

SOP: RR 404 Version No: Effective Date: 01/01/07	CONTINUING REVIEW – CRITERIA FOR RENEWAL	Supersedes Document Dated: 11/05
---	--	--

1. POLICY

The IRB conducts continuing review of research taking place within its jurisdiction at intervals appropriate to the degree of risk, but not less than once per year.

Specific Policies

1.1 Interval for Review for Purposes of Renewal

The IRB must conduct continuing review of protocols for purposes of renewal of the IRB approval period, at intervals appropriate to the degree of risk, which is determined at the initial review, but not less than once per year. "Not less than once per year" means that the research must be reviewed on or before the one-year anniversary of the previous IRB review date, even though the research activity may not have begun until some time after IRB gave its approval.

Investigators are required to submit a Renewal Application form (Form FO 301-B) prior to the expiration of the study or as specified by the IRB, but at least annually. The signed Renewal Application form should normally be filed no less than 30 days before the study approval period ends. [If the study has been completed prior to the approval expiration date, the investigator is required to inform the IRB by submitting a completed Application for Closure (Policy RR 405.)

1.2 Extensions of Approval Period

There is no grace period extending the conduct of the research beyond the expiration date of IRB approval.

However, if the Investigator is in communication with the IRB, the Application for Renewal is forthcoming, and in the opinion of the IRB, subjects participating in such a study would suffer a hardship if medical care were discontinued, appropriate medical care may continue beyond the expiration date for a reasonable amount of time. However, new subjects cannot be enrolled. The IRB will address on a case-by-case basis those rare instances where failure to enroll new subjects would seriously jeopardize the safety or well being of an individual. Prospective research data cannot be collected, and no procedures that are only being performed for the purposes of the protocol may be performed until an Application for Renewal or other progress report, as requested, is reviewed and approved.

1.3 Criteria for Renewal

Continuing review must be substantive and meaningful. When considering whether or not to renew a study, the IRB revisits the same criteria used to grant initial approval. Therefore, the IRB (or the reviewers for protocols reviewed under an expedited procedure) must determine that:

- The risks to subjects continue to be minimized and reasonable in relation to the anticipated benefits;
- The selection of subjects continues to be reasonable in relation to anticipated benefits;
- Informed consent continues to be appropriately documented;

- Additionally, there are:
 - Provisions for safety monitoring of the data,
 - Protections to ensure the privacy of subjects and confidentiality of data, and
 - Appropriate safeguards for vulnerable populations.

Because it may be only after research has begun that the real risks can be evaluated and the preliminary results used to compute the actual risk/benefit ratio; IRB can then determine whether or not the study can be renewed at the same risk/benefit ratio, or if new information has changed that determination.

In order to determine the status of the study, the following will be revisited:

- 1.3.1 Consent document: Each member of the IRB shall review the currently approved consent document and ensure that the information is still accurate and complete. Any significant new findings that may relate to the subject's willingness to continue participation should be provided to the subject in an updated consent document.
- 1.3.2 Current approved research objectives including any amendments to protocol since initial review: Each member of the IRB shall review the Renewal Application form. The primary reviewers will also review a copy of the full protocol that should include any amendments and addenda approved during the approved period. [Amendments and addenda to a research protocol should be submitted as generated during the course of the study, but they may also be submitted at the time of review if generated at the time of continuing review.] If additional amendments are submitted along with the Renewal Application form, a separate cover letter describing the change and all appropriate documentation (approved consent form) must accompany the continuing review application.
- 1.3.3 Continuing IRB review is required as long as individually identifiable follow-up data are collected on subjects enrolled in the protocols. This remains the case even after a protocol has been closed at all sites and protocol-related treatment has been completed for all subjects. These renewal requests may qualify for expedited review.
- 1.3.4 Continuing review of DSMB-monitored clinical trials: When a clinical trial is subject to oversight by a DSMB whose responsibilities include review of adverse events, interim findings and relevant literature (e.g., DSMBs operating in accordance with the National Cancer Institute Policy for Data and Safety Monitoring of Clinical Trials, or internally developed DSM group), the IRB conducting continuing review may rely on a current statement from the DSMB indicating that it has reviewed study-wide adverse events, interim findings and any recent literature that may be relevant to the research, in lieu of requiring that this information be submitted directly to the IRB. However, the IRB must still receive and review reports of local, on-site unanticipated problems involving risks to subjects or others and any other information needed to ensure that its continuing review is substantive and meaningful.
- 1.3.5 Progress report: All IRB members shall receive a progress report as part of the Renewal Application prepared and submitted by the Investigator along with the number of subjects entered to date and since the last review. The

progress report shall summarize adverse event experiences, amendments, changes in training of personnel and new COI disclosure as applicable, and provide a reassessment of the risk-to-benefit ratio.

