VA Portland Health Care System

Institutional Review Board

Policies & Procedures

*IRB Approved*

*R&D Committee Approved*

*Effective 8/1/2022*

Substantive changes in this revision:

1. Guidance regarding exemption from IRB oversight and review criteria that was removed and included in the Exemption Subcommittee P&P added back to the IRB SOP (i.e., Section VIII. Exemption From IRB Oversight/Review and Appendix 2).
2. Background Information: The 2018 Revised Common Rule removed the requirement for annual

review of some human studies, including exempt studies, and also increased those studies that would qualify as exempt by adjusting the definition. At the time, exempt studies were required to be overseen by the R&D Committee, but the Directive governing the R&D Committee (VHA Directive 1200.01) required annual review of all studies under its oversight. The Office of Research and Development (ORD) provided guidance to help facilities create an Exemption Subcommittees (ESC) to alleviate the workload of the annual review and the added burden on the R&D Committee. However, January 2021 ORD posted a technical amendment to VHA Directive 1200.01 that removed the annual review requirement for exempt studies. On June 30, 2021, the ESC was dissolved, and all exempt studies were realigned back under the oversight of the R&D Committee and in accordance with VHA Directive 1200.01.

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# INTRODUCTION

The VA Portland Health Care System (VAPORHCS) Institutional Review Board’s (IRB) Standard Operating Procedures (SOP) for the protection of human subjects in research is a reference for IRB members, IRB Analysts, researchers, and other individuals associated with the Human Research Protection Program (HRPP). This SOP details the policies and procedures based on the regulations and policies governing human research and the requirements for submitting research proposals for review by VAPORHCS IRB #1. The IRB shall adhere to the policies and procedures outlined in this SOP document. Other SOPs not included in this document are referenced by title and are available on the VAPORHCS Research & Development Web page.

Questions regarding the VAPORHCS IRB SOP may be directed to the IRB Analysts and/or the Research Assurance Officer.

Additional information about the Research Program and the Human Research Protection Program may be accessed on the VAPORHCS Research & Development Home Page at <https://www.va.gov/portlandresearch/>.

