ADVARRA, INC. IRB Review Processes
VA Portland Health Care System Supplemental SOP

Purpose:

The purpose of this Standard Operating Procedure (SOP) is to document the process for communication between the VA Portland Health Care System (VAPORHCS) and the Advarra IRB.

Background:

VAPORHCS has received approval from the Veterans Health Administration (VHA) Office of Research and Development (ORD) to enter into an agreement with Advarra, Inc. to serve as an IRB of record for funded or industry sponsored cooperative research studies or ORD approved expanded access programs. The reliance agreement content was approved at the national level by the Office of Research Oversight (ORO), ORD, and Advarra, Inc. so no local changes are required. A Master Services Agreement is in place between the Office of Research and Development (ORD), and Advarra, Inc. which includes VA specific requirements for IRB review.

This SOP is supplemental to the IRB Policies and Procedures (P&P), the VA medical facility IRB SOPs stored on the VAPORHCS Research & Development website, which is located at: https://www.portland.va.gov/research/documents/irb/irb-sop.doc, and is consistent with the Advarra IRB Standard Operating Procedures (SOPs), located at: https://www.cirbi.net/CIRBI/sd/Rooms/DisplayPages/LayoutInitial?Container=com.webridge.entity.Entity[OID[AC482809EC03C442A46F2C8EEC4D75D3. The Advarra IRB Handbook for Investigators, Sponsors, and Sponsors' Representatives is located on the Advarra IRB website and should be disseminated and reviewed by all applicable research and study staff. Any changes to the Handbook are communicated via the IRB's cloud based Advarra Center for IRB Intelligence CIRBI Platform (www.cirbi.net) and will be posted in the Reference Materials section of CIRBI for immediate access.

Advarra utilizes a cloud-based electronic platform to facilitate research study submissions, regulatory compliance, and e-processing and tracking of research studies. The electronic platform is called the Advarra CIRBI Platform and allows real-time communication among sponsors, research sites, institutional representatives, and Advarra staff and IRB members. All parts of the IRB process from initial submission to study close-out/termination are supported by CIRBI. Note: Please contact the CIRBI Help Desk at 1-866-99CIRBI (1-866-992-4724) or email CIRBI@advarra.com with any questions.

Institutional Official Responsibilities:

(1) The VAPORHCS Institutional Official (IO) signs the Advarra, Inc. IRB Institutional Authorization Agreement and Division of Responsibilities. This agreement replaces the VA Memorandum of Understanding (MOU) for IRB services (VHA Directive 1058.03). The agreement is updated as required by the Advarra IRB, and copies of the initial agreement and each update are sent to ORD and ORO

when fully executed. ORO does not require updates to the agreement for changes of Institutional Official.

(2) Appoints the Local VA Facility Liaison to serve as the administrative liaison between the VAPORHCS and the IRB. The name of the liaison will be reported to ORD. Any liaison change must be reported to Advarra and ORD.

(3) Formally reports unanticipated problems, serious and/or continuing non-compliance, and suspension or termination of study activities originating at VAPORHCS as required by VA policy to ORO and external federal agencies or oversight bodies.

(4) Ensures that the Federalwide Assurance (FWA) and VA Addendum to the FWA are kept current as required by VHA Directive 1058.03.

Research & Development Committee (R&DC) Responsibilities:

(1) The convened R&DC and sub-committees may review the protocol prior to the Advarra IRB review and then the R&DC through designated review may grant final approval.

(2) Ensures that the investigator and study personnel have the resources, experience and training needed to conduct the research, all members of the research team have been credentialed, privileged, have an approved Scope of Practice if applicable, and have completed all training required by VA and Advarra, Inc. in the protection of human subjects.

(3) Ensures that the Advarra IRB is provided with current state law requirements.

(4) Determine if non-Veterans should be enrolled in a study at VAPORHCS if the VA Investigator requests non-Veteran enrollment in the study.

(5) Ensures Information Systems Security Officer (ISSO) and Privacy Officer (PO) preliminary reviews were provided to Advarra IRB for review during the approval process and that all required final reviews are complete with all stipulations resolved before R&D Committee final approval is given and before the study is initiated.

(6) Ensures the VAPORHCS conflict of interest policy will be followed, and relevant determinations and/or management plans will be forwarded to Advarra IRB per Advarra SOPs.

(7) Ensures reviews by all applicable R&DC subcommittees are complete before the study is approved.

(8) Ensures that the study may not begin at VAPORHCS until the R&D Committee approves the research study and the ACOS/R notifies the Principal Investigator in writing that he/she is authorized to initiate the study.

(9) Oversees the local regulatory aspects of the research and reviews protocol non-compliance reports.

