TITLE: Review of Projects by the Convened IRB

1.0 PURPOSE

This Standard Operating Procedure (SOP) sets forth the policies and procedures the VA Central IRB uses for reviewing research projects by the convened IRB. This includes initial review of new project submissions, continuing reviews, and requests for amending or modifying approved projects. Procedures for the review of other actions by the convened IRB, such as serious adverse events, unanticipated problems involving risks to subjects or others, protocol deviations, reports of noncompliance, complaints, and other reports, can be found in the SOPs addressing those issues.

2.0 REVISION HISTORY

Date of Initial Approval	July 29, 2008
Revision Dates	August 21, 2009 September 24, 2009 March 23, 2010 August 19, 2010 February 7, 2011 August 8, 2011

3.0 SCOPE

This SOP applies to all VA Central IRB members. It also applies to VA Central IRB administrative staff involved in the processing of project documentation for review by the convened IRB, documenting the results of the IRB review, and relaying the results of the review to investigators and local participating sites.

4.0 POLICY

4. 1 It is the policy of the VA Central IRB that research involving human participants not classified as exempt or not qualifying for review under the expedited review procedure, is reviewed at a meeting of the convened IRB. See VA Central IRB SOP 107, Requests for Exemption Review and Determination, for exemption classification criteria and VA Central IRB SOP 110, Expedited Review Process, for expedited review criteria.

4.2 The convened VA Central IRB utilizes a Primary and Secondary Reviewer System. Projects that require informed consent and that will be reviewed by the convened IRB are also assigned an Informed Consent Reviewer. See VA Central IRB SOP 108, VA Central IRB Convened Meeting Preparation, for procedures on how reviewers are assigned and complete specific checklists as part of their pre-meeting responsibilities.

4.3 It is the policy of the VA Central IRB that if an investigator's written responses to reviewer questions or concerns alter any of the documents previously forwarded to the VA Central IRB members, the altered documents are made available to all members before the meeting, if time permits. If time does not permit, copies are made available to all members at the meeting, including uploading the documents to the VA Central IRB SharePoint meeting folder or faxing them to those participating via video or teleconference who cannot access the SharePoint site at that time. Members are given sufficient time to review the altered documents before any discussion of that particular project.

4.4 The VA Central IRB uses ad hoc consultants as needed to supplement member review if there is no member who has the specific expertise needed to provide an appropriate review. This is done in accordance with VA Central IRB SOP 108. The VA Central IRB has no other procedure or subcommittee to supplement its review.

4.5 It is the policy of the VA Central IRB that all meetings are conducted in a professional manner. All members, whether voting or nonvoting, are given an opportunity to participate, to include all members participating via audio or video conferencing. Members may not participate in the meeting discussion or vote by e-mail.

5.0 DEFINITIONS

See VA Central IRB SOP 128, Definitions Used in VA Central IRB SOPs.

6.0 RESPONSIBILITIES

6.1 The VA Central IRB Co-Chairs are responsible for the following:

6.1.1 The Co-Chairs manage the meeting in accordance with the agenda. The Co-Chairs set the tone of the meeting and exercise sound judgment in facilitating the discussion, while still ensuring all controverted issues are adequately discussed. They are responsible for appropriate time management while ensuring that all agenda items receive a comprehensive and qualitative review. The Co-Chairs may alter the order of the agenda as necessary to accommodate reviewer schedules and to ensure quorum requirements are maintained.

6.1 2 The VA Central IRB Co-Chairs ensure that the VA Central IRB makes a determination on all required IRB approval criteria for each research project reviewed at the meeting, whether it involves an initial application, a continuing review, or a request for an amendment. The Co-Chairs use the agenda tool prepared by each Coordinator for the specific projects being reviewed to structure the discussion and formulate the IRB's determination regarding each project.

6.1.3 The VA Central IRB Co-Chairs are voting members of the VA Central IRB and vote on each motion and are subject to the same voting restrictions as the

members concerning conflicts of interest. The Presiding Co-Chair calls for a motion and then for a vote after a motion is seconded.

6.1.4 Each Co-Chair is responsible for reviewing the minutes and at least one of the Co-Chairs must sign the minutes of the meeting once they are approved at the next convened meeting. Each Co-Chair is also responsible for reviewing and signing the VA Central IRB determination letters for the specific protocols for which he/she chaired the review at the meeting.

6.2 The Primary Reviewer completes the applicable reviewer checklists for the type of project action being reviewed, briefs the members about the research project in accordance with the agenda tool, leads the discussion at the convened meeting about any issues or concerns, and makes an approval recommendation to the IRB.

6.3 Secondary Reviewers also complete the applicable reviewer checklists and supplement the Primary Reviewer in the discussion, particularly if there are controverted issues. The Secondary Reviewer for a project may also make approval recommendations to the IRB.

6.4 The Informed Consent Reviewer is responsible for reviewing the informed consent document to ensure it matches the protocol and contains all required and additional elements as applicable; ensuring the consent process protects the privacy and confidentiality of the participant and respects their rights; and evaluating the process for obtaining documentation of the informed consent.

