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Research Ethics

40 years of protecting human and animal subjects (through IRB's)

[Code of Federal Regulations]

[Title 21, Volume 1]

[Revised as of April 1, 2004]

[CITE: 21CFR50.20]

TITLE 21--FOOD AND DRUGS

CHAPTER I--FOOD AND DRUG ADMINISTRATION
DEPARTMENT OF HEALTH AND HUMAN SERVICES

SUBCHAPTER A - GENERAL

PART 50 -- PROTECTION OF HUMAN SUBJECTS
Subpart B -- Informed Consent of Human Subjects

Sec. 50.20 General requirements for informed consent.

Except as provided in §§ 50.23 and 50.24, no investigator may involve a human being as a subject in research covered by these regulations unless the investigator has obtained the legally effective *informed consent* of the subject or the subject`s legally authorized representative. An investigator shall seek such consent only under circumstances that provide the prospective subject or the representative sufficient *opportunity to consider whether or not to participate and that minimize the possibility of coercion or undue influence*. The information that is given to the subject or the representative shall be in *language understandable* to the subject or the representative. No informed consent, whether oral or written, may include any exculpatory language through which the subject or the representative is made to waive or appear to waive any of the subject`s legal rights, or releases or appears to release the investigator, the sponsor, the institution, or its agents from liability for negligence.

[46 FR 8951, Jan. 27, 1981, as amended at 64 FR 10942, Mar. 8, 1999]

Main Ethical Issues

Equipoise (New Tx Vs Current SOC)

- a true null hypothesis should exist

Safety Of The Research Participant

- risk/benefit ratio

Informed Consent

- in writing, after time to consider & ask any pertinent questions.
- ongoing process, not a singular event or a mere formality.

Privacy And Confidentiality Concerns

- how information is protected from unauthorized observation
- how participants are to be notified of any unforeseen findings

How Adverse Events Will Be Handled

- who will provide care (e.g., injury)
- who will pay for that care

Main Ethical Principles

Belmont Report (1979)

- The National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research

3 main principles

- Autonomy
- Beneficence
- Justice

Autonomy

Liberty to follow one's will, personal freedom (OED)

Obligation to respect each person as capable of making an informed decision regarding participation in the research study.

Participant must received

- a full disclosure of the nature of the study
- the risks, benefits and alternatives
- an extended opportunity to ask questions

Autonomy is expressed through informed consent

Beneficence

- Doing good, the manifestation of benevolence or kindly feeling, active kindness. (OED)
- Maximize benefits for the individual participant and/or society, while minimizing risk of harm to the individual.
- Beneficence is expressed thorough risk/benefit calculation

Justice

Upright and impartial in one's dealings; rendering every one his due; equitable. (OED)

Equitable selection of participants

- avoid coerced
  - prisoners & other institutionalized people
  - children
- equality in distribution of benefits and burdens
  - Q: Corporate Research: drug & insurance
  - Q: DOD Research

Justice is expressed thorough sampling design

Informed Consent

Disclosure

- Nature & Purpose
- Procedures
- Expected benefits (participant and/or society)
- Foreseeable risks, stresses, and discomforts
- [Alternatives to participating in the research]
- Procedures: confidentiality or anonymity
- Compensation & medical Tx available (injury)
- Contact for questions

Informed Consent

Understanding

- Docs in lay language - avoid technical jargon
- Must understand what has been explained
- Ask questions and have them answered

Voluntariness

- Free of any coercion or promises of benefits unlikely to result from participation

Competence

- Must be competent to give consent
  - If not: surrogate iff: in the participant's best interest

Consent: In Writing and Witnessed

Nuremberg Code

'Trials of War Criminals Before the Nuremberg Military Tribunals Under Control Council Law No. 10", Vol. 2, Nuremberg, October 1946 - April 1949

" . . . certain types of medical experiments on human beings, when kept within reasonably well-defined bounds, conform to the ethics of the medical profession generally. The protagonists of the practice of human experimentation justify their views on the basis that such experiments yield results for the good of society that are unprocurable by other methods or means of study. *All agree, however, that certain basic principles must be observed in order to satisfy moral, ethical and legal concepts*."

Nuremberg Code

"The voluntary consent of the human subject is absolutely essential."

- **Yield fruitful results, unprocurable by other methods or means of study**
- **Anticipated results will justify the performance of the experiment.**
- **Avoid all unnecessary physical and mental suffering and injury.**
- **No priori reason to believe that death or disabling injury will occur**
- **Risk never exceed the humanitarian importance of the problem**
- **Protect against even remote possibilities of injury, disability, or death.**
- **Subject should be at liberty to stop the experiment**
- **Be prepared to terminate the experiment at any stage, if it becomes dangerous**

Tuskegee Syphilis Study

uskegee, Alabama, 1933

- highest prevalence of syphilis 6 southern States

.S Public Health Service

- chart successive phases of syphilis when NO Tx

ubjects

- 399 African-American men with latent syphilis
- 201 men without disease

Characteristics of Tuskegee

- Rural (Sub were sharecroppers)
- Deprived socioeconomic status
- High Illiteracy
- Poor Access to Medical Care

PHS Docs

- Told *treated* for "bad blood,"
  (a euphemism for syphilis)

Study lasted for 40 years (till 1972)

Sporadic clinical reexaminations

No anti-syphilitic therapy

urther Insult

942 (9 yrs into study)

- Draft Physicals, Told to undergo Tx

Assistant Surgeon General, prevented Tx.

Gave Draft Board list (256 names) to exclude from the list of draftees needing treatment. Board Agreed (still got drafted)

943

- modern-era of anti-syphilitic therapy began (penicillin)
- PHS did not use the drug on the Tuskegee participants unless they asked for it.

esearch Rational

Such individuals seemed to offer an unusual opportunity to study the untreated syphilitic patients from the beginning of the disease to the death of the infected person. An opportunity was also offered to compare the syphilitic process uninfluenced by modern treatment, with the results attained when treatment had been given.“

derlehr RA, Clark T, Wegner OC et al : Untreated syphilis in the male Negro. ***Ven Dis Inform*** *17: 260-265, 1936*

The Results

1972: Study came to light

- *Washington Star,* July 25, 1972, Jean Heller
- & was ended on November 16th

28 men had died of syphilis

100 others were dead due to syphilis related complications

40 wives had been infected

9 children had contracted the disease at birth

The Aftermath

1973: $1.8 billion class action suit filed

- $3 million in damages for each survivor & each heirs of the deceased
- The case never came to trial

1974 settlement with US for $10 million

- $37,500 for each survivor
- $15,000 for each heir

May 16, 1997, Pres Clinton formally apologized

Ethical Findings

Not provided with the adequate information needed to willingly consent to participating

Not Informed about

- The research project
- Its consequences to them
- Alternatives available to them

...various methods were used to maintain and stimulate their interest. Free medicines, burial assistance or insurance, free hot meals on the days of examination, transport to and from the hospital and an opportunity to stop in town on the return trip...all helped."

Ethical Principles re: Human Subjects

World Medical Association

- **Geneva, 1948**
  - **" . . . the health of my patient will be my first consideration"**
  - **" . . . I will not use my medical knowledge contrary to the laws of humanity"**
- **London,1949 International Code of Medical Ethics**
  - **"Any act, or advice which could weaken physical or mental resistance of a human being may be used only in his interest."**

World Medical Assembly

- **Declaration of Helsinki (June, 1964)**
- ***amended October 1975 and October 1983.***

U.S.

- **The Belmont Report (1979)**

stitutional Review Boards

Declaration of Helsinki (1964)

"The design and performance of each experimental procedure involving human subjects should be clearly formulated in an experimental protocol which should be transmitted to a *specially appointed independent committee* for consideration, comment and guidance."

IRB Proposal Items

Sound Scientific Logic
- Preliminary data
- Literature

Worth of the Study

Sound Methods

Safe Procedures

PI Skill

Informed Consent

Risk/Benefit Ratio

Confidentiality

Treatment

Additional Considerations
Clinical Research

- Doc must be free to use a new measure, if it offers hope of alleviating suffering.
- New method weighed against advantages of the best current methods.
- *Every* patient- including control group, be assured of the best proven diagnostic and therapeutic method.
- Refusal to participate must never affect Tx.
- Medical research is NOT professional care
  - Only acceptable to the extent that research is justified by its potential diagnostic or therapeutic value *for the patient*.

IRB @ WSU

WSU Web Page

- Browse A-Z

ORA Home Page

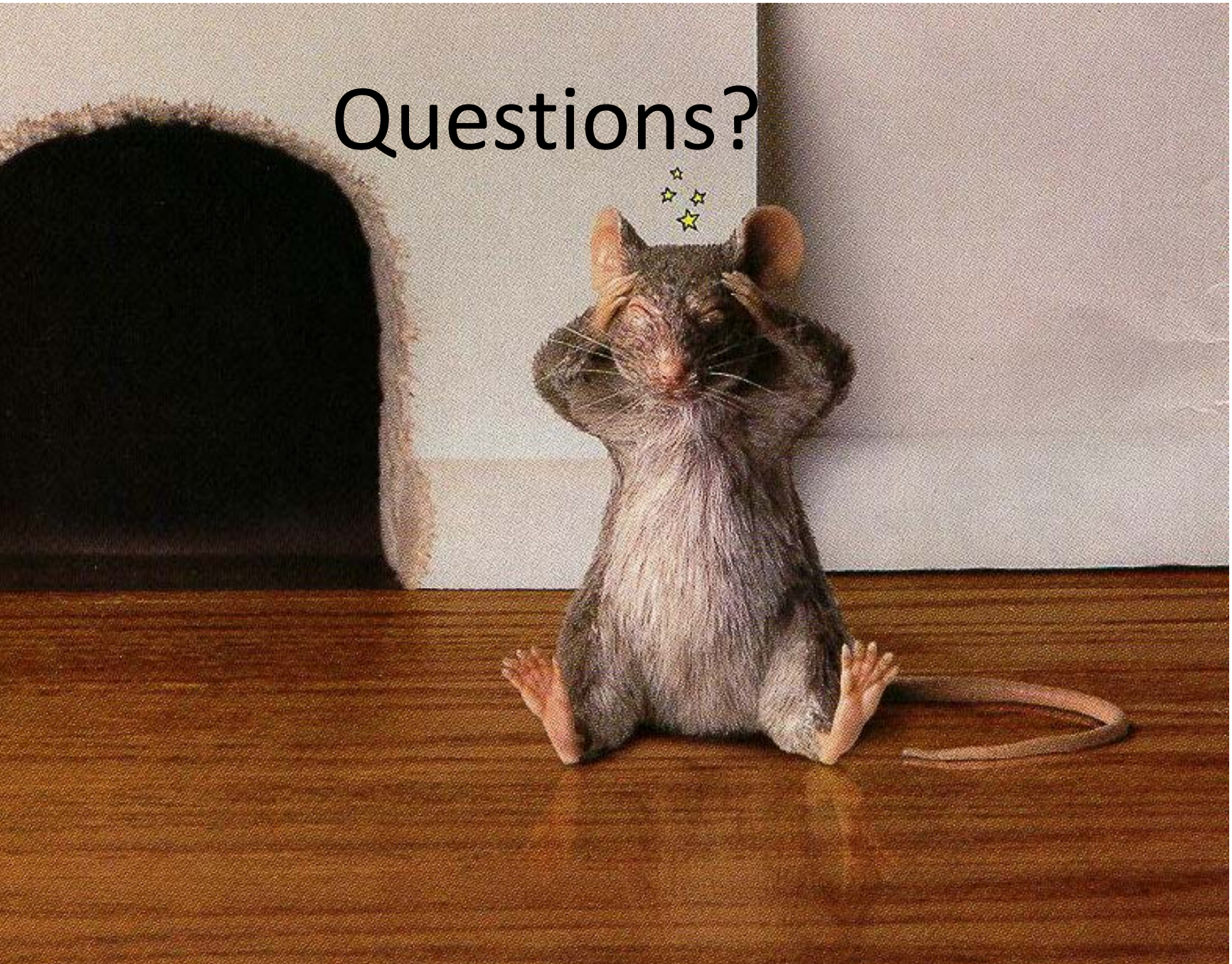
- Forms

RB Form

RB Guide

Example

Checklist


Questions?

o Be Happy In The Presence Of