VA Northeast Ohio Healthcare System (VANEOHS)
Medical Research Service
Standard Operating Policy/Procedure (SOP)

Effective Date: 06/04/2020
SOP Title: Use of ADVARRA, Inc Institutional Review Board
SOP Number: HSP-031
Version: 01

Purpose:

The purpose of this Standard Operating Procedure (SOP) is to document the process for communication between the VA Northeast Ohio Healthcare System (VANEOHS) and the Advarra IRB.

Background:

VANEOHS 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 VA medical facility IRB and Human Research Protection Program (HRPP) SOPs located at https://www.clevelandvaresearch.org/research-sops 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 at the end of this SOP. 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 VANEOHS 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 Handbook 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) If desired, a specific VA research staff member can be appointed as a liaison to the Advarra IRB.
(3) Formally reports unanticipated problems, serious and/or continuing non-compliance, and suspension or termination of study activities originating at VANEOHS as required by VA policy to ORO and external federal agencies or oversight bodies.
(4) Updates and signs the Federal-wide Assurance (FWA) and VA Addendum to the FWA.

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 VANEOHS if the VA Investigator requests non-Veteran enrollment in the study.
(5) Ensures Information Systems Security Officer (ISSO) and Privacy Officer (PO) review is complete before R&D Committee final approval is given and before the study is initiated.
(6) Ensures the VANEOHS 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 VANEOHS 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 VANEOHS.
(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 MOUs or other agreements, 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 VANEOHS 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 sent to the Local Site Investigator as indicated above, for inclusion in the Study Regulatory Binder.
(3) As needed, the R&DC coordinator 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) 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.
(5) Manage evaluation of financial conflict of interest.
(6) Provides tracking for protocols and correspondence.
(7) Ensures notification of the Research Compliance Officer (RCO) of the signed reliance agreement and this supplemental SOP including IRB specific reporting mechanisms.
(8) 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.

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

(10) Receives IRB minutes related to VA research. Minutes are provided to VA medical facilities upon request.

VA Privacy and Information System Security Officers:

(1) The VANEOHS PO and Systems 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) 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. All reports of apparent serious non-compliance, apparent continuing noncompliance, or apparent serious unanticipated problems resulting from an RCO audit will be processed within the facility as specified by VHA Handbook 1058.01. RCOs will have access to the research subjects' records and/or case files for oversight and monitoring activities. RCO audit reports including but not limited to with no findings or no immediate findings for studies overseen by the Advarra IRB will be submitted to the R&D Committee. 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 and coordinated with ORO. 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 VANEOHS procedures. Information regarding the review and any relevant determinations or management plans must be shared with the Advarra IRB during the application process. Detailed information regarding submission and review of OGE 450-AltVA Form can be found in Medical Center Policy (MCP) 151-014 Research Service Financial Conflict of Interest Policy. This MCP be found on the

VANEOHS Sharepoint site
https://dvagov.sharepoint.com/sites/Cleveland/mcp/SitePages/Home.aspx

(3) Ensure ISSO and PO reviews are 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 approval by the R&D Committee.
(7) Ensure all study staff changes are submitted to the Research & Development Committee Coordinator. The PI must keep an up to date study staff list in their regulatory documents.
(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 VANEOHS 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 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 and/or 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 Handbook 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, this Handbook, 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) Responsible for proposing/preparing 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, via email, of documentation going to and from the Advarra IRB to the VANEOHS R&D Coordinator.

(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 VANEOHS, not on behalf of the institution.

Review date for this SOP is June 3, 2023.