1 SCOPE AND APPLICABILITY

1.1 The scope and purpose of this standard operating procedure (SOP) is to describe the overall mission, values, organizational structure, responsibilities, and requirements of the Veterans Health Administration Central Office (VHACO) Human Research Protection Program (HRPP), particularly in relation to the functioning of the VA Central Institutional Review Board (IRB). As such, this SOP also sets forth the authority and responsibilities of the VA Central IRB and contains procedures for identifying and reporting any instances of individuals attempting to exert undue influence on the VA Central IRB, its members, or its administrative support staff.

1.2 This SOP applies to research involving human participants that is conducted and/or overseen by the VHACO HRPP and for which the VA Central IRB serves as the IRB of Record. It includes all components of the VHACO HRPP and the HRPPs of VA field facilities, as well as Non-Profit Corporations (NPCs) associated with the VA field facilities, when involved in the conduct and/or oversight of studies for which the VA Central IRB serves as the VA IRB of Record. This SOP applies to VA Central IRB members and the VA Central IRB administrative staff; local VA Research and Development (R&D) Offices and Committees; the Institutional Official (IO) for the VHACO HRPP and his or her delegates; local participating VA facility IOs and their delegates; local NPC IOs and their delegates; local Research Compliance Officers (RCOs); and all individuals serving as study team members in studies overseen by the VA Central IRB. It also pertains to any other VA employees and students involved in the conduct and oversight of VA research involving human participants in studies overseen by the VA Central IRB.

1.3 It is the policy of the VHACO HRPP to ensure that all VA research under the purview of the VA Central IRB is conducted ethically and in accordance with all VA and other federal requirements for the protection of human research participants, and to promote a culture of shared responsibility and accountability for the following goals: to protect the rights and welfare of human research participants; to minimize the risks and maximize the benefits of participation; and to treat fairly the groups and individuals involved. The VHACO HRPP adheres to the basic ethical principles (respect for persons, beneficence, and justice) governing human research found in the Belmont Report which can be found at the following web link: http://www.history.nih.gov/research/downloads/belmont.pdf.

1.4 The VA is one of the 18 Federal departments and agencies that have agreed to follow the Federal Policy for the Protection of Human Subjects (the Common Rule.) This is incorporated in Title 38 Code of Federal Regulations (CFR) Part 16, Department of Veterans Affairs, Protection of Human Subjects.

1.4.1 The procedures followed by the VHACO HRPP for implementing 38 CFR Part 16 are defined in VHA Directive 1200.05, Requirements for the Protection of Human Subjects in Research. These requirements apply to VA research involving special populations such as pregnant women, children, and prisoners. The VHACO HRPP and the VA Central IRB also adhere to the following additional VA requirements:

- Statutory provisions for protection of VA patient rights, Title 38 United States Code (U.S.C.) Sections 501, 7331, and 7334.

- VA regulations pertaining to protection of patient rights, 38 CFR 17.33a and 17.34.
- VA regulations pertaining to research related injuries, 38 CFR 17.85.
- VA regulations pertaining to hospital care for research purposes and outpatient care for research purposes, 38 CFR 17.45 and 17.92.
- VA confidentiality of medical quality assurance records statute, 38 U.S.C. 5705.

1.4 It is the policy of the VHACO HRPP, that the VA Central IRB operates as an independent authority to carry out all the responsibilities required of an IRB in accordance with VA and other requirements, and that any attempt to exert undue influence on the VA Central IRB or any VA Central IRB member individually or categorically is promptly identified and reported.

1.5 The VA Central IRB oversees VA-funded multi-site research as designated by the Office of Research and Development (ORD) and VHACO. In addition, the VA Central IRB may oversee research funded by other federal government entities such as but not limited to the Department of Defense (DoD), the Department of Energy (DoE), and the National Institutes of Health (NIH). In addition, the VA Central IRB may review research funded by non-profit organization and commercial sponsors if its resources permit.

1.6 The VA Central IRB may serve as an IRB of Record for any VA facility maintaining a federalwide assurance (FWA). In addition, the VA Central IRB may serve as an IRB of Record for a VA facility affiliated NPC, as well as for a DoD or DoE entity having an FWA. In order for the VA to serve as an IRB of record for a VA or other entity, a Memorandum of Understanding (MOU) must be entered into with the applicable facility. This MOU must be signed by both the VHACO HRPP signatory official as well as the signatory official for the other institution before any review for that entity can take place.

1.7 Additionally, the VHACO HRPP adheres to statutes and regulations pertaining to the release of patient information. These include 5 USC 552a, 38 USC 5701a and 7332, and 45 CFR Parts 160-164. VHA requirements are provided in VHA Directive 1605.1, Privacy and Release of Information, and VHA Directive 1605.2, Minimum Necessary Standards for Protected Health Information. For the purposes of these requirements and in accordance with 45 CFR 164.512(i), the VA Central IRB may also approve a waiver of authorization as required by the Health Insurance Portability and Accountability Act (HIPAA) in regard to the research it reviews and may serve as a Privacy Board for VA facilities when it is not the IRB of Record for studies reviewed by other non-VA entities, such as for the NIH "All of Us" study.