6.5 All VA Central IRB members are responsible for participating in the project discussion. If a member has a conflict of interest, the member must recuse his or herself from the discussion and leave the room or video/teleconference in accordance with VA Central IRB SOP 103, Conflict of Interest. Recused members do not count towards quorum.

6.5.1 All VA Central IRB voting members are responsible for casting a vote for or against the recommendations presented, or they may abstain. Conflicted members must recuse themselves and are not counted in the total voting members or toward the quorum.

6.5.2 The non-voting members of the VA Central IRB are responsible for providing applicable guidance prior to and during the project discussion in regard to their area of expertise. They may make recommendations but they may not cast a vote or act in any manner that may be construed as exercising undue influence upon the IRB members.

6.5.3 The Information Security Officer (ISO) and Privacy Office Representatives also complete the applicable compliance certification pertaining to their review of study documents.

6.6 The VA Central IRB Coordinators and the VA Central IRB Administrator are responsible for ensuring that all required determinations and approval decisions made by the VA Central IRB are accurately documented in the meeting minutes, to include a summary of controverted issues discussed and their disposition, as well as providing an accurate record of the vote on each action.

7.0 PROCEDURES

7.1 Conduct of Meeting. The presiding Co-Chair convenes the meeting at the scheduled time if a quorum is present.

7.1.1 The presiding Co-Chair reminds all members of their obligation to declare any conflicts of interest prior to the review of the conflicted project. Members are required to complete and turn-in the VA Central IRB Form 127, Conflict of Interest Declaration, to the VA Central IRB Meeting Coordinator in accordance with VA Central IRB SOP 103, Managing Conflict of Interest.

7.1.2 The following requirements must be met in order for a quorum to be declared.

- The majority of the voting members are in attendance in-person or via audio or video conference
- All members must have received and had time to review all agenda materials
- At least one voting member whose primary concerns are in a non-scientific area must be in attendance
- A voting licensed physician-member must be present for FDA-regulated projects reviewed
- Voting members who leave the room or the phone or video conversation, to include recusing themselves, are not counted towards quorum. If quorum is lost while members are absent, no vote can be taken on any action until a quorum is once again established,
- Members with the knowledge and expertise to review the research are present, or sufficient information has been obtained from an ad hoc consultant.
- A prisoner representative must be present if research involving prisoners is being reviewed.
- If research involving populations vulnerable to undue influence or coercion is being reviewed, at least one member must be present that has experience with those populations or the services of an ad hoc consultant must be obtained.

7.1.2.1 The VA Central IRB Administrator is responsible for informing the Presiding VA Central IRB Co-Chair when quorum is attained to begin the meeting or when quorum is lost. No further business requiring a vote can be conducted until quorum is attained again. The number of members required to attain quorum will be noted in the minutes. The total number of members present for each vote will be documented with each vote count and must meet or exceed the number required to attain quorum or no vote can be taken.

7.1.2.2 The attendance or absence of all members is documented for each meeting and is used to evaluate members. All members are required to attend two-thirds of the convened meetings, whether scheduled or unscheduled. Attendance can be by phone, video conference, or in-person. Exceptions are made in the event of a member's active duty deployment or prolonged or serious illness or illness of a close family member.

7.1.3 The meeting is conducted by the Presiding Co-Chair in accordance with the published agenda and VA and other requirements. Deviations from the agenda can be made as required to accommodate reviewers' time, however, the Presiding Co-Chair must ensure the meeting is managed so that all reviews on the agenda are conducted with a quorum.

7.1.4 All members having a conflict will leave the room or be temporarily excluded from the audio or video feed during the discussion and vote on the project being reviewed. These members will not count towards quorum. If a quorum is not present, the project is tabled. After the vote, the excluded member is asked to return to the room and/or the members who were excluded via audio or video are reconnected.

7.1.5 If a voting member not having a conflict leaves the room or is temporarily unavailable via audio or video, VA Central IRB Administrative staff verifies whether quorum is maintained and, if not, informs the Co-Chair. Discussion of the research being reviewed and voting may continue as long as a quorum is maintained. If a quorum is not maintained, discussion of research projects is put on hold until the member returns. Other business not requiring a vote may be discussed in the interim until quorum is attained.

7.1.6 Motions are not called for until the presiding Co-Chair ensures that all members have had the opportunity to speak. The Primary Reviewer makes the initial motion, which can then be seconded by any other voting member. The presiding Co-Chair then calls for a vote. Vote is by hand for those present at the meeting in-person. A roll call is taken of all voting members participating via audio or video conference. Voting members can vote for the motion, against the motion, or abstain. If the motion does not garner a majority of the voting members making up the convened quorum, or the motion is not seconded, any voting member of the VA Central IRB can make a subsequent motion.

