2011

Research with human subjects

Sarah Fowler-Dixon
Washington University School of Medicine in St. Louis

Research with Human Subjects

Sarah Fowler-Dixon, PhD
Human Research Protection Office (HRPO)
2011

22 N. Euclid Ave, Ste. 233
(In the CWE, across from Jimmy Johns)

314-633-7400

Website: http://hrpohome.wustl.edu

Today's Outline

- What is Research?
- What is Human Subjects Research?
- Brief Historical Perspective
- The elements of the Belmont Report and what that means for individuals participating in research?
- What is the Institutional Review Board (IRB)?

What is Research?

- A systematic investigation including research development, testing and evaluation, designed to develop or contribute to generalizable knowledge.
  - Generalizable: If I follow your procedures, I can expect to see similar results.
- There are various forms of research: bench or pre-clinical, animal studies and human studies.

What is Human Subjects Research?

- **Research that is conducted with human beings or their private, identifiable information.**

- 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*.

  45 CFR 46.102(f)

Definitions

Intervention includes both physical procedures by which data are gathered (for example, venipuncture) and manipulation of the participant or the participant's environment that are performed for research purposes.

Interaction includes communication or interpersonal contact between investigator and participant.

Private information includes information about behavior that occurs in a context in which an individual can reasonably expect that no observation or recording is taking place, and information which has been provided for specific purposes by an individual and which the individual can reasonably expect will not be made public (for example, a medical record). Private information must be ***individually identifiable*** (i.e., the identity of the participant is or may readily be ascertained by the investigator or associated with the information) in order for obtaining the information to constitute research involving human participants.

- 45 CFR 46.102 (f)

Brief Historical Perspective

- Experimentation has always taken place.
- The Hippocratic Oath originally written by Hippocrates in late 5th century first stated:
  - "I will prescribe regimens for the good of my patients according to my ability and my judgment and never do harm to anyone."
- However, in the course of experimentation people were harmed and sometimes killed.

Historical Studies – Nazi Germany 1939-1944

- To test the effects of extremely high altitudes internees were put in vacuum chambers that duplicated low air pressure and lack of oxygen at altitudes as high as 65,000 ft.
- To test hypothermia, internees were: immersed in tubs of ice water; or fed salt water for days; or penned outside without clothing or shelter in sub-freezing temperatures for 12-14 hours and some were sprayed with cold water.

- Battlefield medicine including treatment of wounds, burns, traumatic amputations, chemical and biological agent exposure that was first inflicted on the victim.

Historical Studies - USA

- The Public Health Service Syphilis Study in Tuskegee, AL, 1932-72

- Willowbrook Experiment, 1956-72, Willowbrook State School in New York for mentally disabled children. Children were infected with a mild form of hepatitis.

- Milgram Study, 1963, was designed to study the role of obedience to authority; why ordinary people behave in ways that seem inhumane outside a certain context.

Studies talked about in 2010

- HeLa Cells, 1951. Henrietta Lacks was diagnosed with cervical cancer. Her physician removed some of the cancerous cells and developed the first "immortal" human cells grown in culture.

- Havasupai Tribe, 1992. Blood samples were taken to study occurrence of diabetes amongst tribe members but were used for other studies as well.

- US Public Health Service in Guatemala, 1946. Male prisoners in Guatemala were infected with syphilis using infected female prostitutes.

Establishment of IRBs

- Federal regulations were codified in 1974 that established institutional review boards.

- IRBs are charged with reviewing human subjects research to ensure that it meets federal, state, and ethical codes.

  - WU IRBs Mission: **To protect the rights and welfare of Human Subjects**
    - IRBs follow the guiding principles in **Belmont Report**

The Belmont Report

- Respect for Persons, that includes concepts of Autonomy and Informed Consent as well as extra Protections for vulnerable populations
- Beneficence, that involves Risk vs. Benefit analysis
- Justice, meaning Equitable Subject Selection for a given study.

Respect for Persons

- All individuals are autonomous individuals and can make decisions for themselves when given appropriate information.
  - Consent, whether written, verbal or implied
  - You must consent participants in the manner approved for the protocol
  - All elements of consent should be appropriate whenever appropriate

Elements of Consent

- Purpose of the study
- All steps of participation
- Any costs that will pass along to the participant
- Any payments the participant will receive
- Risks of any and all drugs, devices, treatments and/or procedures
- Benefits to the participant and/or society
- Maintenance of confidentiality

Elements of Consent

- Contacts in case of any emergency
- The right to withdraw at any time.
  - If there are consequences to withdraw as in some investigational drug and device studies, how withdrawal will occur safely and if the participant still needs to come back for follow-up safety visits.
- For studies deemed greater than minimal risk, who will pay in case a research related injury occurs.
- Alternatives to the research, if any

Other Elements of Consent that may need to be included depend on study

- The number of individuals that will be enrolled study-wide if the study is being conducted at more than one site.
- Conditions under which a participant's time in a research study will be terminated by the PI.
- That the social security number will be obtained. This is needed any time a payment or gift is given per IRS regulations.
- Any new significant findings during the course of the study will be passed along to the participant.

