

 OHSU Research Integrity Office	Policies & Procedures	
Title: Continuing Review and Expiration of Research	Date Effective 2/26/2008	Supersedes P&P dated: 10/2002
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Background

IRB review is an ongoing process, not a one-time step. Continuing review is the ongoing monitoring mechanism by which IRBs ensure the continuing protection of subjects who participate in research. While initial review is based on the researcher's and the IRB's best assessment of the anticipated risks and benefits, regular re-evaluation ensures that research is conducted responsibly. Actual risks can truly be understood only after research has begun. Unexpected developments in a project can raise questions about the conduct of the research, and new findings can raise questions about the project. At continuing review, the IRB can then determine the correctness of its initial judgment. Additionally, the regulations for human subjects research are constantly being refined. Changes in laws, regulations and guidance can prompt substantive and administrative modifications to review.

For non-exempt research conducted or supported by HHS, the IRB must conduct continuing review of research at intervals appropriate to the degree of risk, but not less than once per year (45 CFR 46.109(e)). At the time of continuing review, the IRB should ensure that the criteria for IRB approval under HHS regulations at 45 CFR 46.111 continue to be satisfied. In particular, the IRB needs to determine whether any new information has emerged either from the research itself or from other sources that could alter the IRB's previous determinations, particularly with respect to risk to subjects. Information regarding any unanticipated problems that have occurred since the previous IRB review in most cases will be pertinent to the IRB's determinations at the time of continuing review. A study which lapses and has not been reviewed by its expiration date is not considered to be approved by an IRB.

Scope

This applies to all studies with IRB approval from the OHSU IRB and addresses the responsibilities of the OHSU IRB and Principal Investigators.

Authority

- 45 CFR 46.105(b) and 21 CFR 56.108 requiring compliance with requirements for continuing review in order to have federal funding, having written procedures for continuing review
- 45 CFR 46.107(e) and 21 CFR 56.107(e) stating that members may not have a conflict of interest and take part in the continuing review.
- 45 CFR 46.109(e) and 21 CFR 56.109(f) requiring continuing review at least once per year.
- OHRP Guidance on Continuing Review, January 15, 2007

I. Policy

- A. The IRB will conduct continuing review of research at intervals appropriate to the degree of risk, but not less often than once a year. The Board will determine the appropriate review interval.
- B. Continuing review of research will be substantive and meaningful. Each continuing review will ensure that the 45 CFR 46.111 criteria for approval of research are still satisfied in order to re-approve. The IRB will also consider, at a minimum, unexpected

results of ongoing research, unanticipated problems, the effects of the research project itself, regulatory changes and new knowledge gained.

- C. Continuing review will be conducted by the convened IRB, with recorded vote on each study, unless the research is otherwise appropriate for expedited review.
- D. No human subject research may be conducted without prior approval from the IRB. A study that lapses past the review date is considered to have an expired IRB approval and therefore all such research must stop. Subjects may not be enrolled and no research information/data may be collected from currently enrolled subjects until the approval is reinstated. There is no provision for any “grace” or “extended approval” period.
- E. If a study has expired, the PI may appeal to the IRB for continued subject contact during the lapse. Research procedures may only continue if, upon appeal, the IRB finds that it is in the best interests of individual subjects to continue participating in the research interventions or interactions.
- F. All information/data collected and subjects enrolled during a lapse period and without special permission from the IRB are considered to be the result of unapproved research activities.
- G. The OHSU Research Integrity Office (ORIO) will issue continuing review reminders, however the Principal investigator is responsible for ensuring that the IRB receives the continuing review application with sufficient time for review. Late submissions cannot be guaranteed timely review.

II. Procedures

A. Establishing the Continuing Review Date (Expiration Date).

- i. IRB approval, without a continuing review, may not exceed 12 months. Upon review and approval of a proposed study, the IRB will set the continuing review date for 364 days from the most recent approval date, unless the IRB determines otherwise.
- ii. The IRB may set a shorter review period. The expiration date will be indicated on the Review Communication and approval letter. Shorter review periods may be required if the IRB determines that:
 - a. It is in the best interest of subjects or will reduce possible risk to study subjects,
 - b. New information is likely to emerge, or
 - c. The PI requires closer monitoring due to a history of non-compliance.

B. Submitting an Application for Continuing Review

- i. As a courtesy, ORIO will issue continuing review reminders to the PI and the primary contact at 90, 60 and 30 days prior to expiration.
- ii. If re-approval is desired, the PI should submit an application for continuing review 10 to 6 weeks prior to the expiration date.
 - a. Applications submitted more than 10 weeks prior to the expiration date will not receive priority ahead of other studies with earlier expiration dates.
 - b. Applications submitted after the 6 week deadline cannot be guaranteed IRB review prior to expiration of the study. This is especially true for studies requiring full board review.
- iii. If re-approval is not desired, the PI should submit an application for termination. If this step is not carried out, the study will be considered expired and ORIO will follow the policy for expired studies.
- iv. Applications must be submitted through the Electronic IRB (eIRB) by creating a Continuing Review Questionnaire (CRQ) and providing all of the appropriate documentation.

C. Determining Level of Review

- i. If a study was initially reviewed at a full board meeting of the IRB, then continuing review will usually be by the full board. The study may, however, become eligible for expedited review or be moved to exempt status.
- ii. A previously full board study may become eligible for expedited review if:
 - a. Research is permanently closed to enrollment, all subjects have completed research-related interventions and the research remains active only for long-term follow-up of subjects, or
 - b. No subjects have been enrolled and no additional risks have been identified, or
 - c. The remaining research activities are limited to data analysis.

