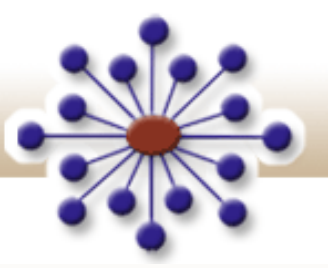


Informed Consent for Human Participant Research

Presented by:

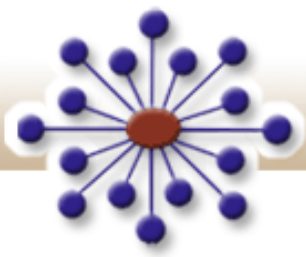
*Lynn Kunkel, M.S., C.C.R.P.
Jennifer Sharpe Potter, Ph.D.*

*The background
The principles
The practice*



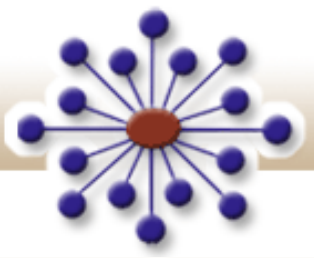
Introduction

This seminar is intended to assist CTN affiliated research staff understand the principles that govern human subject research and the importance of informed consent in research trials.



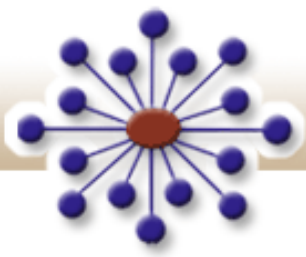
Introductory Polling Questions



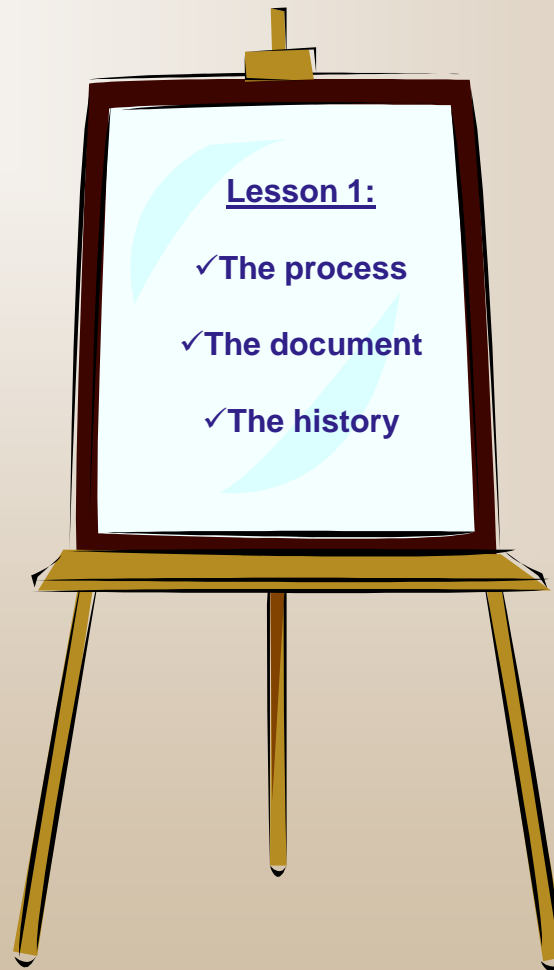


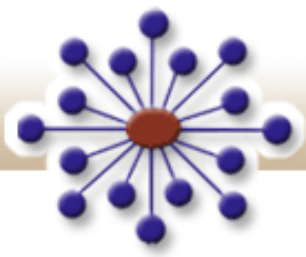
Training Outline

- Lesson 1: Informed Consent Overview
 - The process
 - The document
 - The history
- Lesson 2: The Principles
- Lesson 3: The Requirements Elements
- Lesson 4: The Essence of Informed Consent



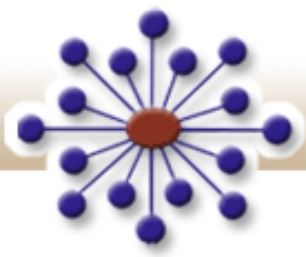
Lesson 1: Informed Consent Overview





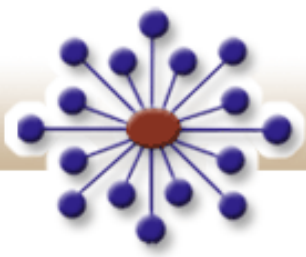
Lesson 1: Informed Consent Overview

- The Informed Consent Process
 - Information exchange between the prospective participant and the investigator and study staff
 - Before, during, and sometimes after the study



