Completing a First-Rate Review:
Your Responsibilities as an IRB Reviewer

Presented by
The Research Integrity Office

Regulatory Bootcamp

- Some basics about the regulations and where they come from...

Essentials of a Good Reviewer

- Knowledgeable
  - The regulations, research, the IRB process
- Thorough
- Thoughtful
- Collaborative
  - With investigators, the IRB staff, colleagues on the panel
- Reasonable

How IRBs Got Started...

- Tuskegee Syphilis Study came to light in the early 1970's
- National Commission created by Congress to develop principles and policy for research oversight (the Belmont Report)
- Peer review (i.e. the IRB) is established as an essential component of research ethics
  - Informed consent
  - Investigator integrity

The IRB Mission

To protect the rights and welfare of research participants

- The IRB is charged with the responsibility of reviewing and overseeing human subject research.
- The IRB review process is designed to protect the rights and welfare of human subjects by ensuring:
  - Equitable selection of participants
  - Assuring adequate informed consent
  - Assessing and minimizing risks
  - Maintaining privacy and confidentiality

The Office for Human Research Protections

OHRP is an office within the Dept. of Health & Human Services (DHHS) that deals with the ethical oversight of research.

- Tip for interpreting the regs: "Know the lingo"
  - "Must" = Required
  - "Should" = Recommended or Suggested

http://www.hhs.gov/ohrp
Title 45 Code of Federal Regulations, Part 46

- 45 CFR 46 consists of Subparts A-D
  - Subpart A: “The Common Rule”
  - Subpart B: Additional protections related to research involving fetuses, neonates, and pregnant women
  - Subpart C: Additional protections related to research involving prisoners
  - Subpart D: Additional protections related to research involving children

Minimizing Risk

- How do we ensure the risks to participants are minimized?
  1. Use procedures consistent with sound research design and which do not unnecessarily expose subjects to risk
  2. Whenever appropriate, use procedures already being performed on the subjects for diagnostic or treatment purposes

Key Points to Consider

- Risk: Is the risk to the participant minimized?
  - Have the investigators done everything they can to ensure the participants are only exposed to risk absolutely necessary to conduct the research?
- Validity: Will the study yield results that matter?
  - More on this in a moment...
- Consent: Is the consent document clear & easy to understand?
  - Is the consent document written appropriately for the population being studied?

The Risk/Benefit Ratio

- What is the risk/benefit ratio?
- The comparison of the risk of a situation to its related benefits.
  - For research that involves more than minimal risk of harm to the subjects, the investigator must assure that the amount of benefit clearly outweighs the amount of risk.

Assessing Risk

- Minimal Risk: The probability and magnitude of harm and discomfort anticipated in research are not greater than those ordinarily encountered in daily life or during the performance of routine physical or psychological tests
- Greater than Minimal Risk: Not minimal, or “less than” minimal risk.

“The job of the IRB is to evaluate ethics...
...it has no business commenting on the science of a research study.”

What do you think?
Validity

- 45 CFR 46.111: In order to approve research, risks to subjects are minimized by using procedures which are consistent with sound research design.

  Ethical Science = Good Science

  ❖ It is unethical to pose any risk to subjects if no valid results will be obtained from the project.

- Declaration of Helsinki (2000):
  - Human research must conform to accepted scientific principles and be based on thorough knowledge of the literature.
  - Human research should only be done if the importance of the objective outweighs the risks and burdens to participants.

When Should the IRB Require a Change in the Study Design?

- If a change in the study design will meaningfully reduce the risk to participants without compromising the study results, the Board should not approve the study until the change is made.

  Note: If the study is less than minimal risk and the design is flawed (but not fatally), there is no real ethical justification for the IRB to require mandatory revisions to the study design.
  - For example, undergraduate student research projects.

Consent

- Is there a thoughtful and thorough plan in place to document informed consent?
- Is the process of obtaining consent adequately described?
- Have any waivers been requested? Are they approvable/appropriate?
- Are all of the required elements of informed consent present?
  - Your Reviewer Checklist, the IRB consent template, and the IRB staff will help you with this...

Criteria for Approval of Research

- Risks are minimized
- Risk/Benefit Ratio is reasonable
  - Risk/Benefit Ratio: The comparison of the risk to its related benefits.
  - Benefit: Includes direct benefit to the participant, and anticipated benefit to society.