(10) Reviews all determinations by the Advarra IRB of any reported incidents or unanticipated problems and/or serious or continuing noncompliance for acceptance or further action. Ensures any remediation is completed.

(11) Notify the IRB when a regulatory deficiency has been cited on an RCO or other regulatory audit that occurred during the time that the IRB was responsible for study oversight.

(12) Provide a mechanism to receive and address concerns from local study participants and others about the conduct of the research.
(13) Is authorized to observe any aspect of the research process including observing the informed consent process. The Advarra IRB retains the authority to direct this to be done when necessary, by VAPORHCS.
(14) Conducts an annual review of the Advarra IRB and submits to the VA Facility Medical Center Director as required by ORD policy in VHA Directive 1200.01. This review includes but is not limited to evaluation of the number of projects handled by the committee, communication between entities, changes in the Institutional Authorization Agreement, change in processes, and challenges. Advarra IRB has agreed to provide an annual summary to assist in R&DC review.
(15) Ensures formal notification in a timely manner to the Advarra IRB whenever there is a proposed change in Principal Investigator.

VA R&D Service/Office:

(1) Verifies that the following forms and agreements are signed and executed by the VAPORHCS prior to use of the Advarra IRB and maintained in a current status:
    a. This Advarra IRB SOP with review by the R&D Committee per local policy.
    b. The Institutional Authorization Agreement, signed by the Facility Director and Advarra, Inc.
(2) Correspondence from the Advarra IRB will be available to the Local Site Investigator through the CIRBI platform as indicated above, for inclusion in the Study Regulatory Binder.
(3) As needed, the R&DC coordinator, RCO, or other facility personnel may apply for an account with the Advarra IRB (CIRBI) http://www.cirbi.net and have access to the files and correspondence to the investigator. Otherwise, the local investigator may download documents from the Advarra IRB web portal and provide copies of the documents to the R&DC coordinator who will, as appropriate, triage documents to oversight committees and oversight officials for action and maintain project files.
(4) Provides tracking for protocols and correspondence.
(5) Manage evaluation of financial conflict of interest.
(6) Ensures a process in place to allow ISSO and PO access to study materials for project review prior to study submission and to facilitate communication between the ISSO, PO and PI so that preliminary stipulations can be addressed by the PI prior to submitting to Advarra IRB.
(7) The VA Endorsement Letter will serve as the site-specific IRB submission cover page. It must be signed by the ACOS/R&D, the AO/R&D or a designee other than the PI confirming that once all required approvals are in place the project may be conducted at the facility, neither the VA nor the NPC is contracting directly for the IRB review and that the PO and ISSO preliminary reviews have been completed. The endorsement letter cannot be signed by the investigator.
(8) In the event of a change in the PI, ensures coordination with the departing Local Site Investigator, the sponsor and the IRB. Coordinates with the new PI a transfer of the approved study, after the R&D office confirms that the proposed new PI has

the appropriate credentials to proceed as PI and the new PI has been approved by the Sponsor and the IRB.

(9) Ensures notification of the Research Compliance Officer (RCO) of the signed reliance agreement and this supplemental SOP including IRB specific reporting mechanisms.

(10) Promptly updates SOPs for changes in the IRB requirements and inform the research community affected (e.g., investigators, study coordinators, investigational pharmacist) as applicable for changes affecting their roles and responsibilities.

(11) Maintains current FWA and access to IRB Rosters.

VA Privacy and Information System Security Officers:

(1) The VAPORHCS PO and ISSO will review studies overseen by Advarra IRB.

(2) The PO will review the HIPAA authorization to ensure it contains all required elements and is consistent with all privacy requirements. The PO reviews the HIPAA authorization, informed consent document, and protocol for consistency.

(3) ISSO and PO preliminary reviews and recommendations must be included in the application information sent to Advarra IRB. All ISSO and PO identified concerns must be resolved prior to study initiation.

(4) Advarra IRB is not storing VA data on their platform; VA is transmitting a copy of VA data for the purpose of IRB review. As part of the ORD approval process for nationwide use of Advarra IRB, VACO ISSO reviewed the methods and systems over which a copy of VA data is securely transmitted to the IRB.

Research Compliance Officers (RCO) Responsibilities:

Complete informed consent audits and study regulatory audits as required in the RCO Audit Plan. RCOs will have access to the research subjects' records and/or case files for oversight and monitoring activities. All reports of apparent serious non-compliance, apparent continuing noncompliance, or apparent serious unanticipated problems resulting from an RCO audit will be reported to the local facility officials per local policy and to the Advarra IRB. RCO audit findings that are reportable to the Advarra IRB will be submitted to the Advarra IRB within 10 business days in accordance with Advarra IRB policy. RCO audit reports with no findings or no immediate findings for studies overseen by the Advarra IRB will be submitted to the R&D Committee and to the Advarra IRB in a study specific batched annual report which may include any IC and HRPP audit reports. The RCO must ensure that the reports are uploaded within the required timeframe by those who have access to the system. RCOs are not required to audit Expanded Access Programs.