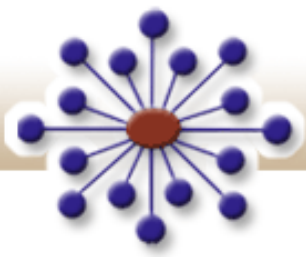
Lesson 1: Informed Consent Overview

- The Informed Consent Process
 - An opportunity to build trust and a rapport with participants
 - Allows for participants to become fully informed about the study
 - Provides time for the participant to ask questions
 - Ensures participant comprehension



Lesson 1: Informed Consent Overview

- **The Informed Consent Document**
 - Provides all information needed for the participant to make and informed decision
 - Also used as a guide for verbal study explanation
 - Regulated by
 - OHRP via 45 CFR 46
 - FDA via 21 CFR 50
 - FDA and OHRP regulations are not exactly the same; both may apply to the study
 - The IRB and the institution the study is being conducted
 - The IRB and institution may have more stringent standards than the federal regulations
 - They cannot have more lenient standards



Lesson 1: Informed Consent Overview

"Those who do not remember the past are condemned to repeat their mistakes."

(George Santayana, philosopher, essayist, poet and novelist 1905-1906)

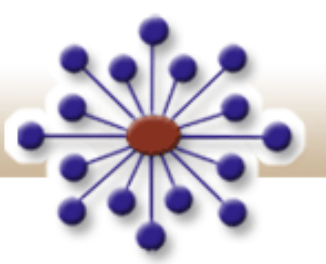
- **The Informed Consent History**
 - Three events had significant impact on Federal Regulations
 - 1940's Nuremberg War Crimes Trial
 - 1960's Thalidomide Tragedy
 - 1972 Tuskegee Syphilis Study
(there are many more.....)



Lesson 1: Informed Consent Overview

- The Informed Consent History
 - 1940's Nuremberg War Crimes Trial (ethical yardstick)
 - Volunteer informed consent obtained without coercion
 - Human experiments should be based on prior animal experimentation
 - Anticipated scientific results should justify experiment
 - Only qualified scientists should conduct medical research
 - Avoid physical & mental suffering
 - No expectations of death or disabling injury
 - International conduct standard





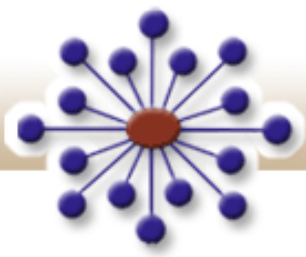
Lesson 1: Informed Consent Overview

- The Informed Consent History

- 1960's Thalidomide Tragedy

- Drug was extremely dangerous to fetus in first trimester. Interfered with the normal development of arms and legs
- Many of the people taking the drug were not informed that they were taking an 'experimental drug' nor had been asked to give their consent
 - 1962 to the Food, Drug and Cosmetic Act Amendment
 - Written consent documentation requirement

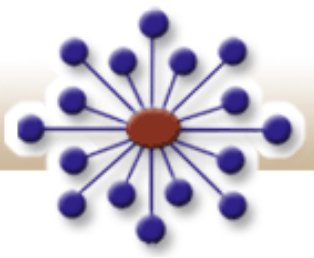




Lesson 1: Informed Consent Overview

- The Informed Consent History
 - 1972 Tuskegee Syphilis Study
 - Individuals were studied to observe the natural, untreated progression of the disease
 - Participants were not required to give consent and were not aware of diagnosis
 - Treatment withheld
 - Lead to the Belmont Report, the
 - Lead to the establishment of
 - National Human Investigation Board
 - Institutional Review Board

