SUBJECT: VA Ann Arbor Healthcare System (VAAAHS) Local Requirements for Submission of a VA Central IRB Protocol

1. PURPOSE:

The research mission of the Department of Veterans Affairs (VA) is conducted within individual VA medical centers according to the highest ethical standards with accountability to all involved stakeholders. This guidance outlines the local requirements for submission of a VA Central IRB (VA CIRB) Protocol.

2. DEFINITIONS:

Research: Research is the testing of concepts by the scientific method of formulating a hypothesis or research question, systematically collecting and recording relevant data, and interpreting the results in terms of the hypothesis or question. It is a systematic investigation including research development, testing, and evaluation designed to develop or contribute to generalized knowledge.

VA Research: VA research is research conducted by VA investigators while on VA time, utilizing VA resources (e.g. equipment), or on VA property including space leased to, or used by VA. The research may be funded by VA, by other sponsors, or be unfunded.

Human Subject: A human subject is a living individual about whom an investigator (whether professional or student) conducts research, and:

(1) Obtains information or biospecimens through intervention or interaction with the individual, and uses, studies, or analyzes the information or biospecimens; or

(2) Obtains, uses, studies, analyzes, or generates identifiable private information or identifiable biospecimens.

VA Central IRB: The purpose of the VA Central IRB is two-fold. First and foremost, its purpose is to enhance the quality of human research protection in multi-site human research projects by performing appropriate ethical and scientific review while ensuring local issues are addressed. The second is to enhance the efficiency of these reviews across participating sites.

Principal Investigator/Study Chair (PI/SC): The Principal Investigator who is the lead on the main study reviewed by the CIRB.

Local Site Investigator (LSI): The investigator at a local participating site who leads the local site project team and serves as the main point of contact for the PI or SC and the CIRB concerning the conduct of the project at that site.

Local Site Liaison: The VA Ann Arbor Healthcare System designee(s) who coordinates communication between Research Administration, Local Research Committees, and the VA CIRB.

3. Instructions for Submission of NEW Project and Protocol:

a) Simultaneously submit your initial VA CIRB PI or LSI application (see Appendix 1) and AAROW Project applications. In AAROW go to the home page, go to your Project Assistant, Project Workspace, select Create a New Project and begin a Project Application including COIs, budget, uploading of protocol, etc.

b) Complete your AAROW Protocol application but DO NOT SUBMIT IT at this time. In AAROW go to the home page, go to your Protocol Assistant, Protocol Workspace, select Create

a New Protocol and begin a Central IRB Application. You will need to upload all of your approved Central IRB documents into this submission, so wait for full approval of your Local Site Investigator (LSI) Application from the VA Central IRB.

c) Your AAROW Project application will go through the usual VA Ann Arbor Research & Development Committee (RDC) review. You can expect to receive an RDC response letter. Note that this will not be a final approval letter, but will be one of two categories:
   - Deferred pending Subcommittee approval: You are required to receive VA Central IRB approval and then local AAROW acknowledgement letters before the RDC will give final approval.
   - Deferred pending PI Response: You are required to respond to questions that the Committee may have, plus notation of the need for pending VA Central IRB approval.
   - Make all corrections as required. You must have VA CIRB Approval and then the local AAROW acknowledgement letter before the RDC will give final approval.

d) Approval for your project from the RDC will be granted only after your project application returns to the RDC. The Committee meets once per month (1st Wednesday of the month). If you have a Safety Component, then please make sure all safety concerns have been addressed with the Subcommittee on Research Safety as well.

e) Submit your Protocol application in AAROW once you receive VA CIRB **Local Site Investigator (LSI) approval**.

   1) The Central IRB Liaison will administratively process the CIRB documents. The local IRB does not have approving authority. An Outcome Letter will be issued, which must occur before the RDC final review and approval. The AAROW protocol serves only to track approved documents and follow your study as an approved protocol at VAAAHS.
   2) As part of your IRB Protocol application, the following documents must be uploaded into AAROW from your CIRB study application and CIRB-approved documents:
      - CIRB approval letter (VAAAHS PI or LSI)
      - Abstract
      - Protocol (Scientific Narrative)
      - Approved CIRB Consent Form
      - Approved CIRB HIPAA AUTHORIZATION FORM
      - Recruitment materials
      - Any other pertinent documents

f) Uploading documents into AAROW:
   - Open the Central IRB Submission and add a new component (mid-screen on the right…)
   - Select appropriate descriptions for your documents: consent, HIPAA, other, etc...
   - Complete and submit your AAROW Protocol application once you have the CIRB LSI approval in hand. **DO NOT SUBMIT WITH ONLY THE MAIN PRINCIPAL INVESTIGATOR (PI) APPROVAL UNLESS YOU ARE THE LEAD SITE!**

g) The Central IRB Liaison will then provide the study team with an outcome letter acknowledging receipt of the CIRB approvals and documents. The Central IRB Liaison will also alert the RDC of this action. The RDC approval letter will be issued after the RDC

meeting followed by the final ACOS approval to initiate study letter, which is the last approval granted. Once the ACOS/R issues the study initiation letter, the study can begin.

h) Order of submission tasks and events:
   1) VA CIRB Application (PI or LSI, depending on site involvement and role – See Appendix 1).
   2) Local VA Ann Arbor Project Application in AAROW (full application which undergoes RDC review, with an issued response letter).
   3) Local VA Ann Arbor Protocol Application in AAROW (Complete in AAROW, DO NOT SUBMIT until you have your LSI Approval from VA CIRB).
   4) If there is a safety component, a separate Safety Protocol Application will be required for submission as well.
   5) When VA CIRB approval is granted, upload VA CIRB Approval and accompanying documents in the Protocol in AAROW and submit.
   6) Final review to occur at monthly meeting RDC Meeting.
   7) You must have 4 documents in hand to begin the study: VA CIRB approval of LSI application, AAROW Acknowledgement Letter from the Central IRB Liaison, VA Ann Arbor RDC Approval, VA Ann Arbor ACOS Notice to Initiate Project.

i) Investigators and Study Team are required to complete all applicable trainings and processes associated with human subjects research. Documentation of study staff training, credentialing and privileging will be maintained by the VAAAHS Research Office, but must also be kept in a required Regulatory Binder.

j) Studies approved by the CIRB will be audited and monitored in accordance with all relevant local policies. All audit reports will be sent to the local study team which should report to CIRB at time of Continuing Review. The CIRB will be notified if a problem is discovered or complaint received.

4. Local Requirements for VA CIRB Amendments:

a) Contact the Central IRB Liaison if an amendment involves any changes to specific aims or changes that will impact patient safety or change in investigators or staff. Examples: study adds new procedures like more blood draws or x-rays.

b) Add the revised protocol, consent, HIPAA, abstract, CIRB approval and any other related documents to the AAROW Protocol, i.e., upload these documents. Do NOT begin an amendment or change the application except to upload documents to the initial protocol in AAROW. If in doubt, contact the Central IRB Liaison.

5. CONTINUING REVIEW: Continuing Review documents will be submitted to the VA CIRB. Once reviewed and approved, the local Central IRB Liaison will receive an email with a link to approved documents. The local database will be updated with a new expiration date by the Central IRB Liaison. You do not need to submit anything to the local IRB. Feel free to contact the Central IRB Liaison if any dates seem incorrect in AAROW.

6. STAFF CHANGES: Please notify local RDC and Central IRB Liaison if the Project is transferred to a NEW Principal Investigator. Follow all VA Central IRB guidelines for staff changes.

7. **SERIOUS ADVERSE EVENTS/PROTOCOL DEVIATIONS:** Contact VA Central IRB within the appropriate timeframe and follow their specific instructions.

8. **PROTOCOL CLOSURE:** Close protocol through the VA CIRB. Notify local Central IRB Liaison to close protocol and provide appropriate documentation. Submit a Project Closure Form.

9. **CONTACTS:**
   Projects (R&D applications and RDC): Sam McVean, RDC Coordinator at 734-845-5602
   Protocols (Central IRB Liaisons): Cathy Kaczmarek, IRB Coordinator at 734-845-3439
   Sheena Hatcher, IRB Coordinator at 734-845-5901

10. **REFERENCE:**
    VA Central IRB Standard Operating Procedures
    VA Central IRB Memorandum of Understanding Template
    Information for VA Central IRB Local Site Liaisons (

11. **FOLLOW-UP RESPONSIBILITY:** VA Central IRB Local Site Liaison

12. **ATTACHMENTS:** Appendix 1 - Submitting a New Study Application to the VA Central IRB

Appendix 1 - Submitting a New Study Application to the VA Central IRB

What projects are submitted to the VA Central IRB?

The VA Central IRB mainly reviews ORD-funded VA research projects that have more than one VA site engaged in human subjects research. The VA Central IRB will also review single site pilot studies that, if successful, will eventually have multiple VA sites engaged in human subjects research. The applicable ORD Funding service should be consulted if you have a question concerning whether your study should be submitted to the VA Central IRB. Studies funded by other sources may be considered for review by the VA Central IRB on a case-by-case basis.

How do I submit a new project to the VA Central IRB?

The VA Central IRB Application process involves two steps. The first step pertains to the submission of the protocol and supporting documents by the Principal Investigator/Study Chair (PI/SC). In addition, the PI/SC submits all waiver requests if they apply to the entire study, as well as model informed consent documents, HIPAA authorizations, and recruitment materials as applicable. The second step involves the submission of Local Site Investigator (LSI) Applications once the PI/SC application has been approved.

All VA Central IRB Application forms can be found by clicking on the forms link on this website: https://www.research.va.gov/programs/orppe/vacentralirb/forms/investigator-forms.cfm. **Prior to filling out any of the listed forms, the PI/SC or Study Coordinator should contact the VA Central IRB Administrator at 202-443-5649 to discuss submission deadlines, potential participating sites, and application procedures.**

The VA Central IRB also has an optional pre-review process. Drafts of the applicable forms and protocol can be submitted and a courtesy pre-review will be performed by one of the staff or by the VA Central IRB Administrator. This pre-review is not a determination of the VA Central IRB and is meant to assist the study team in ensuring the application will be complete at the time of submission. To request a pre-review, please contact the VA Central IRB Administrator.

Below is a more detailed description of the two-step submission process:

Step 1: Submission and review of Principal Investigator/Study Chair (PI/SC) New Project Application

The PI/SC completes a VA Central IRB Form 108, PI/SC New Project Application, as well as all associated forms and documents. The VA Central IRB Form 108 was designed to be self-explanatory but if you have any questions on any areas of the application, please do not hesitate to call a member of the VA Central IRB staff for assistance. Once the VA Central IRB Form 108 and all other associated documents and forms are complete, call the VA Central IRB Administrator at 202-443-5649 to obtain access to the VA Central IRB secure SharePoint site and to have a folder created for upload of the application documents.

Upon submission of the documents on the SharePoint site, send an e-mail message to or call the VA Central IRB Administrator to indicate that the initial submission is complete. The VA Central IRB

Administrator will assign a VA Central IRB Manager to the study. The assigned VA Central IRB Manager will serve as your main point of contact for all VA Central IRB actions related to the study.

The VA Central IRB Manager will perform an administrative review. Depending upon the type of project submitted, additional reviewers from the VA Central IRB will be assigned. At a minimum, the study will receive a review by the Regulatory Advisor to the VA Central IRB, the Privacy Officer Representative, the Information Security Officer Representative, and at least one voting member of the VA Central IRB. If the study is scheduled to be reviewed by the convened IRB, a Secondary Reviewer and an Informed Consent Reviewer may also be assigned. All comments will be consolidated as much as possible and forwarded to the PI/SC or designee via encrypted e-mail for response. However, in the interest of not holding up communications, some reviewer comments may be forwarded separately depending upon receipt. If the study is reviewed at a convened IRB meeting, a letter indicating the determinations made by the IRB, as well as any required modifications, will be forwarded.

Upon approval of the PI/SC Application, or approval contingent upon required minor modifications if the study was reviewed by the convened IRB, the study advances to the next step.

Step 2: Submission of Local Site Investigator (LSI) Applications

After a PI/SC Application has been approved under expedited review procedures, or approved contingent upon required minor modification if reviewed by the convened IRB, LSI Applications, VA Central IRB Forms 104, may be submitted by each Local Site Investigator.

The LSI Application mirrors the PI/SC Application. There are standard sections for study staff and site-specific information. If the LSI does not plan to deviate from the approved PI/SC Application, in many sections, this can just be stated and no further information needs to be completed. If the LSI plans to deviate from the approved PI/SC Application, all deviations must be detailed and justified on the application. Approved model forms should be used and site-specific demographic information completed as appropriate. Any deviations made from approved wording must be indicated through the use of the "track changes" function, and justification provided within the application. LSI Applications should also include changes made in response to any requested modifications to the PI/SC Application as applicable.

LSI Applications must be submitted to the PI/SC study team for review prior to upload to the VA Central IRB SharePoint site. This upload can be done by the PI/SC study team and/or the Local Site Study Coordinator. The PI/SC study team must inform the VA Central IRB Manager for the study via phone or e-mail that LSI Applications have been submitted.

LSI Applications will be reviewed after the comments that were solicited from the local sites to the approved PI/SC Application are reviewed by the VA Central IRB. Upon review of local site comments, additional modifications may be required in the PI/SC and/or LSI Applications. These additional modifications will be detailed for the investigators in writing.

A simplified flowchart detailing the entire VA Central IRB application and review process can be found by clicking on the below Microsoft Publisher file: Flowchart detailing the entire VA Central IRB application