Local Principal Investigator (PI) Responsibilities:

(1) Ensure that study staff have been appropriately credentialed and privileged as applicable and have completed all required VA training in the protection of human subjects.

(2) All Investigators must submit an OGE 450-Alt-VA Form for review through the normal VAPORHCS procedures. Information regarding the review and any relevant determinations or management plans must be shared with the Advarra IRB during the application process. OGE 450 Alt VA forms are not sent to the IRB. The VAPORHCS Conflict of Interest In Research policy is available at: https://www.portland.va.gov/Research/piservices/rd_forms.asp.

(3) Ensure ISSO and PO preliminary reviews are conducted and provided to Advarra IRB for review prior to IRB approval. To limit multiple IRB submissions, any ISSO or PO requirements should be addressed by the PI prior to initial IRB submission. Final ISSO and PO reviews must be complete prior to initiating the study.

(4) Ensures the study is not initiated prior to receiving written ACOS implementation approval.

(5) Develop a recruitment plan. If potential subjects are to be identified from CPRS or any facility list of patients, a HIPAA authorization waiver must be requested and approved prior to viewing records.

(6) Ensure non-Veterans are not enrolled without study specific approval by the R&D Committee.

(7) Ensure all study staff changes are made and submitted to the Research Administration Office for updating in the research protocol tracking system and research personnel database.

(8) Ensure VA required elements are in the informed consent including any language required by VHA Directive 1200.05 for Certificates of Confidentiality if applicable. If the HIPAA authorization is embedded in the consent document, ensure all required VA elements are included. Use the approved informed consent document for use at VA as approved by the IRB.

(9) If the HIPAA authorization is not embedded in the consent document, ensure required VA form 10-0493 is used. The form 10-0493 must be included in the Advarra IRB application packet and reviewed by the VA facility privacy officer prior to study approval by the R&D Committee. Ensure the approved form is used. Ensure the HIPAA authorization includes the VA-required elements if the authorization is combined with the written informed consent document.

(10) Write progress notes as appropriate.

(11) Maintain compliance with state, local, or institutional requirements related to the protection of human subjects.

(12) Comply with all Advarra IRB and VAPORHCS requirements related to the protection of human subjects and adhere to responsibilities detailed in VHA Directive 1200.05 investigator section.

(13) Investigate and notify the Advarra IRB and R&DC of any study-specific incidence, experience or outcome that appears to rise to the level of an unanticipated event per Advarra IRB requirements and VHA requirements in VHA Directive 1058.01 respectively. The IRB requires that sponsors and/or investigators/sites (as appropriate) submit in writing any unanticipated problems (UAPs) involving risks to subjects or others, including adverse events that should be considered UAPs as described in Advarra IRB SOP. Notification to the IRB of a UAP must occur promptly but no later than 2 weeks (10 business days) from the time of identification.

Investigate and notify the Advarra IRB and R&DC of any serious or continuing non-compliance, termination or suspension of research, privacy or information security incidents per local and VHA policies. Investigators are required to follow stricter reporting requirements per VHA Directive 1058.01 for information security incidents.

Sponsors, investigators and/or research staff must notify the IRB in writing of any instance of noncompliance with the regulations, VHA Directive 1058.01 and/or determinations and requirements of the IRB. This notification must be as soon as possible but no later than 2 weeks (10 business days) from the time of the event.

(14) Propose/prepare a management/remediation plan to the R&DC and Advarra IRB for local potential unanticipated problems and possible serious or continuing noncompliance.
(15) Notify the Advarra IRB if a subject becomes incarcerated during participation in a study.
(16) Notify the Advarra IRB if a female subject becomes pregnant during her participation in a study.
(17) Maintain a regulatory file for the study under Advarra IRB purview as per local institution and sponsor policy.
(18) The PI will forward documents/communication to the research office per local policy.
(19) Submit copies of documentation going to and from the Advarra IRB to the VAPORHCS Research Administration Office. These are to be submitted in the online submission system VAIRRS or via email to the RA Office, where appropriate.
(20) Notify the Advarra IRB and research office in the event of a proposed change in PI or a planned leave of absence.
(21) Acts as the point of contact for the Advarra IRB should they have any questions about the research proposed or being conducted at VAPORHCS.