7.1.7 During the meeting both the VA Central IRB Coordinators and the VA Central IRB Administrator take notes and record the IRB determinations per VA Central IRB SOP 115, Preparation and Distribution of VA Central IRB Meeting Minutes. The Coordinators and Administrator assist the presiding Co-Chair and members as needed in ensuring that all required determinations that must be made for each project are addressed by reviewing the agenda tool for that project.

7.1.8 During the meeting, various documents may be projected via computer on a video or other type of screen for discussion and on-line editing by the members as an option. If this option is used, the VA Central IRB Administrator makes all suggested changes to the projected documents using the track changes feature of MS Word if applicable. Copies of both the original document and the edited document are kept in the project file. Members on video conferencing will be able to view the changes while members participating via teleconferencing will need to track the changes on their copies of the documents as they are being made. All changes will be verbally communicated prior to the changes being made on the screen so those members on the phone can comment as needed.

7.1.9 Upon conclusion of the meeting, the VA Central IRB Meeting Coordinator provides members containers to deposit the meeting materials in for shredding if they do not want to keep them for further review. Members who have personal notes regarding the projects are reminded that these must be maintained in accordance with the VA requirements for maintenance of VA-sensitive information. If requested by any of the members, any materials the members want to retain can be forwarded to them via express mail so they don't have to carry them back to their home destination.

7.2 Procedure for Review of New Applications. The following review procedure is followed for the initial review of PI/SC New Project Applications:

7.2.1 The presiding Co-Chair asks anyone who has a conflict of interest to recuse themselves and leave the room, unless they are requested by the Co-Chair to provide information about the project. After providing the requested information, the member will then leave the room. If participating remotely, the member will disconnect.

7.2.2 The Primary Reviewer provides a brief overview of the project for the other members, including the project's purpose and design. The Secondary Reviewer supplements the comments of the Primary Reviewer. Other members may ask questions and present points of clarification as they deem necessary to ensure an accurate and thorough presentation of the project is made.

7.2.3 The VA Central IRB, led by the Primary Reviewer and the Presiding Co-Chair, then discusses whether the project meets the definition of "minimal risk" as defined by VA and other guidelines or if it is "greater than minimal risk" and whether the required IRB approval criteria as specified below have been met:

7.2.3.1 The risk to subjects are minimized by using procedures consistent with sound research design and do not unnecessarily expose subjects to risk and, when appropriate, using procedures already being performed on the subjects for diagnostic or treatment purposes.

7.2.3.2 The 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. The IRB must ensure that studies with treatment or services that constitute "usual care" include a narrative section that clearly differentiates the research interventions from usual care and whether usual care is delivered to only some or to all research participants.

7.2.3.3 The selection of subjects is equitable. The IRB must take into account the purpose of the research and the setting in which the research is to be conducted. The IRB needs to be particularly cognizant of the special problems involving vulnerable populations and other categories of participants who may be potentially susceptible to harm to include children, prisoners, pregnant women, individuals lacking decision making capacity, and VA employees and students. If recruitment of non-veterans is being requested, the IRB must ensure that it is appropriate and justified.

7.2.3.4 Informed consent will be sought from each prospective participant or the subject's legally authorized representative or a request for waiver or alteration of informed consent has been submitted by the investigator, it meets the waiver approval criteria, and it is appropriately justified. The informed consent process must contain all applicable required elements. In addition, if the project involves usual care, the informed consent process must clearly define for the participant which potential risks are related to the research and which risks are associated with the usual care provided. The informed consent process must include language advising subject to review the risks of usual care with their health care provider.

7.2.3.5 Informed consent will be appropriately documented or a request for waiver or alteration of documented informed consent has been submitted by the investigator, it meets the waiver or alteration approval criteria, and it is appropriately justified.

7.2.3.6 When appropriate, the research plan makes adequate provision for monitoring the data collected to ensure the safety of the participants.

7.2.3.7 There are adequate provisions to protect the privacy of participants and to maintain the confidentiality of the data. The IRB must determine that the informed consent form or process, the protocol, and the HIPAA authorization are consistent with each other. In addition, if real social security numbers, scrambled SSNs, or the last four digits of SSNs are to be used in the study, the IRB must determine that appropriate security measures are in place to protect the SSN. *Note: This does not apply if the only use of the SSNs is on the informed consent form or the HIPAA authorization for filing in the participant's health record.*

7.2.3.8 When some or all of the subjects are likely to be vulnerable to coercion or undue influence, additional safeguards have been included in the study to protect the rights and welfare of these subjects. See VA Central IRB SOP 106, Research Involving Vulnerable Populations, for required additional safeguards.

7.2.3.9 Real, perceived, or potential conflicts of interest have been managed, reduced, or eliminated.

7.2.3.10 All investigators have met current educational requirements for the protection of human participants and are qualified to conduct the research or the project will not be granted final approval.

7.2.4 After the VA Central IRB completes its discussion, all controverted issues are adequately resolved, and the VA Central IRB has reached consensus on the risk level of the project and whether it meets all the approval criteria, the VA Central IRB indicates any required changes or modifications that must be made in the project before granting approval. All required modifications are compiled in an orderly fashion per the order of the agenda tool. If the VA Central IRB determined that it had sufficient information and the project met all applicable IRB approval criteria, any required modifications must be minor and specific and directive in nature so as not to require further review by the convened IRB.

