

Institutional Review Board for the Protection of Human Subjects: Training and Continuing Education

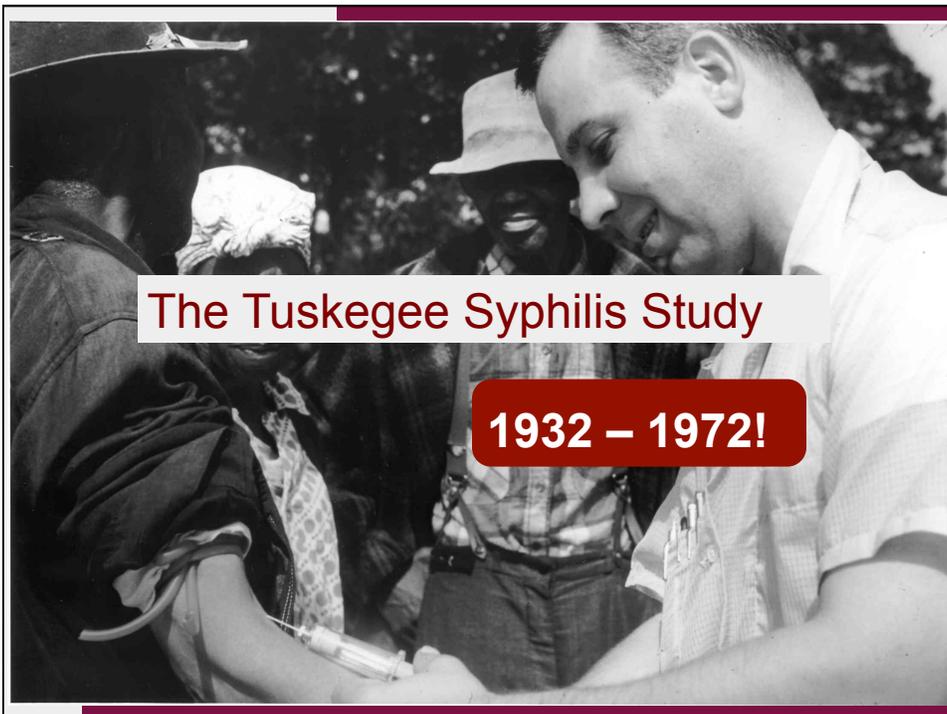
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The Nuremberg Trials



The Nuremberg Code - 1947

- As part of the verdict, rules for “Permissible Medical Experiments”
 - Voluntary consent
 - Benefits outweigh risks
 - Ability of the subject to terminate participation



Stanley Milgram's Obedience Study (1963)



Humphreys "Tearoom" Study



The Stanford Prison Study



1974 Research Act

- Resulted in the “Common Rule”
- The Belmont Report



The Belmont Report

Three Basic Ethical Principles:

- Respect for Persons
 - Individual autonomy
 - Protection of individuals with reduced autonomy
- Beneficence
 - Maximize benefits and minimize harms
- Justice
 - Equitable distribution of research costs and benefits



Top Ten Investigator Responsibilities When Conducting Human Subjects Research



Investigator Responsibility #1

**Design And Implement Ethical
Research, Consistent With
Three Ethical Principles
Delineated In The Belmont
Report**



Investigator Responsibility #2

**Comply With All Applicable
Federal Regulations
Impacting The Protection Of
Human Subjects**



Federal Regulations and Policy

- 45 CFR 46 - Basic DHHS Policy for Protection of Human Research Subjects
Originally adopted May, 1974, Revised January 13, 1981, Revised June 18, 1991
 - Additional protections for vulnerable populations in Subparts B-D
- Federal Policy for the Protection of Human Subjects - “The Common Rule” June 18, 1991
 - Departments of Agriculture, Energy, Commerce, HUD, Justice, Defense, Education, Veterans Affairs, Transportation, and HHS. NSF, NASA, EPA, AID, Social Security Administration, CIA, and the Consumer Product Safety Commission.



Federal Regulations and Policy

Additional Protections Included in 45 CFR 46:

- **Subpart B** - Additional Protections for Pregnant Women, Human Fetuses and Neonates Involved in Research (revised December 13, 2001)
- **Subpart C** - Additional DHHS Protections Pertaining to Biomedical and Behavioral Research Involving Prisoners as Subjects
- **Subpart D** - Additional DHHS Protections for Children Involved as Subjects in Research



Children as Subjects

- In most cases, children may participate only if the research involves no more than minimal risk
- Consent of parent or guardian
- Assent of the child
 - Generally, written assent if the child is 11 years old or older
 - Assent form must be in language appropriate to the age of the child



Investigator Responsibility #3

Ensure That All Research
Involving Human Subjects Is
Submitted To And Approved
By The Appropriate
Institutional Review Board



Definitions

- Research - a systematic investigation designed to develop or contribute to generalizable knowledge.
- Human Subject - a living individual about whom an investigator conducting research obtains
 - data through intervention or interaction with the individual, or
 - identifiable private information



IRB Review

- **Institutional Review Board (IRB):** A campus-wide committee charged with the review of human participants research to assure that the rights and welfare of human participants are adequately protected.
- **Why do we need IRB review?**
 - No one can be objective about their own work
 - People underestimate the risks involved in things they are very familiar with
 - People overestimate the benefit of things that are important to them



Investigator Responsibility #4

Comply With All Applicable
IRB Policies, Procedures,
Decisions, Conditions, And
Requirements



IRB Decision Matrix

BENEFICENCE

Risk/Benefit Analysis
Experimental Design
Qualifications of PI

JUSTICE

Subject selection
Inclusion/exclusion
Recruitment

RESPECT FOR PERSONS

Informed consent
Assent

Privacy & Confidentiality
Protection of subjects
(especially vulnerable
populations)

Regulatory Review Requirements

- The proposed research design is scientifically sound and will not unnecessarily expose subjects to risk
- IRB Q'a
 - Is the hypothesis clear
 - Is the design appropriate
 - Will the research contribute to generalizable knowledge and is it worth the risk?

