

**Department of Veterans Affairs  
Tuscaloosa VA Medical Center**

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**Human Research Protection Program SOP #6**

**October 17, 2007**

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**IRB CONTINUING REVIEW**

**1. POLICY**

The Tuscaloosa VA Medical Center (TVAMC) Human Research Protection Program (HRPP) is committed to protecting the rights and welfare of human research subjects by outlining policies and delineating responsibility and procedures of the Subcommittee on Human Studies (Institutional Review Board [IRB]).

It is the policy of the TVAMC to ensure the applicable Federal, state, and local regulations are carried out in protecting the rights and welfare of subjects who voluntarily participate in investigational studies within this Medical Center. This Standard Operating Procedure (SOP) establishes procedures that ensure the protections of the rights and welfare of subjects who are involved in research by delineating the continuing review procedures. The policies and procedures described within this document provide guidance related to continuing reviews of approved research projects for Research office staff, IRB members, R&D members and research investigators.

**2. RESPONSIBILITIES**

**The TVAMC Director** has ultimate responsibility for ensuring the protection of human research participants. The TVAMC Director is responsible for making final decisions concerning the continuation of research studies based on recommendations from the IRB and R&D Committee. The Director is also responsible for implementing these decisions and for taking any steps needed to assure that the IRB is free from undue pressure in discharging its responsibilities.

**TVAMC Research and Development (R&D) Committee** must ensure all activities of the IRB are in compliance with all Federal, state, and local regulations. The R&D Committee makes recommendations to the Director for approval or disapproval of the actions of the IRB, including those pertaining to continuing review.

**TVAMC IRB** is responsible for the initial evaluation and subsequent progress reviews through continuing review of investigational studies involving human participants. It makes recommendations concerning approval, disapproval, modifications, restrictions, suspensions or termination of such studies to the R&D Committee. Within the review process, the committee is responsible for safeguarding human studies in the areas of informed consent,

voluntary participation, confidentiality, and insures that human experimentation is performed under stipulation and procedures of the written protocol as approved.

**Principal Investigators** are responsible for submitting the research proposal to the IRB for evaluation and decision before initiation and also at the time of continuing review. Under no circumstances may an investigator begin a study involving human participation or continue a study past the continuing review date without approval from the IRB, the R&D Committee, and the Director, who endorses the R&D Committee Minutes.

### 3. **DEFINITIONS**

Refer to HRPP SOP #1-3 for definitions of research and IRB processes.

### 4. **PROCEDURES**

- a. **Continuing Reviews:** The IRB is required to conduct a substantive continuing review of research at intervals appropriate to the degree of risk, but not less than once per year. The IRB approval period for a study begins on the date that the protocol received IRB approval (day of convened IRB meeting when either full approval was granted or approval with contingencies that did not require full IRB to review was granted) and may not exceed one calendar year from the initial approval or previous continuing review approval. The protocol approval expires at 16:30 Central Time on last date of the approval interval (i.e. a protocol approved for one calendar year on May 1, 2000 would expire on April 30, 2001 at 16:30). The IRB may determine and document that certain studies require review more often than annually based on the initial review or continuing review. IRB minutes specify the review requirements (e.g., 12 months, 9 months, 6 months, and 3 months), as appropriate to the degree of risks, and will be communicated to the investigator in writing. The investigator may be notified one month in advance of the due date by email; however, it is the responsibility of the investigator to submit their projects for Continuing Reviews by the due date. If the investigator fails to respond, approval may lapse or may be terminated. Errors or miscommunications on the part of the IRB will not be a cause for disapproval. The study must also be reviewed and approved by the R&D Committee in order to continue.

**Continuing review and need for IRB approval must occur as long as the study has 1) active subjects, 2) active recruitment of subjects, 3) active long-term follow-up of participants, even when research is permanently closed to the enrollment of new participants and all participants have completed all research-related interventions, and 4) remaining research activities include the collection or analysis of private identifiable information.**

- b. **Materials submitted by the investigator and distributed to all IRB members** (except where noted) for their review and consideration include:
- Request for Continuing Approval of Human Use form (status report), which includes a summary of safety monitoring reports (i.e. Expected and Unexpected

Adverse Events, Adverse Drug Events, and Serious Adverse Events, Unanticipated problems that affect risks to subjects or others, if applicable), summary of subject enrollment (including the number of subjects, gender, number of women, and the minority status), enumeration of subjects withdrawn and the reasons for withdrawal

- Abstract (updated with findings to date, if available)
- Updated protocol (same format as initial review) if changes have been made since initial review
- Updated Informed Consent Form (VA form 10-1086) and HIPPA authorization form, (if not previously waived)
- A summary of new knowledge that may change the risk/benefit ratio
- Amended or updated Investigator's Brochure (if applicable; primary reviewer only)
- Advertising material, if applicable and not previously approved
- Updated Subcommittee for Research Safety form (if applicable; for R&D Committee only)

Unless eligible for expedited review (see HRPP SOP #4), the investigator must submit all materials to the IRB Staff 14 days prior to the next IRB meeting.

- c. **Primary Reviewer System:** The TVAMC IRB uses a primary reviewer system for the continuing review. The selection of the primary reviewer and the process is described in detail in HRPP SOP #2 and SOP #3. The primary reviewer uses the IRB Primary Reviewer Continuing Review Checklist to aid in the conduct of the review and document their findings. The primary reviewer reviews the complete IRB protocol file to confirm that all modifications have been approved and all reports of unanticipated events have been included in the summary documents. The primary reviewer leads the discussion at the IRB meeting. As with the initial review procedures, a primary reviewer or IRB member may request a non-voting consultant to review the materials and provide input and recommendations.
- d. **Materials Provided to and Reviewed by the IRB and R&D Committee for Continuing Review:** Prior to the convened meeting (ideally 7 days, but no less than 4 days), all members of the IRB shall be provided with sufficient information to substantially and meaningfully evaluate the proposed research, conduct the continuing review (i.e. review the IRB study file and materials submitted by the investigator), and determine appropriate action during the convened meeting. The IRB Staff prepares the agenda, assembles the materials, and distributes the agenda and materials to the IRB members. The IRB is required to conduct substantive and meaningful continuing review of research at intervals appropriate to the degree of risk, but not less than once per year.

In addition to a copy of the agenda and the previous month's minutes, the primary reviewer AND all other members receive:

- Request for Continuing Approval of Human Use form (status report), which includes a summary of safety monitoring reports, summary of subject enrollment

(including the number of subjects, gender, number of women, type of vulnerable populations, and the minority status), enumeration of subjects withdrawn and the reasons for withdrawal

- Abstract (updated with findings to date; tracked and clean copy)
- Updated protocol (tracked and clean copy) if changes have been made since initial review
- Updated Informed Consent Form (VA form 10-1086) and HIPPA authorization form, (if not previously waived)
- A summary of new knowledge that may change the risk/benefit ratio
- Advertising material, if applicable and not previously approved
- **Stamped approved copy of Abstract, Protocol, and Consent Form**
- **Table summary of all SAEs, ADEs, EAEs, UAEs, unanticipated problems involving risks to participants or others, complaints about the research, protocol deviations, and amendments or modifications with continuing review application.**
- **Site monitoring visit forms**
- **Multi-center trial reports**

The R&D Committee receives that updated Subcommittee for Research Safety form and abstract, as well information regarding the IRB decisions and actions.

e. **The focus of Continuing Review** will be:

- To assure that federally established criteria and conditions of IRB approval are being met (see IRB Primary Reviewer Continuing Review Checklist) and that there are no instances of non-compliance.
- To ensure that the currently approved or proposed consent document is still accurate and complete (or that waiver of informed consent is still appropriate)
- To assess SAEs and Adverse Events for commonalties or oddities that may suggest increased risks, reduced potential benefit, investigator error, or evidence that the TVAMC population is different than others.
- To determine if any new information regarding the research study requires an amendment or consent form revision, or if new information needs to be communicated to research subjects.
- To determine if the risks to subjects have changed.
- To approve, require modifications in (to secure approval), or disapprove/table the project.
- To determine a new Continuing Review date based on degree of risk.
- To consider past protocol violations and/or deviations, and investigator compliance, including compliance with IRB requirements for frequency of periodic Continuing Review
- To determine when projects need verification from outside sources that no material changes have occurred since previous IRB review (Such auditing activities might be prompted by complaints, observations that indicate lack of compliance, unanticipated problems, SAEs. Outside sources may include,

investigational pharmacy records, incident reports, safety reports, source documents, outside monitor reports, and information from staff, research subjects, families of research subjects, research subject surrogates, sponsors, or others.

- To determine if any significant new findings arose that might affect the participants' willingness to continue participation and if it was, or should be provided to participants.

- f. **IRB Actions at the Time of Continuing Review:** The criteria for approval of research with continuing review are the same as for initial review (see HRPP SOP #3). At the Continuing Review, the IRB decides if the research may continue, may continue with modifications, must be suspended, or must be terminated. The IRB may Approve, Contingently Approve with minor stipulations or modifications, Table, or Disapprove a study's continuation. All actions must be made by simple majority consensus of a quorum and are communicated to the PI in writing.
- g. **Communication of Findings and Actions** All actions and stipulations or modifications for contingent approvals or reasons for disapproved or tabled actions are included in a letter to the PI. All actions are communicated to the R&D Committee through verbal exchange from the IRB Coordinator and through written IRB minutes. Actions and recommendations by the R&D Committee are communicated to the TVAMC Director, thru the Chief of Staff, for his/her approval or disapproval. Once all approvals are secured, a copy of the approved consent form containing the stamped approval date is sent to the investigator and filed in the protocol files maintained by the IRB.
- h. **Expiration or Lapse of Continuing Review:** The expiration of approval is set as the due date of a Continuing Review (not to exceed one year). Any study that is approaching expiration of approval should undergo a Continuing Review in the month prior to the expiration date. When a 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 VA ORO as a suspension of IRB approval under HHS regulations. Should a lapse of approval occur, the investigator is immediately informed by the IRB Program Support Assistant or the IRB Chair and instructed to halt all research activity in that study until the IRB has conducted the Continuing Review. However, the PI may submit a memo to the IRB Chair requesting continuation for those subjects currently active in the study, if abrupt discontinuation poses a significant risk to the subject. These potential risks must be detailed in the memo. The Chair may elect to authorize continuation of those subjects already enrolled, but no new subjects can be enrolled until the IRB Continuing Review and approval is obtained. Continuing Review application must be submitted to the IRB on the following month with a response from the PI about precautions taken to reduce subject risk and the steps to prevent future lapses of approvals. Repeated occurrences of approval lapses place the investigator in serious noncompliance of IRB policies and jeopardize his/her continued privilege to conduct research. In addition, the IRB may convene an ad hoc

meeting to review a Continuing Review application to prevent lapses in approval. The IRB will report study expiration to the sponsor, if the study is a sponsored study.

- i. **Suspension or Termination of IRB Approval of Research:** The IRB may vote to suspend or terminate approval of research not being conducted in accordance with IRB or regulatory requirements or that has been associated with unexpected problems or serious harm to subjects. A suspension of approval occurs when the IRB orders the research to stop pending an action (such as an investigation into the causes of adverse outcomes). Termination of approval occurs when the IRB determines that the research study must cease. The IRB shall notify the PI in writing of such suspensions or terminations and shall include a statement of reasons for the IRB's actions. The terms and conditions of the suspension must be explicit. The investigator shall be provided with an opportunity to respond in person or in writing. Where the IRB Chair determines that such action is necessary to ensure the rights and welfare of subjects, the Chair may require an immediate temporary suspension of enrollment of new subjects or of continued participation of previously enrolled subjects, pending review of the situation by the convened IRB.
- j. **Study Closure:** The Continuing Review format will also be used for final study reporting when submitting for study closure.

## 5. **REFERENCES**

- VA Handbook 1200.5
- 38 CRF 16.109(e)
- 45 CRF 46.109(e)
- 21 CRF 56.109

## 6. **ATTACHMENTS**

- Request for Continuing Approval of Human Use form
- Primary Reviewer Checklist for Continuing Review

## 7. **RESCISSIONS**

TVAMC SOP #6 IRB Continuing Review dated May 7, 2007

## 8. **REVIEW DATE**

January 1, 2012

Signature on File in Research Office

Lori L. Davis, MD

Coordinator of Research and Development