7.2.5 The Informed Consent Reviewer then briefs the members on whether all required elements are present in the informed consent form or in the Participant Information Sheet if a wavier of documentation of informed consent was submitted. See VA Central IRB SOP 105, Informed Consent Requirements, for the required elements of an informed consent.

7.2.5.1 Any controverted issues are discussed until a consensus is reached regarding resolution of the specific required element or until the presiding Co-Chair determines no further progress is being made.

7.2.5.2 Any required changes or modifications to the informed consent document are documented. The Microsoft Word track changes function can be used to do this or a specific listing can be compiled.

7.2.6 The Information Security Officer (ISO) and the Privacy Officer Representatives participate in all relevant discussions as indicated above if present at the meeting. If the ISO or Privacy Officer Representatives cannot be present, written comments must be provided prior to the meeting.

7.2.6.1 The ISO Representative turns in the completed VA Central IRB Form 122, Information Security Officer (ISO) Compliance Review, at the meeting or forwards it to the VA Central IRB Administrative Office prior to the meeting. The ISO Representative certifies that the project meets all VA and VHA information security requirements including but not limited to use, disclosure, storage, transfer, and security of sensitive research information. If the project requires modification in order for the ISO Representative to provide the required certification, the ISO Representative submits an interim report specifying the modifications.

7.2.6.2 The Privacy Officer Representative turns in the completed VA Central IRB Form 123, Privacy Officer Compliance Review, at the meeting or forwards it to the VA Central IRB Administrative Office prior to the meeting. The Privacy Officer Representative certifies that the project is in compliance with all VA and VHA requirements for safeguarding protected health information in accordance with the Health Insurance Portability and Accountability Act (HIPAA), for meeting all requirements for participant privacy and data confidentiality. If the project requires modification in order for the Privacy Officer Representative to provide the required certification, the Privacy Officer Representative submits an interim report specifying the modifications.

7.2.7 The VA Central IRB also determines if the participant's medical record needs to be flagged to protect the participant's safety and welfare by identifying the participant's involvement in the project.

7.2.7.1 The VA Central IRB will require medical records to be flagged if it is determined that it is important for the health and welfare of the participant that other providers caring for the participant know the participant is taking part in a specific research project. The participant's health record must be flagged if the subject's participation in the study involves:

- Any invasive research procedures (e.g., muscle biopsy or bronchoscopy)
- Interventions that will be used in the medical care of the subject or that could interfere with other care the subject is receiving or may receive (e.g., administration of medications, treatment, or use of an investigational device)
- Clinical services that will be used in the medical care of the subject (e.g., orders for lab tests or x-rays ordered as part of the study), or that could interfere with other care the subject is receiving or may receive
- The use of a survey or questionnaire that may provoke undue stress or anxiety unless the IRB determines that mandatory flagging is not in the best interests of the participant

7.2.7.2 The VA Central IRB might not want to require the medical record to be flagged if:

- Participation in the study involves only one encounter that does not involve any of the above mandatory flagging requirements
- Participation in the study involves the use of a questionnaire that should not cause anxiety or stress
- The study only involves the use of previously collected biological specimens.
- Identification as a participant in a particular study will place the participant at greater than minimal risk.

7.2.8 If the project application indicates there is a difference between federal or VA and state or local law, the VA Central IRB will make a determination on which laws must be followed based on the most restrictive criteria. If the VA Central IRB cannot resolve the differences, the issue will be forwarded to the Office of General Counsel (OGC) Representative serving on the VA Central IRB as a nonvoting member who will be responsible for obtaining an official OGC position on the issue.

7.2.9 Upon completion of all discussion, the presiding Co-Chair can ask the VA Central IRB Administrator or the VA Central IRB Coordinator assigned to the study to review all required modifications if needed. The presiding Co-Chair then asks the Primary Reviewer for a motion. The Primary Reviewer can make one of the following approval recommendations as part of the motion:

7.2.9.1 Approve Contingent Upon Required Minor Modifications. The specific modifications are detailed in writing for the investigator. Upon submission of the changes by the investigator, the changes are verified by one of the Co-Chairs and the project does not have to be reviewed again by the convened IRB unless there are comments from the local sites requiring review by the convened IRB or the investigator appeals one or all of the modifications.

7.2.9.2 Approve Contingent Upon Receipt and Review of Local Site Comments. All IRB approval criteria have been met and there are no required modifications. The project and the IRB's determinations will be forwarded to the local sites for a local context review to determine if there is a local issue that impacts on the IRB's approval decision. No further review by the convened IRB is required unless one of the sites raises an issue that the presiding Co-Chair determines requires review by the convened IRB. If review by the convened IRB is not required, the Co-Chair will review all comments, require any minor changes as needed, and make the final approval determination.

