

What You Should Know About IRB Review of Research

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Why IRB Review?

- Public scandals related to the use of humans in research in the 50's and 60's
 - Scientists overlooked harms and overestimated benefits
 - Scientific self regulation was not enough
- Most of this research was sponsored by the US government
 - Constitutional green light to regulate human subject research
- Congressional action
 - National Research Act (1974)
 - The National Commission published the Belmont Report (1979)
 - 45 C.F.R. 46, Protection of Human Subjects (1981)

From Bioethical Principles to Law

The Belmont Report

- Respect for person
- Beneficence
- Justice



45 C.F.R. 46 (“The Regs”)

- Informed consent; protecting autonomy, voluntary participation
- Minimize potential risks; favorable risk-benefit analysis
- Equitable subject selection; equitable distribution of burdens & benefits

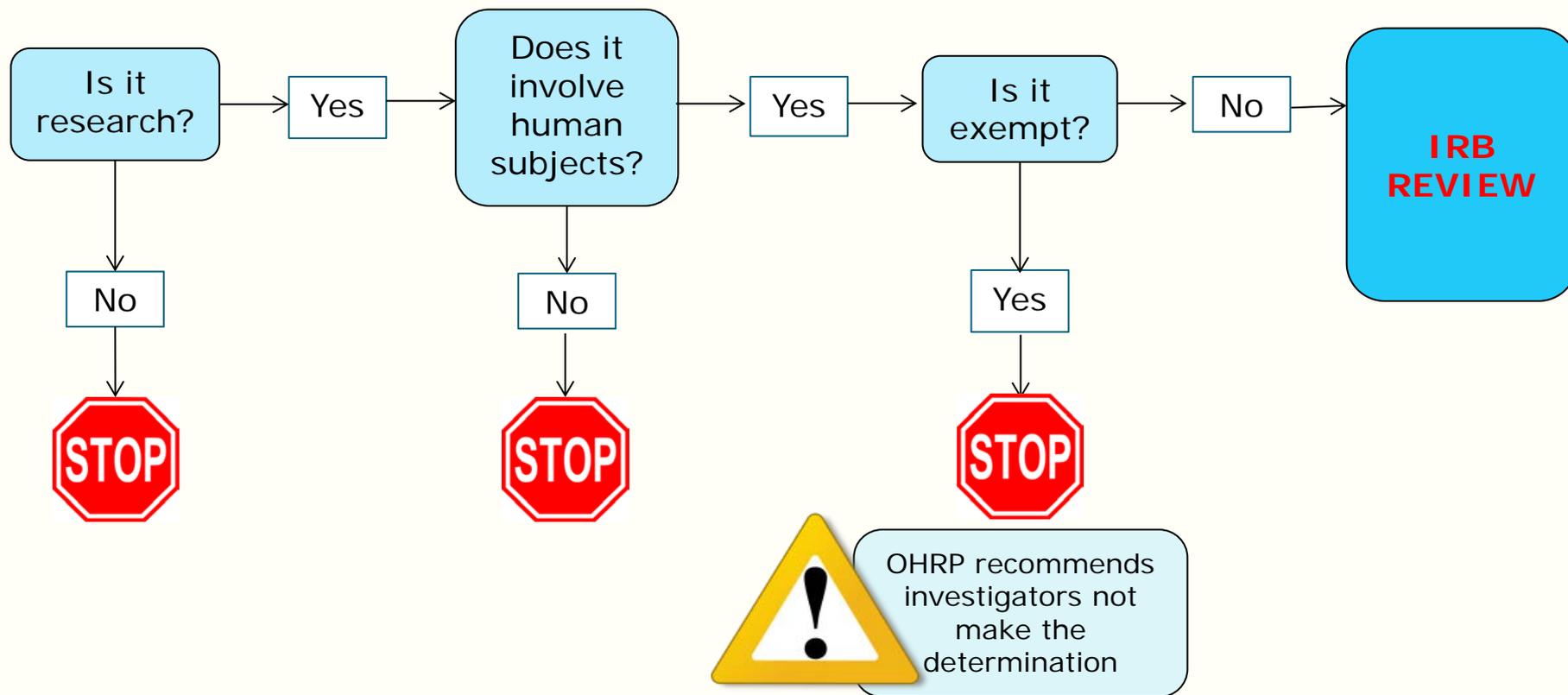
Composition of the IRB

- At least five members
 - Various backgrounds
 - Consideration of race, gender, and cultural backgrounds
 - Sensitivity to such issues as community attitudes
- At least one scientist and at least one nonscientist
- At least one member who is not otherwise not affiliated with the institution
 - Could be a scientist or a non-scientist
- Members with conflicts of interest may not participate
- Non-voting consultant o.k.