1.8 When the VA Central IRB reviews FDA-regulated clinical investigations, it applies and adheres to the FDA regulations pertaining to the protection of human participants and the conduct of IRBs. These include 21 CFR 11, 50, 54, and 56. The following additional FDA regulations are also applied when research involves the use of specific test articles as follows:

- Investigational New Drug Applications (IND) (21 CFR 312 and 314)
- Radioactive Drugs for Certain Research Uses (21 CFR 361)
- Biological Products (21 CFR 600)

- Investigational Device Exemptions (IDE) (21 CFR 812 and 814)

1.8 VA research supported by the Department of Health and Human Services (DHHS) must also adhere to the provisions in 45 CFR 46, to include when pregnant women, children, prisoners, and impaired decision-making individuals might take part in the research.

1.9 VA research overseen by the VA Central IRB must comply with the state and local laws of the appropriate jurisdiction of the VA facility where research is conducted.

2 DEFINITIONS

2.1 **Assurance.** A written commitment by the institution to protect human research subjects and comply with the requirements of the Common Rule. *Note: Assurances are further discussed in VHA Directive 1058.03, Assurance of Protections for Human Subjects in Research. For the purposes of the VA Central IRB SOPs, "assurance" is synonymous with "Federalwide Assurance."* (VHA Directive 1200.05)

2.2 **Conflict of Interest (COI).** Any situation in which financial or personal obligations or interests may compromise or present the appearance of compromising an individual's or group's professional judgment in conducting, reviewing, or reporting research. An appearance of COI is when the circumstances would cause a reasonable person with knowledge of the relevant facts to question an employee's impartiality in the review and conduct of human research protocols.

An institutional COI may occur when the institution, or any of its senior management, has an external relationship or financial interest in a company or organization that itself has a financial interest in a VA investigator's research project.

2.3 **Federalwide Assurance (FWA).** An assurance approved for Federalwide use by the Office of Human Research Protections (OHRP) in accordance with the Common Rule (see 38 CFR 16.103(a)). (VHA Directive 1200.05)

2.4 **Human Protections Administrator (HPA).** The individual named in an FWA as a primary contact responsible for directing, or having in-depth knowledge of, the daily operations of an Institution's program for protecting human research subjects (VHA Directive 1058.03).

2.5 **Human Research Protection Program (HRPP).** An HRPP is a comprehensive system to ensure the protection of human subjects participating in research. At a local VA facility the HRPP consists of a variety of individuals and committees such as: the VA Facility Director, Associate Chief of Staff for Research and Development (ACOS/R&D), the Administrative Officer (AO) for R&D, the R&D Committee, the IRB, other committees or subcommittees addressing human subjects protection (e.g., Biosafety Committee, Radiation Safety, Radioactive Drug Research, Conflict of Interest) investigators, IRB staff, research staff, health and safety staff (e.g., Biosafety Officer, Radiation Safety Officer), research compliance officers (RCOs), Information System Security Officers (ISSOs, Privacy Officers (POs), and research pharmacy staff. The objective of this system is to assist the institution in meeting ethical principles and regulatory requirements for the protection of human subjects (VHA Directive 1200.05).

The VHA Central Office HRPP is composed of the VA Central IRB, the VHACO institutional leadership as appointed by the Under Secretary for Health; investigators of multi-site projects approved by the VA Central IRB; local medical center directors and affiliated non-Profit Corporation NPC IOs; local R&D Committee at participating local VA facilities; Office of Research Oversight (ORO), and local RCOs per the MOU with each VA facility; and many others who are involved in human subjects research. The VHA Central Office HRPP does not replace or duplicate the efforts of the local VA facilities' HRPPs. Instead, it only serves as the IRB of record for specified studies at each site and as such operates within the context of the local site HRPP and, as such, its minutes are reviewed by local R&D Committees as part of their local oversight functions. The VHA Office of Research Oversight (ORO) has oversight responsibility for the VHA Central Office HRPP. An organizational chart of the VHACO HRPP can be found at Attachment 1.

2.6 **Human Subject.** A human subject is a living individual about whom an investigator (whether professional or student) conducts research and: (1) obtains information or bio specimens through intervention or interaction with the individual, and uses, studies, or analyzed, t the information or bio specimens; or (2) obtains, uses, studies, analyzes, or generates identifiable private information or identifiable bio specimens. (VHA Directive 1200.05)

Note: Individuals who receive test article or who serve as controls in clinical investigations, including clinical investigations as defined under Food and Drug Administration (FDA) regulations in 21 CFR 50.3, 312.3(b), and 812.3(h), are also considered human subjects for the purposes of these SOPs.

2.7 **Institutional Official (IO).** The IO is the individual legally authorized as Signatory Official to commit an institution to an FWA. The Signatory Official assures that human subjects research to which the FWA applies is conducted in accordance with the terms of the assurance. A senior leader in the Office of the Under Secretary for Health is the IO for VHACO Office and VA facility Directors are the IOs for local VA facilities. (VHA Directive 1200.05)

2.8 **Institutional Review Board (IRB).** A board, committee, or other group, formally designated by an institution to review, approve, require modification, disapprove, and conduct continuing oversight of human subject research in accordance with the Common Rule (38 CFR 16) and other applicable regulations. (VHA Directive 1200.05)

2.9 **Investigator.** Any individual who conducts research including, but not limited to, the Principal Investigator (PI), sub-investigator or co-investigator, and Site Investigator or Local site Investigator (LSI). All VA investigators on a VA research study or program must hold a VA appointment. (VHA Directive 1200.05)

2.9.1 **Principal Investigator (PI).** The PI is a qualified person who directs a research study or program. The PI oversees scientific, technical, and day-to-day management of the research. If a study is conducted by a team of indivduals, the PI is the responsible leader of that team.

2.9.2 **Sub-Investigator or Co-Investigator**. A qualified person designated by the PI or LSI to perform critical research procedurs and/or to make important research-related decisions. Both

terms are interchangeable. These investigators are key personnel on a research study or program.

2.9.3 **VA Investigator.** Any individual who conducts research while acting under a VA appointment including full and part-time employees, without compensation (WOC) employees, or individuals appointed or detailed to VA under the Intergovernmental Personnel Act (IPA of 1970 (5 U.S.C. 3371 et seq.). Individuals working under a contract with VA cannot conduct research as VA investigators under a WOC appointment while simultaneously working as a contractor.

2.10 **IRB of Record.** The IRB(s) designated under a VA facility's FWA for review and oversight of the facility's human subject research (VHA Directive 1058.03, paragraph 4m).

2.11 **Memorandum of Understanding (MOU).** A written agreement between two VA facilities or between a VA facility and a non-VA Institution documenting their relationship and defining their respective roles and responsibilities within that relationship (VHA Directive 1058.03).

2.12 **Non-Profit Corporations (NPCs).** VA-affiliated NPCs are authorized by Congress under 38 U.S.C. 7361-7366 to provide flexible funding mechanisms for the conduct of research and education at one or more VA facilities. Research approved by a facility R&D Committee and education approved by the facility Education Committee are considered to be a VA research project or a VA education activity respectively, regardless of the source of funding, the entity administering the funds, or the research or education site. (VHA Directive 1200.05)

2.13 **Research.** A systematic investigation, including research development, testing, and evaluation, designed to develop or contribute to generalizable knowledge. Activities that meet this definition constitute research for the purposes of VHA Directive 1200.05, whether or not they are conducted or supported under a program which is considered research for other purposes. Clinical investigations, including clinical investigations as defined under FDA regulations in 21 CFR 50.03, 312.3(b), and 812.3(h), are considered research. (VHA Directive1200.05)

Note: For an expanded definition to include activities not considered research see VA Central IRB SOP 102, Requests for Exemptions and Requests for Determination of Human Subjects Engagement.

2.14 **Research and Development (R&D) Committee**. The R&D Committee is a committee responsible, through the Chief of Staff (COS) to the VA facility Director, for the oversight of the facility's research program and for maintenance of high standards throughout that program (see VHA Directive 1200.01, Research and Development (R&D) Committee.) (VHA Directive 1200.05)

2.15 **VA Research**. Research that is conducted by investigators (serving on VA compensated, WOC, or IPA appointments) while on VA time or on VA property. The research may be funded by VA, by other sponsors, or be unfunded. VA research must have R&D Committee approval before it is considered VA research and before it can be initiated. All research activities approved by the R&D Committee are considered VA research. (VHA Directive 1200.05)

3 RESPONSIBILITY

3.1 VHACO Institutional Official (IO). The IO is designated by the Under Secretary for Health to represent the VHACO HRPP, assume the obligations of the VHACO FWA as the Signatory Official, and to ensure compliance with its terms.

3.1.1 The VHACO IO is appointed from the senior VHACO leadership and is advised by the Chief Research and Development Officer (CRADO); the Chief, Office of Research Oversight (ORO); and the Human Protections Administrator (HPA) for the VHACO HRPP. The VHACO IO is responsible for maintaining a current FWA, ensuring compliance with its terms, and establishing written procedures as required by the Common Rule and VHA policies.

3.1.2 The following are the duties and responsibilities of the IO that are inherent in the IO function and cannot be delegated:

- Fostering an institutional culture that supports the ethical conduct of human subjects research
- Serving as signatory authority for the VHACO Office HRPP Federalwide Assurance (FWA)
- Completing required Federalwide Assurance training
- Appointing the VA Central IRB Chair or Co-Chairs, and suspending or terminating the appointment of any Chair or Co-Chair who is not fulfilling the responsibilities and/or obligations of the Chair position.
- Ensuring that the VA Central IRB functions independently and that its Chair, or Co-Chairs, and members have direct access to the IO for appeal if they experience undue influence or if they have concerns about the operations of the VA Central IRB
- Ensuring that resources, including funds, space, and personnel are provided to support the operation of the VHACO HRPP

3.2 Human Protections Administrator (HPA). for the VHACO HRPP is responsible for ensuring that the VHACO HRPP carries out all functions and responsibilities of the HRPP as detailed in VHA Directive 1200.05. The IO appoints the HPA in writing from among the senior management officials within the VA Office of Research and Development (ORD). Currently, the HPA has been delegated the following specific duties by the IO:

- Managing and administering funds, personnel, space, and other resources allocated to the VHACO HRPP in support of the VA Central IRB;
- Reviewing and approving the Standard Operating Procedures (SOPs) for the VA Central IRB to include a written procedure for determining when a research activity approved by the IRB, prior to January 21, 2019, can transition to the 2018 requirements, if applicable, and that this procedure lists what individuals or groups are designated to make the determinations.;

- Overseeing the daily operations of the VA Central IRB in accordance with its published SOPs;
- Recruiting qualified applicants for membership on the VA Central IRB, to include expert ad hoc advisors;
- Appointing VA Central IRB voting and nonvoting members, with the exception of the Chair or Co-Chairs;
- Suspending or terminating the VA Central IRB appointment of any individual for whom it is determined that he/she is not fulfilling VA Central IRB member responsibilities and/or obligations, with the exception of the VA Central IRB Chair or Co-Chairs;
- Reviewing and signing MOUs between the VHACO, local VA facilities, and other entities, concerning use of the VA Central IRB as an IRB of record for those facilities;
- Being the point of contact for correspondence addressing human subjects research with the Offfice of Human Research Protections (OHRP), the FDA, and VHACO;
- Developing and implementing an educational plan for VA Central IRB members, staff, and investigators that ensures they are appropriately knowledgeable to review and/or conduct research in accordance with ethical standards and all applicable VA and other requirements;
- Performing an annual evaluation of the performance of the VA Central IRB Co-Chairs;
- Performing an annual evaluation of the VHACO HRPP and reporting the results to the VHACO HRPP IO and to local VA facilities that have an active MOU with the VHACO HRPP.

3.3 Local VA Facility IO. The local facility IO is the Signatory Official for the institution when entering into an MOU with VHACO designating the VA Central IRB as an IRB of record on its FWA. The local facility IO is responsible for ensuring that the facility meets all the obligations as set forth in the MOU and that no research submitted to the VA Central IRB is otherwise approved or begun at the facility until it is approved by the VA Central IRB and by the local facility in accordance with VHA Directive 1200.01. In VA facilities, the IO is the Medical Center Director.

3.4 Local R&D Committees. The local R&D Committees are responsible for fulfilling all responsibilities required in VHA Directive 1200.01, Research and Development Committee, for all research in which the local facility is engaged, and for all research within other VA facilities for which it serves as the R&D Committee of record. The local R&D Committees also includes the VA Central IRB in the annual review of their facilities' HRPP if the VA Central IRB is listed as one of their IRBs of record.

3.5 VA Central IRB. The VA Central IRB is responsible for fulfilling all responsibilities and performing all functions of an IRB as specified in VHA Directive 1200.05 to include but not limited to the authority to perform the following activities:

3.5.1. Conducting initial and continuing review of research and reporting findings and actions to investigators, the R&D Committees, and the participating institutions for specific studies.

3.5.2. Determining which projects require review more often than annually, and which projects need verification from sources other than the investigators that no material changes have occurred since previous IRB review.

3.5.3 Ensuring prompt reporting by an investigator to the IRB of proposed changes in a research activity, and for ensuring that investigators will conduct the research activity in accordance with the terms of the IRB approval until any proposed changes have been reviewed and approved by the IRB, except when necessary to eliminate apparent immediate hazards to subjects.

3.5.4 Ensuring prompt reporting to the IRB, appropriate institutional officials, department or agency head, ORO, and OHRP of: (1) any unanticipated problems involving risks to subjects or others, or any serious or continuing noncompliance with VA policies or the requirements or determinations of the IRB, and (2) any suspension or termination of IRB approval.

3.5.5 Determining whether a study meets the criteria for exemption from the requirements of the Common Rule and when a study requires limited IRB review.

3.5.6 Observing or having a third party observe, research activities, including the informed consent process, when the IRB determines this to be appropriate.

3.5.7 Conducting expedited review and reporting findings and actions to the IRB, R&D Committee, and investigator; and

3.5.8 Training and education of the IRB Chair, voting members, and alternates in human subjects protections, ethics, and regulatory requirements.

3.6 VA Central IRB Administrator. The VA Central IRB Administrator is responsible for overseeing the daily administrative activities of the VA Central IRB to include ensuring the FWA and IRB registration with OHRP are kept current, all written policies and procedures governing the operation of the VA Central IRB are up-to-date, and that the VA Central IRB operates according to approved policies and procedures. The VA Central IRB Administrator is also responsible for the following:

- Assisting local VA facilities and NPCs if they do not have an approved MOU in place, and/or have not designated the VA Central IRB as an IRB of record on their respective FWA, in submitting and processing the required documents;
- Maintaining a database of all local VA facilities with approved MOUs and their renewal dates;
- Updating the MOU as changes occur and ensuring it is reviewed with each facility no less than every three years; and
- Educating and assisting local sites and study teams on meeting VA Central IRB and VHACO HRPP and other VA requirements concerning the conduct of human subjects research.

3.6 VA Central IRB Managers. The VA Central IRB Managers are responsible for ensuring the following:

- That all local VA sites participating in a multi-site project submitted to the VA Central IRB for review, have an approved MOU on file and that the VA Central IRB has been designated as an IRB of record on the local site's FWA;

- Conducting the daily activities of the VA Central IRB including, but not limited to, coordinating all project review functions of the VA Central IRB with the designated VA Central IRB Reviewers, the VA Central IRB Co-Chairs, and the study teams in accordance with established policies and procedures.
- Maintenance of all required documentation, including but not limited to required documentation for actions taken by the VA Central IRB in regard to each Manager's assigned projects.

3.7 VA Investigators and research staff. All VA investigators, research staff and students (including VA employees or students from a VA-affiliated academic institution) are expected to adhere to the ethical standards required by the VA to conduct human subjects research and for meeting all the responsibilities for investigators as detailed in VHA Directive 1200.05 and VA Central IRB SOPs, to include completing all forms and documents required by the VA Central IRB in a timely manner and for promptly reporting any issues that require VA Central IRB review.

3.8 VA-affiliated NPCs. NPCs that are affiliated with local VA facilities for the purpose of providing a flexible funding mechanism for the conduct of and/or to facilitate functions related to the conduct of approved VA research and education, must have and keep up-to-date an FWA designating the VA Central IRB as an IRB of record. The NPC is responsible for ensuring that its FWA is kept current in accordance with VHA Directive 1058.03. The NPC is also responsible for ensuring it enters into an MOU with the local VA facility and the VHA Central Office. This MOU sets forth the respective authorities, roles, and responsibilities of these three entities.

3.9 VA Central IRB Local Site Liaison. Local Site Liaisons are responsible for facilitating communication with the VA Central IRB as needed and ensuring that all approved study documents on the VA Central IRB SharePoint site are made available for the site Research Office files, as applicable. Liaisons also assist other designated site personnel in performing review functions and relaying the results to the VA Central IRB. Liaisons ensure that the VA Central IRB is immediately informed of all local site actions involving restriction, suspension, or termination of research privileges for research team members associated with a VA Central IRB-approved project. Local Site Liaisons also keep the VA Central IRB updated on changes in local Research Office and Institutional personnel in accordance with the MOU. (See VA Central IRB SOP 108 for more information concerning VA Central IRB Local Site Liaisons)

4 PROCEDURE

4.1 Maintenance of VHACO FWA. VHACO will maintain a current FWA on file with both ORO and OHRP.

4.1.1 The Under Secretary for Health appoints in writing a member of the senior leadership for VHACO to serve as the IO for the VHACO HRPP. As such, this individual serves as the Signatory Official for the VHACO FWA.

4.1.2 The FWA includes all components within the VHACO that conduct research. These offices do not have to be listed on the FWA. Only significant VHACO components, where the program office is remotely located or OHRP would not recognize the office as a VHACO program,

need to be listed individually on the FWA.

4.1.3 The FWA and ORO VA addendum are updated upon the appointment of a new Under Secretary of Health, IO, or HPA. The FWA is also updated if there is a change in the IRB of record or if a significant component of the VHACO needs to be added or deleted.

4.1.4 Upon appointment to their positions, the Under Secretary for Health, IO, and HPA, will complete the three OHRP FWA Online Training modules if they have not already done so. Copies of their Certificates of Completion for each of the three modules are forwarded to the VA Central IRB Administrator and kept in the files of the VA Central IRB. The OHRP Human Subjects Assurance Training modules are available on the OHRP website or through the VA Training Management System (TMS).

4.1.5 FWA updates are prepared as necessary by the VA Central IRB Administrator using the automated OHRP registration system. The update is then submitted through the HPA to the IO for signature through the VHACO automated correspondence system. The VA Central IRB Administrator also coordinates the update through ORO, to include an updated VA addendum to the FWA (as specified in VHA Directive 1058.03) which must be signed by the Under Secretary for Health, in addition to the VHACO IO. The OHRP electronic submission is not finalized until clearance is received by ORO and all signatures have been obtained as required on the FWA.

4.1.6 In addition, any appointment letters and /or delegation of authority letters must be updated based on the FWA changes and will also be prepared by the VA Central IRB Administrator and included as part of the package forwarded for signature. All delegation of authority letters expire upon the appointment of a new IO.

4.2 Designation of the VA Central IRB as the VHACO IRB of Record. The VA Central IRB is listed as the IRB of record on the VHACO FWA.

4.2.1 The VA Central IRB is registered with OHRP as a single IRB. Additional IRB panels may be established as needed based on the volume and types of human research projects submitted. The turnaround time and workload of the IRB is evaluated on a periodic basis, but no less than annually, by VA Central IRB staff, VA Central IRB members and Co-Chairs, as well as ORD and VHACO stakeholders to determine whether additional panels are needed based on current and projected workload.

4.2.2 If there is a change in the voting membership, the VA Central IRB Administrator submits an updated registration form to OHRP through ORO within 30 days of the change.

4.2.2.1 Registration updates are completed on-line through the OHRP website. Once the information is entered into the system by the VA Central IRB Administrator, ORO is informed and given the access codes for the updated registration.

4.2.2.2 ORO reviews the updated registration information on-line for completeness and accuracy and then informs the VA Central IRB Administrator when the review is complete. The update is then submitted to OHRP.

4.2.2.3 The VA Central IRB Administrator ensures that the VA Central IRB registration is renewed at least once every five years or within five years of the last previous update.

4.2.2.4 Changes in the non-voting membership do not need to be reported to OHRP or ORO until the next time there is a change in the voting membership. However, those changes will be posted on the listing maintained on the VA Central IRB website and on the VA Central IRB SharePoint site.

4.2.3 The VA Central IRB membership roster as reported to OHRP and ORO contains the following information on the members:

- Name
- Gender
- Earned degrees
- Scientific status (scientist or non-scientist)
- Primary scientific or nonscientific specialty
- Affiliation status
- Indications of experience sufficient to describe each IRB member's chief anticipated contributions
- Employment or other relationship between each IRB member and the Department of Veterans Affairs
- Role on the IRB or representative capacity (i.e., vulnerable populations, prisoner representatives)
- IRB position (e.g., Co-chair)
- Voting Status
- Alternate Members
- The primary members or class of members for whom each alternate member could substitute

Non-voting members are listed on the roster per the request of ORO and are indicated as such in the "Comments." Rosters are maintained permanently.

4.4 VA Central IRB Serving as an IRB of Record for VA Facilities. Each VA facility having its own FWA must enter into an MOU with VHACO, irrespective of other IRB arrangements, in order for the VA Central IRB to serve as one of the facility's IRBs of record.

4.4.1 The MOU spells out the specific authorities and responsibilities of each party to the MOU. The same MOU template is used for each facility and is not subject to change by a local facility as the MOU has been coordinated through both VHACO, ORD, and ORO. This template can be found at Attachment 2.

4.4.2 The associated NPC for a facility is also a party to the MOU and also must add the VA Central IRB as an IRB of record. If the VA facility does not have an NPC, then the MOU at Attachment 3 should be used.

4.4.3 If an MOU is not in place, the local VA facility follows these procedures to establish one:

4.4.3.1 Complete the applicable MOU template (with or without NPC), add the VA Central IRB as an IRB of record to the facility FWA on the OHRP website, and obtain the signature of the local VA facility IO, and NPC IO if applicable, which can be a VA-approved electronic signature. Forward the signed MOU to the applicable VA Integrated Service Network (VISN) Director, along with the ORO FWA Addendum, which can be found on the ORO website.

4.4.3.2 The local VA facility notifies ORO when the amended FWA and ORO addendum are ready for ORO's review. ORO electronically reviews the revisions and notifies the facility when to electronically submit the FWA revisions to OHRP.

4.4.3.3 The local VA facility then submits the signed copy of the MOU to the VA Central IRB (an electronic file can be submitted). Personnel in the VA Central IRB Administrative Office will obtain the signature of the VHACO HPA, and forward a signed copy to both the local VA facility and ORO.

4.4.4 If there is a change in VA facility or local NPC IO, the MOU must be amended through submission of VA Central IRB Form 143, Amendment to Memorandum of Understanding (MOU) which can be found at Attachment 4. Upon receipt of a notice from OHRP of a change in Signatory Official on the FWA for a VA facility or NPC and the VA Central IRB has not received the required amendment form with the new IO's signature, VA Central IRB staff will contact the VA Central IRB Liaison at the site and ask that an amendment be submitted within 30 days. Changes in HPA or a change in the IO's title, such as "Acting" Director to "Director" do not require submission of an MOU amendment form.

4.4.5 One provision of the MOU is for the VA facility IO to appoint a VA Central IRB Liaison to serve as the main point of contact between the VA Central IRB and the local VA facility, as well as a Local Site Designee to review VA Central IRB initial approval determinations for new studies and provide any local site comments. Details on this appointment process and the duties and responsibilities of these positions can be found in VA Central IRB SOP 108, VA Central IRB Communications with Investigators, Local Participating Sites, and Community Outreach.

4.4.6 Another provision of the MOU is that the local sites must incorporate applicable VA Central IRB policies and procedures in the VA facility's SOPs. The VA Central IRB makes its SOPs and forms available on its public website to facilitate this process. In addition, the VA Central IRB maintains a public listing on its website of all VA facilities and other entities for which it currently serves as an IRB of record.

4.5 VA Central IRB Serving as an IRB of Record for DoD or DoE Facilities. Currently the VA Central IRB is serving as an IRB of record for eight DoE Laboratories and may also serve as an IRB of record for DoD facilities.

4.5.1 VHACO has negotiated a standard MOU with the DoE similar to the one for VA facilities. The standard template for this MOU can be found at Attachment 4. Liaisons are also appointed for each laboratory and several points of contact have been appointed to represent the DoE overall. These central points of contact are to be copied on all MOU approvals, amendments, and study approvals and other actions as well as the laboratory specific liaisons.

4.5.2 When a signatory authority for one of the laboratories changes, a VA Central IRB Form 144, Amendment to Memorandum of Understanding (MOU)–DOE Laboratories (Attachment 5), is submitted by the applicable DoE Laboratory. The VA Central IRB tracking system is updated with the new information and the amendment is filed with the original MOU. A copy is also sent to ORO. Some DoE facilities do not list the VA Central IRB as an IRB of record on the laboratory's FWA while some do. The VA Central IRB will not follow-up to obtain the most current FWA information since part of the amendment is a certification by the signatory official that the laboratory's FWA is current and accurate.

4.6 MOUs with other Non-VA Organizations. The VA Central IRB and/or VHACO will occasionally enter into other MOUs with various organizations to provide a variety of services and/or for the organization to perform services for or in conjunction with the VA Central IRB. These can be, but not limited to such things as serving as an IRB of Record for VA facilities for which a non-VA IRB is serving as the IRB of Record for non-VA facilities in the same study and for which there is a coordinating center that that will be managing issues between the two IRBs. MOUs can also be entered into for providing outside consultant or other services in the management of some aspects of IRB review or pre-reviews. These are just two examples.

4.7 Required Written Procedures. The VA Central IRB must establish written procedures for, but not limited to the following:

4.7.1 Conducting initial (See VA Central IRB SOP 104) and continuing review (See VA Central IRB SOP 105) of research and for reporting the findings and actions to the investigator, the applicable local R&D Committees, and appropriate local VA participating facility IOs and designees per the MOU with the facility for use of the VA Central IRB as an IRB of record for the facility.

4.7.2 Determining which projects require review more than annually and which projects require verification from sources other than the investigator that no substantive modifications or changes have occurred since the previous review. (See VA Central IRB SOP 105)

4.7.3 Ensuring prompt reporting by an investigator to the VA Central IRB of proposed changes in a research activity and for ensuring that investigators will conduct the research activity in accordance with the terms of the VA Central IRB approval until any proposed changes have

been reviewed and approved, except when necessary to eliminate apparent immediate hazard to the participants. (See VA Central IRB SOP 106)

4.7.4 Ensuring prompt reporting to the VA Central IRB, appropriate institutional officials, department or agency heads, ORO, and OHRP of: (1) any unanticipated problems involving risks to subjects or others, or any serious or continuing noncompliance with VA policies or the requirements or determinations of the VA Central IRB, and (2) any suspension or termination of IRB approval. (See VA Central IRB SOP 107)

4.7.5 Observing, or having a third party observe, the informed consent process when the VA Central IRB determines it to be appropriate. (See VA Central IRB SOP 107)

4.7.6 Conducting expedited review and reporting findings and actions to the IRB, applicable R&D Committees, local facility designees per the MOU, and investigators (See VA Central IRB SOPs 104 and 108.)

4.7.7 Training and education of the VA Central IRB Co-Chairs, voting members, and alternates in human subject protections, ethics, and regulatory requirements. (See VA Central IRB SOP 101)

4.8 Reporting Findings and Actions to the VHACO IO. The VA Central IRB Co-Chair and/or HPA meets with the IO on a periodic basis to review the status of the VHA HRPP, to include the operations of the VA Central IRB. These meetings take place at a minimum of twice a year and can be more often as required and schedules permit. In addition to these meetings, the VHACO IO is kept informed in the following ways:

4.8.1 The VHACO IO is notified in writing within five working days of any action taken by the VA Central IRB that is further reportable to ORO and/or other federal oversight agencies. This includes finding of serious and/or continuing noncompliance, related unanticipated problems involving risks to subjects or others and any suspensions or termination of research activities by the VA Central IRB.

4.8.2 A report is prepared after the end of each quarter by the VA Central IRB Administrator and sent to the VHACO IO through the HPA within 30 days of the quarter's end containing the following information:

- New studies approved that quarter to include name, funding source, and number of potential participating sites.
- Average turnaround time (TAT) for the approved new studies
- New studies received and still under review to include name, funding source, and number of potential participating sites.
- Post-approval monitoring workload volume to include the following; 1) number of continuing reviews performed (PI and LSI), 2) Number of amendments approved (PI and LSI), 3) number of LSI Applications approved, 4) number of unanticipated problem reports

and protocol deviation reports reviewed, 5) number of administrative updates processed, 6) number of phone calls received on the Office of Resarch Protections, Policy, and Education (ORPP&E) toll free line, 7) number of pre-reviews completed, 8) number of MOU addenda and FWA updates processed, and 9) number of active protocols open or in process to include number of sites that the VA Central IRB is currently managing.

- Updates on previously reported events that required follow-up of required corrective actions
- Summary of reportable events reported during the quarter for which the report is being submitted.
- Other significant issues or activities

4.9 Independence of VA Central IRB. The VA Central IRB is an independent authority. Its structure and oversight mechanisms have been developed to minimize the possibility of any Institutional COI or undue influence. However, there may be situations in which study teams and sponsors attempt to put pressure on the VA Central IRB or individual members to move studies through the review process more quickly or to overlook certain deficiencies or stipulations that they do not wish to comply with.

4.9.1 To guard against such potential COIs, the VA Central IRB deliberations and decisions are independent of the funding services within ORD. The VA Central IRB has the final authority to approve research. Such independence is established based on the nationally diverse membership of the VA Central IRB, as well as oversight by ORO and the VHACO IO, who is appointed from VHACO senior leadership outside of ORD.

