Office of Human Research Ethics Training Tips

Approval with Conditions, Deferral & Re-Considerations

OHRP SOP: 12.3 Deferral

The term "deferral" is used to describe the situation in which an **IRB determines that substantive changes must be made** before approval may be granted. The PI's response, including any amended materials, **must be reviewed by the convened IRB.**

Subject to IRB discretion, a **proposal may be withdrawn** if the PI does not respond to a deferral within a reasonable amount of time. If the investigator wishes to conduct a study that has been withdrawn, he/she must resubmit an application, addressing comments from the prior IRB review.

Unless otherwise specified, **the approval period** for research protocols that are deferred is one year from **the date of the last convened meeting at which approval was granted or minor changes were stipulated.**

Approval of Research with Conditions: OHRP Guidance (2010)

C. What circumstances preclude the IRB from approving research? (DEFERRAL)

Any time the IRB reviewing a research project cannot make one or more of the determinations required for approval by the HHS regulations at 45 CFR 46.111 and, if applicable, subparts B, C, or D of 45 CFR part 46, the IRB must not approve the research project. This applies to both initial and continuing review of research, and review of proposed changes to previously approved research.

Examples of required changes or clarifications that generally would preclude the IRB from approving the research include the following:

1. Justification for using a placebo
2. Justification for enrolling children
3. Revising the study hypothesis and, accordingly, the study design
4. A description of procedures that the control group will undergo
5. Providing clarifying information needed to assess the risks to subjects, such as clarifying whether individuals who have taken aspirin within 14 days prior to enrollment will be excluded from the study because of concerns about the risks of bleeding
6. Clarifying the timing and circumstances under which the informed consent of prospective subjects will be sought
7. Providing a plan to implement additional subject monitoring in order to reduce risks to subjects, given the number of serious adverse events that have occurred in study subjects since the prior IRB review

D. What circumstances permit the IRB to *approve research with conditions*? (Basic Stips)

The IRB may approve research with conditions if, given the scope and nature of the conditions, the IRB is able, based on the assumption that the conditions are satisfied, to make all of the determinations required for approval under the HHS regulations at 45 CFR 46.111 and, if applicable, subparts B, C, or D of 45 CFR part 46. The authority to approve research with conditions extends to the IRB's initial review of research, continuing review of research, and review of proposed changes to previously approved research. This authority also applies to IRB review of research at a convened meeting or under an expedited review procedure.

The IRB may require the following as conditions of approval of research:

1. Confirmation of specific assumptions or understandings on the part of the IRB regarding how the research will be conducted (e.g., confirmation that the research excludes children);
2. Submission of additional documentation (e.g., certificate of ethics training);
3. **Precise language changes** to protocol or informed consent documents; or
4. Substantive changes to protocol or informed consent documents along with **clearly stated parameters that the changes must satisfy.**

The following examples illustrate the types of conditions IRBs could stipulate when approving research, these examples are not intended to be all-inclusive: **(More Stips)**

1. Submission of documentation
2. Correction of minor grammatical and typographical errors
3. Provide a copy of clinical privileges/hospital staff to confirm that he has approval to perform such procedures.
4. Requiring that the investigator re-locate in the informed consent document the statement "You will receive $500 for participating in this study" from the "Benefits" section of the form to a separate section under the heading "Compensation.
5. Requiring that the investigator – in order to ensure that risks to subjects are minimized – add "a history of aspirin use in the past 14 days" to the exclusion criteria
6. For a randomized clinical trial comparing two types of surgical procedures, requiring that the investigator – in order to ensure that informed consent will be obtained under circumstances that provide prospective subjects with sufficient opportunity to consider whether or not to participate – revise the protocol to indicate that informed consent of the prospective subjects will be sought by the investigator during an outpatient clinic visit at least one week before the surgery.
7. Requiring the investigator to (a) confirm that any standard contrast material used in radiological procedures dictated by the research protocol will be limited to agents and dose levels specified in precise detail by the IRB, and (b) submit a revised protocol which includes the precise agents and dose levels.
8. Requiring that the investigator modify the informed consent document to include standard template language used for research involving college psychology students, stating that comparable non-research alternatives for earning extra credit will be offered to students who choose not to participate in the research.
9. Requiring the addition to the informed consent document of a description of the risks of a standard chemotherapy drug, where the risks are well-described in the research protocol.
10. Requiring revision of the research protocol to include a description of the type and amount of standard contrast material to be used in the radiological procedures dictated by the research protocol.
11. Requiring simplification of the description of the study risks in the informed consent document to be at an 8th grade comprehension level
12. Requiring that the research protocol be revised to include a plan for (a) informing subjects about the results of standard clinical tests performed as part of the research protocol (e.g., cardiac function tests), and (b) referring subjects for appropriate clinical follow-up.

G. May an IRB approve some components of a proposed research study and defer taking action on other components at the time of initial review? (Approval/Deferral Combo)

Yes, at the time of initial review *an IRB may approve some components of a proposed research study* and ***allow an investigator to initiate research activities only related to those approved components, while deferring taking action on other components of the proposed study.*** In such circumstances, the IRB must ensure that the approved components of the research study are scientifically valid and satisfy all criteria required for IRB approval, even if the other components are never approved and conducted. The IRB may require that the investigator, in order for the investigator to secure approval for the unapproved components of the initially proposed research study, submit to the IRB for review (a) changes to the protocol or informed consent documents, or (b) clarifications or additional documents. The following example further illustrates this scenario:

> The investigator proposes a research study involving the enrollment of subjects ages 12-65 years, including pregnant women.
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> Because the investigator did not provide sufficient information regarding the involvement of children and pregnant women, the IRB is unable to make the findings required for approval under subparts B and D of 45 CFR part 46. As a result, the IRB approves the research study for one year only for involvement of non-pregnant adult subjects, and the research may not involve pregnant women or children. Note that the IRB must ensure that the study as initially approved without inclusion of children or pregnant women is scientifically valid and satisfies all criteria for IRB approval under 45 CFR 46.111.
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> The IRB requires that the investigator, in order to secure approval for inclusion of pregnant women and children in the study, submit additional information necessary for the IRB to make the findings required under subparts B and subpart D of 45 CFR part 46.
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> The investigator subsequently submits sufficient information necessary for the IRB to make the determinations required under subparts B and D. The IRB reviews this information, makes the required determinations, and

approves the involvement of children and pregnant women in the study. At this point, the investigator can begin enrolling pregnant women and children.