THE UNIVERSITY OF ALABAMA AT BIRMINGHAM

OB CWRH

IRB Guidance & Common Mistakes

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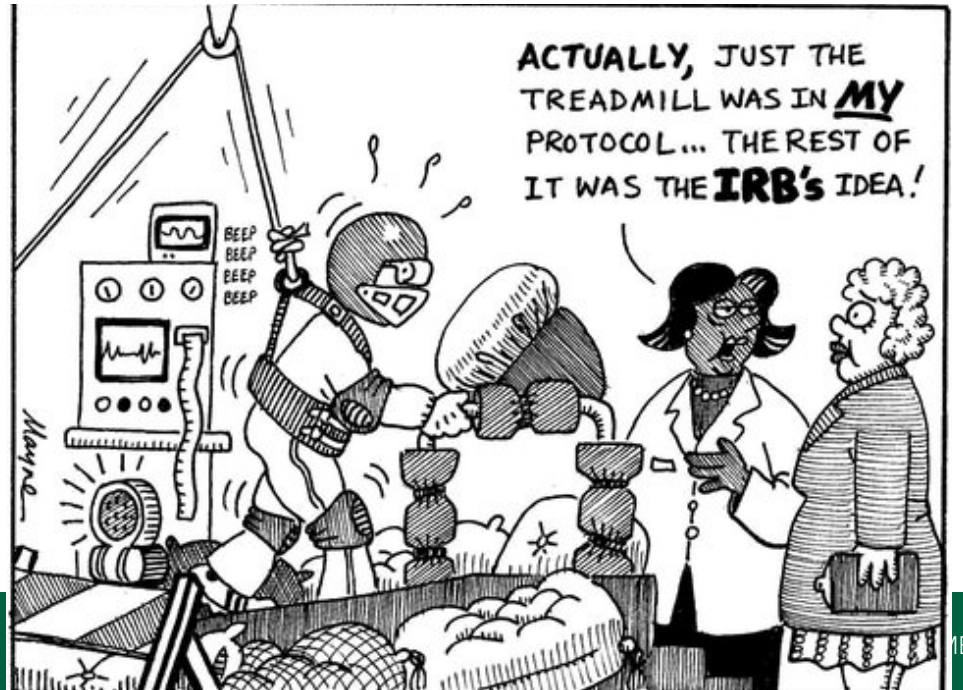
What is the IRB and why does it exist?



What is the IRB and why does it exist?

- U.S. Public Health Service Syphilis Study at Tuskegee (1932-1972)
  - Originally “Tuskegee Study of Untreated Syphilis in the Negro Male”
- N=600 Black men (399 with syphilis and 201 without syphilis)
- Informed consent was not collected. Men were told they were being treated for “bad blood,” a local term used to describe several ailments (syphilis, anemia, fatigue).
- In exchange for taking part in the study, the men received free medical exams, free meals, and burial insurance.

What is the IRB and why does it exist?

- By 1943, penicillin was treatment of choice but not offered to participants.
- In 1972, an AP story about the study led to an Ad Hoc Advisory Panel, which concluded it was “ethically unjustified” and “results were disproportionately meager compared with known risks”.
- The study was stopped, and in 1974 the National Research Act was signed into law.
- The Belmont Report (1979) summarized 3 ethical principles that should guide human research: *respect for persons, beneficence, and justice.*

UAB IRB

- UAB has two IRBs. Together, they review all research conducted at UAB or by UAB faculty, staff and students that involves human subjects.
- The IRB also has jurisdiction over research involving UAB data on human subjects. The IRB can approve, require modifications in, or disapprove all research activities that fall within its jurisdiction.
- The aim of the IRB review is to ensure that research involving human participants is *conducted in an ethical manner*. This includes ensuring that
  - risks are minimized
  - participant selection is equitable, and
  - participants are fully informed of what their participation will entail including potential risks and benefits.