# ABBREVIATIONS

ACOS Associate Chief of Staff

AE Adverse Event

AD Administrative Director

CFR Code of Federal Regulations

COC Certificate of Confidentiality

COS Chief of Staff

CRF Case Report Form

CRQ Continuing Review Questionnaire

CRADO Chief Research and Development Officer

DHHS Department of Health & Human Services

DOD Department of Defense

DPAHC Durable Powers of Attorney for Health Care

DSMB Data and Safety Monitoring Board

FDA Food and Drug Administration

FWA Federalwide Assurance

HIPAA Health Insurance Portability & Accountability Act

HRPP Human Research Protection Program

ICF Informed Consent Form

IDE Investigational Device Exemption

IND Investigational New Drug

IO Institutional Official

IRB Institutional Review Board

IRQ Initial Review Questionnaire

ISSO Information System Security Officer

LSI Local Site Investigator

OHRP Office for Human Research Protections

OHSU Oregon Health & Sciences University

ORD Office of Research and Development, VA Central Office

ORO Office of Research Oversight

PHI Protected Health Information

PI Principal Investigator

PO Privacy Officer

VAPORHCS VA Portland Health Care System

R&D Research & Development

R&DC Research & Development Committee

RAO Research Administration Office

RCO Research Compliance Officer

RSO Radiation Safety Officer

SAE Serious Adverse Event

SOP Standard Operating Procedures

VACO VA Central Office

# DEFINITIONS

* **2018-Requirements:** The federal policies mandating the protection of human subjects are known as the “Common Rule.” The Common Rule was substantially revised in 2017, and entities must comply with the revised version of the rule for all studies approved by the IRB or determined to be exempt by IRB on or after January 21, 2019. The revised Common Rule also allows for continued compliance with the previous 1991 Common Rule for those studies approved by the IRB or determined to be exempt prior to January 21, 2019. For the purposes of this IRB SOP, the revised Common Rule, is referred to as the "2018 Requirements” throughout this document.
* **Adverse event (AE):** any untoward physical or psychological occurrence in a human subject participating in research. An AE can be an unfavorable or unintended event, including an abnormal laboratory finding, symptom or disease associated with the research or the use of a medical investigational test article. An AE does not necessarily have a causal relationship with the research.
* **Serious Adverse Event:** an AE that results in: death; a life-threatening experience; inpatient hospitalization or prolongation of hospitalization (for a patient already hospitalized); persistent or significant disability or incapacity; congenital anomaly; birth defects; or medical, surgical, behavioral, social or other intervention being required to prevent one of the preceding outcomes**.**
* **Administrative Hold:** voluntary interruption of research enrollments and/or ongoing research activities by an appropriate facility official, research investigator, or sponsor (including the VHA ORD when ORD is the sponsor). The term does not apply to interruptions of VA research related to concerns regarding safety, rights, or welfare of human research subjects, research investigators and staff, or others.
* **Administrative Termination**: projects for which the approval period has expired and the PI has failed to complete the continuing review paperwork (provided there are no subjects currently enrolled) may be administratively terminated at the discretion of the IRB. In such a case the PI will be notified of the termination and a new submission will be required if the project is to resume.
* **Administrative Withdrawal:** a new proposal that has received contingent approval or was tabled/deferred at the IRB initial review may be administratively withdrawn if the PI fails to meet the contingencies the IRB has specified. In such a case the PI will be notified of the withdrawal and a new submission will be required if the approval process of the project is to resume.
* **Certificate of Confidentiality:** a Certificate of Confidentiality is a document issued by a component of HHS pursuant to The Public Health Service Act Section 301(d), Title 42 United States Code (42 U.S.C.) 241(d) amended by Section 2012 of the 21st Century Cures Act, Public Law 114-255, to protect the privacy of individuals who are subjects of certain specified research activities by authorizing investigators to withhold from all persons not connected with the conduct of such research the names or other identifying characteristics of such subjects. Persons so authorized to protect the privacy of such individuals may not disclose information in any federal, state, or local civil, criminal, administrative, legislative, or other proceedings to identify such individuals.
* **Children:** Children are persons who have not attained the legal age to consent to treatments or procedures involved in the research under the applicable State law of the jurisdiction in which the research will be conducted.
* **Clinical Trial:** (NOTE: the pre-2018 Requirement provided no definition of a clinical trial.) ***For research that is subject to the 2018 Requirements:*** A research study in which one or more human subjects are prospectively assigned to one or more interventions (which may include placebo or other control) to evaluate the effects of the intervention on biomedical or behavioral health-related outcomes.
* **Collaborative Research:** collaborative research is human subject research activities involving investigators from VA and at least one non-VA institution. Collaborative research may include VA and non-VA institutions.
* **Conflict of Interest:**a conflict of interest exists when an individual’s financial interests or other obligations interfere, or appear to interfere, with the individual’s obligations to act in the best interests of the human research participants and the VAPORHCS and without improper bias. This may include both financial and non-financial conflicts of interest. The mere appearance of a conflict may be as serious and potentially damaging to the public trust as an actual conflict. Therefore, potential conflicts must be disclosed, evaluated, and managed with the same thoroughness as actual conflicts.
* **De-Identified:** health information that is presumed not to identify an individual and with respect to which there is no reasonable basis to believe that the information can be used to identify an individual because the 18 Patient Identifiers (which includes dates related to the individual, such as dates of birth, study or clinic visits, specimen collection, etc.) described in the HIPAA Privacy Rule have been removed or a qualified biostatistician has determined that the health information has been de-identified. De-identified information is no longer covered by the Privacy Act, 38 U.S.C. 7332, or the HIPAA Privacy Rule (see VHA Directive 1605.01, Privacy and Release of Information). Please see the List of 18 HIPAA Identifiers at <https://www.va.gov/portlandresearch/documents/hrpp/18-HIPAA-identifiers.doc>.
* **Exempt Research:** research determined by the Institutional Review Board (IRB) or Exemption Determination Official and member of the Exemption Subcommittee (as detailed in Section VIII) to involve human subjects only in one or more categories as determined by OHRP. ***NOTE:*** *Categories of exemption are listed on the Certification of Exemption form at* <https://www.va.gov/portlandresearch/piservices/rd_forms.asp#alphabetical>.
* Experimental Subject: as defined by the DOD, human subject involved in research under a DOD Addendum that involves an intervention or interaction with the subject for the primary purpose of obtaining data regarding the effect of either.
* Federal-wide Assurance (FWA): A Federalwide Assurance (FWA) is an assurance approved for Federalwide use by the Office of Human Research Protections (OHRP) in accordance with Section 103(a) of the Common Rule (see 38 CFR 16.103(a)).
* FWA: Department of Defense (DOD) Addendum: Addendum to FWA that must be filed by the ORD when a study is sponsored by the Department of Defense and the DOD requires. Such an addendum describes specific DOD responsibilities for the study.
* Fetus: for purposes of this SOP and as defined in Subpart B of the Common Rule (including the 2018 Requirements) for the Protection of Human Subjects, a fetus is the product of conception from the time of implantation until delivery.
* **Human Research Protection Program (HRPP**): 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 VA facility Director, Associate Chief of Staff (ACOS) for Research and Development (ACOS/R&D), the Administrative Director (AD/R&D), the R&DC, the Institutional Review Board (IRB), other committees or subcommittees addressing human subjects protection (e.g., Subcommittee on Research Safety (SRS), 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, information security 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 in research.
* **Human Subjects:** defined by the pre-2018 Requirements version of the federal regulations, at 45 CFR 46.102(f) and 38 CFR 16.102 (f), as "living individual(s) about whom an investigator conducting research obtains (1) data through intervention or interaction with the individual, or (2) identifiable private information."
  + - * + **Intervention** includes both physical procedures by which data are gathered (for example, venipuncture) and manipulations of the subject or the subject's environment that are performed for research purposes.
        + **Interaction** includes communication or interpersonal contact between investigator and subject.
        + **Private information** includes information about behavior that occurs in a context in which an individual can reasonably expect that no observation or recording is taking place, and information which has been provided for specific purposes by an individual and which the individual can reasonably expect will not be made public (for example, a medical record). Private information must be individually identifiable (i.e., the identity of the subject is or may readily be ascertained by the investigator or associated with the information) in order for obtaining the information to constitute research involving human subjects.” The VA regulations furtherdefine human subjects to include investigators, technicians, and other assisting investigators, when they serve in a "subject" role by being observed, manipulated, or sampled.
* **Human Subjects** (***For research that is subject to the 2018 Requirements):*** defined by federal regulations, at 45 CFR 46.102(e) and 38 CFR 16.102 (e), as living individual(s) about whom an investigator (whether professional or student) conducts research and : (1) obtains information or biospecimens through intervention or interaction with the individual, and uses, studies, or analyzes the information or biospecimens; or (2) obtains, uses, studies, analyzes, or generates identifiable private information or identifiable biospecimens.

***Intervention*** includes both physical procedures by which information or biospecimens are gathered (for example, venipuncture) and manipulations of the subject or the subject's environment that are performed for research purposes.

***Interaction*** includes communication or interpersonal contact between investigator and subject.

***Private information*** includes information about behavior that occurs in a context in which an individual can reasonably expect that no observation or recording is taking place, and information which has been provided for specific purposes by an individual and which the individual can reasonably expect will not be made public (for example, a medical record).

* **Human subjects per FDA regulations**: Per the FDA’s Protection of Human Subjects regulations [21 CFR 50.3(g)], “an individual who is or becomes a participant in research, either as a recipient of the test article or as a control. A subject may be either a healthy human or a patient.” In addition, the FDA’s Investigation Device Exemptions regulations [21 CFR 812.3(p)] state a “*Subject* means a human who participates in an investigation, either as an individual on whom or on whose specimen an investigational device is used or as a control. A subject may be in normal health or may have a medical condition or disease.”
* **Identifiable Biospecimen (*For research that is subject to the 2018 Requirements.*** *NOTE: the pre-2018 Requirement provided no definition.)* An identifiable biospecimen in one which the identity of the subject is or may readily be ascertained by the investigator or associated with the biospecimens.
* **Identifiable Private Information (*For research that is subject to the 2018 Requirements.*** *NOTE: the pre-2018 Requirement provided no definition.)* Identifiable private information is information for which the identity of the subject is or may readily be ascertained by the investigator or associated with the information.
* **Institutional Official:** The institutional official (IO) is the individual legally authorized as the 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 (see VHA Directive 1058.03). The Principal Deputy Under Secretary for Health or designee is the IO for VHA Central Office, and VA facility Directors are the IOs for local VA facilities.
* **Institutional Review Board (IRB)**:a formally established subcommittee of the Research and Development Committee (R&DC) with and for the purposes expressed in the Common Rule. The IRB also provides oversight and monitoring of such protections. In accordance with the Common Rule, VA and FDA regulations, the IRB has responsibility for approving, requiring modification (to secure approval), or disapproving research.
* **International Research:** Defined by VA as any VA-approved research conducted at international sites (i.e., not within the United States (U.S.), its territories, or Commonwealths), any VA-approved research using either identifiable or de-identified human biological specimens or identifiable or de-identified human data originating from international sites, or any VA-approved research that entails sending such specimens or data outside of the US, including to individuals with VA appointments at international sites. This definition applies regardless of funding source (funded or unfunded) and to research conducted through any mechanism of support including MOUs, CRADAs, grants, contracts, or other agreements. For additional guidance on international research, see VHA Directive1200.05.

