Why IRB Compliance Is Required for Grant Submissions
Topics to Cover Today

• What is an IRB?

• Why IRB review is required?

• Regulatory Requirements for IRB Review

• What are the red flags to look out for when reviewing grants?
Functions of the IRB

• Ensure that research participants are treated ethically at all times (principles of the Belmont report)

• Ensure that researchers are adequately gaining informed consent from every research participant

• Monitor projects to ensure adherence to protocol

• Provide a contact point for participants if they are concerned about their rights

• Handle reports of violations of participants’ rights or adverse outcomes of the research
RULES—Must Haves!

• Informed consent

• Training to protect participants (what you are doing now)

• Training to protect privacy

• All research on people must have IRB approval!
Regulatory Requirements
Research Equation

Funding + IRB Approval = Study

\[ \downarrow \quad \downarrow \]

Grant \quad Submission
WHAT IS A RESEARCH PARTICIPANT?

- Anybody we gather information about

- Information comes from
  - experiment
  - observation
  - medical records review
HISTORY (not to be repeated)

• What has happened in the past?
  – History --> guidelines --> rules

• Helps us understand the guidelines

• We don’t want to make the same mistakes again!
Historical Events

1900: Walter Reed’s use of consent form in Yellow Fever Study

1947: Nuremberg Code established in response to Nazi atrocities

1955: First Review Board established at NIH

1973: Tuskeegee study exposed and halted


1979: Belmont Report issued
Ice Bath Experiments at Dachau
“Bad Blood”
NUREMBERG CODE
“RULES FOR TREATING PARTICIPANTS”

• Voluntary agreement of the participant is required
• Research must help society
• Research should be based on previous knowledge
• Should not cause mental and physical suffering, and avoid risk of injury and death
NUREMBERG CODE (continued)

- Amount of risk must not be more than the importance of the problem
- Qualified researchers
- Participant must be free to stop at any time
- Researcher must be prepared to stop if there is risk of injury, disability or death
NUREMBERG IMPACT

- American researchers thought something like that could never happen here
- There was no rule that one had to follow the code
- People got more serious when things went wrong in America
DECLARATION of HELSINKI “MORE SPECIFIC RESEARCH RULES”

• Consent should be in **writing**
• Research should build on previous work
• Research must follow written plan
• Review by an independent committee
• Caution if participant is in dependent relationship with researcher
• Participants must receive best **proven** care
Willowbrook State School
Staten Island, 1956-1963

- Institutionalized children
- Infected with hepatitis A on purpose

- Only allowed in the school if they participated in the study
“Ethical lapses are almost never cases of bad people, doing bad things, for no good reason. Rather, they are good people, doing bad things, for good reasons.”

Loosely quoting Marcia Angell, MD
former Editor-in-Chief, NEJM
So, How Does an Idea Become a Medical Advancement?

That becomes an experiment in the lab
How Does an Idea become a New Drug or Device?

- Begins with a scientist who has an idea,
So, How Does an Idea Become a Medical Advancement?

That then is tested on small animals, Then tested on larger animals
Request IND/IDE from FDA

- **Investigational New Drug (IND)**
  - Brand new drug or
  - Off label use of an old drug or
  - Change in dosing and manner of dosing

- **Investigational Device Exemption (IDE)**
  - New device or
  - New use of an existing device or
  - Modification of an existing device
Human Research Subjects

• When individuals agree to VOLUNTEER to be a human research subject in a clinical trial.
Then Humans in ....

- **Phase I** (or 1st. In Humans) Trials with very few subjects

- **Phase II** Trials with a few more subjects
Then Humans in ....

Phase III Trial with a lot of subjects
Phase IV Trials

- Quality of Life Studies (QoL)
- Post Marketing Studies
The FDAs Role

The results of all these studies are compiled and submitted to the Food & Drug Administration (FDA) in an application for the approval of a new drug or device and permission to sell it. But only for what and how you requested in your submission.

If you want to change how it is administered, dosing, format and what it is used to treat, **must start over.**
# Federal Regulations

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**THE UNIVERSITY of NORTH CAROLINA at CHAPEL HILL**
Current Regulatory Structure Creates a “Patchwork Quilt” of Protections

- Not federally funded
- Not FDA regulated
- Not at institution that voluntarily applies 45 CFR 46 to all research via FWA

**Diagram:**
- FDA
- DHHS
  - Subpart A ➔ Common Rule
  - Subpart B
  - Subpart C
  - Subpart D

17 Departments & Agencies

45 CFR 46
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**

* HIPAA (Health Insurance Portability & Accountability Act of 1996) Change
IRB Approved Protocol
Good for 1 year max!

Amendments (ANY change to IRB Approved Protocol)

Final Report Means Final—The IRB Box is Closed
Confidential vs. Anonymous

- **Anonymous** means the research participant’s identity is not known, even to the interviewer.

- **Confidential** means we have identifying information about the research participant (in some cases, only a phone number and/or first name) but we will not reveal that information to anyone.
FDA (Food and Drug Administration) Regulations Related to Human Research

Some studies are also covered by FDA regulations

- Drugs (including nutritional supplements)
- Devices (including mobile apps, software, etc)
- Biologics
- FDA regulations differ from 45 CFR 46 in areas of reporting of adverse events, informed consent waivers, and confidentiality.
Federalwide Assurance (FWA)

An FWA allows the institution’s IRB to approve each project

– UNC’s FWA covers all federally-funded human subjects research

– The FWA must be renewed every three years
Requirements in UNC’s FWA (#4801)

- **The institution** bears full responsibility for ensuring that all human subject research is conducted in accordance with Federal regulations.

- **The IRB** must review and approve or disapprove research involving human subjects according to guidelines set forth in 45 CFR 46.

- **The investigators** acknowledge and accept their responsibility for protecting the rights and welfare of human subjects and for complying with the FWA.
Levels of IRB Review

- **EXEMPT** – Applies to specific categories of research, most often with extremely low risk or anonymous data.

- **EXPEDITED REVIEW** – Applies to specific categories of research with no more than minimal risk.

- **FULL COMMITTEE REVIEW** – All studies which do not qualify as exempt or expedited must be reviewed by a full IRB.

**Note:** The level of review is determined by IRB, not by the investigator or by the client. The requirements for each level are given in the regulations.
Suspension of Research by the IRB

An IRB has the authority to **suspend** or **terminate** approval of research that is not being conducted in accordance with the IRB’s requirements or that has been associated with unexpected or serious harm to subjects.
The Belmont Report

• **Respect for persons:** Informed consent
  – Individual autonomy
  – Protection of individuals with reduced autonomy

• **Beneficence:** Assessment of risks & benefits
  – Maximize benefits & minimize harms

• **Justice:** Selection of subjects
  – Equitable distribution of research costs & benefits
Risk Benefit Ratio
SUMMARY

• Research involving people
  – Helps make better programs or treatments
  – Only done with permission of participants
  – Rules to make it as safe as possible
  – Must be approved by an IRB
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  – Only done with permission of participants
  
  – Rules to make it as safe as possible

  – Must be approved by an IRB
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