7.2.9.3. Defer for Major Modifications. Important information is not included in the application package, major changes are required in the project documentation, or any other situation is identified that affects the IRB's ability to make the required regulatory determinations based on the IRB approval criteria. A deferred project requires re-review by the convened IRB after the missing or requested information is made available and/or the requested major changes are made by the investigator and the project re-submitted.

7.2.9.4 Disapprove. The project is deemed to have risks that outweigh potential benefits or the project is significantly deficient in one or more major areas. The reasons for disapproval will be summarized for the investigator.

7.2.9.5 Table. A vote could not be taken at the meeting. The reason will be relayed to the investigator in writing. Possible reasons include, but are not limited to, a lack of quorum, lack of investigator response to prior inquiries by reviewers, or time constraints.

7.2.10 If the Primary Reviewer makes a motion to approve the project contingent on minor modifications or contingent upon receipt and review of local site comments, the Primary Reviewer also makes a recommendation as to the approval period. The Primary Reviewer and the VA Central IRB take the following factors into consideration when determining the approval period, which can be no more than one year from the date of the VA Central IRB contingent approval:

- Risk level of the project and/or degree of uncertainty regarding the risks
- Vulnerability of the subject population
- Experience of the investigators
- Unusual study design or consenting process
- Project involves a novel therapy
- Projected rate of enrollment
- Other facts based on study design and content

7.2.11 After the motion is made, the vote is then taken in accordance with paragraph 7.1.6.

7.3 Procedure for Review of Local Site Comments

7.3.1 Comments received from local sites concerning the study and the review as performed by the VA Central IRB which must be reviewed at a convened meeting of the IRB are added to the agenda by the VA Central IRB Administrator. Copies of all the comments are provided to the members as part of their agenda packages per VA Central IRB SOP 108, VA Central IRB Convened Meeting Preparation.

7.3.2 The Primary Reviewer for the study briefs the IRB members on the comments. If the comments pertain to differences in federal or VA and state or local laws, the issue will be addressed per the procedure specified in paragraph 7.2.8. The IRB then decides if any further changes need to be made to any part of the PI/SC New Project Application and/or Local Site Investigator Applications.

7.3.2.1 If the IRB decides changes are required based on the comments, it can elect to apply the changes in any of the following ways:

- To the PI/SC Application only as applicable
- To the PI/SC Application and all Local Site Investigator Applications
- To all Local Site Investigator Applications only
- To a specific Local Site Investigator Application(s) based on that specific site's comments. This usually applies when a site has a specific policy or procedure it wants to keep consistent in all studies conducted at that site.

7.3.2.2 The Primary Reviewer then makes a motion concerning the changes and the IRB votes to approve or disapprove the changes in accordance with paragraph 7.1.6.

7.3.3.3 The VA Central IRB can also decide not to require changes but still forward specific comments to the PI/SC or LSIs for consideration as to whether the PI/SC or LSI would want to consider changing their applications based on the comments. If the PI/SC decides to change the application, the changes must be submitted in the form of an amendment. If the PI/SC chooses not to make any changes based on the comments, a memorandum or e-mail stating this must be forwarded to the VA Central IRB.

7.3.3.4 If the Local Site Investigator Applications have already been submitted and are being reviewed in conjunction with the comments from the local sites, the IRB reviews all submitted local site comments prior to reviewing any of the associated Local Site Investigator Applications. If changes are required to the Local Site Investigator Applications, these changes are included as minor modifications during the review of the Local Site Investigator Applications as described in paragraph 7.4.

7.3.3.5 All changes made by the PI/SC and LSI based on local site comments can be reviewed under expedited review procedures, along with any other minor modifications submitted if applicable, unless the change is determined to be a major change. This is determined by the IRB at the time the change is required or forwarded for review by the PI/SC or LSI. It can also be determined by the VA Central IRB Coordinator or VA Central IRB Administrator, in conjunction with the Co-Chair, once all requested and other modifications as applicable have been received. If the change is major, the changes must be referred to the convened IRB for review.

7.4 Review of Local Site Investigator Applications.

7.4.1 The Primary Reviewer briefs the IRB members, supplemented by the Secondary Reviewer, concerning any issues or discrepancies with each of the individual Local Site Investigator Applications submitted. The comparison table of PI/SC model documents as prepared by the VA Central IRB Coordinator is reviewed to ensure that any deviations from the PI/SC Application model documents are adequately justified. If there are any issues pertaining to differences in federal or VA and state or local laws, the matter will be addressed per paragraph 7.2.8.

7.4.2 Each Local Site Investigator Application is reviewed individually and a vote taken on each one after the IRB discussion. The Primary Reviewer makes a motion concerning the approval of each site to participate in the project using the same approval criteria as for the PI/SC Application and the vote taken and recorded in accordance with paragraph 7.1.6. The Primary Reviewer may make one of the following approval recommendations:

7.4.2.1 Approve. The site application meets all approval criteria. Changes can be suggested but are not required.

7.4.2.2 Approve Contingent Upon Required Minor Modifications. The specific modifications are detailed in writing for the investigator. Upon submission of the changes by the investigator, the changes are verified by one of the Co-Chairs and the project does not have to be reviewed again by the convened IRB unless the investigator appeals one or all of the required modifications.