Regulatory Review Requirements

- Risks to subjects are reasonable in relation to benefits
- IRB Qs
 - What does IRB consider level of risk to be?
 - What about the PI?
 - Is there prospect of direct benefit to subjects?



Regulatory Review Requirements

- Subject Selection is equitable
- IRB Qs
 - Who is enrolled? Men? Women? Ethnic Minorities? Children?
 - Rationale for inclusion/exclusion addressed?
 - Are these subjects appropriate for the protocol?

Regulatory Review Requirements

- Additional Safeguards required for subjects likely to be vulnerable to coercion or undue influence
- IRB Qs
 - Are appropriate protections in place for vulnerable subjects, e.g., pregnant women, fetuses, economically-disadvantaged, decisionally-impaired

Regulatory Review Requirements

- Risks to subjects are minimized
- IRB Qs
 - Does the research design minimize risks to subjects?
 - Would the use of a data & safety monitoring board or other research oversight enhance subject safety?

Regulatory Review Requirements

- Subject privacy and confidentiality are maximized
- IRB Qs
 - Will personally identifiable research data be protected to the extent possible from access or use?
 - Are any special privacy & confidentiality issues addressed, e.g., use of genetic information?

Regulatory Review Requirements

- Informed Consent is obtained from research subjects or their legally authorized representative
- IRB Qs
 - Are the 8 required elements included? →
 - Is consent document understandable? →
 - Who will obtain consent?
 - Child assent?
 - Is IRB requested to waive or alter consent?

Request to alter consent or to waive signed consent

- <http://www.hhs.gov/ohrp/humansubjects/guidance/45cfr46.htm#46.116>



Investigator Responsibility #5

Implement Research As
Approved And Obtain Prior
IRB Approval For Changes



Investigator Responsibility #6

Obtain Informed Consent and
Assent In Accord With
Federal Regulations And As
Approved By The IRB





Informed Consent

Beyond the Consent Form



The Consent Process

Informed consent is not a single event or just a form to be signed -- rather, it is an educational process that takes place between the investigator and the prospective subject.

The basic elements of the consent process include:

- full disclosure of the nature of the research and the subject's participation,
- adequate comprehension on the part of the potential subjects, and
- the subject's voluntary choice to participate.



Investigator Responsibility #7

Document Informed Consent
and Assent In Accord With
Federal Regulations And As
Approved by the IRB



Documentation of Consent

Articles in most popular magazines are at the **8th grade level**. Factors that improve readability include the following:

- Technical terms should be replaced with **ordinary language**;
- Use **active tense** rather than passive tense verbs ("We did" rather than "It was done");
- Write **shorter sentences** in general; and
- Make clear the links of **logical sequences** and of cause-and-effect, even if doing so makes the sentence much longer. ("We will do this, because that happened".)



Documentation of Consent

Format can help comprehend and remember complex material. Good format uses: headings; indents; bolded type; lists; extra spacing between sub-topics; repetition; reasonable-size type; and plenty of margins and empty space in general.



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Elements of Informed Consent

- Informed consent is a process - not just a signature
- 1) Statement that the study involves research
- 2) Description of any risks
- 3) Description of any benefits to the subject
- 4) Disclosure of alternative procedures



Elements of Informed Consent

- 5) Statement regarding confidentiality of records
- 6) If more than minimal risk - explanation of available compensation or treatment
- 7) Contact for answers to pertinent questions
- 8) Statement that participation is voluntary





Additional Requirements

- Taping - state in the consent form and indicate what use will be made of tapes
- Written assent if the child is 11 or older, oral assent from younger children
- If questions deal with sensitive issues tell subjects they can refuse to answer individual questions



Additional Requirements

- Do not promise anonymity if there are any identifiers which link the subject and his/her data
- Deception / Debriefing
- Consent is an active process, passive consent is never acceptable.



Investigator Responsibility #8

Report Progress Of Approved Research To The IRB, As Often And In The Manner Prescribed By The IRB



Continuing Review

An IRB shall conduct continuing review at intervals appropriate to the degree of risk, but not less than once per year...

21 CFR 56.109(e) 45 CFR 46.109(e)



Investigator Responsibility #9

Report To The IRB Any Injuries, Adverse Events, Or Other Unanticipated Problems Involving Risks To Subjects Or Others



Investigator Responsibility #10

Retain Signed Consent Documents And IRB Research Records For At Least Three Years Past Completion Of The Research Activity



Exempt Research

- IRB - not the PI - determines exemption
- Conducted in established or commonly accepted educational settings, using normal educational practices
- Educational tests, survey or interview procedures or observation of public behavior unless information is identifiable and sensitive

Expedited Review

- Some protocols may be reviewed by the chair only, or by a trained, experienced member appointed by the chair.
- An IRB may use the expedited review procedure to review either or both of the following:
 - (1) some or all of the research appearing on the list and found by the reviewer(s) to involve no more than minimal risk,
 - (2) minor changes in previously approved research during the period (of one year or less) for which approval is authorized.

Expedited Review

- The expedited review procedure may not be used where identification of the subjects and/or their responses would reasonably place them at risk of criminal or civil liability or be damaging to the subjects: financial standing, employability, insurability, reputation, or be stigmatizing, unless reasonable and appropriate protections will be implemented so that risks related to invasion of privacy and breach of confidentiality are no greater than minimal.

Expedited Categories

- For a complete listing with descriptions and examples, please visit <http://www.hhs.gov/ohrp/humansubjects/guidance/expedited98.htm>



Thank you very much!