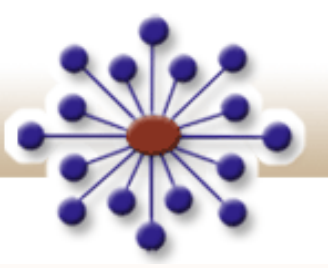




Lesson 1: Informed Consent Overview

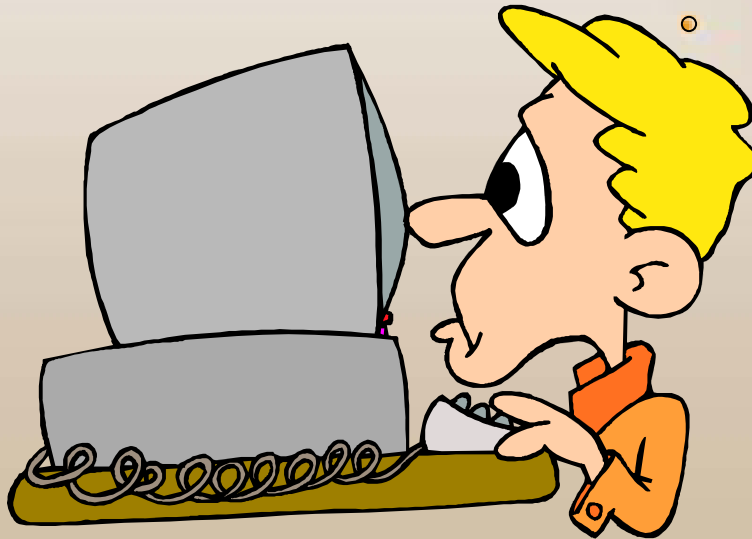
- **Belmont Report**
 - Cornerstone document of ethical principles
 - Principles and guidelines for the protection of human subjects
 - Federal regulation of subject protection





Lesson 1: Polling Questions

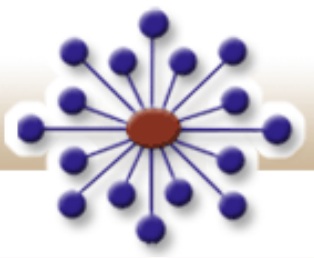
*"Hmm....A...no C,
errr...B, yeah B."*





Lesson 1: Polling Answers

- An informed consent is:
 - ☑ ● A document and a process by which a person agrees to participate in a research study after being fully informed
 - It is **not** a contract
 - It is **not** a release of clinic responsibility



Lesson 1: Polling Answers

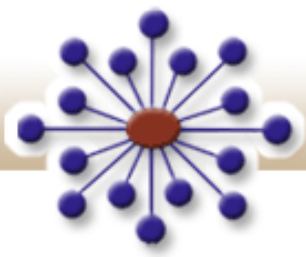
- All CTN members have a responsibility to ensure that the process of obtaining informed consent from research participants respects the participants right to make a voluntary and informed decision, as well as, conforms with federal, state, and local regulations.



- True

- Ethical practice in research protects the study staff, the investigator and the participant.

- False



Lesson 2: The Principles



Respect for Persons

Beneficence

Justice



Lesson 2: The Principles

- **Belmont Report** - Ethical research principles
 - **Respect for Persons – Autonomy**
 - Information needed to make an informed decision
 - Respect participants autonomy
 - Protect those with diminished autonomy
 - **Beneficence**
 - Do no harm
 - Maximize benefits minimize risk
 - **Justice**
 - Benefit outweighs risk
 - Burdens not overly imposed
 - Fair selection process

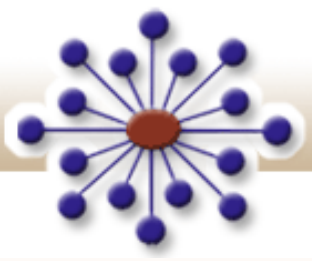


(45 CFR 46 & 21 CFR 50)



Lesson 2: The Principles

- **The Common Rule**
 - Governs research that is conducted or supported by 17 federal agencies
- **Three main protective mechanisms**
 - Independent Review Board (IRB) review of research
 - Institutional assurances of compliance
 - Informed consent of subjects