7.4.2.3 Defer for Major Modifications. Important information is not included in the application package, major changes are required in the project documentation, or any other situation is identified that affects the IRB's ability to make the required regulatory determinations based on the IRB approval criteria. A deferred application requires re-review by the convened IRB after the missing or requested information is made available and/or the requested major changes are made by the investigator and the project re-submitted.

7.4.2.4 Disapprove. The local site is not approved for participation in the project. The reasons for disapproval will be summarized for the investigator and can include such issues as the site not having sufficient resources to ensure the safety and welfare of participants or the study team is not qualified.

7.4.2.5 Table. A vote could not be taken at the meeting. The reason will be relayed to the investigator. Possible reasons include, but are not limited to, a lack of quorum, lack of investigator response to prior inquiries by reviewers, or time constraints.

7.4.3 A general flow chart depicting the IRB review process can be found as an attachment to this SOP. The process for communicating the results of the review to the investigators and to the potential participating local sites can be found in SOP 111, VA Central IRB Communications with Investigators and Local Participating Sites.

7.5 Continuing Review Procedures.

7.5.1 The same procedure as was followed for review of PI/SC New Project Applications is followed for continuing review applications and the same approval criteria applied. There are a few minor differences in the process as follows:

7.5.1.1 The Primary Reviewer, and the Secondary Reviewer if applicable, receive or have access to all materials regarding the project and all other members are provided only those documents as detailed in VA Central IRB SOP 108, VA Central IRB Convened Meeting Preparation. However, any member can have access to all materials upon request. The Secondary Reviewer does not need to complete a checklist unless the Primary Reviewer determines that assistance is required to perform the review due to the nature of the study, the scope of changes

submitted for review, the number of Local Site Investigator applications that must be reviewed, or any other issues requiring additional assistance.

7.5.1.2 The ISO and Privacy Office Representatives do not need to provide a new certification unless the Primary Reviewer requests that this be done due to changes in the way in which sensitive research data or PHI is obtained, accessed, used, transported, or stored since the last review. The VA Central IRB Administrative staff may also request a review by the ISO and/ or Privacy Officer Representative if, upon completion of the administrative review, it is determined that such a review is advisable or required.

7.5.1.3 The Informed Consent Reviewer does not need to provide a review unless a substantial change has taken place in the Informed Consent process since the last review and the Primary Reviewer requests that this be done. However, the IRB must determine that the Principal Investigator, and the Local Site Investigators as applicable, have provided the required certification that all participants entered onto the master list of subjects for the study signed an informed consent form prior to undergoing any study interactions or interventions unless the VA Central IRB has granted a waiver of informed consent or a waiver of documentation of informed consent.

7.5.1.4 If an amendment request is received with the Application for Continuing Review, it can be considered along with the Continuing Review Application and only one vote taken incorporating both actions.

7.5.1.5 After the IRB completes its discussion, the Primary Reviewer makes a motion concerning the continued approval of the PI/SC Application. The vote is taken in accordance with paragraph 7.1.6. The Primary Reviewer may make one of the following approval recommendations:

7.5.1.5.1 Approve. Changes can be suggested but are not required. The IRB could also require that participants receive information of significant new findings reported during the continuing review process if the IRB feels these findings may affect a participant's willingness to continue participation.

7.5.1.5.2 Approve Contingent Upon Required Minor Modifications. The minor changes or corrections must be made and submitted by the investigator before the approval period expires. These can be approved by one of the IRB Co-Chairs by expedited review. See VA Central IRB SOPs 110, Expedited Review Process, and 112, Continuing Review Requirements.

7.5.1.5.3 Deferred for Major Modifications. Changes 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. The investigator must submit a response with the changes in time for review by the convened VA Central IRB prior to the approval expiration period.

7.5.1.5.4 Disapprove. The investigator must terminate or close the project.

7.5.1.5.5 Table. This may be used if information is missing or an investigator has not responded to a reviewer. If the approval period lapses during the deferral period, procedures as detailed in VA Central IRB SOP 112, Continuing Review Requirements, will be followed.

7.5.1.5.6 Suspension or Termination. See VA Central IRB Sop 119, Suspensions and Terminations.

7.5.1.6 The VA Central IRB may also require verification of project requirements from some source other than the PI/SC. Examples of when this may occur include if there has been non-compliance with project requirements in the past, if the project has experienced some unanticipated problems related to the research, or if there have been participant or other complaints. Other examples are if the investigators have recently changed, particularly the PI/SC or LSI at a site, or if the investigators have not been fully responsive or forthcoming in the past.

7.5.2 After the review of the PI/SC Continuing Review Application, each of the Local Site Investigator Applications for Continuing Review is individually reviewed.

