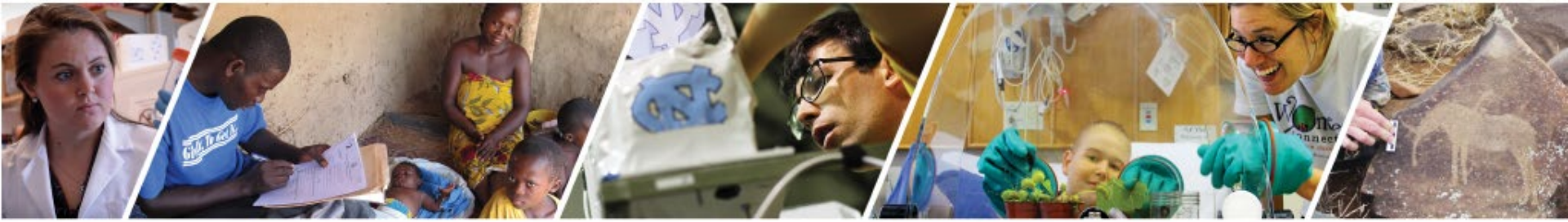
Why Do IRBs Exist?

April 20, 2023



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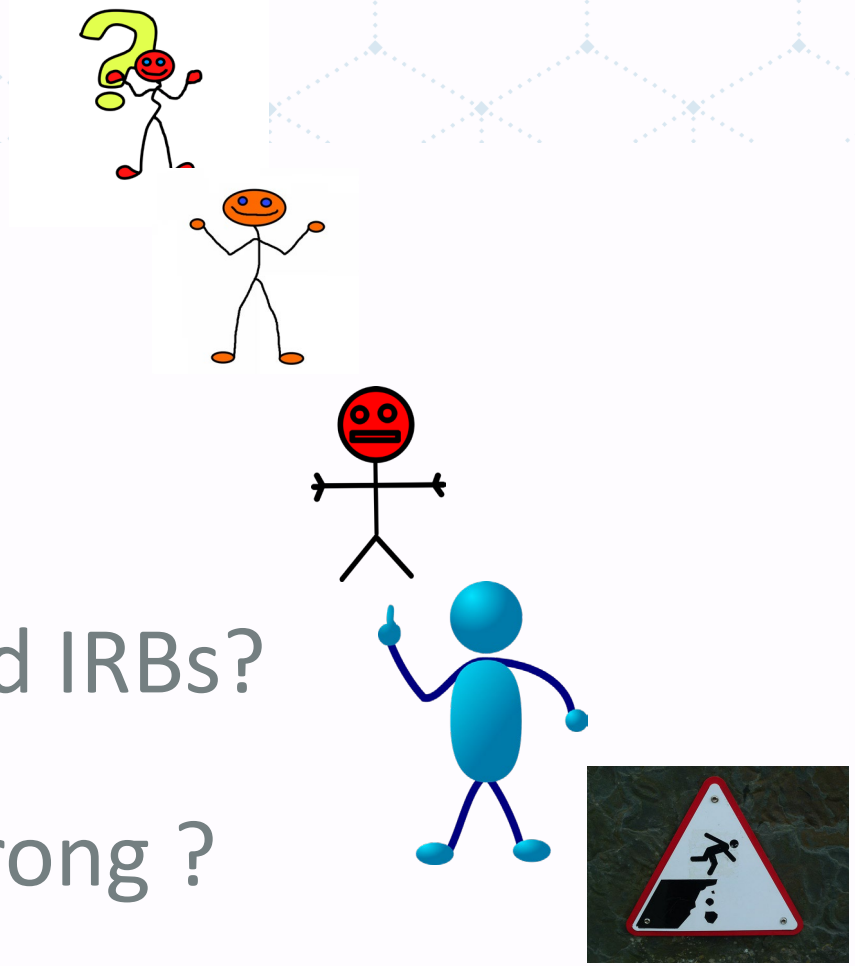
UNC RESEARCH

Today's topics to cover

- Why are there IRBs?
- What do they do?
- How do they do it?
- Do we *really* still need IRBs?
- What can possibly wrong ?



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IRB is Often Seen as a Black Hole: a Mysterious, confusing & a bother (at best)

IRB Basics

- Federally Mandated Review Committee
- Only role is to protect the rights & welfare of research subjects
- Have both federal regulations & ethical standards to uphold
- There are very serious consequences for failure to both PI, IRB & the institution

The IRBs **ONLY** Job is….

To protect research subjects & minimize study risks.

