|  |  |
| --- | --- |
| Policy | P7 |
| Written By: | B. Laurel Elder, Ph.D. |
| Created: | October 30, 2007 |
| Edited | March 1, 2011 |
| Version | P7.5 |

**CONTINUING REVIEW BY THE IRB**

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 IRB approval may be withdrawn at any time if warranted by the conduct of the research.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 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. Continuing review must occur as long as the research remains active for long-term follow-up of participants, even if the research is permanently closed to the enrollment of new participants, and participants have completed research-related interventions. With each continuing review, the IRB will determine whether approval should be continued or withdrawn, and will decide on the frequency of continuing review for each study protocol.

IRB approval for the conduct of a study may be withdrawn if the risks to the subjects are determined to be unreasonably high, (for example, more than an expected number of adverse events, unexpected serious adverse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 Such findings may result in more frequent review of the study to determine if approval should be withdrawn or enrollment stopped until corrective measures can be taken or the study terminated.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

**APPLICABILITY**

The IRB coordinator, IRB chair, and the IRB members at a convened meeting are responsible for review and consideration of approval of protocols during continuing review

1. Continuing review of protocols originally approved by the full board will continue to be performed by the full board.
2. Continuing review of protocols originally approved by expedited review will continue to be reviewed by expedited review. These may be referred to the full committee if it is found that the research activities no longer meet the expedited criteria for review and approval (e.g. are now more than minimal risk).

**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.

For studies that were approved five or more years ago:

1. If the protocol and/or other documents used in the project have been amended within the past five years, and
2. Upon the recommendation of the IRB Coordinator
3. The PI will be requested to submit a new protocol incorporating all amendments into one new submission.

**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 Progress Report is not received as scheduled, the IRB approval expires and the Investigator must stop all research procedures, recruitment, enrollment, interventions, data collection, and data analysis. The termination must be reported to the project sponsor (if applicable). This will be communicated to the investigator in a letter from the IRB. Once a study has expired, IRB re-review and re-approval must occur before the study can resume. The IRB cannot retrospectively grant approval to cover a period of lapsed IRB approval.

Investigators who believe that currently enrolled participant(s) will be at risk if the research project is discontinued must immediately submit to the IRB Chairperson (and to the VA Chief of Staff for VA studies) 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 make the final determination (along with the VA Chief of Staff for VA studies) 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 the research is again reviewed and approved by the IRB.

**Criteria for Continuation/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. These include (but are not limited to):

* 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 obtained and documented;
* Significant new findings that have arisen during the study and which might relate to participants’ willingness to continue participation have been provided to participants
* There are appropriate:

o Provisions for monitoring of the data to assure patient safety,

o Protections to ensure the privacy of subjects and confidentiality of data,

o 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 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. The application for continuing review. This application contains:
   1. A brief summary of the research methodology and procedures
   2. The number of subjects entered and withdrawn (including the reason for withdrawal) for the review period and since the inception of the project
   3. The gender and minority status of those entered into the protocol
   4. The number of subjects considered as members of vulnerable populations
   5. A copy of the proposal (if different from the original submission) and all approved amendments
   6. A copy of the current consent document(s)
   7. A copy of the current HIPAA authorization document (if separate from the informed consent document)
   8. Information that may impact on the risk/benefit ratio such as AEs, unanticipated problems, and complaints regarding the research
   9. Research findings to date (if available)
   10. Summary of the DSMB or DMC meetings (if applicable) or findings based on information collected by the data and safety monitoring plan submitted in the initial proposal
   11. An assurance that all SAEs and UAEs have been reported as required
   12. New scientific findings in the literature, or other relevant findings, tha may impact on the research
2. All IRB members shall receive a copy of the Continuing Review application prepared and submitted by the Investigator.
3. 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.
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.

**IRB Review**

The IRB will determine if it needs verification from sources other than the Investigator that no material changes have occurred since the previous IRB review. In this situation, the IRB may request an independent assessment of information or data provided in the renewal application. Studies with complicated protocols or atypical risks or those conducted by Investigators who have failed to respond to the IRB or IRB Chairperson in the past are examples of when verification may be needed. The IRB staff will alert the assigned reviewer by e-mail when there have been previous problems with an investigator. The reviewer will indicate on the “IRB Checklist for Continuing Review for Full Board Form” if he or she determines that the protocol requires independent verification. 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 or internal audits, literature searches and/or phone call to the sponsor.

**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.

All actions of the IRB, including any changes required to obtain continued renewal approval, shall be provided in writing to the investigators by the IRB staff.

**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 or (for expedited review, the IRB chair). For protocols reviewed by expedited mechanisms, the continuing review must occur within one year of the date the protocol received approval.

**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. The IRB may identify an IRB member or member of the IRB staff to perform site visits or to 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.

**Applicable Regulations:**

45 CFR §46 Protection of Human Subjects

21 CFR §56 Institutional Review Boards

OHRP Guidance on Continuing Review 07/11/2002