

CONTINUING REVIEW – CRITERIA FOR RENEWAL

SOP #:	405	Version #:	1	EFFECTIVE DATE:	8/18/14	SUPERSEDES DOCUMENT:	5/1/09
THIS POLICY PERTAINS TO:			ALL RESEARCH SUBMITTED TO THE IRB				
RESPONSIBILITY FOR EXECUTING POLICY:		ASSOCIATE VICE PRESIDENT FOR RESEARCH AND ECONOMIC DEVELOPMENT, IRB CHAIRPERSON, IRB VICE CHAIRPERSON, IRB STAFF, IRB MEMBERS					
LAST REVIEWED ON:		/ /		RESULTS:	REVISED		
APPROVAL AUTHORITY:		Associate Vice President for Research and Economic Development					
APPROVED BY:					DATE:		08/18/14

1. POLICY

The IRB conducts continuing review (renewal) of research taking place within its jurisdiction at intervals appropriate to the degree of risk, but not less than once per year, and has the authority to observe or have a third party observe the consent process and the research. “Not less than once per year” means that the research must be reviewed before the one-year anniversary of the previous IRB review date, even though the research activity may not have begun until some time after the IRB gave its approval. IRB approval may be withdrawn at any time if warranted by the conduct of the research. The regulations authorize the IRB to establish procedures for the concurrent monitoring of research activities involving human subjects. Periodic review of all human research activities is necessary to determine (1) whether the risk/benefit ratio has changed, (2) whether there are unanticipated findings involving risks to subjects, and (3) whether any new information regarding the risks and benefits should be provided to subjects. With each continuing review, the IRB will determine whether approval should be continued or withdrawn. All research involving human subjects must be reviewed no less than once per year, and the IRB will decide on the frequency of continuing review for each study protocol.

IRB approval for the conduct of a study may be withdrawn if the risks to the subjects are determined to be unreasonably high, for example, more than an expected number of adverse events, unexpected serious adverse events; or evidence that the Investigator is not conducting the investigation in compliance with IRB or Institutional guidelines. Such findings may result in more frequent review of the study to determine if approval should be withdrawn or enrollment stopped until corrective measures can be taken or the study terminated. Continuing review may include, but may not be limited to review of the following:

- Serious, Unexpected Adverse Events, Unanticipated Events
- Non-Compliance
- Amendments
- Significant New Findings
- Interim Results

2. SPECIFIC POLICIES

2.1 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. Investigators or qualified designees are required to submit a periodic report prior to the expiration of the study or as specified by the IRB, but at least annually. The report should normally be filed 40 days before the study approval period ends.

2.2 Expiration and Extensions of Approval Period

There is no grace period extending the conduct of the research beyond the expiration date of IRB approval. Extensions beyond the expiration date will not be granted. If a complete Research Project Review and Progress Report is not received as scheduled, or if the paperwork is not received in a timely manner so that an appropriate review can be conducted, the IRB approval expires and the Investigator must stop all research procedures, recruitment, enrollment, interventions, data collection, and data analysis. The IRB will not accept future research projects from the Investigator until research is current.

Investigators who believe that currently enrolled participant will be at risk if the research project is discontinued must immediately submit to the IRB Chairperson a list of participants for whom suspension or termination of the research would cause harm. The IRB Chairperson or an experienced IRB member designated by the IRB Chairperson will determine whether it is in the best interest of individual participants to continue to take part in the research interventions or interactions. At the discretion of the reviewers, the matter might be brought to a convened meeting. However, new participants cannot be enrolled, prospective research data cannot be collected, and no procedures that are only being performed for the purpose of the protocol may be performed until a Research Project Review and Progress Report is reviewed and approved by the IRB.

Failure to obtain renewal of an approved study in the required time frame is considered serious non-compliance and will be reported to the appropriate institutional officials and regulatory authorities when applicable.

2.3 Criteria for Continuation/Renewal

Research activities initially reviewed by Full Board review must be reviewed by the Full Board at continuation, unless they meet either of the following expedited review categories:

Expedited category #8

Continuing review of research previously approved by the convened IRB as follows:

- (a) where (i) the research is permanently closed to the enrollment of new subjects; (ii) all subjects have completed all research-related interventions; and (iii) the research remains active only for long-term follow-up of subjects; or
- (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.

