Human Subjects in Research

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CREDIT

Some of these slides were shamelessly stolen from ERIC MAH – our beloved IRB Director!
Objectives

Describe

• the IRB, roles and responsibilities
• the principles and application of the principles of the Belmont Report
• the submission process
• the elements of Informed Consent
• how to avoid common mistakes
• the Informed consent process as ongoing
Institutional Review Board

• What is an IRB?
  – The IRB is designated under federal regulations to review and monitor human subjects research
  – IRBs must apply all federal, state, local, and institutional regulations on human subjects when reviewing research projects
  – **UC Davis has 3 IRBs:** 2 clinical committees that meet twice/month; 1 social/behavioral committee that meets once per month
What is a human subject?

A living individual about whom an investigator (whether professional or student) conducting research obtains:

– Data through intervention or interaction with the individual, or

– Identifiable private information
What is research?

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

45 CFR 46.102(d)
IRB Membership

• Must have at least 5 members
• Must include scientific and non-scientific members
• Must include representatives from the community
• Must be diverse in race, sex, profession...
IRB Responsibilities

• IRBs
  – Provide a prospective review of proposed research
  – Provide ongoing review of previously approved research (intervals may be reflective of level of risk)
  – Review amendments
  – Review reports of Non-Compliance
IRB Authority

• IRBs may
  – Approve
  – Table
  – Disapprove
  – Require modifications necessary to secure approval
Unethical Research Practices

• Nazi Experiments on thousands of concentration camp prisoners
  – Nuremberg Code, 1948
    • Advocated for voluntary participation/informed consent
    • World Medical Association’s policy statement of ethical principles to provide guidance to physicians and others in medical research involving human subjects
Unethical Research in U.S.

• Increasing awareness of unethical research occurring in the U.S.
  – Willowbrook Hepatitis Study
  – Jewish Chronic Disease Study
  – Tearroom Trade Study
  – Tuskegee Syphilis Study
Unethical Research in U.S.

• National Research Act 1974
  – Created the National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research
• Belmont Report, 1979
Belmont Report

Three basic ethical principles

– Respect for Persons
– Beneficence
– Justice
Respect for Persons

Two ethical convictions

1. Individual should be treated as an autonomous agent
   – Person may **choose** whether to participate in research/protected by the informed consent process. Informed consent provides the individual with adequate information about a research project and time to make an informed decision.

2. Individuals with diminished autonomy are entitled to protection (i.e., cognitively impaired, children, prisoners)
Beneficence

Two ethical convictions
1. Do not harm

2. Maximize possible benefits and minimize risks
   - Risks can be physical, emotional, social, financial, legal
   - Risks must be reasonable in light of expected benefits
Justice

Ethical Conviction

– There will be an equitable selection, recruitment and fair treatment of research subjects; benefits and burdens are shared

An injustice occurs when:
1. benefits to which a person is entitled are denied without good reason, or
2. when burdens are imposed unduly.
Types of IRB Review

• **Full Board**
  – Greater than Minimal Risk

• **Expedited Review**
  – Minimal Risk and falls into 1 of 9 specific categories for life or until change (no active drug or device studies can be expedited)
  – Anticipated probability of harm or discomfort are not more than those encountered in daily life or doing routine tests
  – Previously approved research that has undergone minor change

• **Exempt Review**
  – Research that exposes human subjects to very small risk; no more than they would encounter in daily life (e.g., telephone survey).
IRB REVIEW PROCESS

1. Initial Submission
2. Review
3. Request for Info
4. PI Response
5. Review (Full or Sub-Committee)
6. Approve, Disapprove, Request for Modification for Approval
What Happens to a Submission?

• Negotiated process of review and response
  – Review of adherence to Belmont Principles and applicable laws, regulations, and UC policy

“You can disagree, just don’t ignore”

- Eric Mah, IRB Director
Informed Consent

• Demonstrates respect for the dignity of the subject

• An ongoing, active, and documented process of communication that facilitates decision making

• The process should in a language understandable to the subject (in terms of literacy, complexity)

• Children provide assent
Capacity to Consent

- Understanding of risks and ability to judge risk/benefit balance for oneself
- Describe how capacity will be determined and by whom in order to assure informed consent
- If decisional ability fluctuate, ongoing process of consent is even more important
- Shared decision-making
- Proxy consent
- Waivers of Consent
8 Elements of Informed Consent

• Statement that the study involves research
• Reasonably foreseeable risks or discomforts
• Reasonably foreseeable benefits—subject or others
• Appropriate alternative procedures or treatments
• Statement describing the extent of confidentiality
• Compensation for research related injury
• Whom to contact to answer questions and subject’s rights
• Statement that participation is voluntary
Writing the Informed Consent

• Simple Language – define and explain jargon
• Short Paragraphs
• Break things apart with headings
• Linear flow
• Focus on the subject experience
“We strongly suspect that the way the human brain processes exteroceptive and proprioceptive sensory inputs differs. External inputs are processed straight away into what is called the sensory system which corresponds to the anterior part of the parietal lobe of the brain. Proprioceptive inputs are probably treated in a more complicated way involving not only the sensory system but also the motor system which is located more anteriorly in the frontal lobe. Little is known about the way that the human brain deals with sensory inputs and this is particularly crucial for proprioceptive inputs.”
Good

“The purpose of this study is to take pictures of your brain to help us understand how it works”
SIX Common Mistakes

ONE:
- Incomplete and/or inconsistent information in the IRB application
- Copy and paste errors
- All questions must be answered
- Spend the time to write the application
SIX Common Mistakes

TWO:
- Informed Consent form is too complex
- Full of jargon
- Missing “Risks” section
- Does not match procedures in other parts of the application
  - Adds new procedures
  - Doesn’t describe major procedures
SIX Common Mistakes

THREE:
- Unresponsive to IRB correspondence
- Do not skip or ignore an issue
- Most things are negotiable
SIX Common Mistakes

FOUR:

- Recruitment and consent process is not well explained
- Give a detailed description of how you will recruit subjects and when you will consent them
- Address how you will minimize coercion if they are your own patients
SIX Common Mistakes

FIVE:

- “De-Identified” not a meaningful term by itself
- Anonymous
  - No code sheet exists
  - No one can determine specimen origin
- Coded
  - Medical Record Number
  - Existing code sheet/Patient names
SIX Common Mistakes

SIX:

• Do not clearly describe standard of care from research procedures
• What is billed to a sponsor, why certain procedures are billed to a subject or 3rd party payor
• Explain in both the IRB application and the ICF
Initial Consent

- Take the time at the initial discussion with subjects so that they have a thorough understanding of what they are undertaking
- Allow subjects to review the consent, take it home, discuss with family
- Verify subject’s comprehension
  - Research versus standard of care procedures
  - Time commitment
  - Randomization
  - Alternatives
  - Potential costs
  - Risks and Benefits
- Taking your time – subjects deserve that
Informed Consent is Ongoing

- Informed consent is not just a signature
- Process that occurs with each interaction with subject
- Discuss new information that may impact a subject’s willingness to continue study participation (i.e., new known risks, benefits, alternatives, changes in study design, etc.)
- Remind subject of study goals and objectives this will improve subject compliance with the protocol and improve retention of subjects
- Documentation of initial informed consent and ongoing informed consent are both crucial
References

IRB Website
www.research.ucdavis.edu

Subscribe to IRB list serv
www.research.ucdavis.edu/humansubjects

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