



Institutional Review Board for the Protection of Human Subjects

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Class Agenda

- Introduction
- Course Objectives
- IRB From an Historical Perspective
- Defining research & IRB
- Federal Regulations on IRB
- Break
- Guidelines for Preparing an IRB
- Hands-on IRB application preparation
- Discussion



Introduction

- An historical perspective and definition of the IRB
- The complex process of the Institutional Review Board (IRB) application
- Clinical trials & IRBs
- Do I need an IRB for my research?
- The basics of an IRB application:
 - general & specific guidelines

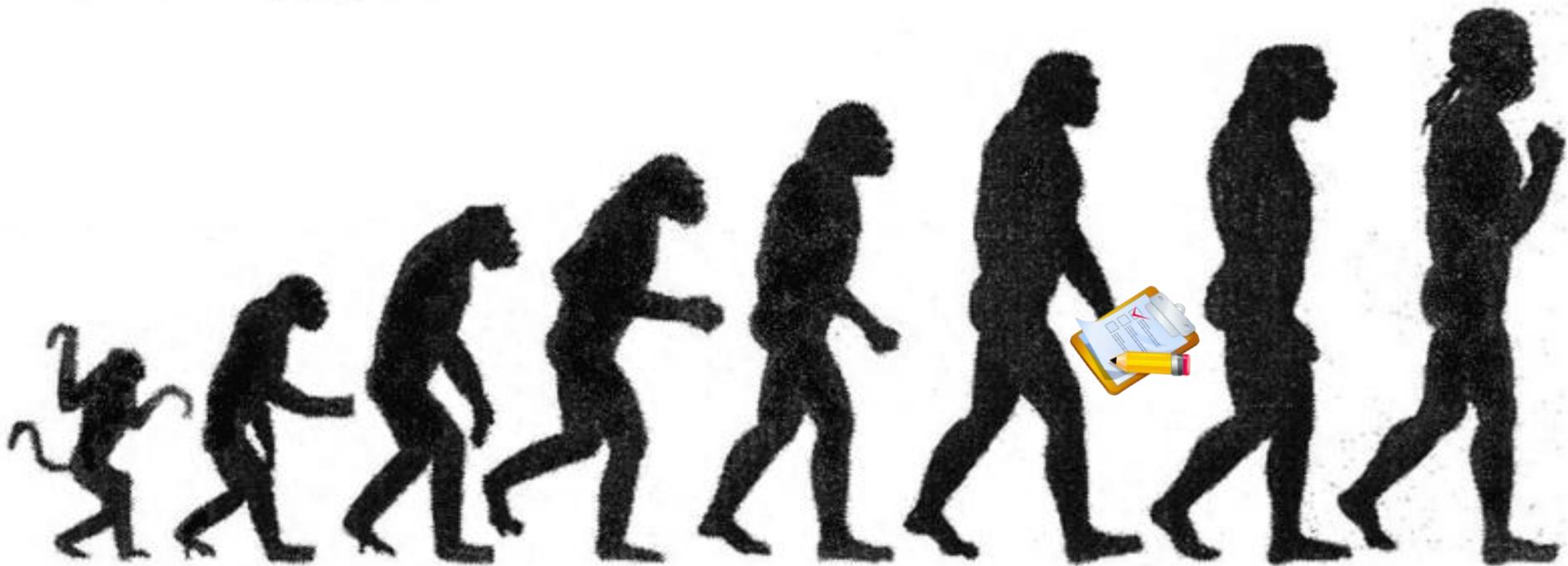


Course Objectives

- Understanding the role of the Institutional Review Board (IRB) in research.
- Understanding what ethical issues to consider when preparing to engage in a research project involving human subjects.
- Understanding what kind of research needs an IRB.
- Understanding what steps are involved in preparing an IRB application.



