

Continuing Review

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Topics

- What is continuing review?
- How is the continuing review date determined?
- What constitutes substantive and meaningful continuing review?
- Expedited continuing review
- What occurs if there is a lapse in continuing review?
- Continuing review best practice

Continuing Review

- Federal regulations require that an IRB conduct continuing review of research at intervals appropriate to the degree of risk, but not less often than once a year (45 CFR 46.109(e) & 21 CFR 56.109(f)).
- Continuing review by the convened IRB, with recorded vote on each study, is required unless the research is otherwise appropriate for expedited review
 - The minutes of IRB meetings should document separate deliberations, actions, and votes for each protocol undergoing continuing review by the convened IRB

Determining Continuing Review Date

- The IRB should decide the frequency of continuing review (no less frequently than once per year) for each study protocol necessary to ensure the continued protection of the rights and welfare of research subjects.
- The continuing review date is based on the date of the last convened meeting where the protocol was reviewed

Determining Continuing Review Date

- The IRB reviews and approves a protocol without any conditions at a convened meeting on April 1, 2008
- Continuing review must occur within 1 year of the date of the meeting, that is, by April 1, 2009

Determining Continuing Review Date

- The IRB reviews a protocol and requests minor changes at a convened meeting on April 1, 2008
- On April 30, 2008, the IRB chair or designee confirms that the required minor changes were made and approves the protocol
- Continuing review must occur within 1 year of the date of the IRB meeting, that is, by April 1, 2009

Determining Continuing Review Date

- The IRB reviews at a convened meeting on April 1, 2008 and has serious concerns.
- The IRB meets on May 1, 2008 to review responses and gives final approval
- Continuing review must occur within 1 year of the date of the final IRB meeting, that is, by May 1, 2009

Grace Periods

- The regulations make no provision for any grace period extending the conduct of research beyond the expiration date of IRB approval
- When continuing review occurs annually and the IRB performs continuing review within 30 days before the IRB approval period expires, the IRB may retain the anniversary date as the date by which the continuing review must occur

Grace Periods

For example:

- Protocol approved April 1, 2008 with one-year approval period
- Continuing review completed March 12, 2009
- Next continuing review due by April 1, 2009

Substantive & Meaningful Review

- Continuing review of research must be substantive and meaningful.
- Federal regulations set forth the criteria that must be satisfied in order for the IRB to approve research (45 CFR 46.111 & 21 CFR 56.111)
 - IRB determinations regarding risk, benefits, equitable subjects selection, informed consent, subject safety, privacy & confidentiality, and vulnerability of subjects
- The IRB must ensure that these criteria are satisfied at the time of both initial and continuing review.

Substantive & Meaningful Review

- When conducting continuing review, the IRB must determine whether the criteria for approval continue to be met
- The IRB should also review information regarding any unanticipated problems involving risk to subjects or other that have occurred during the approval period
- The IRB must review the current consent form to determine that it is still appropriate

Continuing Review Materials

- Protocol Summary
- The number of subjects accrued
- A summary of adverse events and any unanticipated problems, withdrawals or complaints about the research since the last IRB review
- A summary of any relevant recent literature... or modifications
- Any relevant multi-center trial reports
- Any other relevant information, especially information about risks associated with the research
- A copy of the current informed consent document and any newly proposed consent document.

Continuing Review Procedures

- At least one member of the IRB (i.e., a primary reviewer) should review a copy of the complete protocol including any modifications previously approved by the IRB.
- The minutes of IRB meetings should document separate deliberations, actions, and votes for each protocol undergoing continuing review by the convened IRB.

Expedited Review

- IRBs are permitted to use expedited review for the continuing review of research initially approved for expedited review
- When reviewing research under an expedited review procedure, the IRB Chair (or designated IRB member(s)) should receive and review all of the above-referenced documentation, including the complete protocol
- Generally, if research did not qualify for expedited review at the time of initial review, it does not qualify for expedited review at the time of continuing review

Expedited Review Category 8

Expedited review may be used for the continuing review of research previously approved by the convened IRB as follows:

- (a) Where the research is permanently closed to the enrollment of new subjects, all subjects have completed all research-related interventions, and the research remains active only for long-term follow-up of subjects; **OR**

Expedited Review Category 8

- (b) Where no subjects have been enrolled and no additional risks have been identified; **OR**
 - (c) Where the remaining research activities are limited to data analysis.
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- For a multi-center protocol, an expedited review procedure may be used by the IRB at a particular site whenever the conditions of category (8)(a), (b), or (c) are satisfied for that site.

Expedited Review Category 9

Expedited review may be used for continuing review of research ... where categories (2) through (8) do not apply but the IRB has determined and documented at a convened meeting that the research involves no greater than minimal risk and no additional risks have been identified

Lapse of approval

- If an investigator has failed to provide continuing review information to the IRB or the IRB has not reviewed and approved a research study by the continuing review date specified by the IRB, the research must stop, unless the IRB finds that it is in the best interests of individual subjects to continue participating in the research interventions or interactions.
- Enrollment of new subjects cannot occur after the expiration of IRB approval.
- When continuing review of a research protocol does not occur prior to the end of the approval period specified by the IRB, IRB approval expires automatically. Such expiration of IRB approval does not need to be reported to OHRP as a suspension of IRB approval under HHS regulations.

Continuing Review Best Practice

- Although continuing review should be substantive and meaningful, IRBs should focus on determining if the criteria for approval continue to be met
- IRBs should minimize making new requirements at continuing review to
 - Situations where the IRB overlooked something significant
 - Situations where thinking about an issue has changed
- IRBs should recognize that every additional requirement imposed on investigators has a cost and that the cost should be justified by the benefit of the requirement

Summary

- Continuing review is required at least annually
- Continuing review must be substantive and meaningful
- There is no grace period, when approval lapses research must stop
- The IRB should be reasonable in imposing requirements at continuing review