7.5.2.1 The Primary Reviewer discusses each application and any required changes. The comparison table as prepared by the VA Central IRB Coordinator is reviewed to ensure that there have been no changes in the documents submitted by the Local Site Investigators from the prior approved model PI/SC documents and/or the prior approved Local Site Investigator documents.

7.5.2.2 The IRB may also 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.

7. 5.2.3 The Primary Reviewer then makes a motion in accordance with paragraph 7.5.1.5, except that these recommendations would only pertain to the site being reviewed. The vote is then taken and recorded in accordance with paragraph 7.1.6 for each individual site.

7.5.2.4 If an amendment was received from a Local Site Investigator with the Application for Continuing Review for that site, the amendment is considered along with the application and the Primary Reviewer makes one motion incorporating the amendment with the vote then taken and recorded in accordance with paragraph 7.1.6.

7.6 Procedure for Review of Amendments. The following procedure is followed when amendments requiring review by the convened IRB are not submitted as part of a Continuing Review Application.

7.6.1 The Primary Reviewer reviews amendments on his or her assigned projects. If the amendment includes substantive changes in the informed consent document the Informed Consent Reviewer can be involved, in addition to the Primary Reviewer.

7.6.2 The ISO 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.

7.6.3 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.

7.6.4 The Primary Reviewer ensures all the approval criteria for the approval of the research are still met and makes one of the following motions:

7.6.4.1 Approve. No changes or further changes are required.

7.6.4.2 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 one of the Co-Chairs and the amendment does not have to be re-reviewed by the convened IRB.

7.6.4.3 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.

7.6.4.4 Disapprove. The amendment is deemed to have 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.

7.6.4.5 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.

7.7 Documenting the Results of IRB Reviews. The results of the convened IRB review are documented both in the meeting minutes and in Memoranda to the investigators and to the participating sites as applicable.

7.7.1 The VA Central IRB Coordinator prepares a memorandum to the PI/SC, Local Site Investigators, and the participating sites as applicable, within 10 working days of the date of the convened meeting detailing the decision of the IRB for each project action reviewed in accordance with VA Central IRB SOP 111, VA Central IRB Communications with Investigators and Local Participating Sites.

7.7.2 The VA Central IRB Coordinator prepares a draft of the meeting minutes in accordance with VA Central IRB SOP 115, Recording and Distribution of VA Central IRB Meeting Minutes, within three weeks of the convened IRB meeting date to which the minutes pertain.

7.7.3 If the review included an informed consent document that was approved, the date of the current approval is stamped or otherwise entered on the document. This newly dated consent form must begin to be used by the investigators within 5 business days of receipt. This does not include an informed consent document reviewed as part of the continuing review process and for which no revisions were made. In this case the original IRB approval date of the consent form is kept and no new approval date is stamped.

7.8 Other Convened Meeting Reviews. IRB review procedures for reporting and reviewing serious adverse events and unanticipated problems involving risks to subjects or others, complaints, and investigator non-compliance, as well as the use of investigational drugs or devices can be found in the applicable SOPs pertaining to those subjects.

8.0 REFERENCES

8.1 38 CFR 16, Department of Veterans Affairs, Protection of Human Subjects

8.2 VHA Handbook 1200.05, Requirements for the Protection of Human Subjects in Research

8.3 45 CFR 46, Department of Health and Human Services, Protection of Human Subjects

8.4 21 CFR 56, U.S. Food and Drug Administration, Institutional Review Boards

Attachment
VA Central IRB Convened Board Review Process

I have reviewed and approved the contents of this SOP.

