



**VHA Handbook 1200.05: Requirements for the Protection of Human
Subjects in Research (Revised November 12, 2014)
Local Site Responsibilities: VA Facility Director Approvals**

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VHA Handbook 1200.05 Series Goals

- Discuss major topics as they pertain to changes in the revised VHA Handbook 1200.05
- Address questions received on the revised Handbook by integrating responses into select topics.

Revised VHA Handbook 1200.05

- Effective Date: November 12, 2014
- Implementation Date: March 12, 2015 (120 days post release date)
 - Facility Standard Operating Policies and Procedures (SOPs) cannot contradict requirements outlined in the revised Handbook.
 - Facility SOPs can include requirements that go beyond those outlined in the revised Handbook.
 - Facility SOPs should drive practices employed at the facility.

Objectives

- Discuss key Institutional Official (IO) responsibilities:
 - Required human subjects training to be completed by the IO
 - Required approvals for new HRPPs or changes in IRB of Record
 - Procedures to review and approve recruitment materials for advertising non-VA research activities at VA Facilities
 - Certifying VA research involving pregnant women
 - Approving VA research involving children
 - Approving VA international research activities

Required Human Subjects Training To Be Completed by the Institutional Official

- ORD requires individuals involved in the conduct of VA human subjects research to complete training in ethical principles on which human subjects research is to be conducted.
- Institutional Officials are required to complete the Office for Human Research Protections (OHRP) Federalwide Assurance (FWA) Modules.
 - Three (3) OHRP FWA modules to be completed every three years
 - TMS catalog #3855044
- The VA Office of Research Oversight (ORO) must be sent copies of the FWA modules completion certificates.

Institutional Official Approval for New HRPPs or Changes in Institutional Review Board (IRB) of Record

- The IO is responsible for obtaining approval from the CRADO if the VA Facility wants to establish a new Human Research Protection Program (HRPP) or change its IRB of Record.
- Office of Research and Development evaluation includes, but is not limited to, the following:
 - IO support
 - Available infrastructure
 - IRB Roster
 - Number and types of VA research activities
 - Standard Operating Policies and Procedures
 - Agreements (e.g., Memorandum of Understanding)
- Other approvals required in addition to ORD

Institutional Official Responsibility: Procedures to Review and Approve Recruitment Materials for Advertising Non-VA Research Activities at VA Facilities

- The IO is responsible for ensuring that a procedure is in place to review and approve recruiting documents, flyers, and advertisements for research that is not VA research prior to being posted or distributed in any form within or on the premises of a VA Facility.
- Includes announcing, distributing, publishing, or advertising the non-VA study:
 - electronically,
 - hard copy, or
 - other means.
- ORD has no policies which permit the use of VA or personal email to advertise for VA or non-VA studies.
- **Non-VA research activities cannot be advertised on the VA Facebook page.**

Institutional Official Responsibility: Procedures to Review and Approve Recruitment Materials for Advertising Non-VA Research Activities at VA Facilities (cont.)

- Flexibility in how VA Facility Directors develop review and approval procedures.
- Review should include, but not be limited to,
 - considerations as to whether the research is relevant to Veterans and the VA mission;
 - whether the recruitment material clearly conveys that the non-VA research activity is not sponsored or endorsed by VA;
 - whether or not the non-VA research activity should be submitted as a VA research study (e.g., the Principal Investigator (PI) for the proposed non-VA activity is also a VA employee).
- Review can include IRB and VA Research and Development (R&D) Committee member input, but the non-VA recruitment materials cannot be approved by the VA R&D Committee.

Institutional Official Certification for VA Research Activities involving Pregnant Women: IRB and R&D Committee Reviews

- IRB review requirements:
 - All approval criteria have been met in accordance with VHA Handbook 1200.05.
 - 45 CFR, Subpart B, Additional Protections for Pregnant Women, Human Fetuses, and Neonates Involved in Research, Sections 46.203 through 46.207.
- VA Research and Development Committee:
 - Relevant to the VA's mission and the care of Veterans
 - Scientific merit to the proposed research
 - Adequate protections for research subjects and individuals conducting the research
 - Required resources are available
 - Investigator and research team are qualified.
 - All appropriate subcommittee approvals have been obtained.

Institutional Official Certification for VA Research Activities involving Pregnant Women: Certification Documentation

- VA Facility Director required to certify that the VA Medical Facility has sufficient expertise in women's health to conduct the proposed research.
 - Should review IRB and R&D Committee minutes at which the protocol was approved
 - VHA Handbook 1200.01 (Paragraph 7(g)) requires the ACOS/R&D to ensure that all minutes of the R&D Committee and its subcommittees, including those from subcommittees at VA facilities or at the affiliate, are sent to the Medical Center Director and Chief of Staff (COS) for review and appropriate action.
 - Consider whether or not the proposed research should be done at the VA Facility
- Should include a statement that the VA Facility Director is aware of and approves the request for his/her facility to participate in the research activity involving pregnant women
- If the research is greater than minimal risk, the VA Facility Director certification should include a statement that the VA Facility is able to respond to obstetric emergencies.
- VA Facility Director certification documentation should be in the Investigator's study files and in the Research and Development (R&D) file of the Research Office.

Institutional Official Approval for VA Research Involving Children

- Must not involve greater than minimal risk activities
- Requirements apply even if data or specimens are de-identified.
- IRB review requirements:
 - All approval criteria have been met in accordance with VHA Handbook 1200.05.
 - 45 CFR, Subpart D, Additional Protections for Children Involved as Subjects in Research, Sections 46.401 -46.404 and 46.408
- VA Research and Development (R&D) Committee:
 - Relevant to the VA's mission and the care of Veterans
 - Scientific merit to the proposed research
 - Justification for enrolling children or their specimens/data into the study
 - Adequate protections for research subjects and individuals conducting the research
 - Required resources are available
 - Investigator and research team are qualified
 - All appropriate subcommittee approvals have been obtained.

Institutional Official Approval for VA research involving Children: Approval Documentation

- VA Facility Director must approve participation of children in the proposed VA research activity.
 - Should review IRB and R&D Committee minutes at which the protocol was approved
 - If sponsor is not VA, the VA Facility Director should ascertain whether the sponsor has procured appropriate liability insurance.
 - Consider whether or not the proposed research should be done at the VA Facility
- Should include a statement the VA Facility Director is aware of and approves the request for his/her facility to participate in the research activity involving children.
- If the research involves interactions with children at the VA Facility, the Facility Director approval document should include a statement that the facility is able to respond to pediatric emergencies.
- VA Facility Director approval documentation should be in the Investigator's study files and in the R&D file of the Research Office.

Institutional Official Approval for VA International Research Activities

- International Research is research involving conduct at international sites or VA research using identifiable or de-identifiable specimens or data originating from or sending to international sites.
 - Excludes United States, its territories, Commonwealths, U.S. military bases, ships, and embassies
- Includes multi-site trials involving non-U.S. sites where VA is the study sponsor, a VA Investigator is the overall study-wide PI, VA holds the Investigational New Drug (IND) application, or the VA manages the data collection and data analyses
- Does not include studies when VA is one of multiple participating sites, and the PI of the overall study is not the VA Investigator

Institutional Official Approval for VA International Research Activities: Key Review Issues

- Rationale for conducting the research at an international site
- Financial arrangements including funding source, subject payments, and financial arrangements involving the research site and local investigators
- Description of where the research will be conducted
- Research assurances that in place at the international site
- Copies of all IRB/ethics approvals required by the foreign country(ies) and institution(s)
- Oversight plan for the proposed research
- Information on how IRB decisions (both VA and international IRB/Ethics Boards) will be communicated and reconciled
- VA's liability to conduct of research
- Data and security of VA data and VA sensitive information

Institutional Official Approval for VA International Research Activities: IRB Review

- IRB review requirements:
 - All approval criteria have been met in accordance with VHA Handbook 1200.05.
 - If VA is a collaborator, the IRB must ensure that human subjects outside of the U.S. who participate in the research receive equivalent protections as research participants inside the U.S.
 - All International sites should hold an International Federal Wide Assurance (FWA).
 - Research at the international sites should be approved by the IRB or Ethics Board which is listed on the International FWA.
- International FWA
 - Federal Wide Assurance obtained by an international institution
 - Assurance of compliance with HHS regulations at 45 CFR Part 46 approved by the Office for Human Research Protections (OHRP)
 - Same terms of assurance for U.S. and non-U.S. institutions

Institutional Official Approval for VA International Research Activities: VA R&D Committee Review

- VA Research and Development Committee key considerations:
 - Relevant to the VA's mission and the care of Veterans
 - Scientific merit to the proposed research
 - Rationale for conducting the research at an international site
 - Copies of all approvals required by the foreign country(ies) and institution(s)
 - Oversight plan for the proposed research
 - Information on how IRB decisions (both VA and international IRB/Ethics Boards) will be communicated and reconciled.
 - Data and security of VA data and VA sensitive information
 - Financial arrangements including funding source, subject payments, and financial arrangements involving the research site and local investigators
 - Adequate protections for research subjects and individuals conducting the research
 - Required resources are available
 - Investigator and research team are qualified
 - All appropriate subcommittee approvals have been obtained.

Institutional Official Approval for VA International Research Activities: Approval Documentation

- VA Facility Director must approve research activities classified as international research activities according to VHA Handbook 1200.05.
 - Should review IRB and R&D Committee minutes at which the protocol was approved
 - Consider whether or not the proposed research should be done at the VA Facility
- Should include a statement that he or she concurs that the part of the research proposed for the international site including the collection of human biological specimens and data could not be done within the VA or within the United States.
- Should include a statement the VA Facility Director is aware of and approves the request for his/her facility to participate in the international research activity.
- If the international research activities are conducted by the VHA Cooperative Studies program, the CRADO must approve.
- VA Facility Director approval documentation should be in the Investigator's study files and in the R&D file of the Research Office.

Summary

Questions & Contact Information

Questions can be submitted to vhacoordregulatory@va.gov

Presenter's contact information:

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VHA Handbook 1200.05 (November 12, 2014): Requirements for the Protection of Human Subjects in Research

Key Facts Regarding CRADO and VA Facility Director Approvals for Selected VA Research Activities

<u>Pregnant Women</u>	<u>Human Fetuses</u>	<u>Neonates</u>	<u>Children</u>	<u>Prisoners</u>	<u>International Research</u>
Institutional Review Board (IRB) of Record is required to review VA research involving women who are pregnant and/or their fetuses according to 45 Code of Federal Regulations (CFR) Section 46.204.	Research in which the focus is either a fetus, or human fetal tissue, in-utero or ex-utero (or uses human fetal tissue) cannot be conducted as VA research.	Interventional research involving neonates cannot be conducted as VA research.	Research involving children cannot be greater than minimal risk.	Only Chief Research and Development Officer (CRADO) waiver that exists in the revision of VHA Handbook 1200.05 applies to VA research involving prisoners.	International research is research involving conduct at international sites or VA research using identifiable or de-identifiable specimens or data originating from or sending to international sites.
	Embryonic stem cells can be used in VA research as governed by the National Institutes of Health's (NIH's) policies.	Prospective observational and retrospective records review studies involving neonates or neonatal outcomes are permitted to be conducted as VA research.	Research involving biological specimens or data obtained from children is considered to be research involving children even if de-identified.	IRB review of approval of specific requirements in 45 CFR Sections 46.301-46.306 is required prior to CRADO approval.	International research does not include studies when VA is one of multiple participating sites, and the Principal Investigator of the overall study is not the VA Investigator.
The VA Facility Director must certify that the medical facility has sufficient expertise in women's health to conduct the proposed activity.	The VA Facility Director must certify that the medical facility has sufficient expertise in women's health to conduct the proposed activity.	The VA Facility Director must approve participation of children in the proposed VA research activity.	The VA Facility Director must approve participation of children in the proposed VA research activity.	Research involving prisoners cannot be conducted as VA research unless the CRADO has granted a waiver.	The VA Facility Director must approve the proposed VA international research activity unless it is a VHA Cooperative Studies Program (CSP) study.

Note: This worksheet is not an all-inclusive list and does not replace Office of Research and Development policy requirements in VHA Handbook 1200.05 (November 12, 2014).