What Investigators Should Know About IRB Review

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Objectives

• Understand what an IRB is, who is on it, and what it does
• Know the required criteria IRBs use to assess protocols
• Learn tips for submitting a successful protocol
When is IRB Review Required?

1. Is it research?  
   - No: STOP
   - Yes: Does it involve human subjects?
     - No: STOP
     - Yes: Is it exempt?  
       - No: STOP
       - Yes: IRB review

OHRP recommends investigators not make the determination.
What is an IRB?

A committee charged with reviewing research that involves human subjects in order to assure that their rights and welfare are adequately protected.

IRBs:
1) Review proposed research
2) Review ongoing research (at least once a year)
Who is on an IRB?

- Minimum of five members, including:
  - Scientist member
  - Nonscientist member
  - Nonaffiliated member
- Diversity
  - Race, gender, cultural background, experience
  - If prisoners involved, a prisoner representative is required
- Necessary expertise to review research
  - Scientific and technical expertise
  - Experience with communities involved in research
- Consultants may provide expertise but cannot vote
Different Mechanisms of IRB Review

An IRB can review protocols using:

- Full-board review
  - Review by a convened IRB
- Expedited review
  - Review by Chair or designated IRB member(s)
  - Only eligible research activities
# Expedited vs. Full-board Review

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<th>Expedited Review</th>
<th>Full-board Review</th>
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<td>• No more than minimal risk AND only procedures on expeditable list</td>
<td>• Activities that don’t qualify for expedited review</td>
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<td>• Review by IRB chair or designated experienced reviewer</td>
<td>• Majority of IRB members must be present</td>
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<td>• Approve or require modifications</td>
<td>• Nonscientist must be present</td>
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<td>• Approve, modifications, disapprove, or suspend</td>
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Requirements for IRB approval are **THE SAME**, regardless of whether review is full-board or expedited
Understanding the IRB’s Expectations

**The Belmont Report**
Published in 1979, established ethical principles that should undergird regulations

1) **Respect for persons**
2) **Beneficence**
3) **Justice**

**45 CFR 46 (“The Regs”)**
Published in 1981, set out the regulatory requirements for federally sponsored research

1) **Informed consent**
2) **Minimize potential risks; favorable risk-benefit analysis**
3) **Equitable subject selection**
To Approve a Protocol, the IRB Must Determine:

- Risks to subjects are minimized
- Risks are reasonable in relation to anticipated benefits
- Selection of subjects is equitable
- Informed consent is sought from each subject
- Informed consent is properly documented
- When appropriate:
  - Data collection is monitored to ensure subject safety
  - Subject privacy and data confidentiality protected
  - Additional safeguards for vulnerable populations

45 CFR 46.111
Initial IRB Review

- Initial review occurs prior to research commencing
- Requires sufficient information for the IRB to evaluate (such as):
  - Full protocol
  - Informed consent document(s)
  - Recruitment materials
  - Survey instruments
  - Additional info for multi-center trials
Continuing IRB Review

• Investigator submits for IRB review:
  • progress reports
  • any proposed modifications
  • any adverse events reported
  • other information required by institutional policies

• The IRB assesses whether the study continues to meet approval criteria

• Frequency determined by IRB, but at least annually
  • IRB re-approval is required before approval expiry date to continue research without interruption

“Investigators are responsible for fulfilling requirements associated with continuing review in time for the IRB to carry out continuing review prior to the expiration date of the current IRB approval.”

Proposing Changes to a Protocol

- Proposed changes (amendments) must be submitted to the IRB.
- Review and approval **must occur before** changes are implemented.
- Change(s) may not be initiated without IRB approval except to eliminate an apparent immediate hazard to subjects.
  - Follow-up reporting to IRB is required.
TIPS FOR WRITING A SUCCESSFUL PROPOSAL
Understanding the IRB’s Expectations

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1) Respect for persons

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1) Informed consent

2) Minimize potential risks; favorable risk-benefit analysis

3) Equitable subject selection
Example 1: Writing about the Equitable Selection of Subjects

- **Belmont Report:**
  - A moral requirement for fairness in the selection of subjects
  - Equal distribution of burdens and benefits of research
  - Justice and vulnerable populations in research
  - Cautions against inclusion of subjects solely for administrative convenience

- **Criteria for IRB Approval (§46.111(a)(3))**
  - Take into account the purpose and setting of the research
  - Particular attention to research involving vulnerable populations

- **Address in your protocol:**
  - Inclusion/exclusion criteria
  - Recruitment plan
  - Likelihood of coercion and how it will be minimized
**Purpose:** Assess the effectiveness of adding MDMA to cognitive behavioral therapy (CBT) to treat refractory depression

**Inclusion Criteria:** Male patients with refractory depression who are undergoing CBT, and who are not taking SSRIs

Which features likely require explanation regarding the equitable selection of subjects?