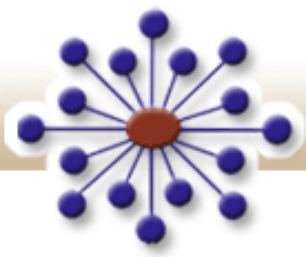
Lesson 2: Polling Questions



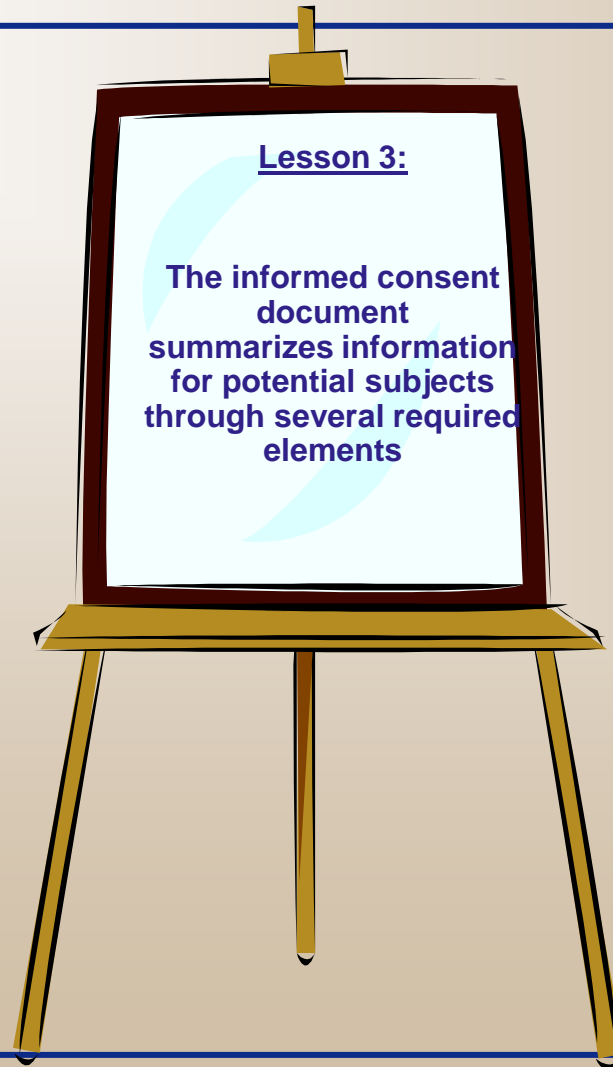


Lesson 2: Polling Answers

- The ethical principles of research (our governing values) are:
 - ☑ ● **Beneficence, justice and Respect for persons (Autonomy)**
 - Justice, comprehension, and autonomy
 - Information, comprehensibility, and voluntariness

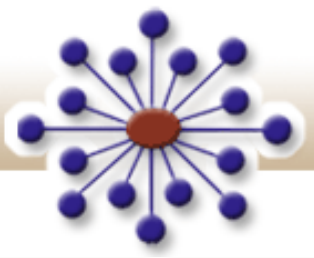


Lesson 3: The Requirements Elements



Lesson 3:

The informed consent document summarizes information for potential subjects through several required elements



Lesson 3: The Requirements Elements

“rules of the road”

- Respect for Persons
 - Information
 - 8 requirements
 - Comprehensibility (understandable)
 - Voluntary Participation

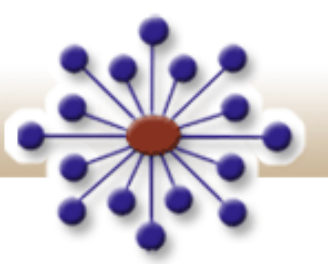
(45 CFR 46 & 21 CFR 50)



Lesson 3: The Requirements Elements

- Eight (8) Required Elements of Information
 - 1) A research statement
 - Purpose, duration, procedures description, experimental procedures
 - 2) Risks/discomforts
 - 3) Benefits
 - 4) Alternatives
 - 5) Confidentiality
 - 6) Information in case of injury
 - 7) Contact for questions
 - 8) Voluntary participation

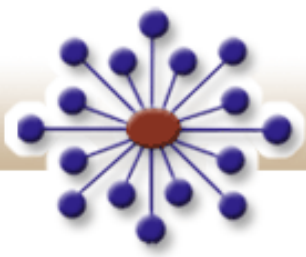
(45 CFR 46 & 21 CFR 50)



Lesson 3: The Requirements Elements

- Additional Elements
 - 1) Unforeseeable risks
 - 2) Participation may be terminated by investigator
 - 3) Cost to participant
 - 4) Significant new findings will be shared
 - 5) Participant withdrawal from study & procedures
 - 6) How many other participants are involved

(45 CFR 46 & 21 CFR 50)



Lesson 3: The Requirements Elements

- **Comprehension**
 - Written in simple, lay terms
 - Verify Understanding
 - Give a quiz
 - Look for questions / Ask questions
 - Avoid Therapeutic Misconception
 - Research goal \neq actual treatment

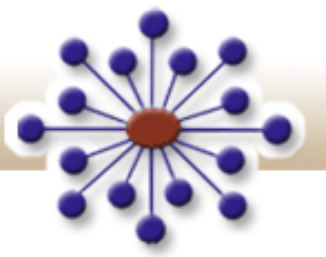
(45 CFR 46 & 21 CFR 50)



Lesson 3: The Requirements Elements

- **Voluntary Participation**
 - Subject's ability to consent participation
 - Without Undue Influence - excessive, inappropriate, improper, or unwarranted reward/benefit used to obtain participation or compliance
 - Without Coercion - forceful or overt pressure on subject to participate or remain compliant
 - The signed consent form is NOT a contract
 - Participation is entirely voluntary. Participant can withdraw at any point in the study
 - Participant can refuse to answer any question they do not wish to answer

**Ethical practice in research
protects the study staff, the investigator and the participant**

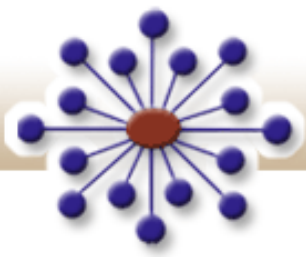


Lesson 3:

The Requirements Elements

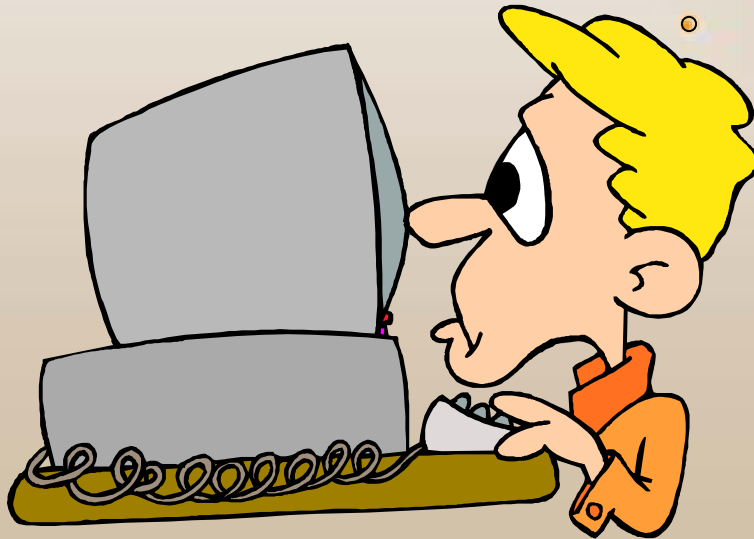
- **Vulnerable/Special Populations**
 - **Children**
 - cannot legally give consent
 - special provisions - parents must give authorization
 - the child must assent to the research as well (excluding children under the age of 7)
 - child that says no cannot be coerced or intimidated
 - even if the parent has said yes
 - **Pregnant Women, Fetuses and Neonates**
 - **Prisoners**
 - Mandatory to be voluntary
 - **Cognitively Impaired**
 - **Others**
 - substance abusers, homeless, elderly (nursing home), students, military personnel, study staff/employees

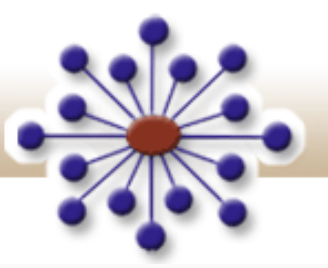
(45 CFR 46 & 21 CFR 50)



