A non-scientific member must always be present at meetings.

Types of IRB review

- Full Committee – vulnerable populations, greater than minimal risk
- Expedited/Exempt – no more than minimal risks, criteria described in regulations

Documents Required for Submittal - IRB Review (Investigator submits the following):

- Application
- Protocol
- Consent form, assent, parental permission form, legally authorized representative – guardian, proxy, health care surrogate as applicable
- Grant
- Questionnaire, survey instrument, testing measurement, interview questions
- Advertisement, flyers
- Application for Renewal – Continuing Review
- Progress Report
- Adverse Events
- Amendments or Changes to Protocol requests

IRB Authority

- Approve research
- Require modification (conditional approval)
- Disapproval
- Conduct continuing review of approved research
- Suspend or terminate previously approved research not in compliance with IRB's requirements, federal regulations, or associated with unanticipated serious harm to subjects

IRB Considerations

- The risks to the subjects
- The anticipated benefits to the subjects and others
- The importance of the knowledge that may reasonably result
- The informed consent process to be employed

IRB Responsibilities

Must report to the appropriate institutional officials, OHRP, FDA, and /or any other sponsoring agency of the federal government:

- Any injuries to human subjects or other unanticipated problems involving risks to subjects or others
- Any serious or continuing noncompliance with regulations or requirements of IRB
- Any suspension or termination of IRB approval of research

Institutional Responsibilities

- Full responsibility pursuant to Assurance
- All requirements must be met for federally sponsored research
- FSU's Assurance commits University regardless of sponsorship
- Designates IRB to review and approve research
- Provides sufficient space and staff to support IRB review and record keeping duties
- Sets the tone for an institutional culture of respect for human subjects

Institutional Official (Vice President for Research)

- Appoints IRB members and Chair
- Provides IRB with necessary resources and staff
- Supports IRB decisions
- Ensures effective institution-wide communication
- Encourages participation in HS educational activities

IRB Chair

- Ensures IRB carries out its responsibilities
- Serves as Moderator
- Conducts expedited review and approval/delegation

IRB Secretary

- Schedules IRB meetings
- Prepares and distributes agenda and reviews materials for IRB members
- Records the minutes of the meetings with required particularity

IRB Staff

- Receive all research protocols, amendments, renewals, other communication
- Intake and entry into database
- Communicate with Investigators on approval status
- Preliminary determinations as to review category
- Maintains IRB records (3 years)
- Arrange access when requested by federal authorities

Investigator Responsibilities

- Has primary duty for protecting the rights and welfare of human research subjects and for complying with all applicable provisions of the Assurance
- Conducts all research according to the IRB approved protocol and complies with all IRB determinations.
- Ensures that each potential subject understands the nature of the research, participation, and comprehension of consent process
- Provides a copy of the IRB approved informed consent document to each subject at the time of consent
- Retains all signed consent documents for at least 3 years beyond completion of the research
- Reports proposed changes/amendments to IRB for review and approval
- Reports progress of research as required by IRB, not less than once per year
- Promptly reports to IRB any unanticipated problems involving risks to subjects or others

Basic Elements of Consent

- Research v. Health Care
- Purpose of Study
- Description of the Procedures
- Description of Potential Risks and Benefits
- Alternative treatments
- Privacy and Confidentiality - HIPAA Releases/Waiver of Authorization- PHI
- Injury Compensation
- Contact Person
- Voluntariness
- Any additional elements required by the IRB

Other Factors for IRB Review

- Gender of Subjects
- Age range of subjects
- Racial and Ethnic origin of subjects
- Recruitment method
- Payment
- Readability of consent document
- Non-English speaking subjects – translation
- Assent for minors/children
- Parental permission
- Legally authorized representatives

Vulnerable Populations

- Children
- Prisoners
- Pregnant Women and Fetuses
- Decisionally impaired persons

Consequences of Noncompliance with Federal Regulations

- Suspension/shut down of research and funding
- Investigation, reporting, increased oversight
- Overhaul and reorganization of Institution reporting structure, offices
- Massive expenditures and lost efforts as consequence of noncompliance
- Initiation of legal actions by federal government, research subjects
- Payment of fines, penalties, damages, findings of liability for negligence and other malfeasance

Current Climate

- Death of Jesse Gelsinger – University of Pennsylvania
- Death of Ellen Roche – Johns Hopkins University
- Numerous suspensions and shutdowns
- Investigations
- Firings, Reorganizations, Reporting, Audits and Oversight
- Lawsuits by federal government, whistleblowers, research subjects, investigators as former faculty, IRB liability, resulting in fines, penalties, and damages.

Contact Information

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