- Equitable selection of participants
- Informed consent is obtained as needed
- Consent is documented as required

Criteria for Approval of Research (continued)

- Data is monitored to ensure safety of participants
- Privacy and confidentiality is protected
  - Privacy: Are embarrassing or sensitive activities conducted in a private room? Are research staff trained not to use participant names in public hallways? Etc.
  - Confidentiality: Are the laptops being used for data entry encrypted? Is the office where the charts are stored locked at all times?

- Vulnerable populations are protected
Establish a routine for reviewing the application

For example:
1. Skim the Consent Document(s).
   - Don't worry too much about taking notes or making revisions, just get an idea of what's going on in the study.
2. Read the Protocol Application
3. Read the supporting documents thoroughly. Take notes as needed.
4. Re-read the Consent Document(s) carefully. Make sure the document makes sense now that you are familiar with the rest of the application. Are participants being informed of everything they need to know?
5. Complete the appropriate checklists.

Enter Your Review In ERICA

- Make sure you submit your checklist
  - This will be the signal to your coordinator that you are done with your review
  - The coordinator will use your checklist as a guide to draft the minutes

Requesting Revisions

- Will a change in the application be likely to improve the welfare of research subjects to a meaningful degree?
  - If not, approve the study without the change.
  - If so, require the change be made prior to approval.

Presenting Your Review:
New Study Application

- Primary Reviewer:
  - Limit the summary of the study to 1-2 minutes
  - Be precise about the changes required to the study
  - End your presentation with a recommendation for the vote (pending the secondary reviewer's comments)

- Secondary Reviewer:
  - Focus on any areas of disagreement with the primary reviewer
  - Discuss the Consent Document and consent process
  - End your presentation with a recommendation for the vote

Requesting Revisions

- Are my revisions clear?
  - The IRB staff will be communicating your requests to the study team. Make sure it is clear what you are asking for.

- Don't sweat the small stuff
  - Don't worry too much about correcting typos, formatting, etc., unless the correction will significantly improve the document or change the meaning of the document.
  - Revisions should be substantive and meaningful.

Presenting Your Review:
Continuing Review Application

- Summarize the study (1-3 sentences)
  - Progress of the study
  - Enrollment status
    - Open/closed, suspended
    - Over/under accrued
  - Number of participants accrued

- Have there been any adverse events (AE) or unanticipated problems (UP) since the last continuing review? Has any new information emerged that changes the risk to participants?
  - DSMB findings, if applicable
  - Withdrawals, complaints, multi-center reports, etc.
Presenting Your Review: Continuing Review Application (Continued)

- Provide a summary of any significant Amendments since last review. Have any of the changes required revisions to the Consent Document?
- Have there been any significant changes to the Consent Document since the last continuing review?
- Is the document still accurate and appropriate?

Presenting Your Review: Modification Application

- Summarize the study (1-3 sentences).
- Describe the changes that are being requested.
- State whether or not the changes will affect the risk/benefit ratio of the overall study.
- State whether or not the changes are acceptable/approvable.

Disapproving a Study

- If I disapprove a study, what happens?
  - The study is returned to the study team for additional revision.
  - The study comes back to the same panel and reviewer the following month for re-review.

Expediting Review

You will likely be designated as an Expedited Reviewer in about 2 months...

The Board Meeting: A Place to Make Decisions, Not Gather Information...

- Ask questions before the meeting
  - Contact the study team
  - Collegial interactions with the research community facilitate the review process and promote respect for the IRB
  - Contact the IRB staff
  - Contact your fellow board members
  - Come with your revisions ready to go
- Keep your meeting coordinator informed
  - If you contact the study team, make sure your coordinator knows what's going on... they are the final gate keepers that ensure your revisions have been included in the final version of the application!

Hot Discussion Topics

Some topics get more discussion time during the meeting than others... it’s helpful to have members in the room that really know their stuff about these issues. The IRB staff can help.

- Vulnerable populations
  - Child Categories
  - Participants with diminished cognitive capacity/LARs
- Waivers
  - Waivers of parental permission
- Randomization to placebo-only arm
- Placebo guidelines
- DSMPs
- Research-Related Injury/Sponsor liability
- IND/IDE
- Tissue/Specimen Banking
Voting

- **Approve as submitted**: No changes required; the study is approved to begin as soon as the final processing is complete.
- **Approve with directed changes**: Minor revisions required. The board approves the study with the understanding that the required revisions will be completed prior to final processing.
- **Disapprove**: The study is not approved. The PI may revise the study and re-submit it as a New Study Application if they choose.
- **Abstain**: Appropriate when the member has insufficient information to make an informed decision (e.g. entered the room late, etc.).

Questions?

**Contact the IRB staff!**

We are here to help you.

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