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Human Subjects Research Ethics & The IRB Review Process

Presentation and discussion with:
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Session Goals

- Clarify the role and authority of the Institutional Review Board (IRB)
- Provide a historical context for the current review process and compliance issues.
- Explain the basic regulatory requirements regarding human subjects research, specifically regarding types of research and levels of review.
- Introduce the IRB application – forms and process.
- Discuss some of the critical elements of human subjects research and review (i.e., risks and benefits, consent forms and process, protected and vulnerable populations, etc.).
- Address questions and issues specific to intended research and areas of interest to participants.

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Institutional Review Board (IRB)

- The IRB's role and responsibility is to ensure safe and ethical research with people.
- IRBs at the UW partner with researchers to protect the rights and welfare of human research subjects recruited to participate in research activities conducted under the auspices of the University of Washington.
- The IRB has the authority to:
  - approve,
  - require modifications in, or
  - disapprove

  all research activities that fall within its jurisdiction as specified by federal regulations, state law, and institutional policy.

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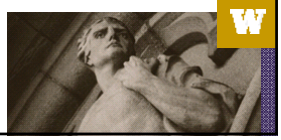
Institutional Review Board (IRB)

Membership must meet federal (and UW) requirements:
Federal Regulations – 5 members (3 = quorum) / UW – 9 members (5 = quorum)
Each Board must have at least:

- 1 Scientist
- 1 Non-affiliated/community member
- 1 Non-scientist (must be present for meeting to occur)
- 1 Student (UW practice)
- Members with sufficient and appropriate expertise to review the research that comes before the Committee.

IRBs at the University of Washington:

- 3 Biomedical Committees (A, B, D)
- 3 Social/Behavioral Committees (C, G, J)
- 1 Combined Committee (K)
- 4 Subcommittees (E/A, E/B, E/C, E/G)
  [Review of Exempt & Minimal Risk]



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Reviews by Non-UW IRBs

Western IRB (WIRB) (http://www.washington.edu/research/hsd/policy_wirb.php)
Reviews industry-sponsored and -initiated clinical trials.

Cancer Consortium IRB (CC-IRB) (http://www.cancerconsortium.org/irb)
Reviews cancer research from consortium members.

Veterans Affairs IRBs (VA & V2)

(http://www.washington.edu/research/hsd/va/)
Reviews research involving veterans and their family members, the VA, or VA funding.

Cooperative Agreements – Affiliated Institutions

(http://www.washington.edu/research/hsd/coopag.php)

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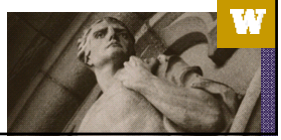
Institutional Review Board (IRB)

What do the IRB committees look for?

1. Risk of harm versus potential benefits of study
   (includes evaluation of study design / scientific merit when risk-benefit evaluation is problematic)
2. Protections of subject privacy and confidentiality
   (primarily within recruitment and data management)
3. Consent process

Why?



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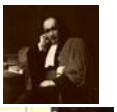
Pre-WWII



Edward Jenner (1789)
Smallpox Vaccine

Claude Bernard (1865)
Ethical Maxims

Louis Pasteur (1885)
Rabies Vaccine

Walter Reed (1900)
Yellow Fever

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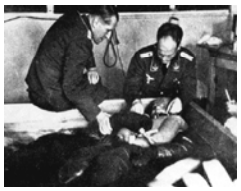
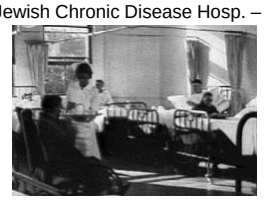
Lessons from Biomedical Research

Nazi War Crimes - WWII

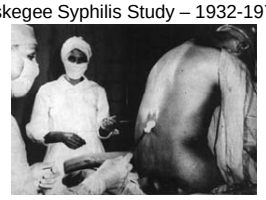


Willowbrook – 1950s

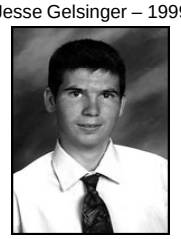
Jewish Chronic Disease Hosp. – 1960s



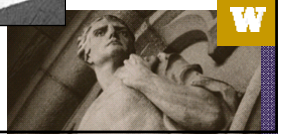
Tuskegee Syphilis Study – 1932-1972



Jesse Gelsinger – 1999



Ellen Roche – 2001



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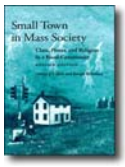
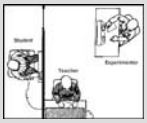
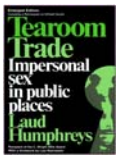
Behavioral Research (just as culpable?)

