Protection of Humans and Animals In Research

Responsible Conduct of Research Series

Informed Consent and Vulnerable Populations

Jill M. Baren, MD

Goal

- “The goal of the informed consent process is to provide people with sufficient information so they can make informed choices about whether to begin or continue participation in clinical research.”

Informed Consent Process

does not equal

Informed Consent Form

The process

- "…involves a dynamic and continuing exchange of information between the research team and participant throughout the research experience…"

The document

- "…a starting point for the necessary exchange of information between investigator and potential participant."
- "…the foundation not the entirety…"

Why do we need it?

- Respect for persons
- Respect for autonomy of decision making
- True limit on investigative authority
- Sense of formality

“It’s a very simple procedure. We slice off the top of your head, scoop out your innards with a spoon, and carve out your eyes and mouth.”

How do we get informed consent

- Varies according to study design and nature of participation
- Verbal vs. Written
- Investigator vs. proxy

Informed Consent Regulations

DHHS:

45 CFR Parts 46.116 and 46.117

FDA:

21 CFR Parts 50.25 and 50.27

Comprehension

- Consent not valid unless subject UNDERSTANDS

- Responsibility for understanding rests with RESEARCHER who must consider:
  - Nature of population
  - Type of information
  - Circumstances and timing
  - Language and culture

General Requirements

- Subject or legally authorized representative
- Language understandable to subject
- Allow subject to consider participation
- Minimize coercion
- Subject does not waive any legal rights

IRB Responsibilities

- Set standards for consent documents
- Create templates
- Agree on “boilerplate language”
- Avoid legal interpretations and language
- Set limits on “marketing” tone
- Avoid jargon

Actual Consent Statements

"The risks associated with participating in this study are minimal, therefore there will be no compensation for injuries during this study"

"I understand that I may be unconscious and may not be able to consent."

Actual Consent Statements

"If you are a woman who is having sex that could lead to pregnancy, you must agree not to become pregnant or make a woman pregnant."

"We will insert 3 catheters, one in each arm."

Informed Consent Documentation

- Use only current IRB approved form
- Subject or legal representative must sign and date
- Provide subjects with copy of form
- Maintain documentation

Investigator Responsibilities

- Train individuals obtaining consent
- Use technology or innovative approaches
- Be sensitive to subjects' needs
- Make adjustments in process, as needed
- Obtain IRB approval for changes

Consent Process

- Typeface standards (font, point size)
- 6th-8th grade reading level
- Translation and/or interpretation
- “Witness” to signature or consent process
- Flowcharts or diagrams (IRB review)
- Video for information and portions of consent process (IRB review)

EM research consent forms

- 94 forms from 96 EM programs performing research
- Mean years of education needed: 10
- Length and complexity increased with risk
- Average EM consent forms may be too difficult for the average participant to understand

- Mader TJ, Playe SJ: Annals of EM April 1997;29:534-539

Informed consent gone wron

- Jesse Gelsinger (gene transplant)
- James Quinn (artificial heart)
- Johns Hopkins (hexamethonium death)

Gene therapy business: The tragic case of Jesse Gelsinger”

- 18 year old with partial ornithine transcarbamylase deficiency
- The first person to die from gene therapy

Reactions

- FDA suspended all gene therapy trials and other experiments
- Hearings on quality of oversight and safety
- President Clinton demanded improvements in consent and access to information about gene therapy research

James “Butch" Quinn: Artificial Heart Recipient

- 52 year old who received an artificial heart
- Lived for 10 months with the device
- Sustained fatal stroke

Reactions

- Lawsuit over consent process
- Recipient's widow says she and her husband were misinformed and misled on risks, benefits and the potential for pain and suffering

Volunteer in Asthma Study

- 24 hours after inhaling hexamethonium reported dry cough, shortness of breath, muscular aches and fever
- 2 days later admitted with concern for possible reaction
- Died one month later

Reactions

- Research suspended
- Federal government temporarily shut down most research involving human subjects at the institution involved
- Hexamethonium not approved by the FDA and IRB did not provide adequate oversight

Are we doing it right?

- Behaviors during informed consent (>1000 ED patients taking a survey)
  - 41% did not read
  - 57% who read spent < 60 seconds
  - 22% asked questions
  - 44% did not accept the form

Baren: AEM 2002

Why do people participate?

- Altruism
- Free medical care and medications
- Trust
- Self-interest
- Attention
- Do we want to constrain people if they are doing things for the wrong reasons?

Healthy volunteers

- May not benefit directly
- Could ultimately contribute to development of a new therapy
- Require particularly close monitoring
- Can pose risk to a volunteer's health or life

Vulnerable populations

- Research on individuals who lack capacity requires prospect of benefit
- Not promulgated in federal regulations except in the case of children
- Family member can consent
  - If consistent with state law

Vulnerable Populations

1. Children
2. Prisoners
3. Pregnant women/fetuses
4. Lactating women
5. Mentally disabled persons
6. Economically disadvantaged persons
7. Educationally disadvantaged persons

Subtle considerations

- Language
- Culture
- Current Events or Incidents
- Age (elderly)
- Age (young)
- Cognitive Impairment
- Chemical Use
- Health Status
- Students
- Employees

Vulnerable Populations: Children

- If child can understand (> age 6-8?)
  - We are obligated to obtain assent
- Limited form of decision making for children
- Promotes investment in the research

Assent (45 CFR 46.408)

- Age
- Maturity
- Psychological state

  OR

- Direct benefit; intervention not otherwis available

Documenting Assent and Permission (45 CFR 46.408)

- Permission document as per consent regulations
- Assent: IRB determines whether and how to document

Assent/Permission

- Can parents overrule?
  - With possibility of benefit
- Studies with more than minimal risk?
  - Not without prospect of benefit

One Parent or Two? (45 CFR 46.40

- One Parent
  - < Minimal risk
  - > Minimal risk but direct benefit
- Both Parents, where possible
  - > Minimal risk, no direct benefit
  - Not otherwise approvable