Lesson 3: Polling Questions

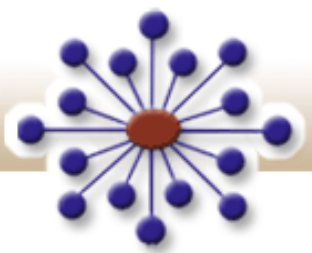
*"Hmm....A...no C,
errr...B, yeah B."*



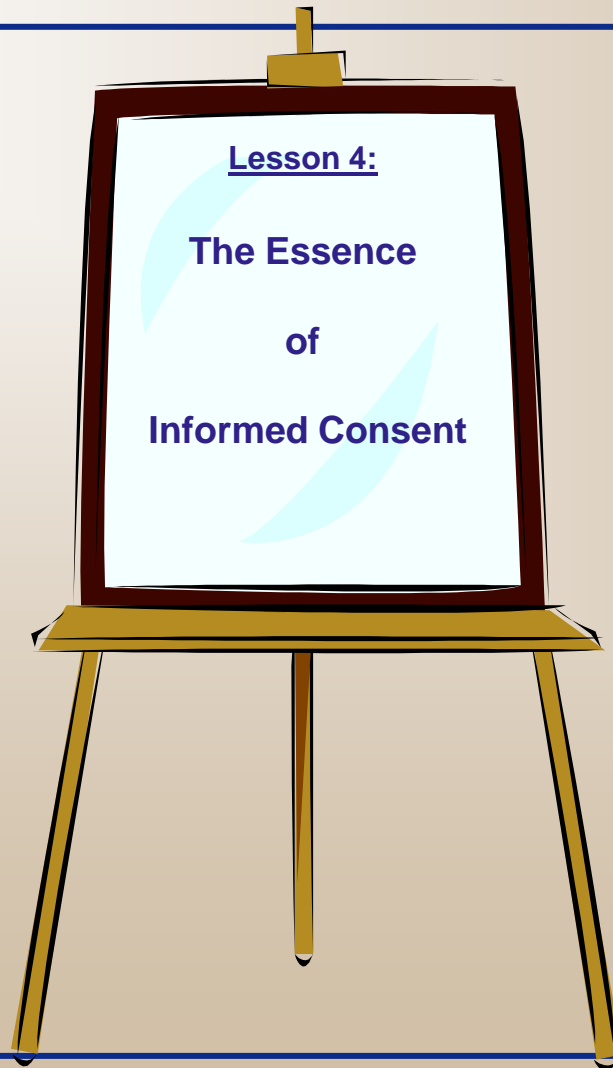


Lesson 3: Polling Answers

- What are three elements required in an informed consent?
 - Individuality, Comprehension, and Autonomy
 - Information, Competency, and Voluntariness
 - ☑ ● **Information, Comprehension, and Voluntariness**



Lesson 4: The Essence of Informed Consent



Lesson 4:

The Essence

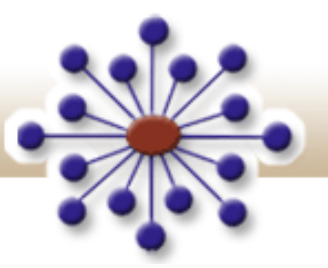
of

Informed Consent

Respect for Persons

Beneficence

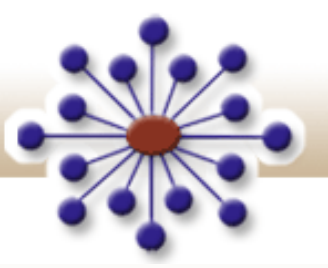
Justice



Lesson 4:

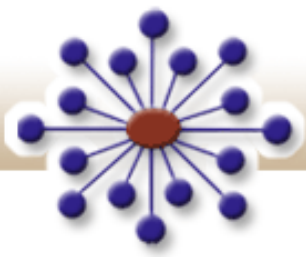
The Essence of Informed Consent

- Who should do it?
 - Knowledgeable research staff
- Where to do it?
 - Private place
 - Talk freely
- When to do it?
 - Allow time to reflect
- How?
 - Review (patience and respect – take as long as needed)



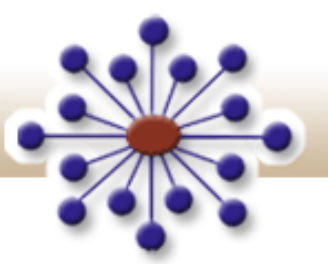
Lesson 4: The Essence of Informed Consent

- Is an opportunity to build trust and a rapport with participants
- Obtaining consent is a process / beginning of an on-going discussion
- An agreement between researcher and participant
 - Explains expectations:
 - What the researcher will do
 - What the participant will do



