Office of Human Research Ethics Training Tips

Primary Reviewer Presentation Tips for Continuing Reviews

IRB Review Process SOP 701

OHRP Background:

Criteria for IRB Approval of Research Undergoing Continuing Review, HHS regulations set forth the criteria for IRB approval of research (45 CFR 46.111, 46.204-207, 46.305, and 46.404-409).

When conducting continuing review, the IRB should:

a. **Start with the working presumption that the research, as previously approved, satisfies all of the above criteria.**
b. **Focus on new information** provided by the investigator, or otherwise available that would change the risk: benefit ratio or require a revision of the protocol and/or the informed consent document.
c. Disapprove or require modifications in (to secure re-approval of) a research activity that does not meet the regulatory requirements.
d. When conducting continuing review & evaluating if the research continues to satisfy the criteria for IRB approval of research, the IRB should pay particular attention to the following four aspects of the research:
   - **Risk assessment and monitoring;**
   - **Adequacy of informed consent process;**
   - **Investigator and institutional issues; and**
   - **Research progress.*** http://www.hhs.gov/ohrp/policy/continuingreview2010.html#section-b1**)**

OHRE SOP 701 2.4 Additional Considerations: 2.4.1 Determination of Risk

At the time of initial and continuing review, the IRB will make a determination regarding the risks associated with the research plan.

OHRP 2010 Guidance: The primary reviewer's summary might highlight any critical issues for consideration by the IRB, identify any key changes being proposed by the investigator, and include recommendations for action by the IRB. A typical primary reviewer's summary might note that no issues of concern have arisen since the prior IRB review, no changes are being proposed by the investigator, adverse events are of the type and frequency expected, the research appears to satisfy all criteria required for approval under 45 CFR 46.111 (and subparts B, C, and D when applicable), and the primary reviewer recommends approval without any stipulated changes.

4. Submission of Documents to the IRB

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. In particular, investigators are responsible for submitting sufficient materials and information for the IRB to meet its regulatory obligations, and should follow the institutional policies and procedures for continuing IRB review of research that are required by 45 CFR 46.103(b)(4) and referenced in the institution's OHRP-approved Federal-wide Assurance (FWA). OHRP recommends that institutions have written procedures for continuing review that require investigators to submit the following documents, as applicable, if not already available to the IRB as part of the existing IRB records for the research:

- A brief project summary (this could be included as part of a progress report described in the next bullet, provided as a separate document, or be addressed by referencing other documents made available to the IRB, including the informed consent document(s));
- **A progress report that includes the following:**

- The number of subjects accrued (for multicenter research studies, the number of subjects accrued at the local institution and the number accrued study-wide, if available, should be provided);
- A brief summary of any amendments to the research approved by the IRB since the IRB's initial review or the last continuing review;
- Any new and relevant information, published or unpublished, since the last IRB review, especially information about risks associated with the research (note that OHRP does not expect the IRB to perform an independent review of the relevant scientific literature related to a particular research project undergoing continuing review; this responsibility rests with the investigators and any monitoring entity for the research);
- A summary of both any unanticipated problems and available information regarding adverse events (the amount of detail provided in such a summary will vary depending on the type of research being conducted; in many cases, such a summary could be a brief statement that there have been no unanticipated problems and that adverse events have occurred at the expected frequency and level of severity as documented in the research protocol, the informed consent document, and investigator's brochure (if applicable); see OHRP's *Guidance on Reviewing and Reporting Unanticipated Problems Involving Risks to Subjects or Others and Adverse Events* at http://www.hhs.gov/ohrp/policy/advevntguid.html);
- A summary of any withdrawal of subjects from the research since the last IRB review, and the reasons for withdrawal, if known; and
- A summary of any complaints about the research from subjects or others since the last IRB review;

- The latest version of the IRB-approved protocol and sample informed consent document(s);
- Any proposed modifications to the informed consent document or protocol;
- For FDA-regulated research, the current Investigator's Brochure, if available, including any modifications; and
- Any other significant information related to subject risk, such as the most recent report from any DSMB or DMC monitoring the research, if available. Even when the DSMB or DMC has identified no problems during its review and simply recommended continuation of the research study as designed, it may be useful for the IRB to be informed of this recommendation.

In developing procedures for continuing review, the IRB might consider use of templates, checklists, or other tools to standardize the request for information or list of materials to be provided to the IRB by investigators at the time of continuing review.

Primary Reviewer Review:

- Assess whether the study is proceeding as expected, using information in the progress report
- Are the number of subjects enrolled greater than the number the IRB approved?
- Have there been unanticipated problems that suggest a change in risk benefit ratio?
- Are there trends in protocol deviations that may need to be addressed?
- Do Data Safety Monitoring Committee reports suggest issues that may need to be addressed?
- Is there new information that changes risk: benefit ratio?
- Is the consent form adequate and up-to-date?
- Are there changes requested for the upcoming approval period?

At the Meeting:

- **Be brief**: Provide an overview of the key points in your oral presentation:
  - Short description of study design, study objectives & progress of the study—is it going as planned?
  - Identification of subjects & enrollment numbers
  - Any changes to study design over the past year.
  - Is an amendment included with the renewal?
  - Recommend stipulations.
    - Make the final motion, including period of approval based on level of risk.

Determination of Renewal Approval Period:

- The length of the approval period is based on the level of risk to subjects and/or an analysis of this risk compared to the risk of alternative care, or standard care if such a standard exists.
- The risk assessment of each protocol is done either by expedited procedure or at a convened meeting.
- In specifying an approval period of less than one year, the IRB may define the period with either a time interval or a research milestone, e.g., number of subjects enrolled. The minutes should clearly reflect any determination requiring a review more frequently than annually."

OHRE 701. 2.4.3 Review More Often Than Annually

The following factors will be considered when determining which studies require review more frequently than on an annual basis:

1. The probability and magnitude of anticipated risks to subjects.
2. The likely medical/psychological/social/legal/educational condition of the proposed subjects.
3. The overall qualifications of the investigator and other members of the research team.
4. The specific experience of the investigator and other members of the research team in conducting similar research.
5. The nature and frequency of adverse events observed in similar research at this and other institutions.
6. The novelty of the research making unanticipated adverse events/unanticipated problems more likely.
7. The involvement of especially vulnerable populations likely to be subject to undue influence or coercion (e.g., terminally ill)
8. A history of serious or continuing non-compliance on the part of the investigator.
9. Any other factors that the IRB deems relevant.

In specifying an approval period of less than one year, the IRB may define the period with either a time interval or a maximum number of subjects either studied or enrolled. If a maximum number of subjects studied or enrolled is used to define the approval period, it is understood that the approval period in no case can exceed one year and that the number of subjects studied or enrolled determines the approval period only when that number of subjects is studied or enrolled in less than one year. If an approval period of less than one year is specified by the IRB, the reason for more frequent review must be documented in the minutes.

Sample Oral Report

Study title & #:
Primary Objective:
Procedures:
Cohort, Numbers:
IND/IDE # ?:

Continuing Renewal Report:

 # Subjects Enrolled in the past year/within the total approved by the IRB initially:
 # Subjects Completed the study in the past year:
 # Subjects withdrawn from the study & why:
Summary of Unanticipated Events reported in the past year:
Summary of any Amendment included with renewal:
Where any complaints received about the study?
New information, published or unpublished, about study topic:
Recommendation: