

**ASSURANCE OF PROTECTION
FOR HUMAN SUBJECTS IN RESEARCH**

1. PURPOSE. This Veterans Health Administration (VHA) Handbook sets forth procedures related to the Human Subject Protection Assurances that facilities are required to provide under Department of Veterans Affairs (VA) regulations at Title 38 Code of Federal Regulations (CFR) Part 16.

2. SUMMARY OF MAJOR CHANGES. This is a new VHA Handbook which:

a. Conforms to the Federal Policy for Protection of Human Subjects (henceforth referred to as the Common Rule) codified by VA at 38 CFR Part 16. *NOTE: For related VHA policy, see VHA Handbook 1200.5, Requirements for the Protection of Human Subjects in Research.*

b. Assigns responsibility to VA medical facilities conducting research involving human subjects, the Veterans Integrated Services Networks, the Office of Research and Development, and the Office of the General Counsel in seeking Federalwide Assurances, or other assurances, satisfactory to the Office of Research Oversight. The assurance is a written commitment to protect human subjects participating in research and to comply with all applicable regulatory and policy requirements pertaining to human subject research. *NOTE: Assurances are required in accordance with 38 CFR 16.103(a).*

3. RELATED ISSUES. VHA Directive 1058, VHA Handbook 1058.1, and VHA Handbook 1050.1.

4. RESPONSIBLE OFFICE. The Office of Research Oversight (10R) is responsible for the contents of this Handbook. Questions may be referred to (202) 565-5184.

5. RESCISSIONS. None.

6. RECERTIFICATION. This VHA Handbook is scheduled for recertification on or before the last working day of May 2012.

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1. PURPOSE

This Veterans Health Administration (VHA) Handbook sets forth procedures related to the Human Subject Protection Assurances that institutions are required to provide under Department of Veterans Affairs (VA) regulations at Title 38 Code of Federal Regulations (CFR) Part 16.

2. BACKGROUND

a. All human subject research conducted or supported by VA must comply with the Federal Policy (Common Rule) for the Protection of Human Subjects, 56 Federal Register (FR) 28001, June 18, 1991, as codified at 38 CFR Part 16.

b. Title 38 CFR 16.103(a) provides that:

(1) Each VA facility engaged in human subject research must provide a written Assurance, acceptable to the Secretary of Veterans Affairs, committing the facility to comply with 38 CFR Part 16.

(2) Each non-VA institution engaged in human subject research conducted or supported by VA must provide a written Assurance, acceptable to the Secretary of Veterans Affairs, committing the institution to comply with 38 CFR Part 16.

c. VHA Handbook 1200.5 stipulates that the VA Medical Center Director or Chief Executive Officer (CEO) is the VA Institutional Official responsible for ensuring that the VA facility conducting research involving human subjects or biological specimens applies through the Office of Research Oversight to the Department of Health and Human Services (HHS), Office for Human Research Protections (OHRP), for an Assurance.

3. SCOPE

The requirements of this Handbook apply to all human subject research and research involving human biological specimens conducted or supported by VA.

4. DEFINITIONS

The following definitions are intended for use only within this Handbook.

a. **Assurance (Assurance of Compliance; Assurance of Protection for Human Subjects; and Human Subject Protection Assurance).** An Assurance is a written commitment to protect human subjects participating in research and to comply with the requirements of 38 CFR Part 16. Assurances are reviewed and approved by the HHS OHRP and various other Departments and Agencies under the Federal Policy (Common Rule) for the Protection of Human Subjects (56 FR 28001, June 18, 1991).

b. **Facility.** The facility is an entity operated by VA, including VA hospitals, medical centers, and health care systems. For purposes of this Handbook, the terms “facility,” “VA facility” and “VA institution” are considered synonymous.

(1) A VA facility includes all VA-operated components within the facility’s management control, regardless of the component’s physical location, and whether housed in space owned, leased, or rented by VA.

(2) A VA facility may include multiple campuses and satellite components.

(3) A VA facility includes all VA space that is “shared” with a non-VA entity, unless the VA space is leased to a non-VA entity and not used by VA for research.

c. **Facility Director.** The facility Director is the Director of a VA Medical Center or the CEO of a VA Health Care System. From this point forward in this Handbook, the terms “Facility Director,” “Medical Center Director,” and “Health Care System CEO” are considered synonymous.

d. **Federal-wide Assurance (FWA).** An FWA is an Assurance approved for Federalwide use by OHRP in accordance with Section 103(a) of the Common Rule.

e. **Human Biological Specimen.** A human biological specimen is any material(s) derived from human subjects, such as blood, urine, tissues, organs, hair, nail clippings, or any other cells, whether collected for research purposes or as a residual specimen from a diagnostic, therapeutic, or surgical procedure.

f. **Human Protections Administrator (HPA).** A HPA is 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.

g. **Human Research Protection Program (HRPP).** An HRPP is a comprehensive system to ensure the protection of human subjects participating in research. The HRPP consists of a variety of individuals and committees such as: the Medical Center Director, Associate Chief of Staff (ACOS) for Research and Development (R&D), the Administrative Officer (AO) for R&D, compliance officers, etc., the R&D Committee, the Institutional Review Board (IRB), other committees or subcommittees addressing human subjects protection (e.g., Biosafety, Radiation Safety, Radioactive Drug Research, Conflict of Interest), investigators, IRB staff, research staff, health and safety staff (e.g., Biosafety Officer, Radiation Safety Officer), 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 in research.

h. **Human Subject.** A human subject is a living individual about whom an investigator conducting research obtains either data through intervention or interaction with the individual or identifiable private information. Individuals who receive test articles or who serve as controls in

clinical investigations, including clinical investigations as defined under Food and Drug Administration (FDA) regulations, generally would be considered human subjects for the purposes of this Handbook.

i. **Institution.** For Assurance purposes, an institution is any public or private entity. This Handbook distinguishes VA institutions from non-VA institutions.

(1) **Non-VA Institution.** A non-VA institution is an entity not operated by VA. Non-VA institutions include, but are not limited to:

(a) Any entity that is not a legal component of VA or of a VA facility, including a Contract Research Organization (CRO); industry or private sponsor; or public or private research company, foundation, or group.

(b) Entities operated under a contract from VA;

(c) Academic institutions, including VA-affiliated medical schools, dental schools, and other academic affiliates;

(d) VA-affiliated Non-Profit Research and Education Corporations (NPCs); and

(e) Other federal departments or agencies.

(2) **VA Institution.** A VA institution is an entity operated by VA, including VA hospitals, medical centers, and Healthcare Systems (see subpar. 4b).

j. **Investigator.** For Assurance purposes, an investigator is any individual who conducts research involving human subjects. This Handbook distinguishes VA investigators from non-VA investigators.

(1) **Non-VA Investigator.** A non-VA investigator is any investigator other than a VA investigator as defined in subparagraph 4j(2). Non-VA investigators who conduct VA-supported research must be covered under an Assurance.

(2) **VA Investigator.** A VA investigator is any individual who conducts human subject research while acting under a VA appointment, including full and part-time employees, without compensation (WOC) employees, and employees under the Intergovernmental Personnel Act (IPA) of 1970.

k. **Institutional Official (IO).** The IO is the individual legally authorized as Signatory Official to commit an institution to an Assurance. For VA institutions, the IO is responsible for ensuring that the institution's HRPP functions effectively and that the institution provides the resources and support necessary to comply with all requirements applicable to research involving human subjects. The IO also serves as the official representative of the institution to external agencies and oversight bodies.

l. **Institutional Review Board (IRB)**. An IRB is 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 38 CFR Part 16 and other applicable regulations.

m. **IRB of Record**. The IRB of Record is the IRB(s) designated under a VA facility's FWA for review and oversight of the facility's human subject research.

n. **Memorandum of Understanding (MOU)**. An MOU is 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.

o. **Research**. Research is a systematic investigation, including research development, testing and evaluation, designed to develop or contribute to general knowledge. Activities which meet this definition constitute research for purposes of this policy, whether or not they are conducted or supported under a program which is considered research for other purposes. For example, some demonstration and service programs may include research activities. Clinical investigations, including clinical investigations as defined under FDA regulations, are considered research for purposes of this Handbook.

p. **VA Research**. VA research is research that has been reviewed and approved by a VA R&D Committee.

5. ASSURANCES FOR VA FACILITIES

a. **Federal-wide Assurances (FWAs)**. Except as indicated in subparagraph 5a(11) of this Handbook, each VA facility engaged in research involving human subjects or human biological specimens must hold an effective FWA approved by OHRP with an effective VA FWA Addendum approved by the Office of Research Oversight (ORO).

(1) The FWA for a VA facility must cover all research conducted at the facility or by the facility's investigators acting in their official VA capacity.

(2) In rare instances and with the written approval of the Office of Research and Development (ORD) and ORO, a VA facility may apply its FWA to the conduct of VA research by a VA investigator from another VA facility that does not operate a human research program. An MOU documenting the arrangement is required.

(3) FWAs for VA facilities may not include or apply to any non-VA institutions or non-VA personnel without written approval of the VHA Chief Research and Development Officer (CRADO) and the ORO Chief Officer and written concurrence from the Office of General Counsel (OGC) in VA Central Office (see subpar. 6e).

(4) FWAs for VA facilities must designate at least one IRB of Record. Where the IRB of Record is operated by an entity other than the VA facility, an MOU is required (see subpar. 6d).

(5) The VA Medical Center Director, Facility Director, or Health Care System CEO must serve as the IO and sign the FWA.

(a) During transitions of leadership, the FWA may be signed by the Acting Facility Director.

(b) Signatory authority for FWAs may not be delegated to accommodate short-term absences, such as travel status or leave, except with prior approval of the ORO Chief Officer, VHA Central Office.

(6) The VA FWA Addendum must be signed by the Facility Director, the Director of the appropriate Veterans Integrated Service Network (VISN), and the ORO Chief Officer, or designee, prior to approval by OHRP. **NOTE:** *The VA FWA Addendum may be found on the ORO web site at: <http://www.va.gov/oro/>.*

(7) The ACOS for R&D, AO for R&D, or other individual knowledgeable about human research protection requirements serves as the HPA for a VA FWA.

(8) In rare circumstances, the VA Facility Director may determine that the best interests of the facility's HRPP require designation of an HPA not employed at the facility. In such cases,

(a) The Facility Director must designate that person in writing;

(b) The designation must be approved by the ORO Chief Officer and the CRADO;

(c) The HPA's supervisor or manager at the non-VA institution, not the designated HPA, must sign the VA Addendum to the FWA, indicating that the non-VA institution approves of the VA facility's HPA designation and accepts responsibility for the HPA's activities on behalf of the VA facility; and

(d) A signature line must be added to the VA Addendum for the ACOS for R&D or equivalent.

(9) If a new Facility Director, Acting Facility Director, or HPA is appointed, the FWA and FWA Addendum must be revised and submitted to ORO within 30 days of the appointment.

(10) All personnel signing the FWA and the VA FWA Addendum must complete the OHRP Assurance Training Modules, as well as any other training required for this purpose by ORD.

(11) In rare cases and with ORD concurrence, ORO may negotiate special Assurances or recognize Assurances issued by other Common Rule Departments and Agencies in lieu of FWAs.

b. **Initial FWAs.** FWAs for VA facilities must be submitted to OHRP through ORO and must be approved by both ORO and OHRP before any human subject research is initiated (see VHA Handbook 1200.5). A VA facility's initial FWA submission must include:

(1) The signed FWA,

(2) The signed VA FWA Addendum,

(3) Certificates of completion of all required parts of the OHRP Assurance Training Module for all personnel signing the FWA and the VA FWA Addendum, and

(4) Where applicable, a signed MOU as described in subparagraph 6d.

c. **Changes to FWAs.** All changes to FWAs must be submitted promptly as they occur to ORO through OHRP. Modifications other than telephone, address, or email changes require a revised VA FWA Addendum signed by the Facility Director, the VISN Director, and the ORO Chief Officer or designee, prior to approval by OHRP. Telephone, address, or e-mail changes may be made electronically through the OHRP web site upon prior notification of and approval by ORO.

d. **FWA Renewals.** Each VA facility must renew its FWA prior to expiration of the FWA's approval period, or in accordance with OHRP and ORO guidance. Renewals of FWAs for VA facilities must be submitted through ORO to OHRP and must be approved by both ORO and OHRP in order to take effect. FWA renewals must include the following:

(1) The signed FWA,

(2) The signed VA FWA Addendum,

(3) Certificates of completion of all parts of the OHRP Assurance Training Module for all personnel signing the FWA and the VA FWA Addendum, and

(4) Where applicable, a signed MOU as described in subparagraph 6d.

e. **Expiration of FWAs.** FWAs for VA facilities are typically approved for a period of 3 years and are inactivated if a renewal has not been approved by both ORO and OHRP prior to the end of the FWA's approval period.

(1) A VA facility may not conduct human subject research under an expired or inactivated FWA.

(2) If a VA facility's FWA expires or is inactivated, the facility's human subject research must cease, pending approval of a new or renewed FWA, except where the IRB, or IRB Chairperson, determines that continuation of the research is necessary to protect the safety, rights, or welfare of subjects currently enrolled in specific research projects (see VHA Handbook 1200.5).

(3) VA facilities must notify the ORO Chief Officer and the appropriate ORO Regional Office of such expiration or inactivation as soon as possible and in accordance with ORO guidance.

f. **Restriction or Suspension of Assurances.** Where the ORO Chief Officer determines that restriction or suspension of a VA facility's Assurance is necessary to safeguard the safety, rights, or welfare of human subjects, the ORO Chief Officer so notifies the Under Secretary for Health and the facility's IO, and provides the IO with a written statement of the reasons for the restriction or suspension.

(1) ORO forwards a copy of the written statement to the entity that approved the Assurance, the VISN Director, the CRADO, and the appropriate regulatory agencies.

(2) The facility must take the following actions upon notification of the restriction or suspension:

(a) In accordance with the determination of the ORO Chief Officer, restrict or cease the conduct of its human subject research except where the IRB, or IRB Chairperson, determines that continuation of the research is necessary to protect the safety, rights, or welfare of subjects currently enrolled in specific projects (see VHA Handbook 1200.5).

(b) Develop an action plan that addresses the deficiencies related to the restriction or suspension and submit it to the ORO for approval.

(c) Fulfill its responsibility to notify facility staff and other entities, including regulatory agencies and sponsors, under any relevant regulations, agreements, or terms of award.

g. **Removal of Suspensions or Restrictions.** The ORO Chief Officer may remove or modify ORO's suspension or restriction of a VA facility's Assurance upon determining that the safety, rights, and welfare of human subjects are protected adequately. The ORO Chief Officer provides written notification of such action to the facility's IO, as well as to the entity that approved the Assurance, the VISN Director, the CRADO, and other regulatory agencies as appropriate.

6. IRB REVIEW ARRANGEMENTS FOR VA FACILITIES

a. **IRBs of Record.** A VA facility may operate its own IRB(s) of Record and/or designate as its IRB(s) of Record one or more IRBs operated by another VA facility, an affiliated medical or dental school, or another entity as permitted under VHA Handbook 1200.5.

(1) Regardless of whether the IRB is operated by the facility or by another entity, the VA facility holding the FWA is responsible for ensuring that its designated IRB of Record is constituted in accordance with all applicable Federal and VA requirements.

(2) A VA facility may not rely upon an IRB until the applicable FWA has been approved by both ORO and OHRP.

(3) Where VA facilities designate more than one IRB, written procedures must clearly describe their respective areas of responsibility and oversight.

b. **IRB Registration.** IRBs used by VA facilities, whether operated by VA or by another entity, must be registered with OHRP and designated as an IRB of Record on the facility's FWA.

(1) IRB registrations must be renewed every three years, or as otherwise required by OHRP.

(2) Initial registrations of IRBs operated by VA facilities, as well as modifications and renewals of such registrations, must be submitted through ORO to OHRP.

(3) A VA facility may not continue human subject research under the oversight of an IRB whose OHRP registration has expired (see subpar. 5e).

(a) If the facility cannot transfer oversight of the research to another registered IRB of Record designated under its FWA, human subject research approved by the IRB with an expired registration must cease pending such designation, except where necessary to protect the safety, rights, or welfare of subjects currently enrolled in specific projects.

(b) VA facilities must notify the ORO Chief Officer and the appropriate ORO Regional Office of such expiration as soon as possible and in accordance with relevant ORO guidance.

c. **IRB Membership Rosters.** VA facilities must maintain accurate membership rosters for their designated IRB(s) of Record.

(1) A membership roster for any IRB operated by a VA facility must be submitted to ORO at the time of registration.

(2) A membership roster for any IRB operated by a non-VA entity must be submitted to ORO at the time of its designation as an IRB of Record in a VA facility's FWA.

(3) In addition to the information required under 38 CFR 16.103(b)(3), membership rosters for IRBs operated by non-VA entities must indicate which members are affiliated with and/or represent the VA facility, which members are affiliated with and/or represent the entity operating the IRB, and which members are not affiliated with either.

(4) Regardless of whether the IRB of Record is operated by the VA facility or by another entity, the VA facility holding the FWA must provide ORO with an updated roster within 30 days of any change in membership.

(5) The VA facility holding the FWA must retain each IRB membership roster for at least 5 years after the date it was superseded or retired.

(6) Updates of IRB rosters do not affect IRB registration renewal dates.

d. **MOU Requirements.** An MOU is required to document pertinent roles and responsibilities relative to the designation of another entity's IRB as a VA facility's IRB of Record.

- (1) The MOU takes the place of the OHRP “IRB Authorization Agreement” and is recognized by OHRP and ORO in lieu of that document.
- (2) MOUs must be revised promptly as conditions change and must be submitted to ORO within 30 working days of any revision.
- (3) VA facilities designating the IRB(s) of another entity as their IRB(s) of Record must review their MOU(s) carefully at the time of FWA renewal, or more frequently as warranted, and make any revisions necessary to reflect current arrangements.
- (4) A VA facility designating the IRB(s) of another entity as its IRB(s) of Record must submit to ORO with its FWA or FWA renewal a signed copy of the MOU describing the current relationship with the entity operating the IRB. ORO routinely forwards a copy of the MOU to ORD upon receipt.
- (5) An MOU determined by the ORO Chief Officer to be inadequate may result in a delay in approval of the FWA, or FWA renewal, pending the resolution of any concerns.
- (6) Suggested elements for MOUs are available on the ORD Web site at <http://www.research.va.gov/> and ORO Web site at <https://vaww1.va.gov/oro/>. VA facilities are strongly encouraged to contact ORD and the ORO Central Office as early as possible for assistance in developing or revising MOUs.
- (7) At a minimum, each MOU is to specify that:
 - (a) The designated IRB(s) of Record must comply with all relevant VA requirements, including but not limited to those of VHA Handbook 1200.5.
 - (b) The entity operating the IRB(s) must provide the VA facility and ORO with access to and copies of any records, documents, or reports relevant to compliance reviews of research conducted or supported by VA, approved by the VA facility’s R&D Committee, or involving individuals with VA appointments.
 - (c) The parties designate and maintain specific communication and cooperation mechanisms sufficient to ensure:
 1. Adequate protections for human research subjects, and
 2. Compliance with Federal and VA requirements (including those of VHA Handbook 1058.1) for reporting adverse events, unanticipated problems involving risks to subjects or others, serious or continuing noncompliance, and for-cause suspensions and terminations of research.
 - (d) The parties designate and maintain specific mechanisms, consistent with VHA Handbook 1058.2, *Research Misconduct*, and other applicable VA and Federal requirements, to address allegations of research misconduct involving VA human subject research or individuals acting as VA employees or agents in VA human subject research.

(8) Each MOU must be signed by the Director of each VA facility, the Director of the VISN in which each VA facility is located, and the IO, or official designee of each non-VA entity taking part in the arrangement.

(9) MOUs must be kept on file at all signatory institutions and made available to ORO and other oversight and accrediting bodies upon request in accordance with applicable law, regulation, and policy. Copies must be retained at least 5 years after the MOU has expired or been superseded.

e. **Use of VA IRBs by Non-VA Institutions.** Non-VA institutions may not designate or rely upon an IRB operated by a VA facility, nor may an IRB operated by a VA facility serve as the IRB of Record for a non-VA institution, without written permission of the CRADO and the ORO Chief Officer and written concurrence from the OGC in VA Central Office. VA facilities operating IRBs are responsible for informing their IRBs and their investigators of this prohibition.

7. PROCEDURES FOR CHANGING VA IRB REVIEW ARRANGEMENTS

a. **IRB Designations.** Before transition to a new IRB begins, the VA facility must designate the new IRB(s) for review and oversight of research under the facility's FWA.

(1) Membership rosters for the new IRB(s) are to be updated as necessary to provide adequate representation of the VA facility for which the IRB(s) review research and to satisfy the requirements of present VHA policy (see VHA Handbook 1200.5).

(2) The previously designated IRB(s) are not to be removed from the FWA until the transition has been completely effected.

b. **Transition MOUs and Standard Operating Procedures (SOPs).** Existing MOUs and SOPs need to be amended as practicable to effect the transition in an orderly fashion and without interruption of IRB oversight.

c. **New MOUs and SOPs.** New MOUs and SOPs are to be developed to reflect the new IRB review arrangements.

d. **IRB Oversight During Transition Period.** During the transition period, the new IRB must review and approve any research projects for which it will assume oversight responsibility. The new IRB may require modifications in the research, to take effect upon assumption of oversight by the new IRB, as a condition for accepting this responsibility.

e. **Completing the Transfer of IRB Oversight.** Once the new IRB and the facility's R&D Committee have formally accepted transfer of oversight to the new IRB, the facility's FWA is to be modified to remove designation of the old IRB(s).

8. ASSURANCES FOR NON-VA INSTITUTIONS

a. **Assurances Required for VA-Supported Research.** In accordance with 38 CFR 16.103(a), non-VA institutions receiving VA funds or other VA support for engagement in human subject research must hold an Assurance acceptable to VA. The following situations are considered indicative of VA support and would typically require an acceptable Assurance for any non-VA institution engaged in the research:

(1) Use by the non-VA institution of VA facilities, resources, or equipment in the conduct of the human subject research.

(2) Transfer from, or through, VA to the non-VA institution of funds, equipment, or other tangible resources for the human subject research.

(3) Transfer from, or through, VA to the non-VA institution of human biological specimens or private information for the research, unless the specimens or information are both de-identified under the Health Insurance Portability and Accountability Act (HIPAA) Privacy Rule at 45 CFR 164.514, and are not identifiable under the human subjects research protection regulations at 38 CFR 16.102(f).

(4) Transfer to VA, from the non-VA institution, of human biological specimens or private information for the research, unless the specimens or information are both de-identified under the HIPAA Privacy Rule at 45 CFR 164.514 and are not identifiable under the human research protection regulations at 38 CFR 16.102(f).

(5) Intellectual or other professional contributions to human subject research that merit authorship credit for individuals acting as VA employees. **NOTE:** “*Authorship*” credit does not include lesser forms of recognition such as “*acknowledgement*.”

(6) Study-wide sponsorship of a multi-site trial by VA or a VA facility.

(7) Possession by VA (or by an individual acting as an employee or agent of VA) of the Investigational New Drug (IND) Application or Investigational Device Exemption (IDE) for a clinical investigation subject to regulation by FDA.

(8) Service as the study-wide principal investigator for a multi-site trial by an individual acting as an employee or agent of VA.

(9) Designation of a VA facility as the study-wide operations center or study-wide statistical center for a multi-site trial.

(10) Designation of a VA facility as the study-wide data repository or study-wide specimen repository for a multi-site trial, unless the data or specimens are both de-identified under the HIPAA Privacy Rule at 45 CFR 164.514, and are not identifiable under the human research protection regulations at 38 CFR 16.102(f).

b. **Assurances Not Required.** The following would generally not be considered research conducted or supported by VA. An acceptable Assurance would thus generally not be required from the non-VA institution if this is the only collaboration between the institutions.

(1) Transfer to or from a VA facility of human biological specimens or private information that are both de-identified under the HIPAA Privacy Rule at 45 CFR 164.514, and are not identifiable under the human research protection regulations at 38 CFR 16.102(f).

(2) Intellectual, professional, or non-research contribution(s) to research involving human subjects or human biological specimens by an individual acting as a VA employee that do not merit authorship credit.

c. **Multi-Site Clinical Trials.** Participation by a VA facility as a research site in a multi-site clinical trial is not, in and of itself, considered indicative of VA support for the overall trial and would not typically require an Assurance for participating non-VA sites, except as indicated in subparagraph 8a.

d. **Acceptable Assurances.** FWAs are recognized as satisfying the Assurance requirements of subparagraph 8a. With ORD concurrence, ORO may negotiate special Assurances or recognize Assurances issued by other Common Rule Departments and Agencies in lieu of FWAs.

e. **Verification of Assurances for Non-VA Institutions.** VA facilities providing support to non-VA institutions or non-VA investigators, as described in subparagraph 8a, must verify that valid Assurances are in place prior to the initiation by the non-VA institution of VA-supported activities involving human subjects. FWAs may be verified by consulting the list available on the OHRP Web site. Other Assurances may be verified by contacting ORO.

f. **Research Not Requiring Assurances.** Prior to approving collaborations that do not require an Assurance from non-VA institutions (i.e., collaborations such as those described in subpars. 8b and 8c), VA facilities need to seek confirmation that:

(1) Participating institutions adhere to appropriate national, international, or study-wide standards for the protection of human subjects; and/or

(2) Data and specimens transferred to VA (even if de-identified under the HIPAA Privacy Rule at 45 CFR 164.514 and not identifiable under the human research protection regulations at 38 CFR 16.102(f)) have been or will be obtained in accordance with widely-accepted standards for the protection of human subjects (e.g., recognized national or international standards or comparable local standards).

***NOTE:** This Handbook does not address VA NPC FWAs. As direct awardees of research support from Federal agencies, OHRP requires that VA NPCs maintain an approved FWA.*

9. INITIATING OR CLOSING A HUMAN SUBJECT RESEARCH PROGRAM

a. **Initiating a Program of Human Subject Research.** VA facilities must contact ORD and the appropriate ORO Regional Office as early in the process as possible for assistance with the logistics of initiating a program of human subject research and establishing the required HRPP.

(1) Prior to submitting an FWA, the facility must notify, in writing, ORD and ORO Central Office, through the VISN within which it operates, of its intention to initiate a program of human subject research.

(2) The facility Director is responsible for:

(a) Establishing an R&D Committee, or arranging through an MOU to use the R&D Committee of another VA facility, to conduct oversight of its human research program (see VHA Handbook 1200.1).

(b) Ensuring that R&D Committee members have sufficient experience and/or training to conduct oversight of human research.

(3) Except as provided under subparagraph 5a(2), no research involving human subjects or human biological specimens may be conducted at a VA facility or by a VA investigator acting in an official VA capacity prior to approval of the facility's FWA by both ORO and OHRP.

b. **Closing a Program of Human Subject Research.** To ensure a safe transition, VA facilities intending to close a human research program must consult with the appropriate ORO Regional Office and the relevant VISN to assist with the resolution and disposition of any ongoing studies or other issues affecting closure.

(1) A VA facility closing its human subject research program must notify ORO Central Office and ORD describing the plans to close its program of human subject research. Such notifications must be in writing and submitted through the VISN.

(2) The facility's R&D Committee and IRB(s) of Record must supervise the transfer or termination of research studies to ensure that there is no harm to the rights, welfare, or safety of human subjects.

(3) The facility's IRB(s) of Record should not be dissolved until all research studies involving human subjects are closed or transferred to another VA facility.

(4) If the facility has no other research activities for which an R&D Committee is needed, its R&D Committee may be dissolved only after all research studies involving human subjects are closed or transferred to another VA facility.

(5) When the program has been properly closed, ORO will issue a letter de-activating the Assurance and, where applicable, the IRB.

(6) ORO will notify ORD and OHRP of the de-activation.

(7) Once de-activated, no human subject research of any kind can be conducted at the facility, or by individuals acting as the facility's employees or agents, unless the facility applies for and receives a new FWA approved by OHRP with an effective VA FWA Addendum approved by ORO, or as provided under subparagraph 5a(2).

(8) The facility must maintain IRB and R&D Committee records in a secure but accessible location for at least 5 years after closure of the program.

10. REFERENCES

a. Title 38 CFR Part 16, Protection of Human Subjects.

b. Title 45 CFR Part 46, Subpart A Protection of Human Subjects; Subpart B, Additional Protections for Pregnant Women, Fetuses, and Neonates; Subpart C, Additional Protections for Prisoners; Subpart D, Additional Protections for Children. Department of Health and Human Services (HHS).

c. Federal Policy ("Common Rule") for the Protection of Human Subjects, 56 Federal Register (FR) 28001, June 18, 1991.

d. VHA Handbook 1050.1

e. VHA Handbook 1058.1.

f. VHA Handbook 1058.2.

e. VHA Handbook 1200.5.