Lesson 4: The Essence of Informed Consent

- **Common Challenges**
 - Providing an environment where the subject is not intimidated or influenced by others
 - Assessing a subject's level of understanding and determining competency
 - Ensuring proper documentation of the consent process

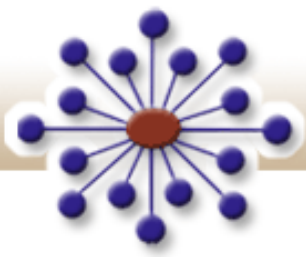


Lesson 4: The Essence of Informed Consent

● Things to Remember

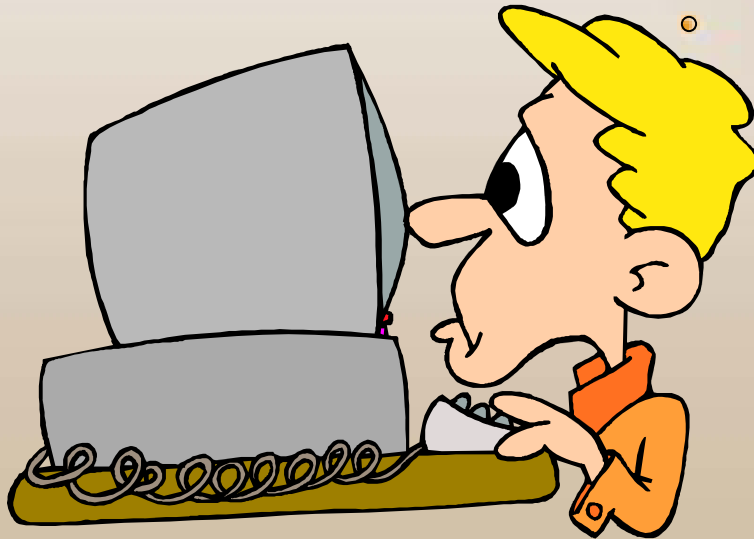
- Allow the participant to have ample time to read the Informed Consent Form
- Obtain all necessary signatures and initials and date (if required by the IRB)
- Use proper correction procedures
 - line through, initial, date
- Ensure the use of the correct ICF version
 - Approved by your IRB
- Obtain a completed ICF document before conducting any study-related procedures
- Remember – A signed consent is NOT a contract

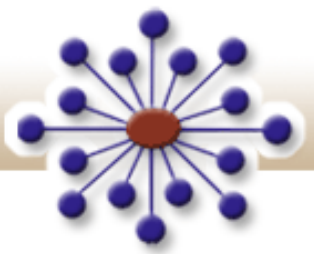
~~Opps~~ *EAB* 01/02/08



Lesson 4: Polling Questions

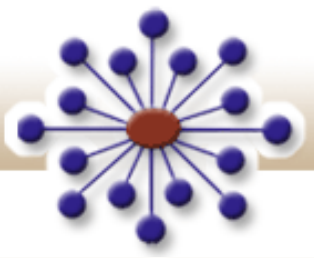
*"Hmm....A...no C,
errr...B, yeah B."*





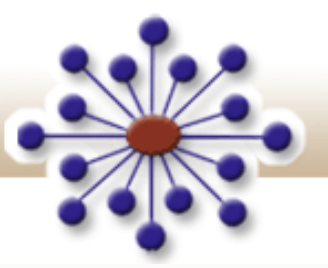
Lesson 4: Polling Answers

- Out of the options provided, which is the best way to discuss and obtain consent?
 - It should be in the investigator's office right before study procedures have to begin.
 - ☑ ● **In a quiet room where both the person obtaining consent and the potential participant can sit down and discuss the consent. The participant should be able to take a copy home for further consideration.**
 - In a quiet room with the person obtaining consent standing before the potential participant presenting the study. Participant should withhold questions until the end of the presentation.
 - In a room with the entire research team present and ready to discuss the study and answer questions about the consent form.



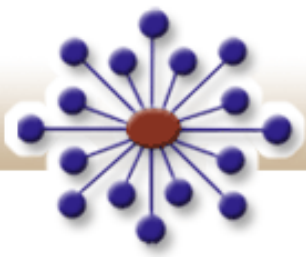
Lesson 4: Polling Answers

- All of the following are key ethical requirements for clinical research except:
 - The methodology used in the research should be scientifically sound.
 - There should be a favorable risk benefit ratio for individual subjects.
 - ❑ ● Subjects should be paid for their participation in the protocol.
 - An IRB should review the research protocol.



