IRB CONTINUING REVIEW

1. POLICY

The Birmingham VA Medical Center (BVAMC) 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 BVAMC 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, research investigators and the ACOS/R&D.

2. RESPONSIBILITIES

The BVAMC Director has ultimate responsibility for ensuring the protection of human research participants. The BVAMC Director is responsible for assuring the continuation of research studies based on the review and approval of the IRB and R&D Committee. The Director is responsible for taking any steps needed to assure that the IRB is free from undue pressure in discharging its responsibilities.

The Chief of Staff is responsible for consulting with the IRB or IRB chair as needed to protect participants previously enrolled in studies that have a lapse of approval or have been suspended.

BVAMC 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 is responsible for initial approval or disapproval of the actions of the IRB. The R&D Committee is not required to conduct a continuing review of studies approved by a subcommittee.

BVAMC IRB is responsible for the initial evaluation and subsequent progress reviews through continuing review of research studies involving human participants. It approves,
disapproves or tables studies, requires modifications, places restrictions on, suspends or terminates research studies and reports this 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.

3. **DEFINITIONS**

Refer to HRPP SOP #24 – HRPP Definitions

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 expires on the last day of approval at midnight. The IRB may determine and document that certain studies require review more often than annually based on the determined degree of risk at 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 is notified (by the IRB administrator) in advance of the due date; 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 expire. Errors or miscommunications on the part of the IRB will not be a cause for disapproval.

**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) **research activities including 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:

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• Continuing Review Application (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
• Updated protocol (same format as initial review) if changes have been made since initial review
• Updated Informed Consent Document and HIPPA authorization form (VA Form10-0493), (if not previously waived)
• All reported SAE’s/AE’s/UAP’s from other sites if multiple site study
• A summary of new knowledge that may change the risk/benefit ratio
• Amended or updated Investigator’s Brochure (if applicable)
• Advertising material, if applicable and not previously approved

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

c. **Materials Provided to and Reviewed by the IRB for Continuing Review:** Prior to the convened meeting 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 Administrator 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 minutes, all members receive:
• Copies of Abstract (if applicable), Protocol (if changed), and Approved Consent Form
• Table summary of all SAEs, ADEs, EAEs, UAPs, unanticipated problems involving risks to participants or others, complaints about the research, protocol deviations, and amendments or modifications with continuing review application, as applicable, including those from multiple sites if applicable.
• Copies of the Continuing Review report including the progress report
• Updated Data Security and Privacy plan (if applicable)
• Data Security Checklist
• Protocol History
• Current statements (or reports) from the data and safety monitoring board or sponsor (if applicable) indicating that it has reviewed study wide adverse events or other events to ensure the safety of participants per agreement (CRADA, if applicable).
• Statement of data and safety monitoring that was conducted for Investigator initiated studies (if applicable)
• Site monitoring visit forms, (if applicable)
• Summary of withdrawn subjects detailing why they withdrew (if applicable)
• Multi-center trial reports (if applicable)
• A statement signed by the PI certifying that all subjects enrolled into the study signed an informed consent form prior to undergoing any study interactions or interventions, unless the IRB has granted a waiver of informed consent (38 CFR 16.116(c) and (d)), or a waiver of the signed informed consent form (38 CFR 16.117(c)).

d. The focus of Continuing Review is:
• To assure that federally established criteria and conditions of IRB approval are being met 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/AE’s and UAP’s for commonalities or oddities that may suggest increased risks, reduced potential benefit, investigator error, or evidence that the BVAMC 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, this should be provided to participants.

e. 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). As part of the continuing review process the IRB may determine whether the study needs verification from sources other than the investigator that no material changes had occurred since previous IRB review and that the current consent document was still accurate and complete. 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 and documented in the IRB minutes.

f. **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. When the study has met all stipulations a letter of approval is sent to the investigator, and if applicable, with the approved consent document containing the stamped date of IRB approval. All IRB actions are communicated to the ACOS/R&D. The ACOS/ R&D will issue a letter to the Investigator acknowledging review and approval of the appropriate subcommittees of the R&D Committee.

g. **Expiration or Lapse of Continuing Review:** Any study that is approaching expiration of approval should undergo a continuing review prior to the expiration date. All studies reviewed within 30 days of their expiration date, (30 days prior to expiration not after) will maintain the same continuing review date. The date will not change, based on an early review. 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. 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 Chair and instructed to halt all research activity in that study until the IRB has conducted the Continuing Review based on materials submitted by the Investigator. The investigator may submit a memo to the IRB Chair requesting continuation for enrolled subjects currently active in the study, if abrupt discontinuation poses a significant safety concern or ethical concerns to the subject. These potential risks must be detailed in the memo. The IRB Chair, after consultation with the Chief of Staff, 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. A continuing review application must be submitted to the IRB at the next convened IRB meeting with a response from the PI about precautions taken to reduce subject risk and the steps to prevent future lapses of approvals. 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.

5. **REFERENCES**

- VHA Handbook 1200.05 Requirements for the Protection of Human Subjects in Research
- Title 38 CRF 16.109(e)
- Title 45 CRF 46.109(e)
- Title 21 CRF 56.109
6. ATTACHMENTS

Continuing Review Application

7. RESCISSIONS


8. REVIEW DATE

January 1, 2021

[Signature]

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ACOS, Research and Development