

# Use of VHA Central Office Institutional Review Board Research Standard Operating Procedures

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## Substantive changes in this revision:

1. **Section V.B.2., deleted the option to review the delegation of authority log throughout document**
2. **Section VI.A.1. & 2., clarified R&DC review of PI/SC or LSI application**
3. **Section VI.A.4., moved flag information to section below**
4. **Section VI.B.1., removed requirement for R&DC review of continuing reviews, clarified review actions of R&DC coordinator re: study staff**
5. **Section VI.C.1., clarified R&DC review actions for modifications, events, etc.**
6. **Section VI.D., replaced “Information Security Officer (ISO)” with “Information System Security Officer (ISSO)” throughout document**

## I. PURPOSE:

To establish the scope, policy, and procedures for the use of the VHA Central Office Institutional Review Board (VA Central IRB) at the VA Portland Health Care System (VAPORHCS)). In 2008, the Office of Research and Development (ORD) established a VA Central IRB in order to be the official IRB of record for VA Cooperative Studies (CSPs). All review of the research by the VA Central IRB must be approved by the R&D Committee.

## II. SCOPE:

The VA Central IRB reviews certain VA funded multi-site trials which intend to include human subject research; this may include human subjects, biological samples from humans, or their medical records. This review is intended to ensure that human subjects are protected. All VAPORHCS applicable R&D Policy & Procedures (P&P) and IRB SOPs will apply to protocols using the CIRB, with this SOP providing the applicable exceptions to those SOPs.

## III. BACKGROUND:

A Memorandum of Understanding (MOU) is in place between the VAPORHCS, the Portland VA Research Foundation (PVARF) and the VA Central IRB for select multi-site VA research projects involving human subjects. The VA Central IRB review will include

initial review, continuing review, review of amendments, reporting, monitoring and other relevant requirements.

As per the MOU, both institutions will adhere to 38 CFR 16 and 17, 45 CFR 46 subpart A, and 21 CFR 50 and 56, as well as other pertinent VA and federal regulations and requirements applicable to human subject research.

The VA Central IRB has been added to the VAPORHCS' Federal-wide Assurance (FWA) with the Office for Human Research Protections as an IRB of record for the facility.

#### IV. DEFINITIONS:

- A. Assurance: An Assurance is also called an Assurance of Compliance, or a Federal-wide Assurance (FWA). It is a written commitment by an institution to protect human subjects participating in research. Under federal regulations, any institution conducting or engaged in federally supported research involving human subjects must obtain an Assurance in accordance with 38 CFR 16.103. NOTE: All research conducted under VA auspices is considered to be Federally-supported. This requirement also applies to any collaborating "performance site" institutions. Under 38 CFR 16.102(f), an institution is engaged in human subject research whenever its employees or agents: intervene or interact with living individuals for research purposes; or obtain, release, or access individually-identifiable private information for research purposes. Assurances are filed through the VA Office of Research Oversight (ORO) with the Department of Health and Human Services (DHHS) Office for Human Research Protections (OHRP). The FWA replaces previous types of OHRP and VA assurances.
- B. Continuing Noncompliance: Persistent failure to adhere to the laws, regulations, or policies governing human research.
- C. Coordinating Site: The main study site where the Principal Investigator/Study Chair (PI/SC) runs the study. The PI/SC New Project Application is submitted from the coordinating site.
- D. Federal-Wide Assurance (FWA): A Federal-wide Assurance is also referred to as an Assurance (see the definition of Assurance in paragraph 3.C).
- E. Investigator: An investigator is an individual under the direction of the Principal Investigator (PI) who is involved in some or all aspects of the research project, including the: design of the study, conduct of the study, analysis and interpretation of the collected data, and writing of resulting manuscripts. An investigator must be either compensated by the VA, be appointed to work without compensation (WOC), or may be an employee assigned to the VA through the Intergovernmental Personnel Act (IPA) of 1970. The FDA considers an investigator and a PI to be synonymous. (VHA Handbook 1200.5)
- F. Local Site: Any study site other than the main coordinating site.
- G. Local Site Investigator (LSI): The investigator who will submit an application to be PI of the study that will be conducted at other VA sites besides the main coordinating site.

- H. Local Site Liaison: The Local Site Liaison is appointed to serve as the main point of contact between the local VA facility and the VA Central IRB. The Local Site Liaison is given access to the VA Central IRB SharePoint site for all studies involving their local site for which the VA Central IRB is serving as the IRB of Record. An Alternate Local Site Liaison may also be added as a local point of contact.
- I. Memorandum of Understanding (MOU): A Memorandum of Understanding is a cooperative agreement between two parties. There is one MOU in place for the purposes of human subject's protection in research. The Memorandum of Understanding (MOU) between the Institution (VAPORHCS) and the VA Central IRB establishes the terms of the cooperative agreement for human subject protection in research between these two entities. This agreement outlines the requirement for both institutions to adhere to VA and other federal requirements for the protection of human participants in research.
- J. Office for Human Research Protections (OHRP): The OHRP is an office within the Department of Health and Human Services (DHHS) that monitors human research subject's protections through educational efforts, clarification and guidance, site visits, and reporting requirements. The OHRP has the authority to suspend research for failure to adhere to the regulations. OHRP replaces the earlier Office for Protection from Research Risks (OPRR).
- K. Office of Research and Development (ORD): ORD is the office within VA Central Office responsible for the overall policy, planning, coordination, and direction of research activities within VHA. NOTE: The Research Integrity Development and Education Program (PRIDE) is the program within ORD that is responsible for training, education, and policy development related to human subjects protection. (VHA Handbook 1200.5)
- L. Principal Investigator (PI): Within VA, a PI is an individual who conducts a research investigation, i.e., under whose immediate direction research is conducted, or, in the event of an investigation conducted by a team of individuals, is the responsible leader of that team. The FDA considers a PI and an investigator to be synonymous. (VHA Handbook 1200.5)
- M. Safety Reports: Safety Reports are written reports from sponsors notifying the FDA and all participating investigators of any adverse experience associated with the use of a drug, biologic or device that is both serious and unexpected.
- N. Serious Adverse Event (SAE): An AE in human research that results in death, a life-threatening experience, inpatient hospitalization, prolongation of hospitalization, persistent or significant disability or incapacity, congenital anomaly, or birth defect. An AE is also considered serious when medical, surgical, behavioral, social, or other intervention is needed to prevent such an outcome.
- O. Serious Noncompliance: The failure to adhere to the laws, regulations, or policies governing human research that may reasonably be regarded as:
1. involving substantive harm (or genuine risk of substantive harm) to the safety, rights, or welfare of human subjects, research staff, or others; or
  2. substantively compromising the effectiveness of a facility's human research protection or human research oversight programs.

- P. Serious Problem: Problem in human research that may reasonably be regarded as involving (a) substantive harm or genuine risk of substantive harm to the safety, rights, or welfare of research subjects, research staff, or others; or (b) substantively compromising the effectiveness of a facility's human research protection or human research oversight programs.
- Q. Unanticipated Problems: An event that is new or greater than previously known in terms of nature, severity, or frequency, given the procedures described in protocol-related documents and the characteristics of the study population.

## V. VA CENTRAL IRB REVIEW PROCEDURES:

### A. PI/SC applications

1. The PI/Study Chair (SC) of the entire project is notified that his/her project is on the Just-in-Time (JIT) Document Manager website. The PI completes the PI/SC New Project Application, VA Central IRB form 104.
2. The PI/SC submits the new project application to the Alternate Local Site Liaison, located in the Research Service office. The alternate liaison obtains the signature of the ACOS on the application and retains a copy for the Research office study file. The alternate liaison returns the application to the PI/study staff to be submitted to the VA Central IRB.
3. The PI/SC contacts the VA Central IRB administrative staff to coordinate the management of study documents. Access to the VA Central IRB SharePoint folder for the study is given to the PI/SC, study staff, and the local site liaisons.
4. The PI/SC application is reviewed by the convened VA Central IRB or via expedited review. The PI and site liaisons will receive correspondence detailing any contingencies that must be addressed if the study is contingently approved. The PI should carbon copy the alternate site liaison on any correspondence to the VA Central IRB in response to the approval contingencies.
5. When the PI/SC New Project Application has been fully or contingently approved, the main study site and the multiple local sites identified in the application are sent a copy of the application package. The PI/SC, and local site investigators and liaisons are required to review the documents and provide comments to VA Central IRB voicing any concerns the study. The PI/SC and the local site investigators and liaisons have 15 calendar days to provide comments on the initial VA Central IRB review of the application. This solicitation is not necessarily related to approval contingencies, if any, but it is the only opportunity for the PI/SC or local site investigator and liaisons to provide input to the VA Central IRB regarding the study design. The local site liaison can request review of the documents by an individual with a particular area of expertise, if necessary.
6. The VA Central IRB will review local site comments and require PI/SC to make changes as applicable. A final determination of the study will be sent to the PI/SC and site liaisons. Whatever revisions are made by the VA Central IRB must be accepted in full by the VAPORHCS, or, if the final approval

documents are not acceptable to the VAPORHCS PI/SC or local site liaison, participation in the study must be declined.

7. When the PI/SC has full approval by the VA Central IRB, the review of local site investigator applications will begin. If the study will include the enrolling of subjects at the VAPORHCS, a local site investigator application must be submitted to the VA Central IRB.

**B. Local Site Investigator Application (LSI):**

1. Once the main PI/SC application is approved, the LSI is instructed to prepare the local site investigator application. The LSI is contacted by the main PI/SC regarding participation as an investigator at the VAPORHCS site.
2. The LSI submits the new project application to the Alternate Local Site Liaison, located in the Research Service office. If the local site investigator is not the main PI/SC of the study, the application must be accompanied by a VAPORHCS PPQ, abstract, Conflict of Interest (CoI) forms for VAPORHCS study staff, Scope of Work forms (IRQ Appendix L) for all VAPORHCS staff, and administrative review form, if applicable. The alternate liaison verifies the credentialing and training of the VAPORHCS staff, obtains the signature of the ACOS on the application and retains a copy for the Research office study file.
3. The LSI coordinates with the main PI/SC to facilitate uploading the documents to the VA Central IRB SharePoint study folder. Study documents are uploaded to the SharePoint study folder by the PI/SC or LSI, or study staff. The local site liaisons do not submit study documents or applications to the VA Central IRB.
4. The LSI application is reviewed by the convened VA Central IRB or via expedited review. The LSI and liaisons will receive correspondence detailing any contingencies that must be addressed if the study is contingently approved.
5. When the approval documents are ready, a link to the folder on the SharePoint site will be sent to PI/SC, LSIS/staff, and local site liaisons. When the signed minutes from the VA Central IRB meeting are complete, a link to a folder on the SharePoint site will be sent to the PI/SC, LSIS/staff, and local site liaisons.
6. When the minutes from the VA Central IRB meeting at which the project was reviewed are posted to the SharePoint site, they will be included for review at the next R&D Committee meeting.

**C. Continuing Reviews:**

1. The VA Central IRB will conduct continuing review of approved projects at least once per year, or more often if determined appropriate. The R&D committee will review and approve the VA Central IRB minutes at which the continuing reviews were discussed and approved.

**D. Modifications, Notifications, and Serious Adverse Events (SAEs):**

1. Modifications, notifications, and SAEs should be submitted by the PI/SC or LSI to the VA Central IRB. No changes to the protocol should be implemented until the proposed modifications are approved by the VA Central IRB. Modifications may only be implemented locally to eliminate apparent immediate hazards to the human subjects in accordance with 21 CFR 56.108(a) and 38 CFR 16.103(b)(4). In such a case, the VA Central IRB must be notified by the PI/SC or LSI within 5 working days. If any local action is mandated by the R&D Committee, the local site liaison should notify the VA Central IRB within 5 working days.
2. The VA Central IRB should be notified immediately by the local site liaison of potential research impropriety, misconduct, suspension, debarment, or restriction of any local research team member associated with a VA Central IRB-approved project.
3. Please refer to the VA Central IRB website: (<http://www.research.va.gov/programs/pride/cirb/sop/default.cfm>) for information on specific reporting requirements and procedures. Refer to *Standing Operating Procedures for Required Reports in Research for VAPORHCS* requirements.
4. A link to notification, amendment, and serious adverse event approval documents on the SharePoint site will be sent to the PI/SC, LSIs/staff, and local site liaisons by the VA Central IRB. Copies of the documents will be stored electronically in Research Service. Notifications, amendments, and serious adverse events do not need to be reviewed by the R&D Committee [per requirements of VHA Handbook 1200.01 and VAPORHCS R&D Committee P&Ps], though they may be discussed during the review of the VA Central IRB minutes.

## VI. VAPORHCS R&D COMMITTEE REVIEW PROCEDURES

### A. Initial Reviews:

1. Once the PI/SC or Local Site Investigator (LSI) application approval documents have been generated and placed on the VA Central IRB SharePoint site, the R&D Committee coordinator confirms the following:
  - a. The credentialing and education requirements are met by the local site investigator and study staff.  
A Scope of Work (IRQ Appendix N) form has been submitted for all VAPORHCS study staff;
  - b. The administrative review is complete (if applicable); and
  - c. If the VA Central IRB has determined that a research flag is required
2. The R&D Committee initial review is scheduled for the next upcoming meeting. Per normal procedures for conducting an initial review, the R&D primary reviewer and R&D Committee members will be provided with the VA

Central IRB approval documents to review, as outlined in the VAPORHCS R&D Committee Policy & Procedures (P&P).

3. When the study receives final initial review approval from the R&D Committee, the R&D Committee initial review approval letter and the notification of approval from the ACOS/Research will be sent by the R&D Coordinator to the PI/SC or LSI. For studies originating from a Cooperative Study Program (CSP) coordinating site, the approval documents will be sent to the CSP program manager, if requested. **NOTE:** *The study cannot start until the PI has received the approval letters from the VA Central IRB and the R&D Committee, and the ACOS/R&D Notification memo.*
- 4.

#### Research Flags Advisory Requirements:

1. If the VA Central IRB determines a research flag should be added to the electronic medical records of all study participants, it will be noted on the PI/SC approval memo. The R&D Committee coordinator will provide the name of the research flag to the LSI and study staff.
2. In general, a VAPORHCS participant may only be enrolled in one research study at a time for which either the VA Central IRB or another VAPORHCS IRB of record has required a flag advisory in the participant's electronic medical record. However, the VAPORHCS investigator (whether he/she is the main PI/SC or a LSI) can request an exception for dual enrollment of an individual participant(s), who already has another research flag advisory on their record, or for the whole study.

In order to request such an exception, the LSI must first contact the LSI (for studies reviewed by the VA Central IRB) or PI (for studies reviewed by the VA IRB or affiliate IRB) of any other flagged study for which they wish to be able to dually enroll a participant(s). The other study's LSI or PI has the discretion to allow dual enrollment for any/all participants, or for a particular participant(s), or they may decline to allow dual enrollment of any kind.

Once the LSI obtains the agreement of the other study's LSI or PI, they must then submit a request for the exception to the R&D Committee. The request should include:

- a memo describing the request;
- written documentation from the other study's LSI or PI that they agree to allow for the dual enrollment of their study's participants or just for a certain participant(s) (if the latter, the applicable participants should be described without using HIPAA identifiers – e.g. all participants who have completed treatment with study drug, or Participant #0001);
- a copy of the abstract for each study; and

- any other applicable materials supporting the request and/or requested by the R&D Committee or Research Administration Office staff.

If the R&D Committee approves the request, the LSI may then enroll the applicable participant(s). The consent progress note of any such participant must include the following:

- the date of R&D Committee approval for the dual enrollment;
- the date that the requesting LSI spoke to the other study's LSI or PI; and
- confirmation that the other study's LSI or PI agreed to dual enrollment and whether the agreement was for a certain participant(s) or for the whole study.

#### B. Continuing Reviews:

1. The R&D Committee will review the continuing reviews of approved projects reviewed by the VA Central IRB when they are presented in the VA Central IRB minutes..
2. The study staff members that are listed in the VA Central IRB continuing review form 115a will reviewed by the R&D Committee coordinator at the time the R&D Committee reviews the VA Central IRB minutes, to make sure that a Scope of Work (SoW) form is on file for each individual.

#### C. Modifications, Notifications, and Serious Adverse Events (SAEs):

1. The R&D Committee is not required to review individual study modifications, notification or SAEs that have been approved by the VA Central IRB. The R&D Committee will review the modifications, notifications, and SAEs of approved projects reviewed by the VA Central IRB when they are presented in the VA Central IRB minutes.
2. If the VA Central IRB, the ACOS/R&D, Research Compliance Officer (RCO), PI/SC or local site investigator requests that local review of such item occur, it will be scheduled by the R&D Committee coordinator.
3. If the modification/notification includes study personnel being added to a study that is reviewed by the VA Central IRB, the R&D Committee coordinator will confirm that credentialing and education requirements are met, and that a Scope of Work (SoW) form has been submitted to the local office.

#### D. Privacy Officer (PO) and Information System Security Officer (ISSO) Review:

1. The VA Central IRB PO and ISSOs perform the required privacy and information security reviews as part of the study reviews. The VAPORHCS PO does not conduct a separate privacy review of studies overseen by the VA Central IRB. The VAPORHCS ISSO may need to review some studies overseen by the VA Central IRB due to local project-specific information security issues. In these cases, the VA Central IRB ISSO will work with the VAPORHCS ISSO to resolve these issues.



2. Any unauthorized use or disclosure of protected health information (PHI) or any violations of VA information security requirements in projects overseen by the VA Central Office must be reported to the VA Central IRB, and the local PO and ISSO.

E. Review of VA Central Office Human Research Protection Plan (HRPP) Annual Report

1. The VA Central IRB HRPP annual report will be reviewed by the VAPORHCS R&D Committee annually. The review will be scheduled according to the R&D Committee annual review schedule of events.

F. Review of Audits:

1. Routine and other compliance audits of VA Central IRB-approved projects conducted by the Regulatory Compliance Officer (RCO) will be reported to the R&D Committee.
2. Special audit requests made by the VA Central IRB as part of its oversight responsibilities for projects for which it serves as the IRB of record will be facilitated by the Research Service office. The results of such audits will be reported to the R&D Committee and the VA Central IRB.