HIPAA Authorization

- HIPAA authorization is different from consent.
  - It is built in to the WU consent templates for studies where this is needed.
- It gives permission to access, use, create and share protected health information outside of treatment, payment, operations functions as in a research study.
  - If PHI is being used, HIPAA authorization language should be in the consent document.

Research Consent Process

- Is longer than a clinical consent process.
- The document is longer and contains more detailed information.
- Process begins at recruitment when you first begin to tell the potential participant about the study.
- The participant should be given adequate time to decide whether or not to enroll.
  - This varies by study

Research Consent Process

- Ideally, the participant is given the consent document to read then a qualified study team member discusses the study and any questions with the potential participant before he/she agrees to enroll.
  - You are a member of the study team and should be familiar with the study procedures as well as what you are expected to do for this study
- Consent does not end with the initial enrollment. Subsequent conversations/contacts are not uncommon and help keep the participant informed all along.
  - This is considered re-consent as you verify continued enrollment with each conversation/contact and note this in your research record.

Respect for Persons also means

- Privacy
- Confidentiality
- Additional Protections for vulnerable populations

Privacy and Confidentiality Definitions

- Privacy: The freedom of the individual to pick and choose for him/herself the time and circumstances under which, and to the extent to which his/her attitudes, beliefs, behavior and opinions are to be shared with or withheld from others. (Levine, p 163)

- Confidentiality: Mode of management of private information. (Levine, p. 163)

Privacy or Confidentiality?

1. Consenting a participant in a private room
2. Keeping data behind two locked doors
3. Devising a recruitment process whereby everyone in the room returns a piece of paper whether or not he/she wants further information about the study
4. Limiting access to identifiable information
5. Using fire walls to secure data

Confidentiality Measures

Type of Confidentiality	Data Protection	Consent Measures
Full identifiers	Research participants fully identifiable	Consent/authorization obtained to collect, use, share
Coded or De-identification of Data or Samples	Those outside the research team cannot identify participants	Consent/authorization to collect and use. Normally shared de-identified or coded.
Data or samples de-identified prior to study initiation	Study team does not have access to any individually identifiable information	Waiver of consent/authorization is appropriate
Anonymous samples	No individually identifiable information was ever collected	Waiver of consent/authorization

Additional Protections for Vulnerable Populations

- Name a vulnerable population.
- What would be an additional protection for this population?

- Examples:
  - Employees – heightened confidentiality so employment is not affected
  - Terminally ill – use of a research advocate to avoid undue influence and increase understanding
  - Socioeconomically disadvantaged – payment not so great that will entice one to enter a study that he/she would not normally consider

Beneficence

- Identification of harms
  - Physical - drug toxicities, exposure to radiation, research injuries
  - Psychological – emotional distress, anxiety in making choice
  - Social – one's reputation, social standing, retaliation
  - Legal – risk of criminal or civil liability
  - Economic – impact on employment, insurance, research costs

- Minimizing those harms
  - Physical – use of standard care procedures
  - Psychological – time to talk to family
  - Economic – letting participant know if there will be any costs

Conflicts of Interest

- Can impose more harms or prevent harms to be minimized, potentially
  - E.g. The PI is the person who developed the device. He/she wants the trial to go well so he/she overlooks some negative results or effects whether intentionally or unintentionally. The participant may/may not be harmed. But, this will affect data validity.
  - So, it's important to know if there is any conflict of interest for any research team member or anyone in his/her immediate family.

Beneficence

- Identification of possible benefits

- Being able to put one participant through the possible risks for the potential benefits.
  - Possible risks: these are known risks that are in current literature, seen clinically, in the investigator's brochure or device pamphlet, seen in previous studies using the same drug/device, etc.

Justice: Equitable Subject Selection

- Given the study and what it is trying to accomplish, are appropriate populations targeted for inclusion and are appropriate populations excluded.
  - We don't want to take advantage of populations or exclude populations inappropriately.

IRB review is required

- Before human subjects research is initiated.
- Anytime there is a change to the research
- When an event occurs that would create an increased risk to research participants.
- At the time of renewal.
  - Most studies are renewed every 12 months.

IRB at WU

- Consists of 12 committees:
  - 10 review new studies and renewals that are either deemed "greater than minimal risk" or cannot be reviewed using expedited review procedures.
  - 1 handles all studies and events considered "minimal risk" and those allowable under expedited review procedures (1 reviewer).
  - 1 handles compliance issues
- Total membership is around 250 individuals comprised of physician scientists, other scientists, and community representatives.

Types of Research Seen by the WU IRB

- Include:
  - Social, Behavioral, and Educational Studies
    - Questionnaires, observations, interviews, studies regarding human behavior
  - Biomedical Studies
    - Medical interventions and therapies, use of investigational drug and devices, studies regarding human physiology

References

- Getz, Kenneth & Borfitz, Deborah. Informed Consent. CenterWatch, 2002, pgs 97-100.
- Havasupai Tribe of the Havasupai Reservation, a federally-recognized Indian tribe v. Arizona Board of Regents and Therese Ann Markow
- HRPO guideline, "What Activities Need HRPO Review and Approval?"
- PRIM&R webinar, "The Inoculation Studies in Guatemala," October 20, 2010.
- Skloot, Rebecca. The Immortal Life of Henrietta Lacks. Crown Publishers, New York, 2010.

When to call the IRB

- Anytime you have a question or concern regarding the study.