Vidich & Bensman (1958)
"Small Town in Mass Society: Class, Power and Religion in a Rural Community."



Milgram (1963)
"Behavioral study of obedience."





Humphreys (1970)
"Tearoom Trade:
Impersonal Sex in Public Places."

Zimbardo (1971)
Stanford
Prison Experiment

Foulks (1979)
Alcoholism in Barrow, Alaska

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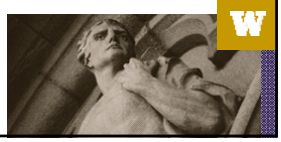
Indian Tribe Wins Fight to Limit Research of Its DNA

The New York Times

Tribal members said prayers over the boxes containing the tribe's frozen blood samples.
Photo: Jim Wilson/The New York Times



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Shocking TV Experiment Sparks Ethical Concerns

npr

An actor prepares to receive "shocks" from the audience on a fake TV game show, staged for a French documentary.
by Joe Palca

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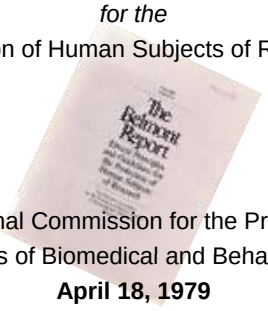
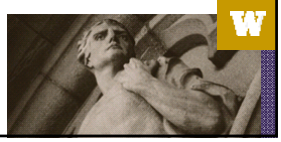
The Belmont Report

Ethical Principles and Guidelines
for the
Protection of Human Subjects of Research



The National Commission for the Protection of
Human Subjects of Biomedical and Behavioral Research
April 18, 1979



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The Belmont Report

Basic 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

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So – defining what is research is pretty straightforward, isn't it?

1. Are you doing research?
   "A systematic investigation, including research development, testing and evaluation, designed to develop or contribute to generalizable knowledge."

2. Are you doing research with humans?
   "A living individual about whom an investigator (whether professional or student) conducting research obtains (1) data through intervention or interaction with the individual, or 2) identifiable private information."

. . . and what difference does this make in what we do?

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Three types of research and levels of review:

1. **Exempt**/Departmental Approval with Administrative IRB Review
   Research that involves human subjects but meets regulations to be exempt from IRB review (six categories), as there is no risk to subjects.
2. **Minimal Risk** ("Expedited")/IRB Subcommittee Review
   Research that poses no more risk to subjects than would be encountered by the average person in his/her typical daily activities (nine categories).
3. **More than Minimal Risk**/IRB Full Committee Review
   Research that poses more risk to subjects than would be encountered by the average person in his/her typical daily activities.
4. **Not Human Subjects Research**/???
   Activities that do not fit the regulatory definition for "human" or "research".

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Five areas to consider carefully in your design & application:

1. **Purpose** – What is it that you're trying to find out?
2. **Subjects** – Who will be involved in your study?
3. **Procedures** – What exactly are you going to do?
4. **Data** – Where is it from? What is it? Who is it from?
   How is it being collected? Where is it being kept? Is it secure?
   How long will you keep it?
5. **Consent** – From the start of subject involvement in your study to the end, how will they know what the study is about, what it means to them, and the results?

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Consent – it's not all created equal . . .

- The consent process and form must be appropriate to the subject population/s and the study.
  - Explains the study in a manner understandable to the subjects.
  - Typically written at a 6th-8th grade level, with adjustments for children and other populations.
  - In a language participants can understand.
  - Such that subjects understand not only what the study is about, but what it will mean for them to participate (and that they can choose not to participate).
- Consent documents need to include all of the elements of consent that are required by federal and state regulations (http://www.washington.edu/research/hsd/consent.php).
- *Is it ever okay not to obtain consent?*
  Written consent?

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Protected & vulnerable populations:

Protected (45 CFR 46)

- Pregnant Women, human fetuses, and neonates (Subpart B)
- Prisoners (Subpart C)
- Children (Subpart D)

Vulnerable

- Decisionally-impaired (Subpart E??)
- Elderly
- Economically disadvantaged
- Culturally disadvantaged
- Native Americans / Alaskan Natives
-
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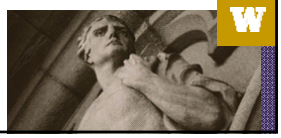

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Criteria for IRB Approval of Research

1 Risks are reasonable relative to benefits

Anticipated benefits include the importance of the knowledge that may be expected to result.

2 Risks to subjects are minimized

- Procedures are consistent with sound research design and do not unnecessarily expose subjects to risk.
- If possible, the research uses procedures already being performed on subjects.