A. Exclusion of women
B. Inclusion of patients with refractory depression
C. Exclusion of patients taking SSRIs
D. A and C only
E. All of the above
Inclusion Criteria: Male and female patients with refractory depression who are undergoing CBT, and who are not taking SSRIs

Procedures: Patients will be randomized to CBT only or CBT plus MDMA

Which are reasonable questions that a reviewer may have regarding subject selection?
A. Will patients with a history of substance abuse be included?
B. Will children be included?
C. Both are reasonable questions
D. Neither seem reasonable, the answers are obvious
Recruitment: The PI provides CBT to patients with refractory depression. During regularly scheduled CBT sessions, the PI will ask her patients to participate in the study, at which point, she will explain the study and obtain their consent.

Is it likely that some patients may feel coerced to participate?

A. Yes, it seems likely
B. No, it doesn’t seem likely
C. It depends on the compensation offered
D. Undecided
Example 2: Writing about Minimizing Risks to Subjects

- **Belmont Report**
  - Concerned with the probability (how likely) and magnitude (how severe) of possible harm
  - Many kinds of possible harms, including psychological, physical, legal, social, and economic harms

- **Criteria for IRB Approval of Research at §46.111(a)(1)**
  - Risks to subjects resulting from the research are minimized

- **Address in your protocol:**
  - What is/are the study intervention(s) and/or procedure(s)?
  - What are the potential risks to subjects from each intervention or procedure?
  - How probable and severe are these risks?
  - How will you minimize the potential risks?
Anticipated Risks to Subjects: The only anticipated short-term risks of low-dose MDMA therapy are mydriasis, insomnia, and sweating. The first two will be minimized by conducting the study early in the morning in a controlled, laboratory setting. The last one, sweating, is only a mild discomfort.

Which are reasonable questions with respect to minimizing risks to subjects?

A. Is there risk of dehydration?
B. Can subjects drive after the session?
C. Can subjects develop an addiction to MDMA?
D. All seem reasonable
E. None seem reasonable, the answers are obvious
**Same Risks, Better Description**

**Anticipated Risks to Subjects:** At the proposed dose, there are no long-term risks anticipated. The only anticipated short-term risks are mydriasis (pupil dilation), insomnia, and dehydration from sweating.

A. **Mydriasis (Pupil Dilation)**
   a. Describe the likelihood, severity, duration, etc. of mydriasis
   b. Describe how the risk will be minimized

B. **Insomnia**
   a. Describe the likelihood, severity, duration, etc. of insomnia
   b. Describe how the risk will be minimized

C. **Sweating and potential for dehydration**
   a. Describe likelihood, severity, duration, etc. of sweating
   b. Describe how the risk will be minimized
Tips for a Successful IRB Review

- Demonstrate you know what the IRB needs
  - Know your institution’s policies and procedures
  - Work with IRB staff
  - Be aware of additional requirements for some populations
- Help reviewers understand how your protocol complies with the regulations
  - Write protocol for the IRB rather than copying/pasting from research protocol
  - Use the regulations and Belmont Report as a roadmap for writing
  - Demonstrate awareness of study risks
  - Anticipate reasonable questions and answer them
Tips (cont.)

• Submit a complete protocol
  • Include informed consent/assent documents, other relevant information such as recruitment materials and survey instruments

• Last but definitely not least:
  • Use simple, clear language
  • Use headings to organize text
  • Pay attention to the details
  • Proofread!
Work with the IRB, not just “to pass” the IRB

- Communicate with your IRB staff
- Invite the IRB or IRB staff to your department for a training session
- Ask to sit in on an IRB meeting as an observer
Thank you!
Any questions?

- Submit your questions to OHRP@hhs.gov
- Stayed connected! Join our listserv at: