Protection of Human Subjects in Research

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Those who cannot remember the past are condemned to repeat it.

- George Santayana
Atrocities in Nazi Germany

Research involving prisoners:

• Claus Schilling - malaria vaccine research at Dachau

• Eugen Haagen – typhus vaccine in Alsace

• Sigmund Rauscher - effects of low oxygen and temperature; drugs on gun shot wounds
Why regulate protection of human subjects participating in research?

• Historical milestones:
  
  ▪ Nuremberg Code - 1947
    • To prevent a repeat of the atrocities committed by Nazi research physicians against the rights and welfare of human beings. This code emphasized the subject’s voluntary consent.

    • Spells out the ethical guidelines for research involving human subjects
The Nuremberg Code

"It was a good code for barbarians but an unnecessary code for ordinary physicians."

– Jay Katz
The Tuskegee Syphilis Study
1932-1972
Congress Gets Involved

• National Research Act of 1974
• Established the National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research
• Belmont Report
• Current regulations – The Common Rule
Belmont Principles

- Respect for persons
  - Autonomy
  - Informed Consent
- Beneficence
  - Benefits outweigh risks
- Justice
  - Equitable selection of participants
  - Fairness in distributing benefits
  - No exploitation

Respect for Persons

Beneficence

Justice
The Common Rule – 45 CFR 46

- Requires Federalwide Assurance (FWA) for federally funded human subjects research (HSR)
- FWA is the contract between institution and the government
- Defines HSR and the IRB review process
- Defines criteria for approval of HSR
IRB Review is required for all research studies involving human subjects.

• So what is research?
  ...and what is a human subject?
• Research means a systematic investigation... designed to develop or contribute to generalizable knowledge.
Human subject means 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.
For research involving human subjects, the IRB may:

- Approve
- Require modifications (to obtain approval)
- Disapprove the research
- Review modifications and continuations of previously approved research.
- Audits
- Suspension and termination of HSR
Requirements for Approval

1. Risks to subjects are minimized and reasonable in relation to benefits
2. Selection of subjects is equitable
3. Informed consent is appropriately sought and documented
4. Provisions for data monitoring
5. Provisions for privacy and confidentiality
6. Other precautions as needed
Exemptions

- IRB review depends on the level of risk involved
- Some research may be exempt from these requirements
  - Defined in 45 CFR 46.101(b) – 6 categories - see Regulations for specifics
  - Includes (in general):
    - Classroom research
    - Surveys and interviews when no risk to participants
    - Some studies using existing data, documents, specimens, etc.
    - Taste tests with foods approved by the FDA, EPA, and/or USDA
  - Some research with minors excluded – See Subpart D
- Exempt determinations MUST be made by the IRB
Informed Consent

• A process – not just a form
• Should be understood by participants
  • Terminology
  • Language
• Opportunity for questions
Informed Consent Form – Essential Elements

- Description of the study - purpose, procedures, expected duration, and explanation of experimental procedures
- Foreseeable risks and/or discomforts
- Potential benefits to subject or others
- Alternative procedures or treatments
- Information regarding confidentiality
- Resources available if injury occurs
- Contact information for questions
- Statement that participation, and continued participation, in the study is voluntary
Informed Consent Form – Additional Elements

- Potential for unforeseeable risk
- When participation might be terminated
- Possible additional costs to the participant
- Consequences of withdrawal from the study
- Information regarding new findings
- The number of participants to be in the study
Institutional Review Board

- Must have a minimum of 5 members
- At least one scientist
- At least one non-scientist
- One community member not associated with institution
- In certain circumstances, a prisoner advocate
Vulnerable Populations

Additional precautions should be considered for vulnerable populations where autonomy is limited such that they cannot fully participate in the consent process:

- Pregnant Women, Fetuses and Neonates – Subpart B
- Prisoners – Subpart C
- Children – Subpart D
- Decisionally impaired, college students, etc.
Importance of Compliance

- Compliance is the shared responsibility of institutions, researchers and society.
- In order for society to agree to participate in research as subjects, they must trust researchers and value research.
- To foster this trust, institutions and researchers must promote and conduct ethical research that promises societal benefits. Anything less will serve to erode the research enterprise.
Review questions

• Why should some research with/on humans be exempted from regulation?

• What should subjects know about proposed research and their protection before they enroll as subjects?

• What other principles could be used for evaluating the ethics of human subjects research besides respect for persons, beneficence, and justice?

• Should subjects be allowed to enroll in experiments that either promise no direct benefit to them or cannot provide them with the opportunity to withdraw completely?
• Why is a person from the local community required to be a member of an IRB?

• Besides the 3 members required by regulation, what other criteria could be used to identify necessary members for IRBs?

• In addition to IRB-approval for a study to commence, what other approvals may be required?
Contact Information

Office of the Institutional Review Board
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Birmingham, AL 35294

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Additional Resources

• Office for Human Research Protections (OHRP)
  http://www.hhs.gov/ohrp/

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

• OIRB Website
  http://www.uab.edu/irb