And is based on the honor system

Ethical Foundations

- Hippocratic Oath (4th century BC)
- Galen (131-201 CE) Roman Physician
- St. Jerome (late 4th Century CE)
- Practical Ethics of the Physician (8th Century CE) Arabic & Islamic Ethics

Belmont Report & 45 CFR 46.111 & 21 CFR 56.111

Whether expedited or full committee review

1)	Risks minimized	Belmont: Respect for Persons & Beneficence
2)	Favorable risk : benefit ratio	Belmont: Respect for Persons & Beneficence
3)	Equitable selection of subjects	Belmont: Justice
4)	Informed consent sought	Belmont: Respect for Persons
5)	Informed consent documented	Belmont: Respect for Persons
6)	Monitoring plan for safety	Belmont: Beneficence
7)	Privacy & confidentiality protected	Belmont: Respect for Persons
8)	Add'l safeguards for vulnerable populations	Belmont: Respect for Persons, Beneficence & Justice

IRB Regulations

RISK

Benefit

Risk:Benefit

Risk (not just physical risks)

- **criminal** or
- **civil liability** or
- **financial standing**,
- **employability**, or
- **reputation**

Benefit

- **NOT any reimbursement or renumeration**
- **Direct Benefit**
- **Benefit to advancement of science**

What is Risk?

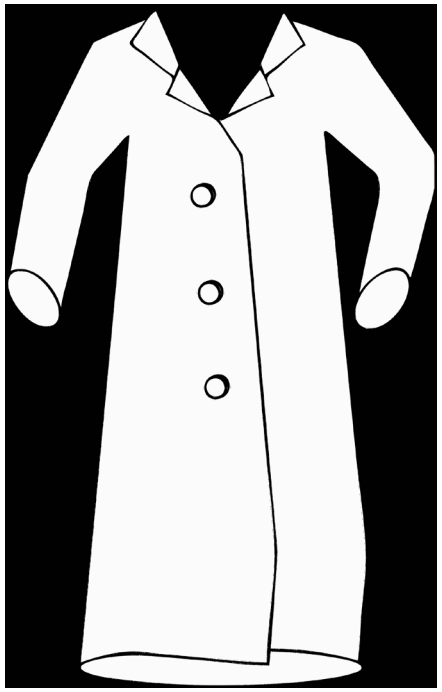
Risk is not harm:

it is the *possibility of harm*, and an analysis of the risks must take into account including both the *magnitude* of the possible harm and the *probability* that the harm may occur.

(The National Commission 1979 and Common Rule)

What Color is Your Lab Coat?

- Physician white?



Researcher Carolina Blue?

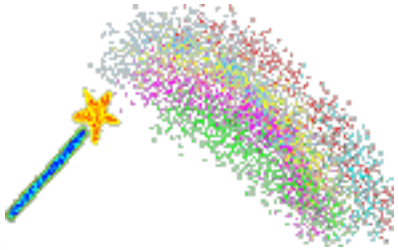
It Depends……

What Color is Your Lab Coat & Which Parallel Universe are you now in?

- Physician researchers work in the parallel universes of clinical care & clinical research.
- Each universe has separate and distinct ethical & regulatory standards.
- In a typical day as a physician researcher you zig-zag multiple times between these separate universes as you meet with patients & research subjects.

Don’t Forget …..

- Is the person you are meeting with a patient or a research subject,
- What color should your lab coat be in this moment & does it match the universe you are now in.
- Think of having magic dust that would switch the color of your lab coat from white to blue to match your current role.



Bad Behaviors lead to Regulations

Regulations created after a problem exists

Rare that laws, regulations, etc. created proactively

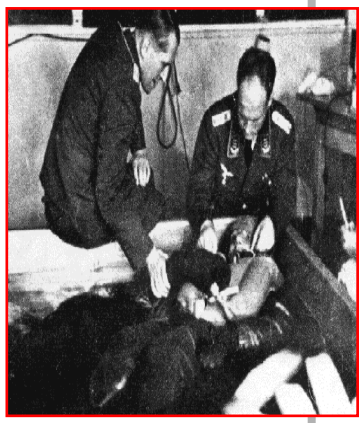
Result:

This is why you see the IRB as a Pain

Critical Events in Research Ethics

***Prison Research 1940s-1970s**

Nuremberg Code 1947



Nazi Medical Experiments WWII

U.S. Scandals 1960s

Willowbrook State School Hepatitis Studies, 1960's

Early NIH Policy 1966

Tuskegee revealed 1972

Nat'l Research Act 1974

Belmont Report 1979

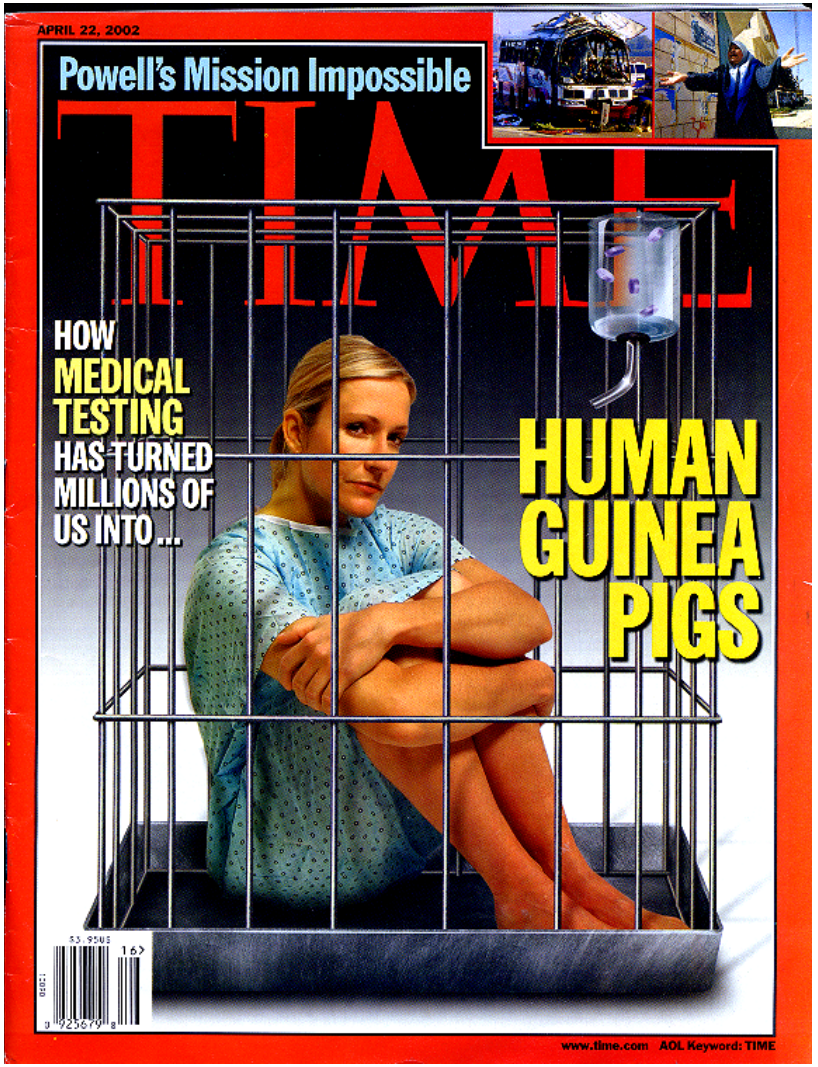
Common Rule

Tuskegee Syphilis Study 1932-1972

1940 1950 1960 1970 1980 1990 2000

Slide Courtesy of Jeremy Sugarman & Dan Nelson

Public View of Research following events at the end of the 20th Century



First Gene Therapy Death & birth of COI

Jesse Gelsinger (1999)

18-year-old with mild OTC deficiency

Conflicts of Interest

- Genovo owned patent on the adenovirus vector
- Genovo provided 20% of the annual research budget for Institute for Human Gene Therapy (IHGT) of University of Pennsylvania
- James Wilson (the PI on the OTC trial) was founder and 30% shareholder in Genovo
- Genovo had exclusive rights to develop Wilson's research into commercial products
- University of Pennsylvania held 5% equity in Genovo

James Wilson's Lessons
(PI on the Jesse Glesinger study)

***"Lessons learned from the gene therapy trial for ornithine transcarbamylase deficiency" Journal* of Molecular Genetics & Metabolism 96 (2008) 151-157**

#1: The clinical protocol is a contract with the research subjects & regulatory agencies that *must* be strictly & literally adhered to.

#2: If you think about reporting—then do so!

#3: It is very difficult to manage real or perceived financial conflicts of interest in clinical trials.

#4: Informed consent may require objective third-party participation.

Healthy Subject Dies, FDA not consulted or IND obtained

Ellen Roche (2001)

Healthy Subject on an Asthma Study

The Headline of IRB Staff Nightmares!