Responsibilities of the IRB

- Conducts initial review of research involving human subjects:
 - Expedited or Full-board review
- Oversees the ongoing conduct of research through:
 - Continuing review,
 - Review of protocol modifications (amendments)
 - Adverse events tracking and reporting

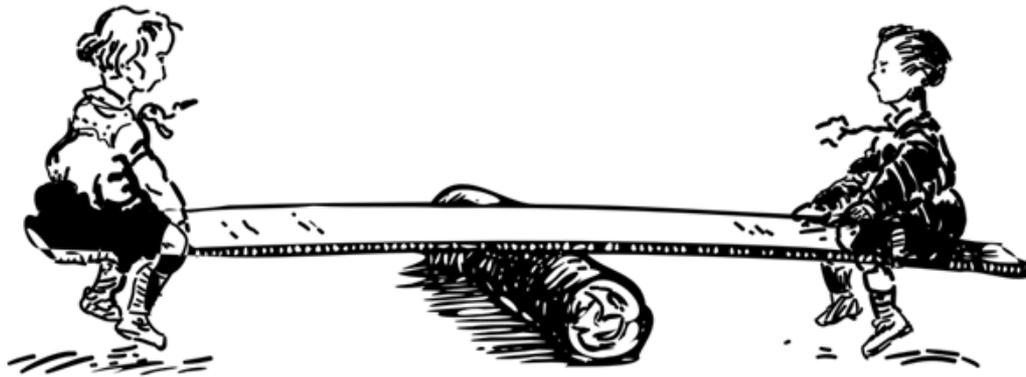
What Requires IRB Review?



Initial Review of Research: Expedited or Full Board?

- Qualifying for expedited review
 1. Procedures must fit into one of the expedited categories (<http://www.hhs.gov/ohrp/policy/expedited98.html>)
- **AND**
 2. Study must be minimal risk
- Full-board Review: everything else
- **NOTE: IRB requirements for approval are the same whether expedited or full board:**
 - Criteria for approval
 - Informed consent requirements

How to Write an Effective IRB Submission?



Societal benefit of science through human subjects research

Respecting research subjects as individuals, not as a means to an end

The Answer is in the Regulations: Section 46.111

- **Criteria for Initial IRB Approval of Expedited and Full-Board Studies**
 - Risks to participants are minimized
 - Risks are reasonable in relation to anticipated benefits
 - Equitable selection of subjects
 - Data monitoring when appropriate
 - Privacy and confidentiality protections when appropriate
 - Additional safeguards for participants likely to be vulnerable to coercion or undue influence
 - Informed consent from each prospective participant
Documentation of informed consent

Translating this into IRB Approval: An Exercise in Good Writing

- Write for a reviewer with different expertise (or a non scientist)
 - Reviewer is likely from a different discipline or specialty
- Organize your writing
 - Use headings and subheadings
- Leave no loose ends
 - Anticipate questions and answer them
- Submit a complete protocol
 - Include ALL instruments, surveys, measurements
- Don't just copy and paste
 - Think through the implementation of your project at every point

Example 1: Writing about the Equitable Selection of Subjects

- Explain why this is a (scientifically) appropriate population for the study
 - Accessibility to investigator does not make the population the most scientifically sound population
- Outline and explain inclusion and exclusion criteria (use separate subheadings for each)
- Address likelihood of coercion or undue influence
 - Additional requirements for pregnant women, fetuses, neonates (Sub Part B), prisoners (Sub Part C), and children (Sub Part D)
 - Many populations can be at risk of coercion
- Explain measures you will implement to minimize the possibility of coercion or undue influence

Example 1: Writing about the Equitable Selection of Subjects *(Cont.)*

Assessing the use of MDMA (ecstasy) in addition to cognitive behavioral therapy (CBT) to treat resilient depression. Patients with depression that has failed to respond to conventional treatments, and who receive CBT only for symptom management, will be randomized to CBT only or MDMA plus CBT. Women and patients taking SSRIs will be excluded from the study.

