

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 administrative staff and VA Central IRB members follow when processing and reviewing submitted requests to amend, modify, or update projects that have already been approved by the VA Central IRB. It also includes requests for one-time protocol exceptions. It does not include review of amendments submitted for studies that have been previously exempted. Refer to VA Central IRB SOP 102, Requests for Exemptions and Requests for Determinations of Human Subjects Engagement.
- 1.2 This SOP applies to all research involving human participants that was submitted by VA investigators for review by the VA Central IRB, was approved, study coordinators, and any other study personnel involved in submitting an amendment. It also applies to VA Central IRB members and to the VA Central IRB administrative support staff.
- 1.3 It is the policy of the VA Central IRB that amendments or modifications in research projects may not be initiated without prior review and approval by the VA Central IRB, except where necessary to eliminate apparent immediate hazard to human participants.
- 1.4 Requests to amend, modify, or update an approved project may be submitted to the VA Central IRB at any time during the current approval period or, for those studies not subject to continuing review, as long as the study or a site have not been closed. This also applies to requests for protocol exceptions. Amendments should only be submitted in conjunction with a continuing review report if the amendment is addressing a deficiency found during preparation of the report and approval of the amendment may have a bearing on the continuing review approval. Otherwise, all amendments submitted with a continuing review application will be separated from the continuing review and processed separately.
- 1.5 For those studies still subject to continuing review requirements, the date when the current IRB approval period for a project expires is not changed based on the approval date of an amendment.
- 1.6 It is the policy of the VA Central IRB that an expedited review procedure may be used to review amendments (modifications) to previously approved research as follows:
 - 1.6.1 Modifications to projects previously approved by the convened VA Central IRB may be reviewed via an expedited review process if they do not pose an increased risk to participants and the modifications constitute a minor change to previously approved research. Examples of minor changes that can be reviewed under the expedited review process include but are not limited to:
 - Minor consent form changes
 - Minor changes to recruitment procedures, recruitment materials, or submission of new recruitment materials to be used in accordance with approved recruitment methods
 - Minor changes to project documents such as surveys, questionnaires, or brochures
 - New project documents to be distributed to or seen by participants that are similar in substance to those previously approved
 - Changes in payment to participants or the amount participants are paid that are not significant enough to affect the risk/benefit ratio of the project

- An increase or decrease in the number and volume of participants or specimen collections as long as they do not negatively affect the risk/benefit ratio or scientific methodology of the project
- Changes that clarify but do not alter the existing meaning of a document
- Addition or deletion of a site as long as the total number of participants to be enrolled remains the same.
- Minor changes in study procedures that do not affect the overall risk/benefit ratio of the study.

1.6.2 Modifications to projects previously approved by the VA Central IRB under the expedited review process may continue to be reviewed via expedited review, if the research continues to pose no more than minimal risk to human participants and the modifications continue to fall under expedited categories 1-7. If a proposed amendment increases risks beyond minimal or introduces procedures not qualifying for expedited review under categories 1-7, the amendment, along with all associated project documentation will be reviewed by the convened IRB.

1.6.3 A Reviewer cannot disapprove an amendment under the expedited review process. A Reviewer must defer review of an amendment otherwise qualifying for expedited review to review by the convened IRB if the Reviewer determines the amendment should not be approved or if the Reviewer has significant concerns and wants the convened IRB to address the issues. The Reviewer may also consult the VA Central IRB Co-Chairs prior to making a deferral decision.

1.7 If the amendment includes a biosafety or radiation safety issue the VA Central IRB cannot grant final approval to the amendment unless the amendment has been granted approval by the applicable committee at the local site and documentation of such approval has been received.

1.8 If an informed consent approved by the VA Central IRB prior to January 21, 23019, requires modification, the general requirements described in VA Central IRB SOP 103, New Project Application Requirements, paragraphs 4.4.6 and 4.4.7 are not applicable unless the study has been transitioned to the 2018 requirements. The VA Central IRB does not plan to transition any studies approved prior to January 21, 2019, that are still in the process of recruiting and consenting participants.

2 DEFINITIONS

2.1 **Expedited Review.** In contrast to a convened IRB review process, the expedited review process consists of a review carried out by the IRB Chair or by one or more experienced voting members of the IRB designated by the IRB Chair in accordance with 38 CFR 16.110(b).

2.2 **Investigator.** Any individual who conducts research including, but not limited to, the Principal Investigator (PI), sub-investigator or co-investigator, and Site Investigator or Local site Investigator (LSI). All VA investigators on a VA research study or program must hold a VA appointment. (VHA Directive 1200.05)

2.2.1 **Principal Investigator (PI).** The PI is a qualified person who directs a research study or program. The PI oversees scientific, technical, and day-to-day management of the research. If a study is conducted by a team of individuals, the PI is the responsible leader of that team.

2.2.2 **Sub-Investigator or Co-Investigator.** A qualified person designated by the PI or LSI to perform critical research procedures and/or to make important research-related decisions. Both terms are interchangeable. These investigators are key personnel on a research study or program.

2.2.3 **VA Investigator.** Any individual who conducts research while acting under a VA appointment, including full and part-time employees, without compensation (WOC) employees, or individuals appointed or detailed to VA under the Intergovernmental Personnel Act (IPA of 1970 (5 U.S.C. 3371 et seq.)). Individuals working under a contract with VA cannot conduct research as VA investigators under a WOC appointment while simultaneously working as a contractor.

2.3 **Minimal Risk.** The probability and magnitude of harm or discomfort anticipated in the research are not greater in and of themselves than those ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests (38 CFR 16.102(i))

2.4 **Protocol Exception.** A protocol exception is a type of planned modification to an approved research project that involves a single subject or a small group of subjects, and the modifications requested do not represent permanent changes to the research project.

2.5. **Reviewer.** An IRB voting member who provides a written review of a submitted project action and/or, for study actions being reviewed under expedited review procedures, grants approval to the action. *Note: The VA Central IRB uses a Primary Reviewer system in which there can be a Primary Reviewer, Secondary Reviewer, and Informed Consent Reviewer. The Privacy and Information Security Officer Representatives, as well as VA Central IRB administrative staff, can also provide written reviews but are not voting members of the VA Central IRB and cannot approve study actions, with the exception of some exemption requests. See VA Central IRB SOP 104, VA Central IRB Review Requirements for New Project Applications (Expedited and Convened) for further definitions of each type of Reviewer and VA Central IRB SOP 102, Requests for Exemption and Determinations of Human Subjects Research Engagement.*

2.6 **Update.** An update is an administrative change in study documents that does not require review and approval by a voting member of the VA Central IRB. This includes but is not limited to such issues as changes in phone or room numbers; correction of formatting issues or obvious typographical errors; or implementation of an approved PI amendment change in LSI-specific documents with no further changes in those documents.

3 RESPONSIBILITY

3.1 **PIs and LSIs.** Both PIs, and LSIs as applicable for their specific site, are responsible for ensuring that all proposed changes to an approved project, or an approved local site application as applicable, are submitted for review in accordance with this SOP prior to initiating any such changes. The only exception is if the change is necessary to eliminate any apparent hazard to human participants. If this is the case, the VA Central IRB should immediately be informed via telephone or e-mail and an amendment or protocol exception requesting the change be submitted within 5 work days. The VA Central IRB staff will consult with a VA Central IRB Co-Chair to determine if a protocol deviation or SAE/UAP report should also be submitted.

- 3.2 VA Central IRB. Assigned VA Central IRB voting members for reviewing all requests to amend or modify an approved project or for a protocol exception in a timely manner via the expedited review process or by the convened IRB; making appropriate approval determinations; and communicating the results of the determinations to the investigators and local participating sites in writing.
- 3.3 VA Central IRB Administrator. Responsible for assisting investigators with meeting VA Central IRB amendment and modification requirements, maintaining the VA Central IRB website, and for ensuring all policies, procedures, and forms pertaining to the research project amendment or modification process are kept current and up-to-date. The VA Central IRB Administrator also tracks the timeliness of amendment and modification processing and ensures all amendments or modifications approved under the expedited review process, with the exception of updates, are reported at the next convened meeting of the VA Central IRB.
- 3.4 VA Central IRB Managers. Responsible for reviewing and processing for approval all requests for amendment, modification, or update of their assigned studies, to include protocol exceptions in accordance with this SOP. This includes performing administrative reviews, preparing Reviewer checklists, sending comments from reviewer to the study team, and reviewing and processing the study team responses. The VA Central IRB Managers also prepare and send out the amendment, modification, or exception approval letters and e-mails, as well as update verification e-mails. The VA Central IRB Managers ensure appropriate upload of all documents to the applicable SharePoint folder and that all documents are filed appropriately on the VA Central IRB shared drive and/or in applicable paper folders for FDA-regulated studies.

4 PROCEDURE

- 4.1 Who Can Submit an Amendment, Modification, or Exception Request. Both the PI/SC (Co-PI/SCs) and the LSI (Co-LSIs) of a VA Central IRB-approved project can submit an amendment, modification, or exception request as detailed below.
- 4.1.1 The PI/SC submits an amendment request when there is a change in how the overall project will be conducted. This can include, but is not limited to, the following:
- Change in project design or procedures;
 - Change in participant population and enrollment target numbers, to include increasing the number of VA sites that will be participating in the project;
 - Change in risk/benefit analysis;
 - Changes in recruitment strategy and/or participant payment procedures;
 - Changes in informed consent procedures or document content;
 - Changes in data collection and storage procedures, to include data banking;
 - Change in PI/SC, Co-PI/SCs, anyone serving in an investigator role, or anyone mentioned by name in the protocol, informed consent, recruitment materials, or other study documents in which current point of contact information is essential; and
 - Change in other study team members when required by the VA Central IRB or the local Research and Development Committees.

- 4.1.2 The LSI submits a request for amendment or modification for the local participating site when there is a site-specific change. These can include, but are not limited to, the following:
- Change in LSI or Co-LSIs;
 - Change in local study team members when serving in an investigator role or when mentioned by name in the informed consent or other study documents where current point of contact information is essential, or when required by local R&D policies or by the VA Central IRB;
 - Changes in local site approved recruitment material specific to that site;
 - Changes in the local site approved informed consent document specific to that site;
 - Changes in resources available at the site to support the project;
 - Changes in state laws or local requirements;
 - Changes in data collection and storage procedures, to include tissue banking specific to that site; or
 - Changes in the local site VA Form 10-9012, Investigational Drug Information Record.
- 4.1.3 Changes in other key study staff not mentioned in paragraphs 4.1.1 and 4.1.2 must be reported at the time of continuing review on the VA Central IRB continuing review application requests for PI/SCs and LSIs for studies being overseen by the VA Central IRB. For those studies no longer subject to continuing review, changes in study personnel who normally receive a copy of VA Central IRB communications must be reported to the applicable VA Central IRB Manager via e-mail so the applicable updates to the study point of contact section of the tracking database can be made. Otherwise, changes in personnel not referenced in 4.1.1 and 4.1.2. do not need to be reported.
- 4.1.4 The PI/SC or LSI submits a request for an exception when there is a specific change that involves a single subject or a small group of subjects only and that is a one-time occurrence for this subject or group of subjects. This can include, but is not limited to the following:
- Change to participant eligibility criteria for a specific subject(s);
 - Change to the procedures used to dispense drugs or devices for a specific subject(s);
 - Change to the timing of study visits or procedures for a specific subject(s); or
 - Requests for continuation of study activities for subjects when a study is suspended or whose approval has lapsed
- 4.1.5 Changes in items such as phone or room numbers, correction of typographical errors, formatting issues, or other minor changes that do not change any of the approved content, are processed as updates and not amendments. The national or local study coordinators submit the updated documents (clean and tracked) with an explanation via a memo or an e-mail describing what needs to be updated and why. If there are a large number of documents that will need to be updated, the updates can be submitted to the Study Team Response and Update folder under the Study folder on the VA Central IRB SharePoint site. These will be processed as administrative updates and not as amendments requiring review by a voting member of the VA Central IRB.

4.2 Completion and Submission of an Amendment Request. When an PI/SC or LSI requests an amendment to an approved project, VA Central IRB Form 116 (Attachment 1), Request to Amend or Modify an Approved Project, must be submitted.

4.2.1 The amendment or modification request must include the following information:

- Type of amendment or modification (PI/SC or LSI);
- Description of the amendment or modification;
- Reason or rationale for each change;
- The anticipated impact on risk-benefit ratio for participants;
- Whether modifications to the informed consent form are needed; and
- Whether it is appropriate to inform participants who have already consented to participate in the project of the changes and/or whether a re-consenting process is requested.

4.2.2 PI/SC amendments to a specific study will be assigned a number in chronological order for each amendment received. Each site amendment will also be assigned a number in chronological order.

4.2.3 The PI/SC or LSI will upload a signed electronic copy of the VA Central IRB Form 116 and all associated documents to the “Initial Submission” folder on the VA Central IRB secure SharePoint site and send an e-mail message to the VA Central IRB mailbox when the submission is complete. Instructions for uploading are available on the SharePoint site. The amendment request and associated documents can also be sent by encrypted e-mail if there are problems with the SharePoint system at the time. If the amendment or modification requires review by the convened VA Central IRB, it is recommended that the documents be submitted no later than 15 working days prior to a scheduled meeting. There is no guarantee that the amendment will be scheduled for review at the next meeting if this submission time is met, particularly if the Reviewer requests clarifications or requests additional documentation. If the amendment or modification and associated documents are submitted later than this, the review may still occur at the intended meeting if the members have sufficient time to receive and review all the documentation. This will be left to the discretion of the VA Central IRB Administrator, assigned VA Central IRB Reviewer and the VA Central IRB Co-Chairs.

4.3 Completion and Submission of Associated and/or Other Documentation. In addition to completing the VA Central IRB Form 116, or in lieu of it, the PI/SC or LSI submits the following documents if applicable for the type of change being requested. When making a change to any currently approved document, the study team must submit a copy with the changes highlighted (or a MS Word tracked changes file) and a clean copy for the official project file.

4.3.1 To add additional new participating sites over the number of sites that was previously approved, the PI/SC submits a VA Central IRB Form 116 while the new site(s) submits a VA Central IRB Form 104, Local Site Application and associated documents.

4.3.1.1 The site must have an active Memorandum of Understanding (MOU) on file with the VA Central Office HRPP in order for the site application to be reviewed by the VA Central IRB.

If no MOU is on file, the VA Central IRB administrative staff will contact the site to assist them in processing the MOU.

4.3.1.2 A VA Central IRB Form 116 does not have to be submitted by the PI if a new site has been identified to replace a site that dropped out before submitting an application, an application was submitted and then withdrawn, or the site was approved but then closed prior to enrolling subjects, as long as the number of VA sites currently approved is not exceeded. A memorandum from the PI or study coordinator explaining the change is sufficient. The new local site would then just submit the VA Central IRB Form 104 or 104b and associated documents.

4.3.2 If there is a change in PI/SC, the addition of a Co-PI/SC, or the PI/SC changes VA sites, a VA Central IRB Form 134a, Change in Principal Investigator/Study Chair (Attachment 2) must be submitted in lieu of the VA Central IRB Form 116, along with a current curriculum vitae or bio sketch; a VA Central IRB Form 102, Local ACOS/R&D Review Supplement; and a COI determination from the PI/SC site or a current OGE Form 450-VA Alternative, Research Financial Conflict of Interest. Copies of all modified forms or other documentation in which the PI/SC is named must also be submitted. If there was a change in PI/SC site and the site is no longer participating in the study due to this change, then a VA Central IRB Form 117b, Local Site Project Participation Closure Report should also be submitted.

4.3.3 If the proposed amendment or modification involves the informed consent or conveying new information, the PI/SC or LSI must indicate whether participants who have already consented to participate need to be re-consented and/or informed. A copy of the new, revised consent form with the changes highlighted, preferably through the use of the MS Word track change function, and a clean copy of the new, revised consent form to be used by the VA Central IRB to stamp the new approval date upon completion of the review must be submitted with the VA Central IRB Form 116. If the PI/SC or LSI does not plan to re-consent participants already enrolled but will inform them of the changes in a letter, a copy of the proposed letter to be sent to participants informing them of the changes must also be submitted.

4.3.4 If there is a change in LSI, a VA Central IRB Form 134b, Change in or Addition of Local Site Investigator (Attachment 3), must be submitted by the new LSI and sent in by the PI/SC study team to include a current curriculum vitae or bio sketch; a VA Central IRB Form 102, Local ACOS/R&D Review Supplement; and a COI determination from the LSI site or a current OGE Form 450-VA Alternative, Research Financial Conflict of Interest. Copies of all modified forms or other documentation in which the LSI is named must also be submitted.

4.3.5 If there is a change in any other documents, such as recruitment materials, the protocol, participant questionnaires/surveys etc., a tracked and clean copy must be submitted if feasible. Where not feasible, the changes must be explained in detail in the VA Central IRB Form 116.

4.4 Submission and Processing of Updates. If there is an approved change to the PI/SC Application that requires changes also be made to approved local site documents for all participating sites, each site only needs to submit the modified documents and they will be processed as administrative updates as follows:

- 4.4.1 The VA Central IRB Manager will enter the requirement for LSI updates in the VA Central IRB tracking system upon approval of the PI amendment and follow-up with each site to ensure all documents are received within 10 work days of notification of the required changes. If documents are not received within 30 calendar days of notification, the issue will be referred to the VA Central IRB Administrator who will consult with a VA Central IRB Co-Chair concerning possible non-compliance action.
- 4.4.2 The VA Central IRB Manager will verify that the required changes were made and file the materials in the study folder and upload verified copies onto the VA Central IRB SharePoint site as a verified update. Each update will be assigned a number in chronological order (for both PI and LSI updates.) A notice that the changes were received, verified, and uploaded will be sent to the LSI study team, the PI/SC study team, and the VA Central IRB Local Site Liaison. If the changes involved the informed consent document, the informed consent document must be updated by the study team with the approved changes and a new version date or version number prior to submission. The informed consent document will then be updated by the applicable VA Central IRB Manager with the current PI/SC amendment date approval and the LSI Verification date of the updated materials prior to posting on the SharePoint site.
- 4.4.3 If there is an administrative change in either the PI or LSI Application as described in paragraph 2.6 not involving the submission of a PI amendment, either the PI or LSI study team as applicable must submit a memorandum detailing the change and submit both clean and tracked changes copies of all documents requiring update. The applicable VA Central IRB Manager will then process the update as detailed in paragraph 4.4.2.
- 4.5 Completion and Submission of an Exception Request. When an PI/SC or LSI requests an exception to an approved project, VA Central IRB Form 127 (Attachment 4), Request for an Exception to an Approved Protocol, must be submitted as detailed below:
- 4.5.1 The exception request must include the following information:
- Confirmation that approval has been received from the PI/SC, if the exception request is being submitted by the LSI, and/or Sponsor, as applicable;
 - The type of exception being requested;
 - A list of subject IDs for those that will be affected by the exception request;
 - A description of the exception;
 - The anticipated impact on risk-benefit ratio;
 - Whether the exception will be discussed with the subject and if so, how;
 - Whether the exception has been previously requested; and
 - The likelihood that the specific exception will be requested in the future
- 4.5.2 Exception requests are to be submitted through the VA Central IRB secure SharePoint site into the Reportable Event folder and an e-mail notification sent to the VA Central IRB mailbox.
- 4.6 Review of Amendment or Modification Requests. Upon notification that an amendment request has been uploaded to the VA Central IRB SharePoint site, a member of the Input team will enter the amendment in the VA Central IRB tracking system, assign an amendment number based on the number of previous PI or LSI amendments submitted, and send an acknowledgement electronically through the

tracking system to the study team copying the applicable VA Central IRB Manager. The Input Team member will create a new folder for the amendment labeled with the amendment number on the VA Central IRB shared drive under either the PI or LSI “Amendment and Update Folder” as applicable and then move the documents from the SharePoint site to the new folder on the shared drive. A copy of the acknowledgement letter will also be filed in the “VA Central IRB Letters” folder for the amendment.

- 4.6.1 Upon notification that an amendment has been received, the assigned VA Central IRB Manager for the study will perform an administrative review to ensure all documents referenced as being changed are included with the submission and that the VA Central IRB Form 116 has been signed by an approved PI/Co-PI or LSI/Co-LSI. If there are missing documents or a problem with the submitted documents, the VA Central IRB Manager will contact the study team via e-mail with a detailed description of the problems that need resolution. If the identified issues are minor the amendment request can be sent to the Reviewer. If the issues will affect the ability of the Reviewer to complete the review, the VA Central IRB Manager will not forward the amendment request to the Reviewer until the requested information and/or corrections have been received and resolved.
- 4.6.2 If the request is ready for review, the Manager will determine if the request can be expedited per paragraph 1.6.1 of this SOP or whether it must be reviewed by the convened IRB and prepare Section 1 of the VA Central IRB Form 120, Reviewer Checklist for Amendments (Attachment 5) accordingly. The Information Security Officer and Privacy Officer Representatives do not need to provide a new certification unless the amendment involves changes in the way in which sensitive research data or PHI is obtained, accessed, used, transported, or stored. If there are such changes in the study documents, particularly the HIPAA waiver and HIPAA authorization, the Manager will prepare VA Central IRB 123, Privacy Officer Compliance Review, and/or VA Central IRB Form 122, Information Security Officer Compliance Review, as applicable. Minor changes in the HIPAA waiver or HIPAA authorization that do not affect these issues will not be automatically sent to the Privacy Officer for review. The Manger will then upload all documents and the VA Central IRB Form 120 onto the VA Central IRB SharePoint site in the folder for “Study Actions for Review” and send a task assignment to the Reviewer via the SharePoint Task List function.
- 4.6.3 The Primary Reviewer for the study reviews all amendments submitted for the study unless the Reviewer is not available within 2-3 days of receipt of the amendment or the response to requested administrative revisions as applicable. Then the Secondary Reviewer may be assigned or one of the VA Central IRB Co-Chairs if the Secondary Reviewer is not available or if there is not a Reviewer currently assigned. If an assigned Reviewer realizes that he or she has a conflict of interest with an assigned project after receiving the checklist and project documents, the reviewer will immediately notify the VA Central IRB Manager and returns the Reviewer checklist indicating that there is a conflict. The VA Central IRB Manager consults, if necessary, with the VA Central IRB Administrator regarding assignment of another reviewer and the Administrator updates the meeting agenda accordingly.
- 4.6.3.1 The Primary Reviewer will have up to ten work days after receiving the e-mail notification of an assigned task to provide a written review and/or a signed checklist indicating approval of the amendment. If the Reviewer has questions, requests

clarifications, or indicates changes need to be made or additional information submitted prior to granting approval, the Reviewer will detail these on the checklist or in an e-mail to the Manager. The VA Central IRB Manager will then relay this information to the study team and ensure a copy is kept in the official file for the study.

- 4.6.3.2 Upon receipt of the response from the study team, the VA Central IRB Manager will check to see whether all information requested was received. If not, the study team will be contacted via e-mail or phone. Once all requested information is received the Manager will load the new documents to the VA Central IRB SharePoint site and update the task assignment.
- 4.6.3.3 Upon notification that the study team response has been received and available for review, the Reviewer will have 5 work days to complete the review. If there are still questions or other issues remaining, the procedures in paragraphs 4.6.4 and 4.6.5 will be followed. If after the second response is received and the Reviewer determines there are still issues to be resolved, one of the VA Central IRB Co-Chairs will be contacted to determine if a teleconference with the study team should be scheduled or if the amendment should be added to the next VA Central IRB meeting agenda. If a call is required, the Manager will coordinate a convenient time with the study team, Co-Chair, and Reviewer if applicable, and prepare a memorandum for the record of the call once complete.
- 4.6.3.4 For amendments requiring review by the convened IRB, once the Reviewer has performed the initial review, provided comments, and recommended approval or disapproval, the Manager will schedule the amendment for review at the next available VA Central IRB meeting. If the Reviewer had questions or required additional information and this is not received at least three work days prior to the scheduled meeting, the review of the amendment may be removed from the agenda and re-scheduled once the response is received if this information is determined by the Reviewer to be necessary for the Board to conduct its review.
- 4.6.4 For amendments undergoing expedited review, the Reviewer ensures all approval criteria for the research are still met and then signs off on the approval, either through completing and signing the checklist or by personally sending an e-mail to the Manager indicating approval. The VA Central IRB Manager will generate an approval letter through the VA Central IRB tracking system. The approval date will be the date of the Reviewer's approval.
- 4.6.5 For amendments reviewed at the convened IRB, the Reviewer will present the amendment to the other Board members. After discussion, the Board members ensure that all approval criteria for the approval of the research are still met and a motion is made, usually by the Reviewer but any voting member may make a motion.
- 4.6.5.1 One of the following motions will be made:
- Approve Contingent Upon Minor Modifications. The modifications are detailed for the investigator. Upon submission of the changes by the investigator, the changes are

verified by the Reviewer or another voting member of the Board. The amendment does not have to be re-reviewed by the convened IRB.

- **Defer for Major Modifications.** Major changes are required in the amendment documentation that are directly relevant to the required determinations that must be made by the IRB based on the IRB approval criteria applicable to the amendment in question. This action requires re-review by the convened IRB when re-submitted by the investigator. The required revisions are detailed for the investigator.
- **Disapprove.** The amendment has risks that outweigh potential benefits or the amendment is significantly deficient in one or more major areas. The reasons for disapproval are summarized for the investigator. The investigator will also be offered the opportunity to appeal.
- **Table.** A vote could not be taken at the meeting. The reason for this is relayed to the investigator. Possible reasons include but are not limited to lack of a quorum, lack of investigator response to prior inquiries by reviewers, or time constraints.

4.6.5.2 All letters resulting from review by the convened IRB will be signed by one of the VA Central IRB Co-Chairs. No letters will be generated for tabled actions. Instead, an e-mail will be sent by the Manager to the study team and filed with the study documentation. If approved, the date of approval will be the date of the convened meeting. If Approved Contingent Upon Minor Modifications, the approval will be the date of approval by the Reviewer via expedited procedures per paragraph 4.6.4. A file of sample letters reflecting the various possible actions is kept on the VA Central IRB shared drive for reference as needed.

4.6.6 The VA Central IRB Manager will post a copy of the letter, along with the approved documents to the study folder on the VA Central IRB SharePoint site. For PI amendments, a notification that the amendment has been approved will be sent to PI/Co-PIs, National Study Coordinators, LSIs, Local Site Liaisons, and Local Study Coordinators, as well as to Coordinating Center personnel if applicable. For local site amendments, all the above personnel will be notified except that only the LSI, Local Site Coordinator, and the Local Site Liaison of the site that submitted the amendment will be notified.

4.6.7 The VA Central IRB Manager will also ensure a copy of the letter and all approved documents, Reviewer checklists, and other applicable documentation are posted to the applicable folder on the VA Central IRB shared drive and that, a paper copy of the documentation is filed in the paper files for all FDA-regulated studies.

4.7 Processing and Review of Exception Requests. The VA Central IRB Input Team monitors the Reportable Event folder on the SharePoint site on a continuous basis during the duty day. Receipt of exception requests will be immediately entered into the VA Central IRB tracking system and will be assigned a chronological number based on the number of exceptions already received and processed for the study. The request for exception will be brought to the immediate attention of the applicable VA

Central IRB Manager. Each exception request will be processed in the same manner as an amendment request per paragraph 4.6 with the below differences:

- 4.7.1 The VA Central IRB administrative staff makes the completed VA Central IRB Form 127, along with any included supplemental materials, available to the assigned Reviewer for that specific project on the secure VA Central IRB SharePoint site and uses the Task Manager function to inform the Reviewer of the assigned task. A copy of the most current, approved protocol is also made available if applicable. In addition, the VA Central IRB Administrative staff will prepare VA Central IRB Form 128, Reviewer Checklist for Protocol Exceptions (Attachment 6), for use by the assigned Reviewer.
- 4.7.2 Exception requests should be reviewed within 5 work days by the Reviewer. If the Reviewer has questions, these should be sent to the study team for a response per paragraph 4.6. Upon a determination being made, a letter will be generated indicating the determination and sent to the LSI and PI, as well as to the local site liaisons and coordinating center personnel as applicable.
- 4.7.3 The Reviewer may choose to refer the Exception request to the convened IRB for review. If this is the case, it will be added to the agenda by the VA Central IRB Manager and the documents posted. Once a determination is made, a VA Central IRB Co-Chair will sign the letter. The same motions that can be made for amendments at convened meetings can also be made for exception requests.

5 DOCUMENTATION REQUIREMENTS

- 5.1 All amendment, updates, and exception requests, along with any associated approved documents, Reviewer checklists, and other study documents are filed in the applicable project folders on the VA Central IRB shared drive while paper copies of FDA-approved studies are maintained in the VA Central IRB paper-based study files.
- 5.2 Copies of approved documents in electronic format are also maintained on the VA Central IRB SharePoint site.

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 VHA Directive 1200.01, Research and Development (R&D) Committee
- 6.4 45 CFR 46, Department of Health and Human Services, Protection of Human Subjects, Subparts B through D
- 6.5 21 CFR 56, U.S. Food and Drug Administration, Institutional Review Boards
- 6.6 21 CFR 50, U.S. Food and Drug Administration, Protection of Human Subjects



Amendments, Modifications, Updates, and Requests for Protocol Exceptions

Document: VA-CIRB-SOP-106

Supersedes: SOP-113 June 29, 2016

Effective Date: 1/21/2019

Page 13 of 13

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.

Marisue Cody, Ph.D.
Director of Operations
VHA Human Protections Administrator
Office of Research and Development

6 Attachments

1. VA Central IRB Form 116, Request to Amend or Modify an Approved Project
2. VA Central IRB Form 134a, Change in Principal Investigator/Study Chair
3. VA Central IRB Form 134b, Change in or Addition of Local Site Investigator
4. VA Central IRB Form 127, Request for an Exception to an Approved Protocol
5. VA Central IRB Form 120, Reviewer Checklist for Amendments
6. VA Central IRB Form 128, Reviewer Checklist for Protocol Exceptions