***NOTE:*** *Remote use of data that is maintained on VA computers within the U.S. or Puerto Rico and accessed via a secure connection is not considered international research.*

* **Investigational Device:** as defined by the FDA, a device, including a translational device, that is the object of an investigation, involving one or more subjects, that is designed to evaluate the safety or effectiveness of the device.
* **Investigational Drug:** a chemical or biological drug that is used in a clinical investigation. The FDA considers the term "investigational new drug” synonymous with “investigational drug.” However, for purposes of this IRB SOP, an Investigational Drug may be: 1) an approved drug that is being studied for an unapproved or approved use, dose, dosage form, administration schedule, or under an IND application; or 2) a new chemical compound not yet released by the FDA for general use. ***NOTE:*** *Concurrent medications, comparators, or rescue medications used in the clinical trial that are not the drug(s) being studied are not defined as investigational drugs unless they are not commercially approved or not available through commercial channels. Prescription drugs, over-the-counter drugs, nutritional supplements, herbal preparations, and legend items used for diagnosis or treatment and meeting the definition of “investigational drug” are considered investigational drugs.*
* **Investigational Device Exemption (IDE):** an application to the FDA that allows an investigational, significant risk device to be used in a clinical investigation to collect safety and effectiveness data. If the device is determined by the IRB to be a non-significant risk device, it is considered to have an approved application for IDE after IRB approval is obtained.
* **Investigational New Drug (IND):** an application to the FDA that allows an investigational drug or biological product to be studied in humans. IND is synonymous with “Notice of Claimed Investigational Exemption for a New Drug.” An IND must be in effect prior to shipment and administration of investigational drug or biological products, except when exempt from those requirements. ***NOTE:*** *For applicability and exemptions, see 21 CFR 312.2(a)-(b) at:* <http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcfr/CFRSearch.cfm?CFRPart=312>*.* Also see definition of Investigational Drug above.
* **Investigator:** Any individual who conducts research, including, but not limited to, the Principal Investigator (PI), sub-investigator, or co-investigators, and Site Investigator or Local Site Investigator (LSI). An investigator must be compensated by VA, be appointed to work without compensation (WOC), or be an employee assigned to VA through the Intergovernmental Personnel Act (IPA) of 1970. The FDA considers investigator and PI to be basically synonymous.
  + - * + **Principal Investigator.** The Principal Investigator (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 individuals, the PI is the responsible leader of that team.
        + **Sub-Investigator or Co-Investigator.** A sub-investigator or co-investigator is a qualified person designated by the PI or LSI to perform critical research procedures and/or to make important research-related decisions. Both terms are interchangeable but are key personnel on a research study or program.
        + **VA Investigator.** A VA investigator is 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. ***NOTE:*** *Trainees can serve as a co- or sub-investigator but must have a VA PI sufficiently experienced in the area of the trainee’s research interest to serve as the PI. Trainee research activities are further discussed in VHA Directive 1200.02, Research Business Operations.*
* **Ionizing Radiation:** particles or rays with sufficient energy to cause the ejection of orbital electrons from absorber atoms. Ionizing radiation should be addressed within the protocol and the informed consent when used in a research study. Ionizing radiation includes diagnostic and therapeutic procedures done for research purposes. Sources of radiation include procedures performed in nuclear medicine, radiation therapy, and radiology.
* **Legally Authorized Representative (LAR):**

1. The Oregon State Law does not define LAR (Oregon Revised Statue (ORS) 677.097. For purposes of signing an ICF, a legally authorized representative (LAR) is defined as an individual, or judicial or other body, authorized under applicable law to consent on behalf of a prospective subject to the subject's participation in the procedures(s) involved in the research.

In accordance with VA regulations and local institutional policy, the following persons are authorized to consent on behalf of individuals who lack decision-making capacity, in the following order of priority:

* 1. Health Care agent (i.e. an individual named by the prospective subject in a Durable Power of Attorney for Health Care)
  2. Legal guardian or special guardian *(Note: Financial or other types of limited guardianship do not always include the authority to make health care decisions.)*
  3. Spouse
  4. Adult children (18 years of age or older)
  5. Parent
  6. Adult siblings (18 years of age or older)
  7. Grandparent
  8. Adult grandchild (18 years of age or older)
  9. Close friend - Any person, eighteen years or older, who: has shown care and concern for the prospective subject’s welfare; is familiar with the prospective subject’s activities, health, religious beliefs and values; and has presented a signed, written statement for the record that describes that person’s relationship to and familiarity with the prospective subject.

***NOTE:*** *The list above contains the only surrogate entities allowed to provide consent for research purposes. Refusal to consent by a person who is a higher priority surrogate shall not be superseded by the consent of a person who is a lower priority surrogate. Additionally, if there are two or more individuals in the same class and the decision is not unanimous among all available members of the class, then no person under this section may provide informed consent. Surrogates may not receive financial compensation for providing consent.*

1. For purposes of signing a HIPAA Authorization, a legally authorized personal representative is defined as follows:
2. A court-appointed legal guardian (Note: *A VA Federal fiduciary administratively appointed by VBA to administer a beneficiary's VA monetary benefits is not empowered to exercise privacy rights of the VA beneficiary who is the subject of that appointment including granting authorization, i.e. Power of Attorney.*
3. A person legally authorized in writing by the individual (or the individual’s legal guardian) to act on behalf of the individual.
4. If the individual is deceased, then Executor of Estate, next-of-kin, or other person who has authority to act on behalf of the individual.

* **Local (for Deaths, S/AEs and Problems):** Occurring in participants, personnel and/or other individuals involved in VAPORHCS research activities.
* **Minimal Risk:**when the probability and magnitude of harm or discomfort anticipated in the proposed research are not greater than those ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests.
* **Neonate:** newborn within the first 4 weeks of birth.
* **Noncompliance:** Failure to adhere to federal regulations and/or other requirements for conducting VA research.
* **Serious noncompliance**:
  1. involving substantive harm, or presenting a genuine risk of substantive harm, to the safety, rights, or welfare of human research subjects, research staff, or others, including their rights to privacy and confidentiality of identifiable private information; or
  2. substantively compromising a facility’s HRPP.
* **Continuing noncompliance**: a persistent failure to adhere to the legal and policy requirements governing human research; this involves knowingly, willfully or intentionally doing something that has been determined to be noncompliant.
* **Nonprofit Research and Education Corporations:** VA-affiliated nonprofit research and education corporations (NPC) 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&DC 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 (see VHA Handbook 1200.17, Department of Veterans Affairs Nonprofit Research and Education Corporations Authorized by Title 38 U.S.C. Sections 7361 Through 7366, dated April 27, 2016 and revised May 9, 2017).
* **Office of Research and Development (ORD):** the office within VHACO responsible for the overall policy, planning, coordination, and direction of research activities within VHA. ***NOTE:*** *The Program for Research Integrity Development and Education Program (PRIDE) is the program within ORD responsible for training, education, and policy development related to human subjects protection.*

**Office of Research Oversight (ORO):** the primary VHA office for advising the Under Secretary for Health on all matters of compliance and assurance regarding human subject protections, animal welfare, research safety and security, research information protection, and research misconduct. ***NOTE:*** *ORD and ORO are two separate offices within VHA. The CRADO reports to the Principal Deputy Under Secretary for Health*. *The Chief Officer of ORO reports to the Under Secretary for Health.*

* + - * **Pregnancy:** period of time from implantation until delivery. A woman is assumed to be pregnant if she exhibits any of the pertinent presumptive signs of pregnancy, such as missed menses, until the results of a pregnancy test are negative or until delivery.

**Prisoner:** any individual involuntarily confined or detained in a penal institution. The term is intended to encompass individuals sentenced to such an institution under a criminal or civil statute, individuals detained in other facilities by virtue of statutes or commitment procedures that provide alternatives to criminal prosecution or incarceration in a penal institution, and individuals detained pending arraignment, trial or sentencing.

* **Program Office:** any office within the VHA Office of the Under Secretary for Health. A Program Office includes all of its component offices and subdivisions, regardless of physical location. ***NOTE:*** The organization chart for the VHA Office of the Under Secretary for Health may be found on the VHA Web site.
* **Program Office Employee:** any individual working under a VA appointment in a VHA Program Office, regardless of duty station, including (but not limited to) full and part-time employees, WOC employees, and employees under the IPA.
* **Qualified Designee:**  an IRB member or Research Administrative Office staff member with appropriate experience and knowledge to perform a specific duty and designated by an IRB Co-Chair to perform that duty as described in this SOP.
* **Quorum:** more than half of the voting members of a committee being present, and including at least one member whose primary concerns are in non‑scientific areas. At meetings of the IRB, a quorum must be established and maintained for the deliberation and vote on all matters requiring a vote. In order for research to be approved, it must receive the approval of a majority of those members present at the meeting.
* **Related S/AE, Death or Problem**: one that may reasonably be regarded as caused by or probably caused by the research (i.e., the event would probably not have occurred without involvement in/of the study).
* **Research:**a systematic investigation, including research development, testing and evaluation, designed to develop or contribute to generalizable knowledge. Research involves the testing of concepts by the scientific method of formulating a hypothesis or research question, systematically collecting and recording relevant data, and interpreting the results in terms of the hypothesis or question.

