

Navigating Drake University's IRB Procedures & Conducting Ethical Research

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Institutional Review Board (IRB)

Duty & Major Mandate from OHSR:

Protect the rights and welfare of human research subjects

Assess subject risk: Physical, psychological, social, economic, legal

Powers:

- Approve/deny protocols based on whether they meet certain standards for the protection of human subjects
- Suspend or terminate approved research that is not being conducted in accordance with IRB requirements, or that has been associated with unexpected serious harm to subjects.

Investigator Quotes

- “Who is going to pay for this requirement (ex. Translation of ICD)?!”
- “The IRB has no business questioning the science.”
- “Why does it take so much time to review, I thought Expedited meant fast?”
- “There is no risk in this research, why does the IRB even need to review it?”

Top 10 Investigator Responsibilities

1. Design & implement ethical research
2. Comply with Federal regulations
3. Obtain IRB approval
4. Comply with IRB/HIPAA requirements
5. Implement research as approved & obtain prior approval for modifications
6. Obtain informed consent/assent
7. Document informed consent/assent
8. Submit progress reports
9. Report unanticipated problems
10. Retain records & document activities

The Belmont Report - 1979

Ethical Principles and Guidelines for the Protection of Human Subjects of Research (45CFR46)

- 1) Respect for persons
 - individuals should be treated as autonomous agents
 - persons with diminished autonomy are entitled to protection
- 2) Beneficence
 - Persons are treated in an ethical manner
 - maximize possible benefits and minimize possible harms
 - respect their decisions
- 3) Justice
 - Ensure burdens/benefits of research are distributed equally

Source: <http://www.hhs.gov/ohrp/humansubjects/guidance/belmont.htm>

Terms

- CFR: Code of Federal Regulations
- FDA: Food & Drug Administration
- FWA: Federalwide Assurance
- HHS: Health & Human Services
- IEC: Independent Ethics Committee
- IRB: Institutional Review Board
- OHRP: Office for Human Research Protections

<http://www.hhs.gov/ohrp/faq.html>

Definitions

- Minimal Risk: "***Minimal risk means that the probability and magnitude of harm or discomfort anticipated in the 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.***"

<http://www.hhs.gov/ohrp/humansubjects/guidance/45cfr46.htm#46.110>

Regulatory Issues and Federal Compliance

- IRB: Functions as IEB
 - Assures ethical principles of autonomy, beneficence, justice are conducted
- Federally regulated:
 - FWA: OHRP requires for ANY institution conducting non-exempt human subjects research
 - Non-compliance with FWA=can withhold conduct of any further research at the institution.
 - Follows CFR

Protecting Human Research Subjects

Does the search for knowledge always justify the "costs" (risks) to subjects?

- Key historical events
- Application of the Belmont Principles
- Drake IRB policies and procedures
 - Exempt reviews
 - Expedited reviews
 - Full board reviews
 - Continuation reviews

Key Historical Events

1940's - Nazi Studies

- Twins studies
- Cold water survival studies
- Simulated sea water drowning
- Simulated high altitude studies
- Social hygiene studies
 - Eye color experiments
 - Secret sterilization experiments
 - Many others

The Nuremberg Code - 1947

Principles for the ethical use of human subjects in research

- Voluntary consent
- Anticipation of scientific benefits
- Benefits outweigh risks
- Animal experiments first
- Avoid suffering
- No intentional death or disability
- Protection from harm
- Subject is free to discontinue
- Qualified investigators
- Safety oversight mechanism

1930-1972: The Tuskegee Experiment

Study of the effects of syphilis on the body

- 399 AA men signed up for free medical care with the U.S. Public Health Service
- men were never told they had syphilis
- denied access to penicillin, even after penicillin was available in 1947

IRB problems:

- physical harm to participants and their relatives
- deceived participants

1963 - New York City's Jewish Chronic Disease Hospital

- Study the nature of the human transplant rejection
- Injection of live cancer cells into elderly patients with various chronic debilitating diseases
- Oral consent, not documented
- Patients were not told that they would receive cancer cells since this would frighten the patients unnecessarily. Investigators defended this view on the basis that they had good cause to predict that the cancer cells were going to be rejected

1963-1966: Willowbrook hepatitis studies

Willowbrook School for "mentally defective persons"

- Studies to assess the natural history of infectious hepatitis and to test the effects of gamma globulin in preventing or ameliorating the disease
- Children were deliberately infected with the hepatitis virus
- Defended deliberate infection since vast majority of pts acquired the infection anyway while at Willowbrook
- School closed its doors to new pts due to overcrowding, but the hepatitis program continued to admit new patients
- Some parents were unable to admit their child to

1961-5: Obedience and Authority Studies (Stanley Milgram)

Were Holocaust accomplices just following orders?

- "Teachers" (research subjects) applied "shocks" to "learners" (actors) if the learners did not remember a list of words correctly
- The "generator" had 30 increments from "slight shock" to "danger: severe shock (300volts)" to "XXX (450volts)"
- Results: 65% of all of "teachers" punished the "learners" to the maximum 450 volts; no subject stopped before reaching 300 volts. Learned that even when pushed to an extreme, people will follow authority

IRB problems: deception, psychological harm

1970: The Tearoom Trade

Study of male homosexual behavior in bathrooms

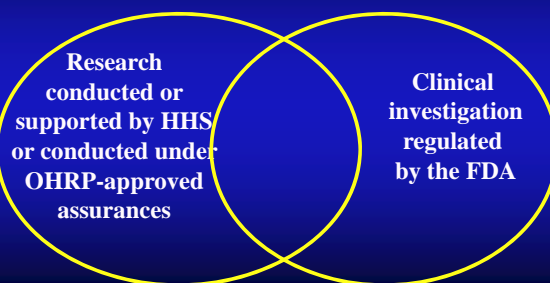
- Designed to learn more about homosexuals
- Researchers followed subjects, got license plates and addresses then interviewed them
- Found that policemen, high school counselors, lawyers were participating
- Changed people's perceptions of homosexuals

IRB problems: no voluntary consent, privacy issues

IRB Application of the Belmont Principles

- 1) Respect for Persons
 - Informed consent
 - Protect privacy and maintain confidentiality
 - Additional safeguards for protection of subjects likely to be vulnerable to coercion or undue influence
- 2) Beneficence
 - Assessment of risk/benefit to include study design
 - Ensure that risks to subjects are minimized
 - Ensure risks are justified by benefits of the research
- 3) Justice
 - Ensure that selection of subjects is equitable and without coercion

Applicability of HHS Versus FDA Human Subject Protection Regulations



HHS Regulations: Title 45 Code of Federal Regulations - Part 46

Protection of Human Subjects

Subpart A - Fundamental Provisions:

- Assurance of Compliance
- IRB requirements
- Legally effective informed consent

Subpart B - Additional Protections for Pregnant Women, Human Fetuses and Neonates Involved in Research.

Subpart C - Additional Protections Pertaining to Biomedical and Behavioral Research Involving Prisoners as Subjects.

Subpart D - Additional Protections for Children Involved as Subjects in Research.

Is the activity research?

- Research (according to 45 CFR - Part 46):
 - A systematic investigation designed to develop or contribute to generalizable knowledge.
- Is the activity designed to produce generalizable knowledge?
- Will the information derived from the activity be applicable to other cases?
- Will the information be gathered systematically? Will it be arranged so that conclusions can be drawn, and so that others can review those conclusions?

If yes....

Does it involve human subjects?

A human subject is involved if:

1. The person is alive and
2. Data about the person will be obtained through:
 - Intervention (e.g., taking a blood sample)
 - Interaction (e.g., administering a survey)
 - A private/confidential source (e.g., from a medical record or school transcript)

If yes....

What type of review* is needed?

Does the project require:

1. Exempt review
2. Expedited review
3. Full board review

*See Drake IRB web page for more information:
<http://www.drake.edu/academics/irb/home.html>

Exempt Review Categories (6)

1. Research conducted in established educational settings, involving normal educational practices
2. Research involving educational tests or surveys, interviews, or observations of public behavior. UNLESS:
 - i. information is recorded in such a manner that the subject can be readily identified (either directly or indirectly) AND
 - ii. subjects' responses could place them at risk (e.g., criminal or civil liability, financial standing, employability or reputation).
3. Research involving educational tests, surveys, interviews, or observations of public behavior, if:
 - i. subjects are elected or appointed public officials or candidates for public office, or
 - ii. federal statutes require confidentiality of identifiable information to be identified permanently.

Exempt Review Categories (6)

4. Research involving the collection or study of existing data, documents, records, pathological or diagnostic specimens. Sources must either be PUBLICLY AVAILABLE or information must be recorded IN SUCH A WAY THAT THE SUBJECT CANNOT BE IDENTIFIED (either directly or indirectly).
5. Research conducted by or subject to the approval of Federal Department or Agency Head.
6. Taste and food quality evaluations involving wholesome and safe foods.