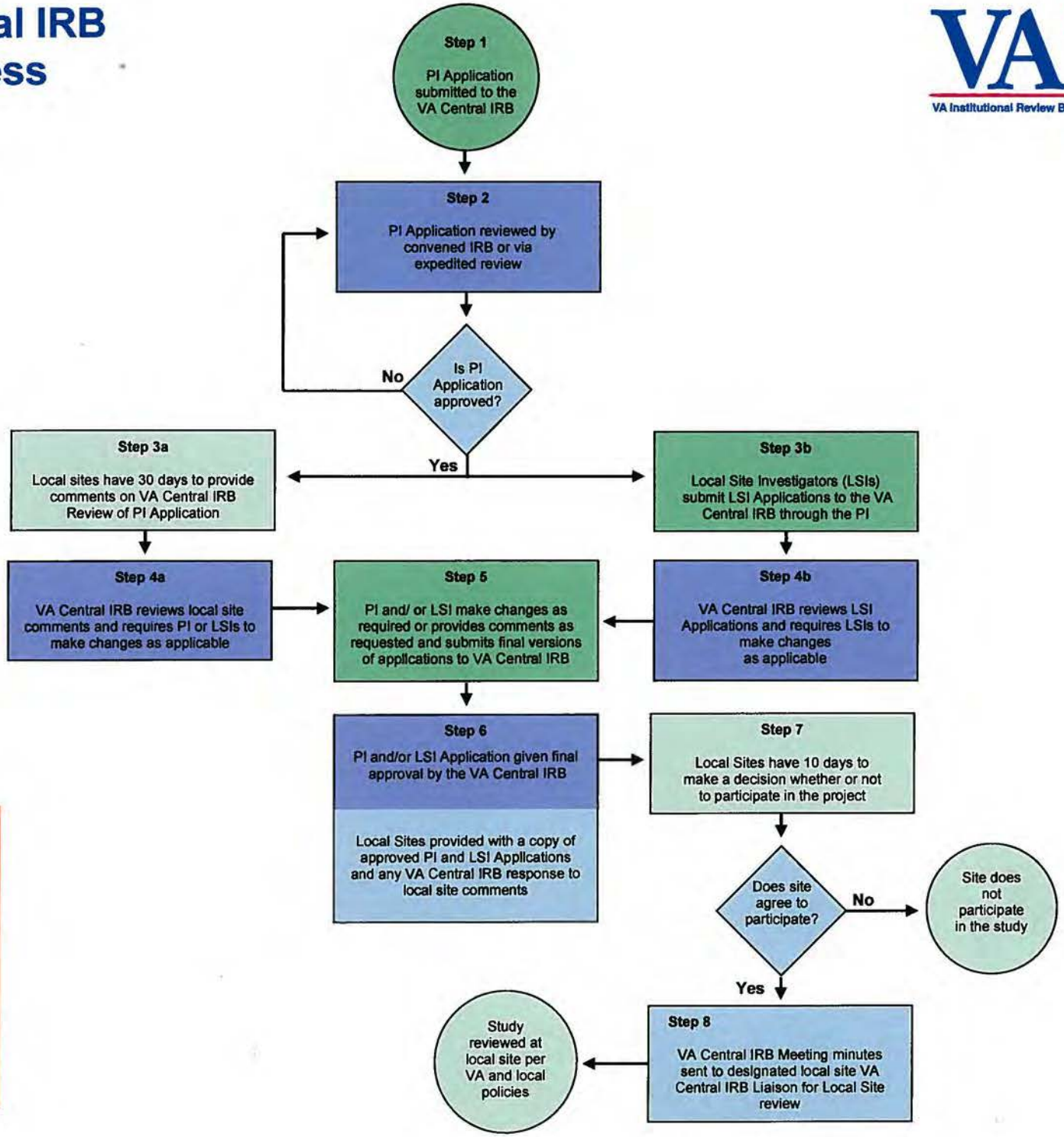
K. Lynn Cates, MD
Director, PRIDE

Date: 8/8/11

The VA Central IRB Review Process

November 2010

VA Central IRB
VA Institutional Review Board for Multisite Studies



Color Key
Investigators
Local Sites
VA Central IRB
Decision Points and Administrative Action
Note: *Local accountability occurs throughout the centralized review process,*

Key Steps in the VA Central IRB Review Process

November 2010

VA Central IRB
VA Institutional Review Board for Multisite Studies

Step 1. The Principal Investigator of a VA Office of Research and Development (ORD)-funded study submits a PI Application with all applicable documents to the VA Central IRB. The PI Application includes the following as applicable:

- Co-PI and Coordinating Center Supplements
- Model Informed Consent Form and HIPAA Authorization
- Waiver Requests (HIPAA/Informed Consent)
- Vulnerable Population Supplements
- CVs and Conflict of Interest Statements for PI
- Model Recruitment Materials
- Other documents as per study design

Step 2. Review Of the PI Application by the VA Central IRB at a convened meeting or by expedited review; if approved or approved contingent upon minor modifications, the PI and participating local sites are informed.

Step 3. This step consists of 2 parts that take place simultaneously:

Step 3a. Local Site Review
Local sites have 30 days to review the VA Central IRB approved PI Application and submit comments to the VA Central IRB.

Step 3b. Local Site Investigator (LSI) Applications
LSIs may begin to submit LSI Applications to the VA Central IRB. LSI Applications include the following as applicable:

- Informed Consent Form
- CVs and Conflict of Interest Statements for LSIs
- Recruitment materials to be used at local site
- Other documents as applicable

Step 4. VA Central IRB reviews Local Site comments and LSI Applications

Step 4a. Review of submitted local site comments; VA Central IRB may:

- Refer comments to PI
- Require changes in PI and/or LSI Applications
- Take no action

Step 4b. Review LSI Applications and include any changes from step 4a.

Step 5. PI and/or LSI submits changes or provides comments.

Step 6. VA Central IRB makes final approval decision and all relevant materials sent to the Local Site, to include the approved PI and the relevant LSI Application and the VA Central IRB response to any local site comments, so the Local Site can determine whether or not it will participate in the project.

Step 7. The Local Site has 10 days to decide whether or not it will participate in the study and to submit a participation decision to the VA Central IRB.

Step 8. The applicable VA Central IRB meeting minutes are provided to the Local Site and the Local Site processes the study in accordance with VA and local requirements.

Note: A VA study cannot begin at a given local VA facility until the PI and LSI applications have been approved by the VA Central IRB, and the local VA facility has complied with the requirements of VHA Handbook 1200.01.