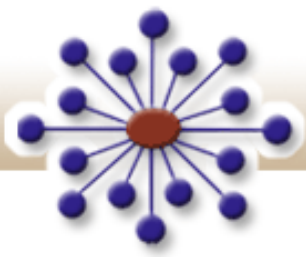
Case Studies





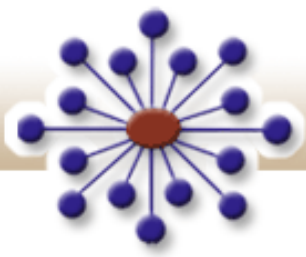
Lesson 4: The Essence of Informed Consent

- Case # 1: Informed Consent Documentation
 - Consent is to be obtained by licensed MD only
 - Research team knows these subjects well
 - Coordinators consent subjects but do not sign the consent form (to comply with PHRC policy)
 - Subjects are asked if they wish to speak with PI, and most subjects decline
 - The PI or co-investigator provides their signature on the consent form
 - Study is amended and requires subject re-consent



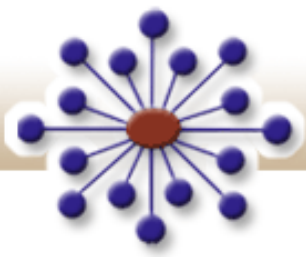
Lesson 4: The Essence of Informed Consent

- **Case # 1: Discussion Points**
 - Does the licensed MD signature on the consent form comply with the institutional policy? What does the signature represent?
 - Can the coordinator re-consent the subjects and sign (seeing as they spoke with them about the study initially and the modification is not investigational drug related)?
 - Anything done well in this scenario?



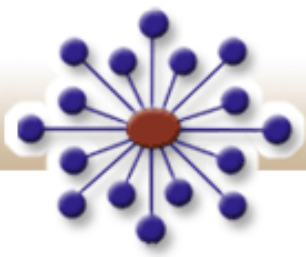
Lesson 4: The Essence of Informed Consent

- **Case #2: Informed Consent Documentation**
 - Subjects are aged 18-25 and do not live on college campuses/dorms
 - Study is of sensitive nature (sexual habits)
 - Majority of subjects are not taking their consent form copy with them as required
 - The copy not taken by the subject is being filed with the original



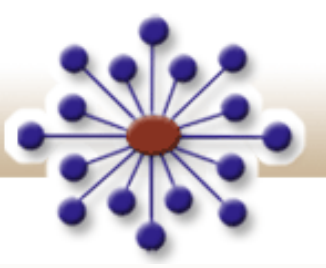
Lesson 4: The Essence of Informed Consent

- **Case #2: Discussion Points**
 - Why might the subject not want to take a copy of their consent form?
 - Should the study site keep the copy on file if the subject refuses?
 - What reporting to the IRB is required to correct this issue?
 - What is a 'next step' to rectify the problem?



Summary of Training

- **Lesson 1: Informed Consent Overview**
 - A process of information exchange
 - A document providing information needed for an informed decision and a guide for discussion and explanation
 - Significant historical events prompted the necessity of ethical principles medical research
- **Lesson 2: The Principles**
 - Belmont Report's
 - Respect for Persons (Autonomy), Beneficence and Justice
- **Lesson 3: The Requirements Elements**
 - Information (8 elements), Comprehension, and Voluntariness
- **Lesson 4: The Essence of Informed Consent**
 - Respect for persons – provide continuous information
 - Avoid coercive statements and conduct



Handouts/Resources

- Journal of Medical Ethics Article
- Annotated Compendium of NIH Resources on Informed Consent
- Informed Consent Checklist
 - <http://www.hhs.gov/ohrp/humansubjects/assurance/consentckls.htm>
- Belmont Report
 - <http://www.hhs.gov/ohrp/humansubjects/guidance/belmont.htm#xbenefit>
- OHRP
 - <http://ohrp.cit.nih.gov/search/asearch.asp>
- WWII Nuremberg War Crimes
 - <http://www.shoah.dk/doctors/experiments.htm>