3 Protection of subject privacy & confidentiality

There are adequate provisions to protect the privacy of subjects and to maintain the confidentiality of data.

4 Adequate safety monitoring plan

The research plan has adequate provisions for monitoring the data collected, to ensure the safety of subjects.

5 Written informed consent obtained

From each prospective subject or the subject's legally authorized representative, unless the IRB, per federal criteria:

- Waives the need for written consent.
- Waives the need for consent.

6 The consent process provides all required and appropriate information

Unless waived by the IRB per federal regulatory criteria.

7 Subject selection is equitable

Taking into account:

- The research purpose and setting, and
- Any special issues associated with vulnerable populations.

8 Additional safeguards for protected & vulnerable populations

- Additional safeguards are included to protect subjects who may be vulnerable to undue influence or coercion.
- Includes: children, prisoners, pregnant women, neonates.
- May also include decisionally-impaired, or economically or educationally disadvantaged subjects.

9 Other ethical & compliance issues

- Researcher conflict of interest.
- Involvement of non-UW institutions and individuals.
- Other compliance requirements.

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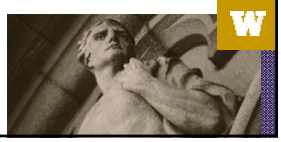
Researcher Responsibilities

The principal investigator (PI) is responsible for all aspects of the study.
Though authority to perform certain aspects of the study may be delegated to others, the PI nonetheless retains full responsibility for all study activities and obligations.

1. **Conduct** the research in accordance with the approved protocol, applicable laws and regulations, and the principles of research ethics as set forth in the Belmont Report.
2. **Consent** is obtained (unless waived by the IRB) without coercion or undue influence, and the potential subjects are provided with sufficient opportunity to consider whether to participate.
   - Use only the most current consent form, bearing the "APPROVED" stamp and date.
   - Provide non-English speaking subjects with an IRB-approved translation of the consent form.
3. **Pre-approval** must be obtained from the IRB for any planned modifications or amendments, including new sources of funding and changes to recruiting materials.



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Researcher Responsibilities – specifics:

4. **Report** promptly to the IRB any new information, unanticipated problems involving risks to subjects or others, or serious adverse events that may affect the welfare or safety of the subjects or the conduct of the research.
5. **Obtain renewal** of IRB approval by providing required Status Reports at least 6 weeks before current IRB approval expires. IRB approval is not automatic and does not occur until the IRB has reviewed and approved the Status Report.
6. **Retain copies** of all IRB-related materials and correspondence, as described in the UW Record Retention Schedule.
7. **Ensure** that there is a system is in place for promptly responding to letters, email or phone inquiries, and messages from subjects and from the IRB.
8. **Inform the IRB** when the research has been completed by completing a Status Report form and checking the box next to "Close IRB Application."

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Contact HSD

University of Washington, Human Subjects Division

http://www.washington.edu/research/hsd/index.php

Staff Contact Information:

http://www.washington.edu/research/hsd/contact.html

To subscribe to *e*-News:

https://mailman1.u.washington.edu/mailman/listinfo/hsd-news

To request training/assistance: hsdtrain@u.washington.edu

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Online Resources

Belmont Report - http://www.hhs.gov/ohrp/humansubjects/guidance/belmont.htm

University of Washington, Human Subjects Division
http://www.washington.edu/research/hsd/index.php

Office for Human Research Protections http://www.hhs.gov/ohrp

Food and Drug Administration http://www.fda.gov/

Health Resources and Services Administration http://www.hrsa.gov/quality/hsrtraining.htm

Council for International Organizations of Medical Sciences
(CIOMS) http://www.cioms.ch/frame_guidelines_nov_2002.htm

CITI – Course in the Protection of Human Subjects [International Course]
https://www.citiprogram.org/default.asp [http://www.irbtraining.org]

Educational Resources on International Research Ethics
http://www.nih.gov/sigs/bioethics/internationalresthics.html#research

Ethical Issues in International Health Research
http://www.hsph.harvard.edu/bioethics/

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The University of Washington is one of the world's preeminent universities and a recognized leader in educating the next generation of leaders, thinkers and doers. A multi-campus institution comprising UW Seattle, UW Tacoma and UW Bothell, as well as a world-class academic medical center, the UW is a focal point of the Puget Sound region's intellectual and cultural life and a key contributor to Washington's increasingly global reputation as a center of innovation and change. A progressive and quintessentially Northwest institution with a uniquely innovative and creative culture, the UW is driven to lead by successfully integrating the full assets of the university and its rich environs to address key issues of pressing human concern that make a lasting difference in the Northwest and around the world.