1.3.6 The IRB should be made aware of any substantive changes in the funding that may impact the project.

1.4 Possible Outcomes of Continuing Review

As an outcome of continuing review, the IRB may require that the research be modified or halted altogether. The IRB may need to impose special precautions or relax special requirements it had previously imposed on the research protocol.

1.5 Expedited Review for Renewal

A protocol that was originally reviewed using the expedited review procedure may receive its continuing review on an expedited basis. Additionally, a standard-review protocol that had no accrual during the previous period, or which has not been awarded funding, or which remains open only to data analysis may be reviewed using an expedited review.

When conducting research under an expedited review procedure, the IRB Chairperson or designated IRB member conducts the review on behalf of the full IRB using the same criteria for renewal as stated in section 1.3 of this policy. If the reviewer feels that there has been a change to the risks or benefits, he or she may refer the study to the full IRB for review.

2. SCOPE

These policies and procedures apply to all research submitted to the IRB.

3. RESPONSIBILITY

IRB Chairperson or IRB Administrator is responsible for establishing and implementing processes for making research renewal decisions.

4. APPLICABLE REGULATIONS AND GUIDELINES

21 CFR 56.108,111

45 CFR 46.111

OPRR Reports 95-01

5. REFERENCES TO OTHER APPLICABLE SOPs

This SOP affects all other SOPs.

6. ATTACHMENTS

FO 301-B Renewal Application Form

7. PROCESS OVERVIEW

All approved projects (expedited or full board) are required to submit a Renewal Application that includes a progress report at the time assigned within the approval letter received by the principal investigator for the project. This project will be reviewed annually or more frequently as determined by the IRB. Appropriate action will be taken if the approval for the project expires prior to review.

Actions may be continuing approval, approval upon recommended changes (approved pending), suspension for cause, or termination for cause. During the review of the progress report (Form FO 301-B – Renewal Application), the degree of risk shall be analyzed. As a component of the analysis, the reviewer(s) should look at the number of Serious and/or Unexpected Adverse Events leading to amendments or consent form

changes. Also, the degree of risk initially assigned by the IRB for the protocol should be reconsidered. Based on these determinations, the reviewer(s) will make a recommendation for re-approval and assignment of a time period for when the next re-approval will occur.

8. PROCEDURES EMPLOYED TO IMPLEMENT THIS POLICY

Who	Task	Tool
<i>IRB Coordinator</i>	Following each IRB meeting, generate a summary from the database of all studies with IRB approvals that include study approval expiration dates.	
<i>IRB Coordinator</i>	<p>Sixty (60) days prior to the approval expiration date, a reminder letter is generated and mailed to the principal investigator with a copy to the research coordinator, if applicable, indicating approval expiration date and the consequences of no response.</p> <p>If response is not obtained by the deadline submission date (thirty (30) days prior to the approval expiration date), the Investigator/Contact Person is sent a reminder that the study approval is about to lapse via email or phone call. Make note of this contact for the study record.</p>	
<i>IRB Coordinator</i>	<p>If a Renewal Application is not received, the study is placed on the IRB agenda under a separate section titled Closed (IRB approval has expired) prior to the expiration date. A letter of permanent closure for investigator noncompliance will be mailed to the principal investigator via certified mail.</p> <p>The IRB will determine what sanctions are necessary in order to reactivate the protocol in question and/or educate the principal investigator of the importance of completing the Renewal Application.</p>	
<i>IRB Administrator and/or Coordinator</i>	When the Renewal Application is received, the OROC staff will assess the renewal request for expedited or full board review, send Renewal Application to the primary reviewers, and place on agenda.	

<i>IRB Chairperson and IRB Administrator</i>	Notify the Investigator as to the outcome of the review. If the IRB does not re-approve the research by the specified expiration date, the research suspension letter will be sent per SOP CO 601. It will also outline the terms of the suspension according to the terms of the suspension according to the three regulatory categories (screening, enrolling of new subjects, and continuation of interactions/interventions in already enrolled subjects) as decided by the IRB or reviewer(s).	
<i>IRB Coordinator</i>	Coordinate faxing (if needed) and mailing the IRB action letter regarding re-approval to the Investigator.	