Minor Versus Major Modifications

Spectrum Health IRB Guidance Document

Purpose

This guidance provides information on how the IRB determines the difference between minor and major modifications and the level of review that each receives. The IRB will review and determine which type of review is appropriate.

Regulatory Citations

The following regulations form the foundation for the discussion and guidance in this document.

Minimal risk means "that the probability and magnitude of harm or discomfort anticipated in the research are not greater in and of themselves than those ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests."

Expedited review procedure for certain kinds of research involving no more than minimal risk, and for minor changes in approved research (45 CFR 46.110).

Categories of Research that may be Reviewed Through an Expedited Review Procedure (1998) https://www.hhs.gov/ohrp/regulations-and-policy/guidance/categories-of-research-expedited-review-procedure-1998/index.html

Discussion and Guidance

All changes to an approved human research study that has been determined to be eligible for expedited review or has been determined to be greater than minimal risk research must be submitted to the IRB for review and approval prior to implementation unless the changes are necessary to "eliminate an apparent immediate hazard to the subject."

Minor modifications are amendments to the research that do not alter the previously determined overall risk and benefit(s) of the study and does not substantially alter the overall scientific aims or design of the study.

Additionally, the modifications must add no more than minimal risk to subjects and any added procedures must fit within expedited categories of review. Examples of minor modifications include (but are not limited to):

- Administrative, typographical, and editorial changes for clarification to the protocol, investigator's brochure, informed consent form, questionnaires, recruitment material or other study documents;
- Addition or change of study personnel or study sites;
- Addition of research procedures that are minimal risk and fall under categories qualifying for expedited or exempt review;
- Alterations to the research study that decrease risk such as decreasing enrollment size, restricting eligibility, decreasing biological sample collected provided that it does not alter safety evaluations, changing data collection points or amounts of data collected as long as it does not alter safety evaluations, decreasing length of subject participation as long as it does not alter scientific merit;
- Alterations of, or addition of, payment schedule and amounts with proper justification;
- New study recruitment material;

- Minor increases in the sample size (e.g., 100 to 105) or study duration (e.g., 12 months to 36 months observational follow-up) as long as there is sufficient justification for the change, and it does not significantly alter the overall risks and benefits of the study;

Modifications that may potentially alter the previously determined risk/ benefit ratio and/or substantially alters the overall scientific aims or design of the study would be considered “major modifications” and would require review and approval by the convened IRB. Examples of major modifications include (but not limited to):

- New risks identified or an existing risk has been found to occur more frequently or with increased severity;
- Adding new inclusion criteria or removing exclusion criteria;
- Adding new greater than minimal risk procedures;
- Re-opening enrollment of a study after a hold for safety concerns;
- Significant changes to study design, such as the addition of new treatments or new arms to the study;
- Deleting safety labs with no replacement of other safety analysis;
- Addition of a new vulnerable population for greater than minimal risk research

Study teams should submit modifications to the IRB via the Modification of Approved Human Research xForm.

Select all changes to the study within the xForm and provide both the details and the reason for the modification. Include the tracked changes versions of updated documents, if applicable, or a summary of changes document. If you are unsure of what to include in your submission reference the IRBs Guidance on “Types of Supporting Materials that Require IRB Approval.”

If there is a change to the risk/benefit analysis this should be conveyed to the IRB and any plans for re-consent should be provided.

Conclusions

It is important to note that this is not an exhaustive list and context matters. Modifications can be reviewed via expedited procedure or at a convened IRB meeting based on how it affects the risks of the study and the current subjects (i.e., how the changes fit into the overall study and if the modification would impact one’s decision to continue participation).

The IRB will ultimately make the decision regarding whether a study is a minor or major modification and what processing route is appropriate. If you have additional questions about a study review path please contact the IRB at irbassist@spectrumhealth.org.