The Evolution of Human Subject Protections



Research Involving Humans

Includes the areas:

- Medical and administrative record data
- Research that uses leftover tissues
- Health services research
- Biomedical and other clinical research
- Behavioral research
- Survey research

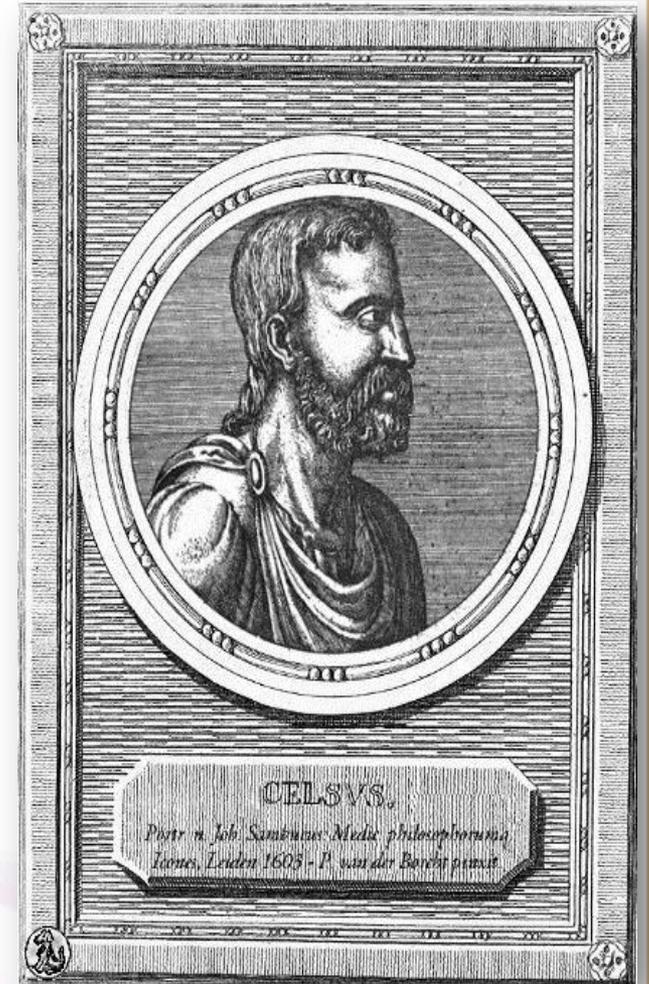


Egypt: 1 CE

"Is it not cruel to inflict on a few criminals sufferings which may benefit multitudes of innocent people through all centuries?"

- Celsus (physician)

Image credit: <http://www.general-anaesthesia.com/images/cornelius-celsus.html>



Nuremberg, Germany, 1947

23 Nazi physicians, **countless** concentration camp inmates,
10 points in the Nuremberg Code ruling



Image credit:

http://upload.wikimedia.org/wikipedia/commons/3/39/Defendants_in_the_courtroom_at_nuremberg_trials.jpg

The Nuremberg Code

- Informed consent is essential
- Research should be based on prior animal work.
- The risks should be justified by the anticipated benefits.
- Only qualified scientists must conduct research.
- Physical and mental suffering must be avoided.
- Research in which death or disabling injury is expected should not be conducted.



Access the full text of the code at

<http://history.nih.gov/research/downloads/nuremberg.pdf>

Helsinki, 1964

World Medical Association develops the Declaration of Helsinki:

“Concern for the interests of the subject must always prevail over the interests of science and society.”

Nuremberg legacy and medical therapeutic research

The publisher role & building the IRB



Henry K. Beecher, 1966

Beecher HK. "Ethics and Clinical Research" NEJM June 16, 1966

22 major journal studies with ethical breaches published in:

- New England Journal of Medicine (5)
- JAMA (2)
- Science

Heightened awareness among

- Researchers
- Press
- Public

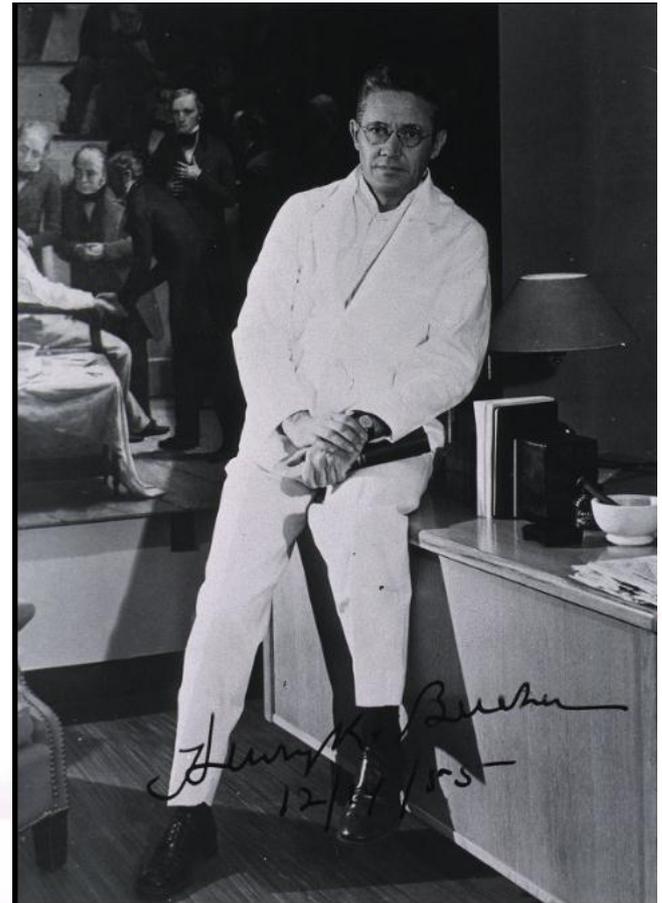


Image credit:

<http://ihm.nlm.nih.gov/luna/servlet/detail/NLMNLM~1~1~101410247~169599:-Henry-K--Beecher->

Tuskegee Study, 1932-1972

- Begun by the United States Public Health Service (USPHS)
- Purportedly designed to determine the natural course of untreated latent syphilis in 400 African American men in Tuskegee, Macon County, Alabama.
- Research subjects were matched against 200 uninfected subjects who served as a control group.

MEMORANDUM DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE
OFFICE OF THE SECRETARY

TO : Director
Center for Disease Control
THROUGH: Administrator, HS *MD* 1/22

DATE: NOV 16 1972

FROM : Assistant Secretary for Health

SUBJECT: Termination of USPHS Study of Untreated Syphilis (the Tuskegee Study)

As recommended by the Tuskegee Syphilis Study Ad Hoc Advisory Panel, I have decided that the "Tuskegee Study" as a study of untreated syphilis must be terminated. I will advise you of the necessary steps to be taken to assure that appropriate medical care be given to all remaining participants in the "Tuskegee Study" as a part of the close-out phase of the project.

Merlin K. DuVal, M.D.
Merlin K. DuVal, M.D.

Image credit:

http://www.examiningtuskegee.com/gallery_usph.html

Tuskegee Study, 1932-1972

The longest nontherapeutic experiment on human beings in medical history.

- Arthur L. Caplan
Emmanuel and Robert Hart Professor of Bioethics
Director, Center for Bioethics
University of Pennsylvania



Image credit:
<http://blackhistorywall.files.wordpress.com/2010/02/picture-device-independent-bitmap-51.jpg>

Tuskegee: Ethical Issues

- Recruitment & “special free treatments”
- Informed consent
- Heavy metals therapy vs. antibiotic therapy in 1940s
- 1950s & penicillin availability
- USPHS preventing treatment
- 1969 Center for Disease Control decision
- 1972: the media & the Department of Health, Education & Welfare



Image credit:

http://upload.wikimedia.org/wikipedia/commons/d/d2/Tuskegee_study.jpg

Willowbrook State School, 1963

1963 – 1966

Medical researcher Saul Krugman

Oral & injection inoculations of Hepatitis A virus

Gamma globulin treatment



Image credit:

<http://willowbrookstateschool.blogspot.com/>

Milgram Experiment, 1961

Yale University social psychology

Authority figure instructions vs. personal conscience

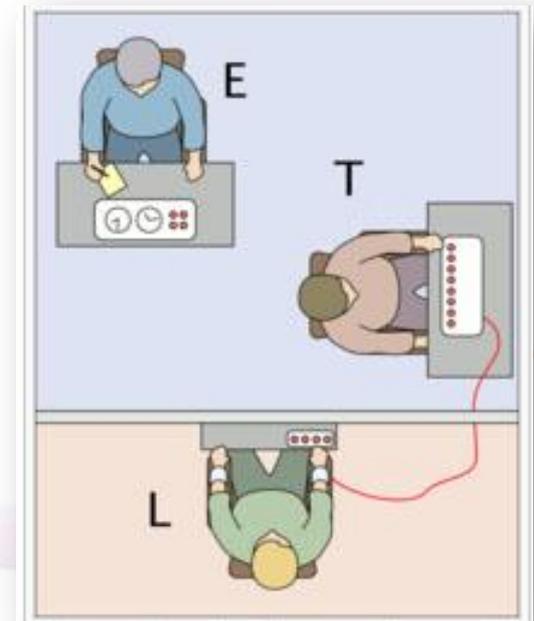


Image credit:

http://en.wikipedia.org/wiki/File:Milgram_Experiment_v2.png

Tearoom Trade Study, 1970

Ph.D. dissertation & book by Laud Humphreys

Lack of research disclosure & subject notification

Collection of personal information under false pretenses

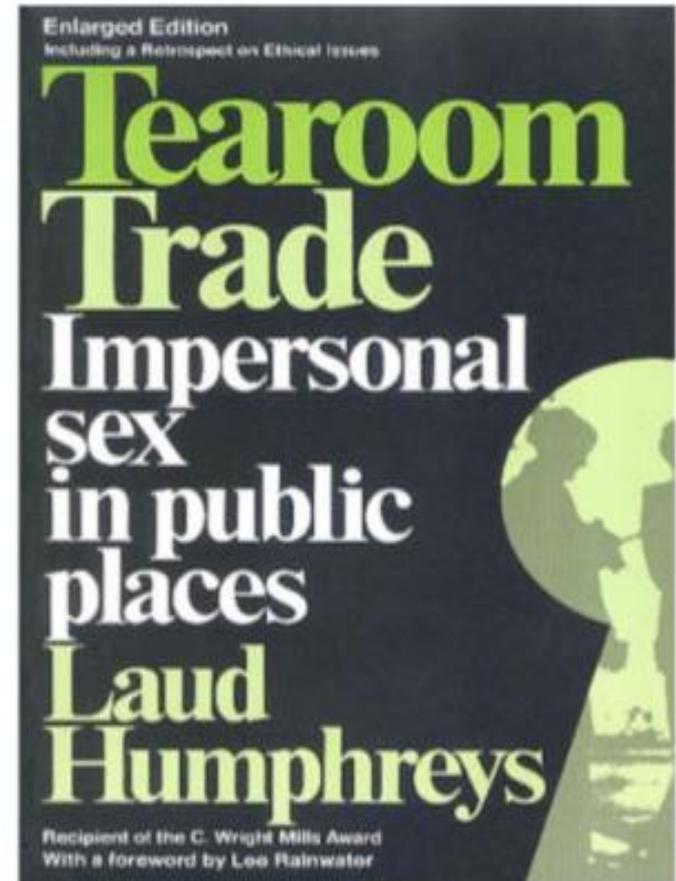


Image credit:

http://books.google.com/books/about/Tearoom_Trade.html?id=NZjAEZsBWvMC

Developing the Regulatory Process: 1970s

- 1973 U.S. Congressional hearings on “Quality of Healthcare - Human Experimentation”
- 1974 National Research Act:
 - National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research
 - IRB **required** at institutions receiving funding from the Department of Health, Education, & Welfare (now Health and Human Services)



Charge of the National Commission

- Identify the basic ethical principles that underlie the conduct of human research.
- Develop guidelines to ensure that human research is conducted in accordance with those principles.
- Current federal regulations to ensure compliance to guidelines.



Code of Federal Regulations (45 CFR 46)

The Common Rule:

- requirements for assuring compliance by research institutions;
- requirements for researchers obtaining and documenting informed consent;
- requirements for Institutional Review Board (IRB) membership, function, operations, review of research, and record keeping.
- additional protections for certain vulnerable research subjects -- pregnant women, prisoners, and children

1991: 16 federal agencies & 45 CFR 46



The Belmont Report, 1979

Underlying ethical principles of human research:

- Respect for persons
- Beneficence
- Justice

Definition of research



Research Defined

A systematic investigation, including research development, testing and evaluation, designed to develop or contribute to generalizable knowledge.

- Code of Federal Regulations 45 CFR 46.102d

Including: interviews, publication in scientific journal or presentation at a scientific meeting.

Not Including: market research/user satisfaction (that doesn't contribute to generalizable knowledge)



Human Research, or Not?

- Pilot studies
- Interview procedures
- Surveys
- Observation
- Case studies
- Oral histories
- Analysis of existing data (*identifiable, private information about human subjects*)
- Program evaluations
- Curriculum improvement research
- Marketing research



Adapted from

http://www.ius.edu/acadaffairs/pdf/Do_You_Need_IRB_Approval.pdf

IRB Defined

- A group that reviews and approves any type of research to protect the people who take part in it.

IRB actions:

- IRBs check to see that the research is well designed, legal, ethical, does not involve unnecessary risks, and includes safeguards for participants.
- Does every organization have an IRB?



IRB: Who & Why

- There should be at least five members on the board.
- An IRB is made up of medical and non-medical professionals, as well as lay people, who represent a cross-section of the community
- At least one member who is not affiliated with the institution or the trial site
- Review of research involving human subjects is required by federal law.
- Federal laws and regulations regarding research on human subjects have specific requirements for IRB and study administration.



IRB & Clinical Trials

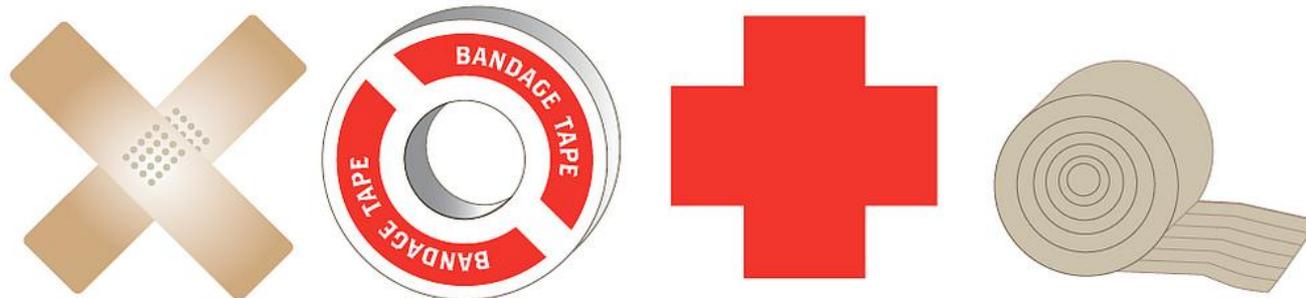


Image Source: <http://www.flickr.com/photos/opensourceway/5754766455/>



Clinical Trials Defined

- A test or study of a drug, therapy, surgical procedure, medical device, or of nutrition or behavioral changes in people.
- The tests are done to find out if the drug, therapy, procedure, etc. is safe and effective for people to use.
- The overall purpose of a clinical trial is to learn, not to treat patients.



ClinicalTrials.gov

- Public Law 110-85, Title VIII
- On September 27, 2007, a U.S. law was enacted that expands the types of clinical trials that must be registered in ClinicalTrials.gov, increases the number of data elements that must be submitted, and also requires submission of results data.
- There are penalties for non-compliance.



Clinical Trial Registration

- The sponsor of the clinical trial or the principal investigator is responsible for registering the trial.
- Failure to register penalties:
 - Civil monetary penalties.
 - The penalties for federally-funded trials may be the withholding or recovery of grant funds.



International Committee of Medical Journal Editors (ICMJE)

Policy on publishing clinical trials:

[http://www.icmje.org/publishing_10register.ht
ml](http://www.icmje.org/publishing_10register.html)



ICJME Obligation to Register

- The ICMJE member journals will require, as a condition of consideration for publication in their journals, registration in a public trials registry.
- The ICMJE encourages editors of other biomedical journals to adopt a similar policy.
- The ICMJE requires registration of trial methodology but **does not** require registration of trial results.



ICJME Membership

- Annals of Internal Medicine
- British Medical Journal
- Chinese Medical Journal
- JAMA
- New England Journal of Medicine
- New Zealand Medical Journal
- The Lancet
- The Medical Journal of Australia

700 journals follow ICMJE policy.

Note! Non-member journals reports that they follow the ICMJE's Uniform Requirements for Manuscripts Submitted to Biomedical Journals



Different Trial Methodologies

- Randomized trials
- Blinded studies
- Clinical trial phases



Randomized Trial

- Half the patients are chosen at random to get the treatment or drug being tested.
- The group getting the treatment or drug is referred to as “treatment group” or “investigational group”.
- The other group, called the “control group”, receives the standard treatment or a placebo* if a drug is being tested.
- The researcher compares the outcomes of the treatment group to the control group.

*sugar pill



Blinded Studies

- In a *single-blind study*, patients do not know whether they are in the treatment group or the control group.
- In a *double-blind study*, neither the patients nor their doctors know which group they are in.

The purpose of blinded studies is to make sure the results are not biased by anyone's hopes for a certain treatment.



Clinical Trial Phases: Phase I

Researchers test a new drug or treatment in a small group of people (20-80) for the first time to:

- test that the treatment is safe
- identify the maximum tolerated dose,
- find a safe dosage range and identify side effects.



Clinical Trial Phases: Phase II

The drug or treatment is given to a larger group of people (100-300) to see if it is:

- effective,
- to further evaluate its safety and
- to gather additional information regarding safe dose range.



Clinical Trial Phases: Phase III

The drug or treatment is given to large groups of people (1,000-3,000) to:

- confirm its effectiveness,
- monitor side effects,
- compare it to commonly used treatments and
- collect information that will allow the drug or treatment to be used safely.



Clinical Trial Phases: Phase IV

- Investigators are looking for additional information, including the drug or treatment's risks, benefits, and optimal use. This trial may occur after the drug or treatment has been approved for use by the FDA.
- Trials may be conducted to determine better dosing guidelines, new formulations, or effects on different populations or new indications.



Clinical Trials & the IRB

- An IRB reviews the appropriateness of the clinical trial protocol as well as the risks and benefits to study participants.
- It ensures that clinical trial participants are exposed to minimal risks in relation to any benefits that might result from the research.
- It ensures that clinical trial participants are exposed to minimal risks in relation to any benefits that might result from the research.



Clinical Trials & the IRB, con't.

- Ensuring that patients' rights, safety and well-being take precedence over the interests of science and society.
- Review of trial-related documents, such as protocols, the informed consent document, advertisement materials, or any other written materials to be provided to human subjects.
- How health sciences librarians can support clinical trial IRBs.



Librarian Research & IRB



What Librarians Should Ask:

- Is it research?

Research, as defined by the **Belmont Report** is :

“an activity designed to test an hypothesis, permit conclusions to be drawn, and thereby to develop or contribute to generalizable knowledge”

- Will the results of the study be compared to other research in the field?
- Will the data be disseminated to the library community, academic community, or the general public?
- If the answer to **any** the above is **yes**, IRB approval is needed.



Types of Library Research

- Research studies that involve students, faculty, and other library patrons.
- Information-gathering interviews where questions focus on services, products, or policies.
- Service surveys for the intent and purposes of improving services/programs or for developing new services or programs.



BREAK

IRB Goals and Responsibilities

Ensure the right and welfare of human subjects are protected.

- Risks to subjects are minimized.
- Risks to subjects are reasonable in relation to anticipated benefits, if any.
- Selection of subjects is equitable.
- Informed consent will be sought from each prospective subject.
- The possibility of coercion or undue influence is minimized.
- Require that additional information be given to subjects “when in the IRB's judgment the information would meaningfully add to protection of the rights and welfare of subjects”.
- IRBs are also responsible for ensuring that members who review research have no conflicting interest.



IRB General Application Guidelines

- Use a simple, descriptive title on the application and consent form.
- Use a readable font size and appropriate spacing.
- Check your spelling and grammar.
- Write recruiting documents and consent forms at reading levels appropriate to the sample being recruited, simpler is better.
- Avoid using jargon.



IRB Application Requirements

- Study Title
- Principle Investigator
- Study Team Members
 - Credentials (CV)
 - Role in project
 - Conflict of interest
- Project Summary
- Select the appropriate IRB body (e.g., Medical, Health Sciences and Behavioral Sciences)
- Estimated project start and end dates
- Performance sites (department affiliation)



IRB App Requirements, con't.

- Research Design
 - Objective (s)
 - Specific Aim(s) / hypothesis
 - Background information
 - Interaction types (e.g., information gathering, survey, interview, focus groups)
 - Statistical design
- Benefits and risks
- Subject participation (number and age)
- Recruitment (may include screening)
- Informed consent
- Confidentiality/security
- Retention of data



Levels of IRB Review

- Exempt
- Expedited
- Full



Exempt Research

- Research that meets the categories set forth by the federal regulations (45 CFR 46) that expose participants to no more than minimal risk.

May qualify:

- Studying educational methods
- Interviewing public figures
- Use of publicly available data sets
- Use of existing data and/or specimens stripped of identifiers



Exempt Research, con't.

- Research conducted in established or commonly accepted educational settings, involving normal education practices, such as:
 1. Research on regular or special educational instructional strategies, **or**
 2. Research on the effectiveness of or the comparison among instructional techniques, curricula, or classroom management methods.



Exempt Research, con't.

Using educational tests (cognitive, diagnostic, aptitude, achievement), survey procedures, interview procedures or observation of public behavior, **unless:**

1. Information obtained is recorded in such a manner that human subjects can be identified, directly or through identifiers linked to the subjects; and
2. Any disclosure of the human subjects' responses outside the research could reasonably place the subjects at risk of criminal or civil liability; or be damaging to the subjects' financial standing, employability, or reputation.



Exempt Research: Public Data

Research involving the collection or study of existing data, documents, records, pathological specimens, or diagnostic specimens, if these sources are publicly available or if the information is recorded by the investigator in such a manner that subjects cannot be identified, directly or through identifiers linked to the subjects.



Decision Charts for Human Subject Regulations

A guide for institutional review boards (IRBs), investigators, and others who decide if an activity is research involving human subjects must be reviewed by an IRB under the requirements of the U.S. Department of Health and Human Services (HHS) regulations:

<http://www.hhs.gov/ohrp/policy/checklists/decisioncharts.html>



Decision Tree Chart Overview

Chart 1: Is it an Activity Research Involving Human Subjects?

Chart 2: Is the Human Subjects Research Eligible for Exemption?

Chart 3: Does the education setting exemption apply?

Chart 4: Does the tests, surveys, public behavior exemption apply?

Chart 5: Does the existing data exemption apply?

Chart 6: Does the public benefit/service exemption apply?

Chart 7: Does food taste and acceptance exemption apply?

Chart 8: May the IRB review be expedited?

Chart 9: May the IRB continuing review expedited?

Chart 10: May informed consent be waived or consent elements altered?

Chart 11: May documentation of informed consent be waived?



Hands-On Group Activities



Create an IRB Application

- Study Title
- Principle Investigator
- Study Team Members
 - Credentials
 - Role in project
 - Conflict of interest
- Project Summary
- Select the appropriate IRB body (e.g., Medical, Health Sciences and Behavioral Sciences)
- Estimated project start and end dates
- Performance sites
- Informed Consent (brief)
- Research Design
 - Objective
 - Specific aim(s)/ hypothesis
 - Background information
 - Interaction types (e.g., information gathering, survey, interview, focus groups)
 - Statistical design
- Benefits and risks
- Subject participation (number and age)
- Recruitment (may include screening)
- Confidentiality/security
- Retention of data

IRB Application Presentations & Discussion



Class Evaluations

