

1 SCOPE AND APPLICABILITY

- 1.1 The scope and purpose of this standard operating procedure (SOP) is to describe the policies and procedures the VA Central IRB uses for conducting continuing review and approval as required by 38 CFR 16.109e. In addition, this SOP establishes an annual status update requirement for studies for which continuing review was not or is no longer required. This SOP includes responsibilities of Principal Investigators/Study Chairs (PI/SCs), Local Site Investigators (LSIs), Coordinating Centers, and VA Central IRB members and administrative staff in completing these requirements.
- 1.2 This SOP applies to all VA investigators and their project team members who have received approval from the VA Central IRB to conduct a research project involving human participants, to include Coordinating Center staff, if applicable. In addition, this SOP applies to all the VA Central IRB members and administrative support staff who are responsible for monitoring continuing review requirements, processing continuing review requests, reviewing and approving requests, and communicating the results to investigators and local sites. It also applies to study team members and staff completing and reviewing the annual status updates as applicable.
- 1.3 Continuing review approval is required for all non-exempt studies that are greater than minimal risk that were approved under the 2018 Common Rule requirements, and for all studies approved prior to January 21, 2019, that have not been transitioned to the 2018 requirements. Sufficient information must be submitted by investigators to allow the VA Central IRB to perform a substantial and meaningful review to include the following:
- Review of the ongoing level of risks and benefits,
 - Assessment of the need for special safeguards to protect subjects, and
 - Review of the adequacy of ongoing protection for potentially vulnerable subjects.
- 1.4 Continuing review approval of research must occur **on or before** the date when VA Central IRB approval expires. When continuing review is not completed prior to the expiration of the current approval period, there is an automatic expiration of IRB approval. All research must stop unless the investigator contacts the CIRB and a VA Central IRB Co-Chair determines that it is in the best interest of individual participants to continue the research interventions or interactions.
- 1.5 Continuing review must be conducted at intervals appropriate to the level of risk, but not less than once per year for all non-exempt studies still subject to continuing review per paragraph 1.3.
- 1.6 For those non-exempt projects not subject to continuing review requirements, an annual consolidated project status update must be submitted for all active sites that details changes in personnel and the project status.
- 1.7 It is the policy of the VA Central IRB that when a project is closed or terminated, the PI/SC submit a closure report, along with a closure report for each site that has not been previously closed. When sites close prior to the PI/SC site being closed, LSIs must submit a closure report at the time of site closure.

1.8 For studies approved prior to implementation of the 2018 Common Rule requirements, the study will be considered for transition to the 2018 requirements at the time the continuing review reports are submitted to the VA Central IRB for review if it meets one of the following criteria: 1) the study is a data use and collection only study or 2) the study is closed to enrollment, has completed all interventions and follow-up activity, and is in the data analysis only stage. This does not apply to FDA-regulated studies.

2 DEFINITIONS

2.1 **Approval Period.** The period of time the VA Central IRB determines the protocol may be approved prior to a requirement for another review. The VA Central IRB may approve a study for a period of up to one full calendar year, i.e., May 1, 2019 through April 30, 2020. The approval period would expire April 30th at midnight. If the approval period is for a shorter period of time, such as six months, the approval period would encompass the full six months, i.e., May 1, 2019 through October 31, 2019. The approval period would expire on October 31, 2019, at midnight.

2.2 **Expiration of IRB Approval.** One minute after midnight on the day after the IRB approval expiration date. There is no provision for any grace period.

2.3 **Transition.** The process by which studies approved prior to January 21, 2019, that are subject to the pre-2018 Common Rule requirements, are reviewed and approved to transition in compliance with the 2018 requirements.

3 RESPONSIBILITIES

3.1 Principal Investigator/Study Chair (PI/SC). The PI/SC is responsible for:

3.1.1 Submitting continuing review applications from all participating LSIs, along with the completed PI/SC continuing review application, to the VA Central IRB by the deadline established by the VA Central IRB in order for the IRB to have sufficient time to review the applications and grant continued approval of the study prior to the expiration date.

3.1.2 Stopping all research activities if VA Central IRB approval expires, unless otherwise notified by a VA Central IRB Co-Chair that the research can continue in the best interest of the participants.

3.1.3 Submitting notification of suspension or termination of a study.

3.1.4 Ensuring sites submit local site closure reports upon closure of the project at a specific site and submitting a project closure report upon completion or termination of the study.

3.1.5 Submitting a study status report on an annual basis by the due date established by the VA Central IRB for all studies not subject to continuing review approval.

3.1.6 Notify the LSIs of upcoming expiration of the protocol.

3.2 Local Site Investigator (LSI). The LSI is responsible for:

- 3.2.1 Submitting continuing review applications and any supporting documentation to the PI/SC by the timeframe established by the PI/SC study team.
- 3.2.2 Stopping all research activities if VA Central IRB approval expires unless otherwise notified by a VA Central IRB Co-Chair that the research can continue in the best interest of the participants.
- 3.2.3 Submitting a local site closure report to the VA Central IRB upon study activities ceasing at the site.