Criteria for IRB Approval (Code of Federal Regulations)

1. Informed consent is appropriately sought
2. Requirements for informed consent is waived only when specific criteria are met.
3. Additional protections for subjects likely to be vulnerable to coercion.
4. Risks to subjects are minimized and reasonable in relation to benefits.
5. Provisions for data and safety monitoring.
6. Provisions for privacy and confidentiality.
7. Selection of subjects is equitable.

Levels of IRB Review

IRB approval or a determination of NHSR or exemption MUST be obtained prior to initiating research

Not Human Subjects Research

- Not research and/or
- No human subjects

Expedited IRB Review

- Minimal risk
- Fits expedited category

Exempt from IRB Review

- Minimal risk
- Fits exempt category

Full IRB Board Review

- More than minimal/undetermined risk
- No applicable expedited category

Definitions

Research = **Systematic** investigation designed to contribute to **generalizable** knowledge

Human subject = living individual about whom an investigator obtains information or biospecimens through **interaction** with the individual OR obtains **identifiable** private information or identifiable biospecimens

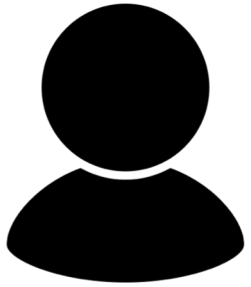
Minimal risk = the probability and magnitude of harm or discomfort anticipated in the research are **not greater** than those ordinarily encountered in **daily life** or during the performance **of routine physical or psychological examinations or tests**

More Definitions: Identifiability

Identifiable

Identity of subject available

Jane Doe

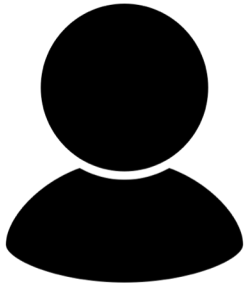


UAB VTE database *during* data collection

Coded

PHI replaced by code (key stored separately)

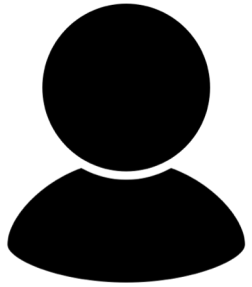
#35



UAB VTE database *after* data collection

Deidentified

Code removed or key file deleted

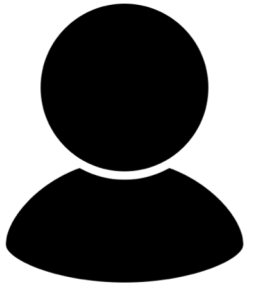


MFMU released database

Anonymized

PHI never linked to data

?



Anonymous survey

Levels of IRB Review

IRB approval or a determination of NHSR or exemption **MUST** be obtained prior to initiating research

Not Human Subjects Research

Secondary analysis of MFMU database (*deidentified*)

Expedited IRB Review

- Minimal risk
- Fits expedited category

Exempt from IRB Review

- Minimal risk
- Fits exempt category

Full IRB Board Review

- More than minimal/undetermined risk
- No applicable expedited category

Why is MFMU database “not human subject research”?

- Research = **Systematic** investigation designed to contribute to **generalizable** knowledge

- Human subject = living individual about whom an investigator obtains information or biospecimens through interaction with the individual OR obtains **identifiable** private information or identifiable biospecimens

*Remember IRB approval **or a determination of NHSR** or exemption must be obtained prior to initiating research

Levels of IRB Review

IRB approval or a determination of NHSR or exemption MUST be obtained prior to initiating research

Not Human Subjects Research

- Not research and/or
- No human subjects

Secondary analysis of MFMU database

Expedited IRB Review

- Minimal risk
- Fits expedited category

Exempt from IRB Review

- Minimal risk
- Fits exempt category

Full IRB Board Review

- More than minimal/undetermined risk
- No applicable expedited category

Exemption Categories

1. Educational Practices
2. Educational Tests, Surveys, Interviews, or Observations of Public Behavior
3. Benign Behavioral Interventions
4. Secondary Use of Data
5. Public Benefit/Service Program Research
6. Taste and Food Quality

Exemption Category 4 – Secondary Use of Data

Secondary research uses of identifiable information or specimens if:

1. The identifiable private information or identifiable biospecimens are publicly available.
2. Use of Information, which may include identifiers, but not readily identifiable.
   - May contain dates (date of birth, date of graduation, date of event, etc.)
   - May **NOT** contain names, medical record number, phone number, address, etc.
3. Use of information/specimens regulated by HIPAA
4. Research conducted by or on behalf of the federal government using information generated or collected by the government for non-research purposes.