1. Systematic: designed to answer a question or test a hypothesis that addresses a research intent by an organized method.
2. Generalizable: knowledge that may be applied to populations or settings different from the ones used in the investigation.
3. FDA regulations define clinical investigation, rather than research. That definition is “any experiment that involves a test article and one or more human subjects and that either is subject to requirements for prior submission to the Food and Drug Administration under section 505(i) [i.e. changes in labeling] or 520(g) [i.e. any activity that evaluates the safety or effectiveness of a device] of the act, or is not subject to requirements for prior submission to the Food and Drug Administration under these sections of the act, but the results of which are intended to be submitted later to, or held for inspection by, the Food and Drug Administration as part of an application for a research or marketing permit.”
4. Any prospective or retrospective collection of clinical data with the intent to develop or contribute to generalizable knowledge constitutes research, as defined by VA regulations. Examples of such clinical data collection include research seminars, posters, abstracts, manuscripts, and pilot data.
5. Research involving human subjects means any activity that either:
6. Meets the VA definition of research and involves human subjects as defined by VA; or
7. Meets the FDA definition of research and involves human subjects as defined by FDA.

* **Research** **(*For research that is subject to the 2018 Requirements):*** 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 this SOP, whether or not they are conducted or supported under a program that is considered research for other purposes. For example, some demonstration and service programs may include research activities.

1) Systematic: designed to answer a question or test a hypothesis that addresses a research intent by an organized method.

2) Generalizable: knowledge that may be applied to populations or settings different from the ones used in the investigation.

3) Clinical Investigations (also see Clinical Trial definition), including those defined under FDA regulations in 21 CFR 50.3, 312.3(b), are considered research.

4) FDA regulations define clinical investigation, rather than research. That definition is “any experiment that involves a test article and one or more human subjects and that either is subject to requirements for prior submission to the Food and Drug Administration under section 505(i) [i.e. changes in labeling] or 520(g) [i.e. any activity that evaluates the safety or effectiveness of a device] of the act, or is not subject to requirements for prior submission to the Food and Drug Administration under these sections of the act, but the results of which are intended to be submitted later to, or held for inspection by, the Food and Drug Administration as part of an application for a research or marketing permit.”

5) Any prospective or retrospective collection of clinical data with the intent to develop or contribute to generalizable knowledge constitutes research, as defined by VA regulations. Examples of such clinical data collection include research seminars, posters, abstracts, manuscripts, and pilot data.

6) Clinical reviews (reviews of four or more clinical records, whether or not care team members are involved) are considered human subjects research and must have IRB and R&DC approval. Case Reports (reviews of three or fewer clinical records by one or more members of the care team) are not considered research but do require submission of an Application for Case Report Review to the RAO.

7) Research involving human subjects means any activity that either:

a. Meets the VA definition of research and involves human subjects as defined by VA; or

b. Meets the FDA definition of research and involves human subjects as defined by FDA.

8) The following activities are deemed not to be research, but the RAO must be contacted prior to initiation of activities to assure all regulations, including those required by the VA, are met:

a. scholarly and journalistic activities (e.g., oral history, journalism, biography, literary criticism, legal research, and historical scholarship), including the collection and use of information that focus directly on the specific individuals about whom the information is collected. (note, these fields have their own codes of ethics, including oral consent);

b. public health surveillance activities including the collection and testing of information or biospecimens, conducted, supported, requested, ordered, required, or authorized by a public health authority. Such activities are limited to those necessary to allow a public health authority to identify, monitor, assess, or investigate potential public health signals, onsets of disease outbreaks, or conditions of public health importance (including trends, signals, risk factors, patterns in diseases, or increases in injuries from using consumer products). Such activities include those associated with providing timely situational awareness and priority setting during the course of an event or crisis that threatens public health (including natural or man-made disasters);

c. collection and analysis of information, biospecimens, or records by or for a criminal justice agency for activities authorized by law or court order solely for criminal justice or criminal investigative purposes; and

d. authorized operational activities in support of homeland security, defense or other national security missions.

* **Research Records:** Research records include, but are not limited to, IRB and R&DC records, records of all observations, other data relevant to the investigation, progress notes, research study forms, surveys, questionnaires, and other documentation regarding the study (see VHA Records Control Schedule (RCS) 10-1).