Expedited category #9

Continuing review of research, not conducted under an investigational new drug application or investigational device exemption where categories two (2) through eight (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.

Research activities that were originally reviewed using expedited criteria may receive continuing review on an expedited basis, unless the research activities no longer meet the expedited criteria for review and approval.

Research activities that had previously met criteria for expedited review may change with the review and approval of amendments, such that Full Board review would be required at the time of continuing review (e.g., risk has changed to be greater than minimal).

When conducting research under an expedited review procedure, the IRB Vice Chairperson or experienced IRB member conducts an in-depth review on behalf of the Full IRB using the same criteria for continuation as stated in section 2.3 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.

2.4 Continuing Review

Continuing review must be substantive and meaningful. The IRB Vice Chairperson or designee serves as Primary Reviewer for all continuing reviews, and will be provided a copy of the protocol, consent document, and Research Project Review and Progress Report to determine whether the proposed research continues to fulfill the criteria for approval. 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 IRB Vice Chairperson or designated 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, if any, to subjects, and the importance of the knowledge that may be expected to result;
- The selection of subjects continues to be equitable and reasonable in relation to anticipated benefits;
- Informed consent continues to be appropriately documented;
- Additionally, there are appropriate:
 - Provisions for safety monitoring of the data,
 - Protections to ensure the privacy of subjects and confidentiality of data,
 - Appropriate safeguards for vulnerable populations.

Members must determine whether the proposed research continues to fulfill the criteria for approval. Because it may be only after research has begun that the real risks can be evaluated and the preliminary results used to assess the actual risk/benefit ratio, the IRB can then determine whether or not the study can be continued, or continued only with protocol modifications. In order to determine the status of the study, the following will be revisited at a meeting of the Full IRB when expedited review cannot be used:

1. Research Project Review and Progress Report: All IRB members shall receive a copy of the Report prepared and submitted by the Investigator. The progress report shall summarize adverse event experiences, protocol changes, number of subject enrolled and new COI disclosures as applicable.
2. 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.

3. Protocol file and applicable IRB minutes: The IRB Vice Chairperson or Designee will act as primary reviewer and review the protocol file and applicable minutes before the convened meeting and indicate whether the protocol is ready for Full IRB review. These documents will be available to IRB members for reference before and during the convened meeting.
4. Continuing IRB review of research must occur even where the remaining research activities are limited to the analysis of data that include identifiable private information as defined in 45 CFR 46.102(f)(2). 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 requests may qualify for expedited review.
5. Review for Continuation review of Data Safety Monitoring Board (DSMB-monitored clinical trials): When a clinical trial 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), the IRB conducting continuation 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. However, the IRB must still receive and review reports of local, on-site unanticipated problems involving risks to subjects or others, interim results and any other information needed to ensure that its review is substantive and meaningful.

2.5 IRB Review

If the IRB determines that it needs verification from sources other than the Investigator that no material changes have occurred since the previous IRB review, the IRB may request an independent assessment of information or data provided in the renewal application. The IRB will obtain verification from sources other than the investigator that no material changes have occurred since previous IRB review when:

1. The IRB doubts the veracity of the information provided by the investigator.
2. The information provided by the investigator is internally inconsistent and the inconsistency cannot be resolved through discussion with the investigator.
3. The information provided by the investigator is inconsistent with other information known to the IRB and the inconsistency cannot be resolved through discussion with the investigator.
4. The investigator has been found to be in serious or continuing noncompliance in the previous year.
5. Any other situation where the IRB requests verification from sources other than the investigator that no material changes have occurred since previous IRB review.

The scope and extent of such an independent assessment is determined on a case-by-case basis, and sources for such outside information could include copies of FDA audits, literature searches and/or phone call to the sponsor.

2.6 Possible Outcomes of Review for Continuation

As an outcome of continuing review, the IRB may authorize continuation of the research, or 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, such as frequency of monitoring, requirement for interim reports, or duration of approval period. Appropriate continuing review intervals are addressed with each review conducted by the IRB. The following factors are taken into consideration when determining the appropriate review interval, but are not limited to:

- Involvement of vulnerable populations;
- Involvement of recombinant DNA or other types of gene transfer protocols;
- Use of waiver of informed consent procedures;
- Classified research;
- Research for which participants would be exposed to additional risks, e.g., breach of confidentiality, phase I studies, disproportionate number or severity of adverse events; and
- Previous suspensions of the research due to non-compliance, record-keeping or other concerns.

Any changes required to obtain continued renewal approval shall be provided to the Investigators by the IRB staff.

2.7 How the Continuing Review Date is Determined

When the IRB has determined that continuing review will occur no sooner than within one year, the date of continuing review is determined by using the date the protocol was reviewed and approved by the convened IRB. For protocols reviewed by expedited mechanisms, the continuing review must occur within one year of the date the protocol received approval.

The period of approval will be indicated on the cover page of the Research Project Review and Progress Report. A copy of the Research Project Review and Progress Report will be sent to the Principal Investigator. If the Principal Investigator is a student, a copy of the face page of the progress report will be sent to the student's adviser. If the Principal Investigator is a faculty member, a copy will be sent to the Department Chair.

2.8 Site Visits/Audits and Third Party Verifications

The IRB has the authority to observe, or have a third party observe, the consent process of research it has approved, and to verify that the study is being conducted as required by the IRB and within the University Policies and Procedures as appropriate. IRB Staff or IRB members may perform site visits or use another party either affiliated with the institution or not, to verify information in the study application, or in any interim, continuing review or renewal submissions.

3. RESPONSIBILITY

The IRB Chairperson and/or IRB Vice Chairperson are responsible for establishing and implementing processes for making research renewal decisions.

The IRB Vice Chairperson is responsible for reviewing all Research Project Review and Progress Reports.

The IRB Vice Chairperson or designee serves as Primary Reviewer for all continuing reviews.

4. APPLICABLE REGULATIONS AND GUIDELINES

21 CFR 56.108,111

45 CFR 46.111

OHRP Guidance on Continuing Review 7/11/02

5. ATTACHMENTS

RR 405-A Research Project Review and Progress Report

6. PROCEDURES EMPLOYED TO IMPLEMENT THIS POLICY

Who	Task
<i>IRB Secretary</i>	<p>Generate a monthly summary for the entire month of the studies with IRB approvals due to expire in 9 weeks.</p> <p>Generate and mail corresponding notification letters and continuing review forms.</p>
<i>IRB Secretary</i>	<p>The Investigator must submit a complete Research Project Review and Progress Report to the IRB by the submission deadline date. If not received by deadline date, a second notice will be sent.</p> <p>If a response to the second notice is not received before the one-year anniversary of the previous IRB review date, or not in sufficient time to have an appropriate review conducted, a third notice will be emailed to the Investigator informing him or her when the IRB approval of the project will expire.</p>
<i>IRB Vice Chairperson, IRB Members</i>	<p>When the Research Project Review and Progress Report is received, the IRB Vice Chairperson will review the report and associated materials to determine the status of continuation of the study. If the IRB does not re-approve the research by the specified expiration date, subject accrual will be suspended. The protocol will need to be re-submitted and re-reviewed by the IRB. Enrollment of new subjects cannot occur after the expiration of IRB approval. Continuation of research interventions or interactions in already enrolled subjects will only continue when the IRB finds that it is in the best interests of individual subjects to do so. OHRP and the IRB must address on a case-by-case basis those rare instances where failure to enroll would seriously jeopardize the safety or well-being of an individual <u>prospective</u> subject.</p> <p>(Note: Only the Full IRB may disapprove a study continuation.)</p>
<i>IRB Secretary</i>	<p>Notify the Investigator as to the outcome of the review. If the IRB does not re-approve the research by the specified expiration date, or if an Investigator does not submit the Research Project Review and Progress Report in time for it to be reviewed before the project expiration date, send a letter to the Investigator that the project no longer has IRB approval.</p> <p>(Note: Only the Full IRB may disapprove a study continuation.)</p>