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Levels of IRB Review

IRB approval or a determination of NHSR or exemption **MUST** be obtained prior to initiating research

Not Human Subjects Research

- Not research and/or
- No human subjects

Secondary analysis of MFMU database

Expedited IRB Review

- Minimal risk
- Fits expedited category

Exempt from IRB Review

VTE study
Secondary analysis of VTE

Full IRB Board Review

- More than minimal/undetermined risk
- No applicable expedited category

Convened (Full) Review

- All research involving human subjects that does not qualify for Exempt or Expedited review
- All research that involves:
  - Greater than minimal risk
  - Investigational drugs
  - Investigational devices
  - Prisoners

Levels of IRB Review

IRB approval or a determination of NHSR or exemption **MUST** be obtained prior to initiating research

Not Human Subjects Research

- Not research and/or
- No human subjects

Secondary analysis of MFMU database

Expedited IRB Review

- Minimal risk
- Fits expedited category

Exempt from IRB Review

- Minimal risk
- Fits exempt category

VTE / Secondary analysis of VTE

Convened (Full) IRB Review

RCT of new Hep C drug in pregnancy

Expedited Review (7 Categories)

1. Clinical studies of drugs/devices (not new/investigational)
2. Collection of blood samples (within max limits)
3. Prospective collection of biological specimens by noninvasive means
4. Collection of data through noninvasive procedures routinely employed in clinical practice
5. Research involving materials that have been or will be collected solely for non-research purposes (diagnosis, treatment)
6. Collection of data from voice, video, digital or image recordings for research
7. Research on individual or group characteristics or behavior

Exempt Category 4 vs Expedited Category 5

1. How do I know if my chart review can be classified as exempt or expedited?
   - Most research involving a research question to be addressed via chart review is likely reviewable under Exempt Category 4 and should be submitted using the IRB Exemption Review Application, not the Human Subjects Protocol (HSP). These projects were previously submitted as Expedited Category 5; however, with the Revised Common Rule (2018), this type of research is generally covered under this expanded exemption definition.
2. Can research utilizing biospecimens be conducted under Exempt Category 4?
   - The use of biospecimens in Exempt 4 is limited to identifiable specimens that are publicly available. Otherwise the use of biospecimens would either fall under Not Human Subjects Research (e.g., completely stripped of all identifiers prior to receipt) or Expedited 5.
3. Can data registries or biorepositories be established under Exempt Category 4?
   - Data Registries and Specimen Repositories (those that are created to do multiple future research projects) should be submitted for Expedited review using the HSP.

Levels of IRB Review

IRB approval or a determination of NHSR or exemption **MUST** be obtained prior to initiating research

Not Human Subjects Research

- Not research and/or
- No human subjects

Secondary analysis of MFMU database

Expedited IRB Review

RCT of oxytocin vs miso IOL
Prospective diabetes database

Exempt from IRB Review

- Minimal risk
- Fits exempt category

VTE / Secondary analysis of VTE

Convened (Full) IRB Review

- More than minimal/undetermined risk
- No applicable expedited category

RCT of new Hep C drug in pregnancy

UAB IRAP Submission (General Questions)

- Name/Title/Purpose/Background/Methods
- Retrospective?
  - Will the study involve the collection or analysis of existing data/records?
  - Will the study involve the collection or analysis of existing biospecimens?
- Prospective?
  - Will the study involve prospective collection or analysis of new data/records?
  - Will the study involve prospective collection or analysis of new biospecimens?
- What is the expected end date (including data analysis)?
- Total number of subjects to be included
- **Methodology:** procedure(s) & indication of whether protocol driven or routine