- iii. Any approved study, whether expedited or full board, can be moved by the IRB to exempt status if the remaining research activities are limited to data analysis and the investigator has recorded the data in such a way that the data are not identifiable and cannot be re-linked to personal identifiers. Research that is determined by the IRB to be exempt will no longer require annual review. PIs can request that the IRB reconsider a study's status.

D. IRB Continuing Review of Research

- i. Each IRB continuing review, whether full-board or expedited, will consider the following:
 - a. Continued fulfillment of the 45 CFR 46.111 criteria for approval of research.
 - b. Unexpected results of ongoing research.
 - c. Any new knowledge gained or emerging information that affects risk.
 - d. Protection of vulnerable populations.
 - e. The sufficiency of the last IRB review.
 - f. Any unanticipated problems.
 - g. Regulatory changes that may impact the study.
- ii. Research will be re-approved if all of the considerations are satisfied.
- iii. The IRB may impose additional precautions or reassess special requirements it had previously imposed on the research protocol.
- iv. No member may participate in the continuing review of any project in which the member has a conflicting interest, except to provide information requested by the IRB.

E. Expired Studies

- i. 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.
- ii. If an investigator has failed to provide continuing review information to the IRB in time for review 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 certain circumstances exist.
 - a. In all cases, enrollment of new subjects cannot occur after the expiration of IRB approval.
 - b. Except for emergency care, the PI may not conduct any research activities without prior approval from the IRB. When subject safety is at issue, the PI may provide emergency medical care, to the extent the physician is permitted to do so under applicable federal, state, or local law.
 - c. The PI may appeal to the IRB for continued subject contact during the lapse. Research procedures may only continue if, upon appeal, the IRB or IRB Chair finds that it is in the best interests of individual subjects to continue participating in the research interventions or interactions.
- iii. Expiration due to late PI submission (later than 6 weeks pre-expiration)
 - a. PI's will receive notice of the expiration and be given 10 working days to submit for continuing review.
 - b. After 10 days, the PI will receive another notice advising that within 10 working days, the study may be terminated by the PI or the IRB will terminate the study and charge the PI's department an administrative fee.
 - c. In order for the PI to continue any research activities during a lapse, the PI must send a memo to the Board, prior to those activities, requesting approval to conduct the listed activities.
 - d. The IRB can only approve the request if it finds that it is in the best interests of individual subjects to continue participating in the research interventions or interactions. This process will be facilitated by the Chair's with appropriate consultation from the Board.
 - e. Generally, the IRB will not approve any research activities during an expired period which are not direct interactions with living subjects and are only interactions with data or identifiable information.
 - f. The memo to the IRB must include an explanation of the cause of the lapse and a plan to avoid future lapses.
- ii. Expiration due to IRB failure to review

- a. When the IRB has received a timely submission from the PI, but has failed to conduct the review prior to expiration of the study, the IRB will move the study to highest priority status once the IRB becomes aware of the expiration.
 - b. During the lapse, the Chair will contact the PI to identify and approve any research activities that should occur during the time until re-approval in order to protect the best interests of the subjects.
- iii. Expiration occurs during full board review process
- a. If research is approved with required changes, research may continue as approved at last review, enrollment may continue and the previously approved consent form may be used until a new approved form is available. Changes to the research may not be instituted until final IRB approval is given. Subjects may need to be re-consented with the newly approved consent form if there have been changes.
 - b. If a study is deferred, expired research procedures for PI induced lapse should be followed.

III. Definitions

- A. **Approval Date** – The date which the IRB, through either an expedited procedure or full board review, determines that, for the proposed research, all of the §46.111 criteria for IRB approval of research have been satisfied.
- B. **Continuing Review** - Regularly scheduled complete re-appraisals of a project. The goals of continuing reviews are to ensure that the risk/benefit ratio is still acceptable, that the measures taken to safeguard subjects are adequate, that the approved protocol is followed, that the project reflects any changes that have been made in the regulations for human subjects research since the last approval and that all of the §46.111 criteria for IRB approval of research are still satisfied.
- C. **Expiration Date** – The date at which time IRB approval expires. This is also referred to as the continuing review date or the lapse date. Research must be re-reviewed and approved prior to this date in order to avoid expiration of IRB approval.
- D. **Expired** – State in which a study is no longer considered to have IRB approval.
- E. **IRB Approved Research** – Research that the IRB, through either an expedited procedure or full board review, has determined that all of the §46.111 criteria for IRB approval of research have been satisfied. The §46.111 criteria include:
 - Risks to subjects are minimized
 - Risks to subjects are reasonable in relation to anticipated benefits, if any, to subjects, and the importance of the knowledge that may reasonably be expected to result.
 - Selection of subjects is equitable.
 - Informed consent will be appropriately sought.
 - Informed consent will be appropriately documented.
 - Adequate provision for monitoring the data collected to ensure the safety of subjects.
 - Adequate provisions to protect the privacy of subjects and to maintain the confidentiality of data.
 - All vulnerable population protections have been considered.
- F. **Lapse** – When an IRB-approved study passes its expiration date and no longer has IRB approval.
- G. **Research-Related Intervention** – An activity that is required as part of the IRB approved protocol, is occurring to contribute to research results, or is follow-up to approved research activities.
- H. **Review Communication** – The memo issued by ORIO to the PI to communicate the results of full board review and any board requirements that must be satisfied for re-review or approval.