4.9.2 Anyone who wishes to report what they believe is an attempt to unduly influence the VA Central IRB or one of its members can report such an attempt to one or more of the following entities:

- VA Central IRB Co-Chair
- VA Central IRB Administrator
- VA Central IRB Manager
- The Director, ORPP&E
- HPA for VHA Central Office HRPP
- CRADO, Deputy CRADO, or ORD Administrative Officer
- VHA CO IO

4.9.3 Upon receipt of a report to unduly influence the VA Central IRB or one of its members, the individual receiving the report immediately informs the VHACO IO. The IO will appoint an individual or individuals to investigate the allegations and prepare a report of findings.

4.9.3 Depending upon the allegations and the outcome of the investigation, the VA Central IRB, HPA, or IO as applicable may take one or more of the following actions:

- Bar an investigator from submitting any further research to the VA Central IRB (VA Central IRB, HPA, or IO)

- Suspend or terminate any currently approved research projects pertaining to the allegations in accordance with approved procedures (VA Central IRB)
- Terminate the membership of any VA Central IRB members involved (HPA and IO)

4.9.4 Other administrative or disciplinary actions may be taken by the appropriate supervisory authorities as applicable depending upon the results of the investigation.

5 DOCUMENTATION REQUIREMENTS

5.1 All approved MOUs for local VA facilities and DoE or DoD facilities will be tracked in the VA Central IRB administrative tracking system with copies of the signed MOUs maintained on the VA Central IRB shared drive, to include any MOU Addenda. Other MOUs will be filed on the VA Central IRB shared drive.

5.2 Certificates of completion by the Under Secretary for Health, the VHACO IO, and HPA for each of the three modules of the OHRP Online FWA training, will be maintained in VA Central IRB files on its shared drive.

5.3 All current VHA FWA and VA Central IRB registration updates will be maintained on the VA Central IRB shared drive. The updated VA Central IRB membership roster will also be posted on the VA Central IRB SharePoint site for access by VA Central IRB Local Site Liaisons.

5.4 The quarterly reports to the IO will be filed on the VA Central IRB shared drive.

Note: For other documentation requirements see VA Central IRB SOP 109

6 REFERENCES

6.1 38 CFR 16, Department of Veterans Affairs, Protection of Human Subjects

6.2 38 CFR 17, Department of Veterans Affairs, Medical

6.3 VHA Directive 1200.05, Requirements for the Protection of Human Subjects in Research

6.4 VHA Directive 1200.01, Research and Development (R&D) Committee

6.5 VHA Directive 1058.03, Assurance of Protection for Human Subjects in Research

6.6 VHA Directive 1605.1, Privacy and Release of Information

6.7 VHA Directive 1605.2, Minimum Necessary Standards for Protected Health Information

6.8 45 CFR 46, Department of Health and Human Services, Protection of Human Subjects, including subparts A through D.

6.9 45 CFR 160 and 164, General Administrative Requirements and Security and Privacy (The HIPAA Privacy Rule)

6.10 21 CFR 11, Electronic Records; Electronic Signatures

6.11 21 CFR 54, Financial Disclosure by Clinical Investigators

6.12 21 CFR 56, U.S. Food and Drug Administration, Institutional Review Boards

6.13 21 CFR 50, U.S. Food and Drug Administration, Protection of Human Subjects

6.14 21 CFR 312, U.S. Food and Drug Administration, Investigational New Drug Application

6.15 21 CFR 314, U.S. Food and Drug Administration, Applications for FDA Approval to Market a New Drug

6.16 21 CFR 361, U.S. Food and Drug Administration, Prescription Drugs for Human Use Generally Recognized as Safe and Effective and Not Misbranded: Drugs Used for Research

6.17 21 CFR 812, U.S. Food and Drug Administration, Investigational Device Exemptions

6.18 21 CFR 814, Pre-Market Approval of Medical Devices

6.19 OHRP Registration of an IRB: Instructions for registering and updating the current registration of an IRB can be found at http://www.hhs.gov/ohrp/assurances/

6.20 OHRP Terms of the FWA: These can be found at **http://www.hhs.gov/ohrp/humansubjects/assurance/filasurt.htm**

6.21 MOU checklists on ORO website

As the responsible authority delegated by the VHA Central Office Institutional Official for administrative oversight of the VA Central IRB, I have reviewed and approved the contents of this VA Central IRB Standard Operating Procedure.

Marisue Cody 103512

Digitally signed by Marisue Cody 103512
Date: 2019.01.22 09:08:59 -05'00'

Marisue Cody, Ph.D.
Director of Operations
VHA Human Protections Administrator
Office of Research and Development

6 Attachments

1. VHACO HRPP Organizational Chart
2. Template MOU with VA Facilities and Associated NPCs
3. Template MOU with VA Facilities without NPCs
4. Template MOU with DoE Laboratories
5. VA Central IRB Form 143 – Memorandum of Understanding (MOU) Addendum
6. VA Central IRB Form 144 – Memorandum of Understanding (MOU) Addendum - DOE