Working with the IRB: A Primer

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Determining When the Common Rule Applies

- Is it research?
  - Yes → Does it involve human subjects?
    - Yes → Is it exempt?
      - Yes - Does it involve exemptions 2(iii), 3(i)(C), 7, or 8?
        - Yes → Proceed to IRB review
        - No → STOP
      - No → STOP
    - No → STOP
  - No or Activities deemed not to be research

Legend: New with the revised Common Rule
The IRB

- What does the IRB do?
  - Reviews research involving human subjects to assure that their rights and welfare are adequately protected
  - Conducts initial review of research
  - Oversees the ongoing conduct of research through:
    - Continuing review, protocol modifications (amendments), and adverse events reporting
Who is on the IRB?

- At least five members
  - Various backgrounds
  - Consideration of race, gender, and cultural backgrounds
  - Sensitivity to community attitudes
- At least one scientist
- At least one nonscientist
- At least one member who is otherwise not affiliated with the institution
- Members with conflicts of interest may not participate
- Consultants o.k., but they cannot vote

How does the IRB work?

Initial Review of Research
(non-exempt, human subject research)

Expeditied
- No more than minimal risk AND only procedures listed
- Reviewed by IRB chair or an experienced reviewer

Full Board
- Research that does not qualify for expedited review
- Reviewed at a convened meeting
- Majority of IRB members AND nonscientist must be present

IRB requirements for approval and informed consent are THE SAME, whether expedited or full board
What are the expectations of the IRB?

- Protocol complies with the Criteria for IRB Approval of Research at 45 C.F.R. 46.111
  - 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 (unless waived)
  - Documentation of informed consent (unless waived)

- Applicable to BOTH expedited and full-board studies

Understanding the expectations of the IRB: The Belmont Report

<table>
<thead>
<tr>
<th>The Belmont Report</th>
<th>45 C.F.R. 46 (“The Regs”)</th>
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<tbody>
<tr>
<td>Respect for persons</td>
<td>Informed consent</td>
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<tr>
<td>Beneficence</td>
<td>Minimize potential risks; favorable risk-benefit analysis</td>
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<tr>
<td>Justice</td>
<td>Equitable subject selection</td>
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PRACTICAL TIPS FOR WRITING A SUCCESSFUL IRB SUBMISSION

Practical Tips for Writing a Successful IRB Submission

- Organize your writing
  - Use headings and subheadings
Why headings and Subheadings?

Practical Tips for Writing a Successful IRB Submission

- Organize your writing
  - Use headings and subheadings
  - Use the regulations and the Belmont Report as a road map

- Submit a complete protocol
  - Include ALL instruments, surveys, measurements
  - Leave no loose ends
  - Don’t just copy and paste from similar submissions or grant applications

- Know your audience
  - Reviewer is likely from a different discipline or specialty
  - Show the reviewer how your protocol complies with the regulations

- Anticipate reasonable questions from IRB and answer them
Consider this Protocol:

• Purpose: To assess the effectiveness of MDMA in addition to cognitive behavioral therapy (CBT) to treat refractory depression

• Inclusion: Adult patients who have been diagnosed with refractory depression and are undergoing CBT

• Procedures: Participants will be randomized to CBT+MDMA therapy (experimental arm) and CBT only (control arm)

Example 1: Writing about Minimizing Risks to Subjects

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

• Belmont Report
  - Concerned with the probability (how likely) and magnitude (how severe) of possible harm
  - Many kinds of possible harms, such as psychological, physical, legal, social, and economic harm (non-inclusive list)

• What to address in your IRB submission
  - What is/are the study intervention(s) and/or procedure(s)?
  - What are the potential risks to subjects resulting from each intervention and/or procedure?
  - How probable and severe are these risks likely to be?
  - How are you going to minimize these potential risks?
**Inclusion:** Adults with refractory depression who are undergoing CBT

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

In an IRB submission, you must discuss the risks related to:

A. CBT
B. MDMA therapy
C. Both
D. Neither

**Anticipated Risks to Subjects:** The only anticipated short-term risks of low-dose MDMA therapy are pupil dilation (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.

If this is the entire description of risks included in an IRB submission, this description is:

A. Inadequate
B. Adequate
C. Adequate, but could be explained better
D. Undecided
Compare: Same Risks, Better Drafting

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

A. **Dosage** (dose selection and lack of long term effects, citations)
B. **Pupil Dilation (Mydriasis)**
   a. Describe mydriasis (likelihood, severity, duration, etc.)
   b. How will the risk of mydriasis be minimize
C. **Insomnia**
   a. Describe insomnia (likelihood, severity, duration, etc.)
   b. How will the risk of insomnia be minimize
D. **Sweating**
   a. Describe sweating (likelihood, severity, duration, etc.)
   b. How will the risk of sweating be minimize

**Potential Risks:** 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 that a reviewer may have regarding minimizing risks to subjects?

A. What about dehydration?
B. Can subjects drive after participating?
C. Can subjects develop an addiction to MDMA?
D. All are reasonable questions
E. All are **UN**reasonable questions
Conclusion:
Tips for a Better IRB Submission

• Organize your writing
• Use 45 C.F.R. 46.111 and the Belmont Report
• Submit a complete protocol
• Write for a reviewer with different expertise (or for a non-scientist)
• Anticipate reasonable questions from the perspective of protecting human subjects

WORK WITH THE IRB, NOT “TO PASS” THE IRB

• 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
THANK YOU