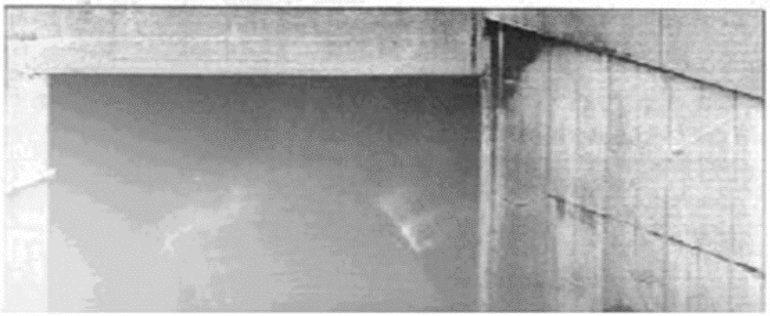
THE SUN

Friday, July 20, 2001 HOWARD COUNTY Baltimore, Maryland : 50 cents

U.S. halts Hopkins research

CHEMICAL TRAIN FIRE

Burning cars in rail tunnel resist control



Most experiments on human subjects ordered suspended

Federal funding withheld

Oversight agency decries safety lapses in volunteer's death

By Jonathan Bor and Tom Pelton

The response

Excerpts from the Johns Hopkins University's response to the federal Office of Human Research Protection

"This action was taken in utter disregard of patients' health and potentially of life. ... The suspension seems to us to be an extreme example of regulatory excess."

Full text [Page 16a]

More inside

Legal: When regulators shut down research on human subjects, "it's devastating," one university official

FDA Audit Findings @ Hopkins

"… an investigation into the death of a healthy volunteer…"

- "You failed to submit an IND…"
- "You did not supply adequate animal toxicity data"
- "You failed to submit a summary of previous human studies"
- "…you failed to promptly report unanticipated problems…“
- ***These comments prompted ALL IRBs to ask more questions & require more documentation from researchers.***

Bad Behaviors lead to Regulations

Regulations often created ***after*** a problem exists

Rare that laws, regulations, etc. are created proactively

Result:

This is why you see the IRB as a challenge & we do too.

Welcome to observe a meeting

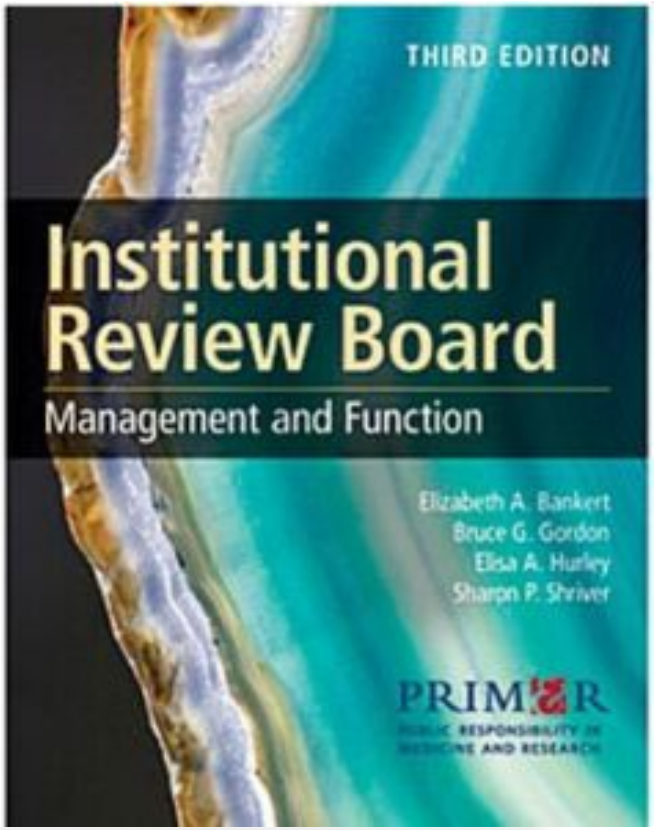
- IRBs A,B,C &D meet on Mondays @ 1pm
- IRB E meets on the 2nd Tuesday @ 1pm
- IRB F meets on the 4th Thursday @ 1 pm
- IRB meetings are via zoom
- If research is your career path, then join an IRB .

IRB Resources

- IRB Staff (see website for listing: http://research.unc.edu/offices/human-research-ethics/)
- Website: *IRB and Office of Human Research Ethics - UNC Research*
- **Telephone: 919-966-3113**
- Education Programs
  - ***http://www.hhs.gov/ohrp/***
  - ***https://www.youtube.com/watch?v=hsUS0k3Ie_g&list=SP5965CB14C2506914&index=8***

This books are available online from the UNC Library.
You will need to *log in with your ONYEN and password*.

Click on the book image to go directly to the library.



OHRE/IRB Contact Information

- **Office of Human Research Ethics Website(OHRE):**

http://research.unc.edu/offices/human-research-ethics/

- **E-mail:irb_questions@unc.edu**

- **Phone:** 919-966-3113

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