- Explain why this is the most appropriate population
 - Subjects have not responded to conventional therapies
- Outline and explain inclusion and exclusion criteria
 - Why excluding SSRIs? Explain any clinical need for this and cite to prior research
 - Why excluding women?
 - Is this an adults only study? Will you exclude subjects under 18?

Example 1: Writing about the Equitable Selection of Subjects *(Cont.)*

- Address likelihood of coercion or undue influence
 - Failure to respond to conventional treatment can unduly influence subjects desperate for an effective treatment
- Minimizing coercion or undue influence
 - E.g., work with treating physicians to ensure potential participants are able to consent and understand that this is only an experimental treatment
- Anticipate and address reasonable questions from the reviewer:
 - Will you exclude subjects with a history of substance abuse?
 - Can severely depressed people consent to research or do we need guardians? (Cite to literature on depression and consent)

Example 2: Writing about Minimizing Risks to Subjects

- Identify the study intervention(s)
 - Use a heading for each study intervention
- Identify reasonably potential risks resulting from each study intervention
 - Use subheading for each reasonably anticipated risk
 - Address how you are minimizing the risk
- Anticipate and address other reasonable risk-related concerns even if unlikely to occur
 - Explain, for example, that the concern is not a reasonably anticipated risk, but don't ignore it
 - Cite prior research in support of your explanations

Example 2: Writing about Minimizing Risks to Subjects *(cont.)*

Assessing the use of MDMA (ecstasy) in addition to cognitive behavioral therapy (CBT) to treat resilient depression. Patients with depression that has failed to respond to conventional treatments, and who receive CBT only for symptom management, will be randomized to CBT only or MDMA plus CBT.

- Clearly identify the study intervention
 - MDMA therapy; not CBT
- Identify reasonable potential risks resulting from the study intervention; i.e., reasonable risks of therapeutic MDMA use
 - Difficulty sleeping
 - Explain how you are minimizing this risk (e.g., providing sleeping pills)
 - Hyperactivity
 - Explain how you are minimizing this risk (e.g., intervention conducted in control, clinical setting; subjects to stay until determined safe to leave)

Example 2: Writing about Minimizing Risks to Subjects *(cont.)*

- Anticipate and address other reasonable risk-related concerns even if unlikely to occur
 - Overdose and dehydration
 - Explain dosage, cite prior safety studies
 - Explain that subjects will be kept hydrated, and how
 - Patients may become addicted to MDMA
 - Discuss whether MDMA is addictive
 - If you think this is not a risk, address it nonetheless (it is a reasonable question)

Informed Consent Process and Documentation of Consent

- **Informed consent as a process**
 - Describe the consent process in your proposal
- **Required elements of consent and waivers:**
 - Describe and thorny issue in the consent form
 - Provide a rationale for waiver of any requirement
 - E.g.: “Participants will be deceived into thinking they are taking MDMA. This is important because Participants will later be debriefed by P.I.”
- **Additional elements of consent (required where applicable)**
 - E.g.: Explain any circumstances for terminating the subject’s participation and risk management associated with early termination
- **Documentation of consent:** Use form approved by the IRB

Tips for a Better IRB Submission

- Write for a reviewer with different expertise (or a non scientist)
- Organize your writing
- Use 45 C.F.R. Sec. 46.111 as a roadmap
- Anticipate reasonable questions from the subject-protection perspective
- Cite references in support of your writing
- Submit a complete protocol
- Don't just copy and paste
- Communicate with your IRB
- Invite the IRB to your department for a training session
- Ask the IRB to let you sit in a meeting as an observer

1 TIP FOR A BETTER IRB SUBMISSION

Don't just write to PASS the IRB
instead

**WRITE A PROTOCOL THAT IS BOTH
SCIENTIFICALLY AND ETHICALLY SOUND**