UAB IRAP Submission (Research Determination)

- Is the activity a systematic investigation?
- Is the activity designed to develop/contribute to generalizable knowledge?
- Does the project involve obtaining information about living individuals?
- Does the project involve an intervention or an interaction with participants?
- Is the information individually identifiable? NOTE: If at any time you will have access to any identifiable data, select yes. Select yes for chart reviews.
- Is the information private?
- Does the project involve an FDA regulated test article?
    - Is the project defined as a clinical investigation?

UAB IRAP Submission (continued)

- Select Risk Level
- Select Exempt Category (if applicable)
- Select Expedited Category (if applicable)
- Sources of Private Information (select all that apply)
- Non-UAB Personnel/Sponsors/Locations/Pediatric/Patients
- Risks (don't forget about *risk of breach of confidentiality* if using PHI at any time)
- Benefits
- Privacy and Confidentiality (data storage, HIPAA)
- Consent

IRB Approved, Now What? Amendments

- Personnel Amendment
- Study Revision/Amendment
  - Change study protocol
  - Update consent form (tracked changes & clean copies)
  - Add patient flyer/recruitment material
- **Continuing Review** (for Convened/Full IRBs) - every 1 year
  - Enrolling
  - Follow-up
  - Data analysis
  - Final report
- **Expedited Status Update** (for Expedited IRBs) – every 3 years

Closing Out an IRB

1. Is enrollment complete?
2. Is follow-up complete?
3. Is data analysis complete?
4. Have all proposed aims/objectives been answered?
5. Have all manuscripts of proposed objectives been published?

Is there a possibility that someone in the future might want to use the data collected in this study to answer a different research question?

Example: VTE Database

- Dr. Lu and colleagues want to study complications related to pharmacologic prophylaxis in pregnancy and postpartum
  - Is the study “research”?
  - Does the study involve ”human subjects”?
- Investigators plan to review electronic medical records in order to abstract data necessary for the research study. They will use the patient’s name and medical record to look up the needed information and store everything in REDCap.
  - Is this data identifiable?
  - The IRB asks what length of time the identifiers will be stored?
- Is this project eligible for an Exempt review? Expedited review?
  - Submitted for Expedited review under category 5 (research involving materials collected for non-research purposes)
  - With revised Common Rule (2018) could be submitted as Exempt category 4

Example: VTE Database (continued)

- Dr. Lu receives IRB approval and starts data collection. She quickly realizes she needs more help collecting the data. What does she need to do?
  - Personnel amendment
- Even with additional help, the research team is still collecting data the next year. They decide that they want to extract ultrasound data from AS instead of collecting by hand. What do they need to do?
  - Revision/Amendment – change in protocol (add AS as a new source of data)
- Data collection is complete. Should she close the IRB?
  - No. Still need to keep IRB open during data analysis as IRB is still in place to protect risk of breach of confidentiality. A reviewer could also ask that she abstract more details about a maternal death, and she would need IRB approval to review the electronic medical record.

Example: VTE Database (continued)

- Dr. Lu submits her manuscript, and while it is under review Dr. Cozzi decides she wants to look at anemia and pregnancy outcomes using the VTE database. What does she need to do?
  - Was her research question included in the original study?
  - *Never wrong (maybe even better) to submit a separate, new IRB proposal*
- Dr. Cozzi doesn't need to review any charts or add any new data to the existing VTE database. What type of IRB proposal should she submit?
  - **Exempt (Category 4)** – Analyst could even use data from initial VTE database without any identifiers/code
- Dr. Battarbee wants to create a "living" database/registry to do multiple future projects evaluating anticoagulation in pregnancy. What does she need to do?
  - Submit new IRB for **Expedited review (Category 5)** - research involving materials collected for non-research purposes

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Questions?