<http://www.drake.edu/academics/irb/admin5-2.html#review5.1.5>

Exempt Reviews

- Means study is exempt from full/expedited review - **Does NOT mean that IRB review is unnecessary**
 - Research exposes subjects only to very small physical, social, or psychological risks - similar to the risks they take in everyday life
- Investigators cannot make this determination - can advise the IRB only
- Receive written authorization from the IRB of exempt status
- IRB cannot deny the project; can only deny its exempt status. If denied exempt status, the investigator must resubmit for expedited or full review.
- **Time frame for review: 7-14 days**

Link to exempt forms: <http://www.drake.edu/academics/irb/forms/index.html>

Expedited Reviews

- 1) For research activities that present no more than minimal risk to human subjects
- 2) May NOT be used where identification of the subjects and/or their responses would reasonably place them at risk of criminal or civil liability or be damaging to the subjects' financial standing, employability, insurability, reputation or be stigmatizing, unless reasonable and appropriate protections will be implemented so that risks elated to invasion of privacy and breach of privacy and breach of confidentiality are no greater than minimal.
- 3) May NOT be used for classified research on humans.

Expedited Reviews

- IRB cannot deny the project; can only deny its status. If denied expedited status, the investigator must resubmit for full review
- Requires all investigators demonstrate human subjects training (see web page below)
 - recertification required every 3 years (see web page)
- Proposal sent to 2-3 members for review
- **Time frame for review: ~14-21 days**

Link to training: <http://www.drake.edu/academics/irb/training.html>
 Link to expedited forms: <http://www.drake.edu/academics/irb/forms/index.html>

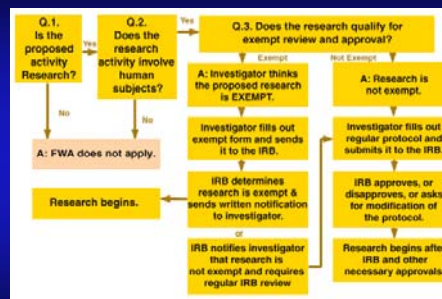
Vulnerable populations

- May include persons from the following groups:
 - Prisoners
 - Institutionalized Persons
 - Cognitively Impaired Persons
 - Comatose Persons
 - Children
 - Minorities
 - Terminally Ill Persons
 - Persons with Low Literacy
 - Drug Addicts
 - Prostitutes
 - Elderly Persons
 - Employees
 - **Students**
 - Pregnant Women

Full Board Reviews

- Projects that do not meet exempt/expedited review criteria and all studies funded by federal government.
- Requires full, convened meetings in which:
 - a majority of the IRB members must be present
 - at least one member of the non-scientific community
 - all members review proposal
 - must receive approval of a majority of members present
 - project can be denied
- Requires demonstration of human subjects training
 - recertification required every 3 years (see web page)
- **Time frame for review: 2-4 weeks**

Link to exempt forms: <http://www.drake.edu/academics/irb/forms/index.html>



Continuing Reviews

Appropriate to risk; not less than once per year.

A status report on the progress of the research:

- The number of subjects accrued
- A summary of adverse events and problems
- Withdrawal of subjects and/or complaints about the research since the last IRB review
- A summary of any relevant recent literature, interim findings, and amendments or modifications to the research since the last review
- A copy of the current informed consent document

Link to continuation form: <http://www.drake.edu/academics/irb/forms/index.html>

Key Elements of Informed Consent Documents*

1. Researcher's affiliation and sponsors
2. Purpose of the research study
3. Statement that participation is voluntary
4. Discuss potential risk(s) to subject
5. Discuss potential benefits to subject and general population
6. Statements assuring confidentiality
7. Provide assurances that decision not to participate will not influence services, grades, benefits, etc to subject.

*Relatively similar requirements are needed for studies involving implied consent mechanisms

Informed Consent

- Elements to be addressed in the consent form:

http://cme.cancer.gov/c01/e01_01a.htm

- Informed consent checklist:

<http://hhs.gov/ohrp/humansubjects/assurance/consentcls.htm>

- Certificates of Confidentiality

<http://hhs.gov/ohrp/humansubjects/guidance/certconf.pdf>

Resources

Drake IRB web page:

<http://www.drake.edu/academics/irb/home.html>

Office for Human Research Protections (OHRP):

<http://www.hhs.gov/ohrp/>

Stanford University IRB web page:

<http://humansubjects.stanford.edu/medical/index.html>



Case studies:

- http://www.stanford.edu/dept/DoR/hs/Case_Studies/cs01.html
- **Blood samples**
 - You are asked to help analyze frozen human blood samples. How should you proceed?
- **Web-based survey research**
 - A class project includes gathering opinions via a web site. Is a protocol approval needed?
- **Educational assessment**
 - You want to compare alternative educational methods. Is a protocol approval needed?
- **Observational study**
 - Your student wants to observe behavior in a public place. How should you advise her?