1. **IRB Records:** IRB records include, but are not limited to, copies of all research proposals and amendments reviewed; scientific evaluations, if any, that accompany the proposals; approved informed consent documents; progress reports submitted by investigators; reports of injuries to subjects; reports of complaints from subjects; minutes of IRB meetings; reports of expedited review activities; records of continuing review activities; copies of all correspondence between IRB and researchers; reports of deviations from IRB-approved protocol; a list of IRB members; written procedures for IRB in the same detail as described in 38 CFR 16.103(b)(4) and (5); and statements of significant new findings provided to subjects as required by 38 CFR 16.116(b)(5).
2. **Investigator Research Records**: all relevant research documents, including copies of: all IRB-approved versions of the protocol and amendments; case report forms and supporting data (including but not limited to signed and dated ICFs forms); documentation for each subject (including signed and dated ICFs and HIPAA authorizations, as well as copies of all information given to subjects), interactions with subjects by telephone or in person, recruitment activities, observations, interventions, progress notes, research study forms, surveys, questionnaires, and other data relevant to the research study; reports of adverse events; data analyses; codes and keys used to de-identify and re-identify participants’ information; reports (including, but not limited to abstracts and other publications); all correspondence (including, but not limited to, that with the funding source or sponsor) and with applicable oversight entities (including, but not limited to, IRB, R&DC, ORO, and FDA); the grant application; documents related to budget and funding; and a master list of all subjects for whom signed informed consent has been obtained in the study.

* **Research and Development (R&D) Committee:** The R&DC is a committee responsible, through the Chief of Staff (COS) to the VA facility Director, for 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).
* **Research Protocol:** A research protocol details the aims and objectives of a research study, scientific rationale, the methods used to carry out the research, and how data will be analyzed. For human subjects research it also entails how subjects will be accessed/recruited, any foreseeable risks, and how these risks will be mitigated.
* **Serious Problem:** a problem in human subjects research or research information security that may reasonably be regarded as:
  + presenting a genuine risk of substantive harm, to the safety, rights, or welfare of human research subjects, research personnel, or others, including their rights to privacy and confidentiality of identifiable private information; or
  + substantively compromising a facility’s HRPP or research information security programs.
* **Signatory Official:** The Signatory Official is the individual legally authorized to commit an institution to the requirements of an FWA.
* **Suspension of Research:** a temporary interruption in selected research activities (e.g., new enrollments or specific interventions) due to concerns about the safety, rights, or welfare of human subjects, research personnel, or others, regardless of whether the action to suspend was taken by an investigator, facility official, research review committee, or external entity. ***NOTE:*** *This does not refer to interruptions for other reasons, including lapses of IRB approval.*
* **Termination of Research:** a permanent halt of all research activities due to concerns about the safety, rights, or welfare of human subjects, research personnel, or others, or about the welfare of laboratory animals, regardless of whether the action to terminate was taken by an investigator, facility official, research review committee, or external entity.
* **Test Article:** a drug, device, or other article including a biological product used in clinical investigations involving human subjects or their specimens.
* **Unanticipated/Unexpected**: event or problem in human subjects research that is new or greater in nature, severity, or frequency than previously known, given the procedures described in protocol documents and the characteristics of the study population.
* **VA Research:** research conducted by VA investigators with a VA appointment (Compensated, Without Compensation-WOC, or Intergovernmental Personnel Agreement-IPA) while on VA time, using VA resources (e.g., equipment), and/or on VA property (including space leased or used by VA). The research may be funded by VA or other sponsors or may be unfunded. VA research must have R&DC approval before it is considered VA Research and before it can be initiated. All research activities approved by the R&DC are considered VA Research. ***NOTE:*** *VA Research must be conducted in VA space and/or third-party space that VA has the legal authority to use for the intended purpose, and for which the parties have entered into an appropriate agreement that complies with the applicable law and VA policy.*
* **VA Facility**: any entity operated by the VA, including but not limited to VA hospitals, medical centers, and healthcare systems; space owned, leased, or rented by VA; and space shared with a non-VA entity (unless the VA space is leased to a non-VA entity and specifically designated in writing not to be used by VA or VA employees for research).

# PURPOSE AND ETHICAL FRAMEWORK

## Purpose of the IRB

The VAPORHCS IRB’s primary responsibility is to ensure that the rights and welfare of subjects are protected in the VAPORHCS human research program. In doing so, the IRB must ensure that human research is conducted ethically, and in compliance with VA and other federal regulations, applicable Oregon and Washington state laws (applicable if determined by Regional Counsel to be more stringent than federal law), the signed FWA, and the VAPORHCS’s institutional SOPs.