3.3 Coordinating Center. The assigned Coordinating Center, if applicable as part of their function for a particular study, is responsible for assisting the PI/SC in collecting and evaluating data from the sites; tracking adverse events, protocol deviations, and problems involving risks to subjects or others that require reporting to the VA Central IRB in summary format; and assisting the PI/SC in preparing and submitting the PI/SC Continuing Review Application. The Coordinating Center's participation in the study will be reviewed as part of the PI/SC Application.

3.4 VA Central IRB. The VA Central IRB is responsible for:

- 3.4.1 Applying the IRB approval criteria described in 38 CFR Part 16.111 and in paragraph 12 of VHA Directive 1200.05, Requirements for the Protection of Human Subjects in Research, during the continuing review and approval process of a study. For FDA-regulated studies, 21 CFR 56.111 will also apply.
- 3.4.2 Transitioning studies to the revised 2018 Common Rule requirements in accordance with the policies and procedures set forth in this SOP.

3.5 VA Central IRB Administrative Office. The VA Central IRB administrative staff is responsible for the following:

- 3.5.1 Notifying the PI/SC prior to the current VA Central IRB approval expiration date of the continuing review requirement and providing instructions for submitting a request for continuing review or a closure report.
- 3.5.2 Ensuring all required information is received and coordinate review of the continuing review application with a voting member of the VA Central IRB via expedited review procedures or prepare it for review at a meeting of the convened IRB as applicable.
- 3.5.3 Notifying investigators and local site liaisons in writing of the results of the VA Central IRB review and documenting these as part of the VA Central IRB meeting minutes as applicable.
- 3.5.4 Notifying the PI/SC and/or LSI(s), the local site liaisons, and the sponsor if VA Central IRB approval of a project expires.

- 3.5.5 Notifying the PI/SC that an annual status report is due, reviewing the report upon receipt, and updating information in the IRB tracking system on the status of the study and changes in personnel who are to receive notices of IRB actions.
- 3.5.6 Keeping the IRB tracking system updated so that the information in the system is current and available to generate all required reports.
- 3.5.7 Reviewing PI/SC and LSI closure reports for impact on any related studies and to ensure there are no ongoing research activities which would require the study or site to remain open. Upon completion of review, report closure to the IRB and send an acknowledgement of the closure report to the site and study team as applicable.

4 PROCEDURES

4.1 Notification of Continuing Review Requirements.

4.1.1 Notification of the requirement for continuing review will be conducted as follows:

- 4.1.1.1 An electronic notice is sent through the IRB tracking system, either the Central Administrative Tracking System (CATS) or the VA Innovation and Research Review System (VAIRRS) upon implementation, to the PI/SC with instructions on how to complete and submit the request for continuing review approval no earlier than 120 days and no later than 90 days prior to the VA Central IRB expiration date of an approved research project. The due date will be 60 calendar days from the current expiration date. A copy of the notice is also sent to the Coordinating Center for those studies utilizing one.
- 4.1.1.2 The initial notification consists at a minimum of:
- Name of Study and PI/SC,
 - Current approval expiration date,
 - Deadline for submission to the VA Central IRB in order to allow time for review at a convened meeting if applicable and/or for the submission and review and approval of any required modifications prior to the current approval period expiration date (usually at least two months prior to the expiration date); and
 - VA Central IRB Form 115b, Application for Continuing Review: Local Site Investigators (Attachment 1), or VAIRRS equivalent if applicable; and
 - VA Central IRB Form 115a, Application for Continuing Review: Principal Investigator/Study Chair (Attachment 2) or VAIRRS equivalent.
- 4.1.1.3 A follow-up reminder notice is sent to the PI/SC via the IRB tracking system if a continuing review request or closure report is not received within 60 days of the expiration date. The VA Central IRB Manager then sends via e-mail another reminder notice to the PI/SC study team if a continuing review request or closure report is not

received within 30 days of the due date and then weekly thereafter until the report is received. Inclusion of PI/SC supervisory staff on emails and phone calls are made as needed to ensure timely submission.

4.1.2 Upon receipt of the notification, the PI/SC notifies the Local Site Investigators at all approved engaged sites of the submission requirement and sends them a copy of the VA Central IRB Form 115b, Application for Continuing Review: Local Site Investigator Application, or provides them instructions on how to complete an equivalent form in VAIRRS. The PI/SC must establish a submission deadline for the LSIs to submit the VA Central IRB Form 115b or VAIRRS equivalent to the PI/SC, while still allowing sufficient time for the PI/SC to review the submitted applications and prepare and submit the PI/SC Application (115a) to the VA Central IRB by the established deadline.

4.2 Local Site Investigator Applications. All participating LSIs must complete the VA Central IRB Form 115b, Application for Continuing Review: Local Site Investigators, or VAIRRS equivalent, in its entirety and submit it to the PI/SC by the established deadline date, along with any additional documents required to complete the continuing review application. All LSI applications must be signed by the LSI, or Co-LSI if applicable. Electronic signatures using the VA PIV card are acceptable.

4.2.1 Additional documents to be included in the LSI's continuing review application include, but are not limited to the following, if applicable:

Prior to the implementation of VAIRRS:

- Copy of the current VA Central IRB-approved informed consent document,
- Copy of the current HIPAA authorization,
- Copies of current HIPAA waiver and Informed Consent Waivers if approved for a site-specific purpose
- Copy of informed consent and/or regulatory audit(s) conducted by local RCO since the initial approval or last continuing review and any other reports from oversight agencies that have not been previously forwarded to the VA Central IRB, as well as copies of the VA Central IRB determination or acknowledgement letter for those reports already reviewed since the last continuing review.

After the implementation of VAIRRS, copies of the approved informed consent document, current HIPAA authorization and any approved waivers will be available in the VAIRRS system. The investigator must indicate on the reports that these are the current documents that are being used and that the study is operating under. RCO audit reports must still be submitted unless they have been uploaded into the VAIRRS platform.

4.2.2 If an LSI application is approved by the VA Central IRB after the due date set by the PI for submission of the LSI applications to the PI for inclusion in the PI/SC overall submission, then the LSI must submit (through the PI/SC) a memorandum stating nothing has changed in the approved LSI application since the VA Central IRB approval, or if there has been a change, the

LSI must state what the change is and indicate when the amendment with this change will be submitted if required. If there has been a change in personnel that does not require submission of an amendment, this can be stated in the memorandum.

4.3 Principal Investigator/Study Chair Applications. The PI/SC must complete VA Central IRB Form 115a: Application for Continuing Review: Principal Investigator/Study Chair, or VAIRRS equivalent and submit it to the VA Central IRB along with any additional documents required to complete the continuing review application. The VA Central IRB Form 115a or equivalent must be signed by the PI/SC, or a Co-PI/SC if applicable. Electronic signatures using the PIV card are acceptable.

4.3.1 Additional documents in the PI/SC's continuing review application include, but are not limited to the following, if applicable:

- Continuing review applications for all participating LSIs,
- VA Central IRB-approved protocol and an abstract addressing the subheadings as indicated on the VA Central IRB Form 115a,
- Current VA Central IRB-approved model informed consent document (VA Form 10-1086), if applicable;
- Current model HIPAA authorization,
- Current HIPAA and Informed Consent Waivers,

The above documents should be available in the VAIRRS system after implementation. The below documents must also be loaded to CATS and must still be uploaded to VAIRRS upon completion of the reports.

- Copy of informed consent or regulatory audits conducted at PI/SC's VA facility since the initial approval or last continuing review and any other reports from oversight agencies that have not been previously forwarded to the VA Central IRB,
- Summary of unanticipated problems (UAPs) and serious adverse events (SAEs) that were not immediately reportable, as well as a summary on noncompliance issues that were not immediately reportable.

4.3.2 If the PI/SC has not received a particular LSI Application by the deadline date, the PI/SC should not hold-up the entire package. The PI/SC should submit the package without the missing LSI Application and provide a reason for the delay. Enrollment figures for the site should be included in the PI/SC Application with a note that these will be verified upon submission of the LSI Application.

4.4. Administrative Screening. VA Central IRB Continuing Review staff will perform an administrative screening of the continuing review applications upon receipt that will include the following:

- That all sites that have been approved and not yet closed have submitted a completed and signed VA Central IRB Form 115b or VAIRRS equivalent. A closure report may be submitted in lieu of a continuing review report. .

- That all required documents and any additional documents have been submitted as indicated on the VA Central IRB Forms 115a and 115bs or VAIRRS equivalents.
 - If additional personnel have been added since last continuing review that their training is current and that anyone serving in an investigator role has been previously added per an IRB-approved amendment or an amendment has been submitted and is in the process of review
 - Verifying that there are no changes in conflict of interest for all study personnel serving in an investigator role since the last continuing review by verifying the responses on the VA Central IRB Form 115 or VAIRRS equivalent. If there are identified conflicts, that an OGE memorandum concerning resolution of the conflict has been submitted with the report.
 - That the protocol abstract has been updated since the last continuing review or initial approval
 - That the amendment summary table matches the record of amendment approvals on file for both the PI and LSI Applications
 - That all applicable sections on the VA Central IRB Forms 115a and 115b or VAIRRS equivalents have been completed.
 - That any submitted RCO audits have been noted and none involve apparent serious noncompliance that have not already been reviewed by the VA Central IRB. If an audit report that has not yet been reviewed by the VA Central IRB does identify apparent serious noncompliance it must be immediately forwarded to the VA Central IRB Administrator and is handled separately from the continuing review.
- 4.4.1 If any information is incomplete, missing, or requires correction, the PI study team is contacted via e-mail and asked to submit the required information as soon as possible. A record of the contact is kept in the continuing review file on the VA Central IRB shared drive. Upon implementation of VAIRRS, all such communications will be captured in the system.
- 4.4.2 If an amendment (PI or LSI) was submitted with the continuing review submission, it will be logged in separately and forward to the assigned Manager for review if it does not pertain to any action affecting the review and approval of the continuing review applications. If it does affect the continuing review application, it will still be logged in separately but will be processed with the continuing review applications.
- 4.4.3 The Continuing Review staff prepares the VA Central IRB Form 114a, Reviewer Checklist for Continuing Review (PI/SC Application) (Attachment 3) and VA Central IRB Form 114b, Continuing Review Checklist for Local Site Investigator Applications (Attachment 4), or VAIRRS equivalents, for completion by the Primary Reviewer and completes any administrative sections of the forms. If the review will involve a large number of local site investigator applications, audit reports, or other documents requiring review, or there is a significant change in the study, i.e., in the risk level, the Primary Reviewer will be consulted as to whether additional assistance is needed to conduct the review. If additional assistance is needed, an additional set of checklists will be prepared for the Secondary Reviewer, if one was assigned, or if there is none, an additional Expedited Reviewer will be assigned.

- 4.4.4 The VA Central IRB administrative staff will indicate on the VA Central IRB Form 114a or VAIRRS equivalent, whether a study requires review by the convened IRB or whether the review can be done through the expedited review process. For studies subject to the pre-2018 Common Rule requirements, the administrative staff will also indicate whether the study is eligible to be transitioned.
- 4.4.5 All LSI continuing review applications are reviewed using expedited review procedures, even if the PI/SC application is scheduled for review at a convened meeting of the IRB. However, the Reviewer can also refer one or more of the VA Central IRB Forms 115bs or VAIRRS equivalents from the local sites for a particular study to be reviewed at the convened IRB meeting, regardless of whether the PI/SC application is also being reviewed at the meeting.
- 4.4.6 If the PI/SC application requires review at a convened meeting, or any LSI Application is referred by the Reviewer for review at a convened meeting, the VA Central IRB administrative staff adds the review to the agenda of an upcoming meeting at least one meeting date prior to the expiration date or preferably two meetings prior to the expiration date if possible. If the approval period will expire prior to the next regularly scheduled convened meeting, the VA Central IRB Administrator will consult with the VA Central IRB Co-Chairs to determine if an unscheduled meeting should be called to review the action.
- 4.4.7 The VA Central IRB administrative staff will then process the applications for review by uploading the documents to the VA Central IRB SharePoint site and completing and sending a task notice to the Reviewer(s) as applicable through the SharePoint Task Manager system. If a study is eligible to be transitioned, the administrative staff will also upload a copy of the current, approved informed consent waiver. Upon implementation of VAIRRS, this will be accomplished within the system.
- 4.5 Review by the VA Central IRB. The assigned Primary Reviewer for the study is responsible for either granting continued approval for projects undergoing expedited review or for making an approval recommendation to the convened IRB for those studies to be reviewed at a meeting. When possible, the assigned Primary Reviewer will be the Primary Reviewer that was assigned to the study when it was originally approved.
- 4.5.1 The assigned Reviewer completes both the VA Central IRB Form 114a, and the associated VA Central IRB Forms 114b if applicable, or VAIRRS equivalent, during his/her review. If there are comments the study team needs to address before the Reviewer can complete his/her review, these will be sent to the VA Central IRB Manager responsible for the continuing review, who will in turn send them to the study team.
- 4.5.2 The study team must then address each comment and forward a response back to the VA Central IRB Manager. Responses can be sent via e-mail or loaded to the SharePoint Response/Update folder for the study if there are revised documents in the response. Upon implementation of VAIRRS this will be done in the system.

- 4.5.3 The VA Central IRB Manager will then review the response and, if the required revisions were only administrative in nature, the Manager may sign-off on the verification of revisions and document this using a VA Central IRB Form 152, Documentation of Administrative Review (Attachment 5), or VAIRRS equivalent.
- 4.5.4 If the required changes need to be reviewed by a voting member of the IRB, the Reviewer will be tasked by the Manager (in either VAIRRS or Sharepoint depending on the status of the VAIRRS implementation) to review the response and complete the checklists, if this was not already done, and verify that the response is satisfactory and the continuing review approval letter can now be released to the study team. If not, the above procedure will be repeated.
- 4.5.5 For studies undergoing expedited review the Reviewer will accomplish the following during completion of the checklists as applicable:
- 4.5.5.1 Determine if all of the following IRB approval criteria continue to be met:
- Risks to subjects are minimized: (i) By using procedures which are consistent with sound research design and which do not unnecessarily expose subjects to risk, and (ii) by using procedures already being performed on the subjects for diagnostic or treatment purposes whenever appropriate.
 - Risks to subjects are reasonable in relation to anticipated benefits, if any, to subjects, and the importance of the knowledge that may reasonably be expected to result.
 - Selection of subjects is equitable.
 - Informed consent is being sought from each prospective subject or the subject's legally authorized representative, in accordance with, and to the extent required by 38 CFR 16.116 and 21 CFR 56.116 as applicable, the informed consent form contains all applicable elements to include appropriate blocks for signatures and dates, and the informed consent form is consistent with the protocol and, if applicable, the HIPAA Authorization. *Note: Alternatively, IRB-approved waivers could be in place.*
 - Informed consent is appropriately documented, in accordance with, and to the extent required by 38 CFR 16.116, 21 CFR 56.116, and VHA Handbook 1200.05. *Note: Alternatively, an IRB-approved waiver can be in place.*
 - The research plan makes adequate provision for monitoring the data collected to ensure the safety of subjects.
 - There are adequate provisions to protect the privacy of subjects and to maintain the confidentiality of data.
 - VHA and VA information security policies pertaining to research have been implemented and are continually monitored to ensure compliance as set forth in VA Directive 6500 and 6501.
 - When some or all of the subjects are likely to be vulnerable to coercion or undue influence, such as children, prisoners, pregnant women, individuals lacking decision making capacity, economically or educationally disadvantaged persons, VA employees and students, or any others whom may be at increased susceptibility to harm, additional safeguards have been included in the study to protect the rights and welfare of these subjects.

- The investigators are qualified to perform the research, all required training is up-to-date, and there have been no new conflicts of interest identified.
- 4.5.5.2 For those studies subject to the 2018 Common Rule requirements that had been eligible for expedited review at the time of initial approval, but continuing review approval was mandated, the Reviewer must determine whether continuing review is still required. If it is still required, a justification for the continuing review and approval requirement must be provided by the Reviewer.
- 4.5.5.3 For studies subject to the pre-2018 Common Rule requirements, the Reviewer must determine whether the study now meets one of the below two requirements:
- The study is a data use only study for which there are no consent forms or participant interventions.
Or
 - The study is in data analysis only and all participant interventions and follow-up actions have been completed.

For studies that meet one of the above criteria, they are eligible to be transitioned to the 2018 requirements. However, if the study is FDA-regulated, it may not be transitioned. *See paragraph 4.8 for procedures when studies are transitioned.*

- 4.5.5.4 After the checklist has been completed the Reviewer will make a final determination regarding the study. At any time during the review process, the Reviewer can refer a project undergoing expedited review for review at a convened IRB meeting or to one of the VA Central IRB Co-Chairs for consultation. If this is done, the Reviewer will notify the VA Central IRB Manager for the study and the Manager will add the study for review to the next available meeting agenda or task the applicable Co-Chair with the review as applicable. The Reviewer cannot disapprove the study. If the Reviewer recommends the study be disapproved, the study must be added to the next meeting agenda for review by the convened IRB.
- 4.5.5.5 Once the checklists are completed, the Reviewer must sign both the PI and LSI checklists if applicable. Electronic signatures using PIV cards are acceptable. The Reviewer then closes out the task which then alerts the assigned VA Central IRB Manager that a final decision has been made regarding the study.
- 4.5.6 For studies reviewed by the convened IRB, the following actions will be taken:
- 4.5.6.1 Upon receipt of the completed checklists from the Reviewer, the assigned VA Central IRB Manager will load all finalized documents to the SharePoint file for the meeting at which the study is scheduled to be reviewed. Upon implementation of VAIRRS, these will already be in the system.

4.5.6.2 At the meeting, the Reviewer will brief the members on the contents of the submitted reports, any problems identified and resolved during the review, and any problems remaining that need to be addressed by the Board. The IRB may require verification of project requirements from some source other than the Local Site Investigator. Some examples of when this may occur include if there has been non-compliance with project requirements in the past, if the site has experienced some unanticipated problems, or if there have been participant or other complaints from the site.

4.5.6.3 Upon completion of discussion the Board reviews the same approval criteria as referenced in paragraph 4.5.5.1 and makes one of the following determinations:

- Approved. No modifications required. The study continues to meet all approval criteria.
- Approved contingent upon required minor modifications. Stipulated minor modifications not affecting the approval criteria must be made and submitted for review by a reviewer designated by the IRB.
- Deferred for Major Modifications. This may be used when changes, that cannot be stipulated, are required that are directly relevant to the required determinations that must be made by the VA Central IRB based on the IRB approval criteria, or in the course of review it is discovered that information central to the review is missing. The investigator must submit a response with the changes in time for review by the convened VA Central IRB prior to the current approval expiration. If the approval period expires during the deferral period, procedures as detailed in paragraph 4.7 will be followed.
- Table. This may be used if a consultant is unable to attend the meeting to lend expertise to the review, or the IRB loses quorum, or any situation where the IRB is unable to review the report.
- Suspension or Termination. If this is recommended the procedures in VA Central IRB SOP 107, Review of Reportable Events and Other Reported Issues, must be followed.

4.5.6.4 If any LSI applications were referred for review by the convened IRB, the same process will take place. If more than one LSI application was referred for review, each one will be considered separately and can be voted on either together or separately.

4.6 Approval Expiration Date. The VA Central IRB continuing review approval expiration date is the last date the study can be conducted without further VA Central IRB approval.

4.6.1 If the VA Central IRB performs and completes the review within 30 days before the original expiration date of the current IRB approval period, the VA Central IRB can retain the original anniversary date (day and month) as the date for the next IRB approval expiration date of the study. This includes studies reviewed via expedited procedures and by the convened IRB. All LSI applications receive the same continuing review approval expiration date regardless of the date when the LSI continuing review application was approved.

- 4.6.2 If the project is approved outside the 30-day window, the new continuing review approval period will be set as the day prior to the day of the final approval of the next calendar year, whether approval was at a convened meeting or the approval is via expedited review (if a one year approval period is granted). The final date of approval is the date the Reviewer signed the Reviewer checklists indicating approval for studies undergoing expedited review and the date of the meeting for studies approved at the convened IRB.
- 4.6.3 When the IRB approves the research with conditions at the time of continuing review before the expiration date of the preceding approval period, the current IRB approval does not expire, even if the investigator needs additional time to satisfy some or all of the conditions. The IRB will establish a date by which the investigator must respond to the conditions and will then determine if the conditions are met or other action needs to be taken. If the investigator does not respond in a timely manner, the IRB may take additional action, such as suspension of enrollment and/or study activities.
- 4.7 Expiration of Approval. If a PI/SC has not provided continuing review application materials to the VA Central IRB, or the VA Central IRB has not approved or conditionally approved the PI/SC continuing review application by the IRB approval expiration date, the VA Central IRB approval automatically expires and all research activities must stop, including data analysis of personally identifiable information. No enrollment of new participants can occur.
- 4.7.1 If the PI/SC continuing review application is not approved by the VA Central IRB approval expiration date, all research activities by the PI/SC and LSI(s) must stop.
- 4.7.2 If an LSI continuing review application is not approved by the VA Central IRB approval expiration date, all research activities under the study at that site only must stop.
- 4.7.3 The PI/SC, or LSI as applicable, must immediately submit to the VA Central IRB Co-Chair a list of participants for whom stopping or interrupting interventions or interactions would cause harm, as well as the name of the Chief of Staff at the participating VA Facility(s). The VA Central IRB Co-Chair must determine within two business days whether it is in the best interests of individual participants to continue participating in the study.
- 4.7.4 The VA Central IRB will notify the PI/SC, the sponsor funding the project, affected participating sites, and affected LSIs of any expirations of study approval. Correspondence will be prepared by the VA Central IRB administrative staff to be reviewed and signed by the VA Central IRB Co-Chair. Correspondence will then be disseminated to the study teams and local site officials as applicable.
- 4.7.5 If the expiration occurred due to non-submission of the continuing review applications by the PI/SC or LSI, the PI/SC or LSI may submit the request for continuing review application, along with a justification for the delay in submission, up to 30 days after the expiration of approval date in order for the review to still be conducted by the VA Central IRB. If the expiration only affected a particular site(s), the LSI Application must be submitted through the PI/SC's office.

After the 30 days have elapsed, the project or site will be considered noncompliant and the Board will proceed in accordance with VA Central IRB SOP 107 and consider the study or site for termination. If study or site termination is not in the best interest of participants, the study may be continued until the participants have safely completed the study or can be withdrawn but no new enrollment can take place.

4.7.5.1 If the PI/SC wants to re-open a study that expired and it has been over 30 days since the expiration occurred, a new PI/SC study application must be submitted, or the PI/SC can consult with the VA Central IRB Administrative office, who will then consult with the Reviewer and VA Central IRB Co-Chairs regarding any documentation that may be required, in addition to the continuing review application, for the review to take place.

4.7.5.2 If an LSI wishes to re-open the study that expired at their site and it has been over 30 days since the expiration occurred, the PI/SC must concur and consult with the VA Central IRB Administrative Office regarding any additional submission requirements for that site.

4.7.6 If the PI/SC submitted all the required documents by the expiration date, but the approval period expires, all the actions as described in paragraphs 4.7.1 through 4.7.4 must still take place. The VA Central IRB will review the submitted materials as soon as practicable.

4.8 Transition of Studies. For studies that meet the criteria for transition in accordance with paragraph 4.5.5.2, the Reviewer completes that portion of the checklist pertaining to the review requirements for transitioning the study. This includes the following:

4.8.1 The Reviewer must indicate on the checklist that the study is approved or not approved for transition. If not approved for transition, the Reviewer must provide justification for not transitioning the study.

4.8.2 If approved, the Reviewer must also determine if the study has an informed consent waiver that must be re-approved under the revised 2018 approval criteria for informed consent waivers. Projects that had an informed consent waiver for recruitment only do not have to have the informed consent waiver re-approved as one of the criteria for transitioning a study is that enrollment has closed, and the study is in data analysis only.

4.8.3 Projects that are still actively collecting and accessing data under an informed consent waiver and or projects that are still analyzing identifiable data and/or specimens under the current waiver (there is no consent form or waiver of documentation of consent form) must have the waiver re-reviewed using the current 2018 informed consent waiver approval criteria. This waiver criteria are indicated on the VA Central IRB Form 114a or VAIRRS equivalent. The Reviewer must indicate which set of criteria the informed consent waiver meets if approving the waiver or the Reviewer must indicate how the informed consent waiver needs to be modified to meet current requirements.

4.9 Notice of Continuing Approval and/or Transitioning of the Study Sent to Study Teams and Sites. Upon continued approval, and transitioning if applicable, the VA Central IRB administrative staff will accomplish the following:

4.9.1 For studies that receive continuing review approval via expedited review and the studies are not eligible for transition, the VA Central IRB administrative staff will verify that the Reviewer checklist has been appropriately completed and signed. If the checklist was previously signed indicating approval once minor issues were addressed, the Reviewer may indicate via e-mail that those issues were now addressed and the study approved. The VA Central IRB administrative staff then drafts the PI/SC approval letter through the electronic system. The approval letter will be addressed to the PI/SC/Co-PI/SC(s) and indicate at a minimum the following:

- Continued approval of the study
- What expedited review categories pertain to the study, if applicable
- The new continuing review period
- Risk level
- Acknowledgement of any audit reports reviewed and staff additions and departures that were reported at continuing review
- Version date of currently approved master informed consent form if applicable
- List of documents that will be added to SharePoint with approval letter. Upon implementation of VAIRRS, this will already be in the system.

A separate approval letter addressed to the local LSI/Co-LSI(s) of each approved site indicating the above information specific to their site will also be prepared.

4.9.2 For studies that receive continuing review approval via expedited review and are also approved for transition, the VA Central IRB administrative staff verify that the Reviewer checklist has been appropriately completed and signed. If the checklist was previously signed indicating approval once minor issues were addressed, the Reviewer may indicate via e-mail that those issues were now addressed and the study approved. The VA Central IRB administrative staff then drafts the approval and notice of transition letter through the electronic system. The approval letter will indicate at a minimum the following:

- Continued approval of the study
- Listing of all participating sites whose applications were also reviewed
- An acknowledgement of any audit reports received and staff additions and departures for the PI/s site
- Criteria under which the study was transitioned
- Re-review and approval of the informed consent waiver if applicable

Separate letters will not be generated for each local site. However, all LSIs/Co-LSIs will be copied on the approval letter to the PI/SC.

4.9.3 For studies reviewed and granted continued approval at the convened IRB, the approval letter can be generated in the electronic system if using VAIRRS or can be done separately. These letters will be addressed to the PI/SC/Co-PI/SCs and contain at a minimum the following:

- Continued approval of the study
- The new continuing review period
- Risk level
- Acknowledgement of any audit reports reviewed and staff additions and departures that were reported at continuing review
- Version date of currently approved master informed consent form if applicable
- List of documents that will be added to SharePoint with approval letter. Upon VAIRRS implementation, these will already be in the system.

Separate letters will be issued for any LSI applications that were also reviewed at the convened IRB meeting, as well as those that were reviewed via expedited procedures. One of the VA Central IRB Co-Chairs must sign all letters that were reviewed at a convened meeting or, upon implementation in VAIRRS, document approval.

4.9.4 Once the approval letters have been finalized, an e-mail is generated through the electronic system or manually and sent to all addressees that are listed in the electronic system as getting notifications of a study action. This includes not only the PI/SCs and LSIs but also the study coordinators, coordinating center program managers, and VA Central IRB site liaisons for all the sites at which the study is open. Sample letters are available as needed and/or can be generated through the electronic system. Documents are then uploaded to the Continuing Review study folder on SharePoint (CATS only) and the e-mail is sent. Copies of the letter and the e-mail are filed in the applicable study folder on the shared drive. Upon implementation of VAIRRS all of the above will be done and stored within the VAIRRS platform. A paper copy is made for all FDA-regulated studies and filed, along with a paper copy of all the study documents and checklists until the VAIRRS platform is in place and then all documents will be maintained on the electronic system that is 21 CFR 11 compliant.

4.10 Status Reports. For all non-exempt studies that are still active and open but that are not subject to continuing review or that were transitioned, in lieu of a continuing review report, the PI/SC study team will be required to submit VA Central IRB Form 130, Status Report for Studies Not Subject to Continuing Review Approval (Attachment 6) or VAIRRS equivalent. The procedures regarding sending notices when the report is due, submission of the report, and review of the report are as follow:

4.10.1 VA Central IRB administrative staff will send notification to the PI/SC study team on a no less than annual basis through CATS or the VAIRRS platform and set a due date 30 days from the date the notice is sent. As part of this notification, the VA Central IRB administrative staff will provide lists of all PI/Co-PIs, LSIs/Co-LSIs, national study coordinators, local site coordinators, and CSP program managers that the VA Central IRB currently lists in the electronic system as receiving notices on study actions.

- 4.10.2 The PI/SC study team can choose to submit a summary report to include all sites on one report or it can ask each individual site to submit a report to the PI/SC study team which can then be submitted with the PI/SC report. The PI/SC team would then not have to summarize the information on one report if this option is used.
- 4.10.3 Upon receipt of the report(s), the VA Central IRB administrative staff will accomplish the following:
- 4.10.3.1 Verify there were no changes in personnel that required an amendment and update the electronic system concerning any departures or arrivals who will need to receive study notifications.
- 4.10.3.2 Check the reports to see if any audit reports, amendments, or other reports were also submitted. If there were, the reports will be reviewed to determine if there are any findings. If there are findings that require review by the IRB, actions will be taken per VA Central IRB SOP 107. If there are no findings or no findings requiring any action, the reports will be filed with the status report in the study folder.
- 4.10.3.3 Bi-weekly follow-up reminders will be sent to the study team if a status report has not been received. If, after 60 days, a report has still not been received the matter will be referred to the convened IRB for review as noncompliance with VA Central IRB policies and procedures and the review will be conducted in accordance with VA Central IRB SOP 107, Review of Reportable Events and Other Reported Issues.
- 4.11 Project Closure. Upon completion or termination of an approved project, the PI/SC must submit a VA Central IRB Form 117a, Project Closure Report (Attachment 7) or VAIRRS equivalent, to the VA Central IRB. This should be done when the study is completed. The study team should not wait until the next continuing review or status report is due.
- 4.11.1 The VA Central IRB Administrative staff will review the submitted report to ensure it is complete. If not, comments will be sent to the LSI or PI/SC as applicable to address. The VA Central IRB Administrative staff may consult with the Primary Reviewer or a VA Central IRB Co-Chair if needed to resolve any issues.
- 4.11.2 Once all issues are resolved, the VA Central IRB Administrative staff documents on the VA Central IRB Form 152 that any issues identified were resolved (CATS only), closes the study in the system, and sends the PI/SC an acknowledgement and concurrence memorandum indicating that the VA Central IRB considers the study to be closed. The closure action is reported at the next convened meeting of the VA Central IRB as part of the expedited listing.
- 4.11.3 If only the participation of a local site is closed or terminated, the LSI completes a VA Central IRB Form 117b, Local Site Project Participation Closure Report (Attachment 8) or VAIRRS equivalent. Upon submission, the VA Central IRB Administrative staff review the report for completeness and sends any comments to the study team if the report is not complete or if there

are questions. VA Central IRB Administrative staff may consult with the Primary Reviewer or VA Central IRB Co-Chair as needed. Upon resolution of all issues, the VA Central IRB administrative staff document on a VA Central IRB Form 152 that all issues were resolved or there were no issues (CATS only), close the site in the system, and sends an acknowledgement and concurrence memorandum indicating that the VA Central IRB considers the study at that site to be closed to the LSI, PI/SC study team, and to the local site liaison. The site closure action is reported at the next convened meeting of the VA Central IRB. If applicable, the closed paper VA Central IRB project files are then archived in accordance with VA Central IRB SOP 109, VA Central IRB Documentation, Program Evaluation, and Quality Assurance Requirements.

- 4.11.4 On the rare occasion when a previously closed site needs to re-open again, the PI must submit a signed memorandum detailing the reason for the site to re-open and include appropriate justification. This will be forwarded to the Reviewer of the study for a recommendation to approve the re-opening or not. The Reviewer's recommendation will be sent to one of the VA Central IRB Co-Chairs for concurrence. If the Co-Chair approves the re-opening of the site(s), a letter will be drafted for the signature of the Co-Chair to the PI/SC and the LSI. The LSI must still be at the site and willing to have the site re-opened or an amendment submitted with the re-opening request to appoint a new LSI. Once the site is ready to close again, a new closure report must be submitted and processed in accordance with paragraph 4.11.3.

5 DOCUMENTATION REQUIREMENTS

- 5.1 Continuing review approvals, disapprovals and other determinations are documented on the applicable VA Central IRB forms or letters or VAIRRS equivalents and archived or stored in accordance with VA Central IRB SOPs and VHA and federal requirements.
- 5.2 Records on closed studies will be stored in separate folders from the active folders on the shared drive and in the VA Central IRB SharePoint system while using CATS for tracking. VAIRRS will continue to store all study documents but show the study status as closed. Paper files will be maintained in separate storage from the active files and kept in accordance with the VA Records Control system until destruction is authorized.

6 REFERENCES

- 6.1 38 CFR 16, Department of Veterans Affairs, Protection of Human Subjects
- 6.2 VHA Directive 1200.05, Requirements for the Protection of Human Subjects in Research
- 6.3 21 CFR 56, U.S. Food and Drug Administration, Institutional Review Boards
- 6.4 Office for Human Research Protections January 15, 2007 Guidance on Continuing Review
- 6.5 VHA Directive 1605.1, Privacy and Release of Information



VA Central IRB Continuing Review Requirements, Annual Status Updates, and Project/Site Closures

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Supersedes SOP 112

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As the responsible authority delegated by the VHA Central Office Institutional Official for administrative oversight of the VA Central IRB, I have reviewed and approved the contents of this VA Central IRB Standard Operating Procedure.

Mary M. Klote, MD
VHA Human Protections Administrator
Office of Research and Development

Attachments:

1. VA Central IRB Form 115b, Application for Continuing Review: Local Site Investigators
2. VA Central IRB Form 115a, Application for Continuing Review: Principal Investigator/Study Chair
3. VA Central IRB Form 114a, Reviewer Checklist for Continuing Review (PI/SC Application)
4. VA Central IRB Form 114b, Continuing Reviewer Checklist for Local Site Investigator Applications
5. VA Central IRB Form 152, Documentation of Administrative Review
6. VA Central IRB Form 130, Status Report for Studies Not Subject to Continuing Review Approval
7. VA Central IRB Form 117a, Project Closure Report
8. VA Central IRB Form 117b, Local Site Project Participation Closure Report