## Ethical Principles Governing the IRB

VA Research must be carried out in an ethical manner. The basic ethical principles governing research involving human subjects are provided in:

### The Nuremberg Code

The modern history of human subject protections begins with the discovery after World War II of numerous atrocities committed by Nazi doctors in war-related human research experiments. The Nuremberg Military Tribunal developed ten principles as a means of judging their “research” practices, known as *The Nuremberg Code.* Significantly, the Code addresses the necessity of requiring voluntary consent of the human subject and that any individual “who initiates, directs, or engages in the experiment” must bear personal responsibility for ensuring the quality of consent. The Nuremberg Code can be accessed through <http://www.hhs.gov/ohrp/archive/nurcode.html>.

### The Declaration of Helsinki

Similar principles to The Nuremberg Code have been articulated and expanded in later codes, such as the World Medical Association Declaration of Helsinki: Recommendations Guiding Medical Doctors in Biomedical Research Involving Human Subjects (1964, revised 1975, 1983, 1989, 1996, 2000), which call for prior approval and ongoing monitoring of research by independent ethical review committees. The Declaration of Helsinki can be accessed through <https://www.wma.net/policies-post/wma-declaration-of-helsinki-ethical-principles-for-medical-research-involving-human-subjects/>

### The Belmont Report

The Belmont Report contains three basic ethical principles central to human research that guide the IRB in assuring protection of the rights and welfare of subjects. The Belmont Report can be accessed through <http://www.hhs.gov/ohrp/policy/belmont.html>. These three principles are:

1. **Respect for persons** recognizes individual autonomyand isapplied by obtaining informed consent, consideration of privacy and confidentiality, and assuring additional protections for vulnerable populations.
2. **Beneficence** requiresthat possible benefits are maximized and possible risks minimized for research subjects.
3. **Justice** is evidenced in the equitable selection of subjects with regard to distribution of burdens and benefits.

## The Regulatory Mandate to Protect Human Subjects

The Department of Veterans Affairs (VA) and other Federal regulations require specific protections for human subjects:

### The Common Rule

In January 1991, the VA joined 16 other Executive Branch Departments and Agencies in simultaneously adopting the Federal Policy (Common Rule) for the Protection of Human Subjects. Codified by the VA at 38 CFR 16, the Common Rule is also codified by the Department of Health and Human Services (DHHS) as Subpart A of the DHHS regulations at 45 CFR 46. DHHS has three additional Subparts in the regulations, as well, that are not in 38 CFR 16. **All** human subject research conducted at the VAPORHCS must adhere to the regulations at 45 CFR 46 and 38 CFR 16. ***NOTE:*** *It is VHA policy that all research involving human subjects must adhere to the 2018 Requirements, except that research which is subject to the pre-2018 Requirements need not comply with standards which are specifically stated in this SOP to be subject to the 2018 Requirements.*

### Other VA regulations and requirements relevant to the protection of human subjects

1. 38 CFR 17.33 - Patients’ rights
2. 38 CFR 17.85 - Treatment of research related injuries to human subjects
3. 38 CFR 17.45 - Hospital care in research studies
4. 38 CFR 17.92 - Outpatient care for research studies
5. VHA Directive 1200.05 – Requirement for the Protection of Human Subjects in Research
6. VHA Directive 1058.01 – Research Compliance Reporting Requirements
7. VHA Directive 1058.03 – Assurance of Protection for Human Subjects in Research

### Food and Drug Administration (FDA) Regulations

The following FDA regulations must also be adhered to when appropriate:

1. 21 CFR 50 – Protection of Human Subjects
2. 21 CFR 56 – Institutional Review Boards
3. 21 CFR 54 – Financial Disclosure by Clinical Investigators
4. 21 CFR 312 - Investigational New Drugs (IND)
5. 21 CFR 812 – Investigational Device Exemptions (IDE)
6. 21 CFR 814 – Premarket Approval of Medical Devices (Humanitarian Use Devices)

### DHHS Office for Human Research Protections (OHRP) – Federalwide Assurance

DHHS mandates that every institution conducting non-exempt human research with federal funds register itself with OHRP and obtain an assurance of compliance approved by the OHRP. Under this OHRP-issued Federalwide Assurance (FWA), the IRB that reviews the human research projects is responsible for adhering to and fulfilling the requirements of the Federal regulations of 45 CFR Part 46.

Information regarding the VAPORHCS FWA number and associated IRB registration numbers can be found on the R&D website: <https://www.va.gov/PORTLANDRESEARCH/hrpp/index.asp?tab=3>

All Community Based Outpatient Clinics over which the VAPORHCS has legal authority are covered by the VAPORHCS’s FWA. Information regarding the FWA may be found by accessing the U.S. DHHS OHRP web site <http://ohrp.cit.nih.gov/search/> and entering the FWA number. The VAPORHCS IRBs abide by the terms in the FWA.

### Department of Defense (DOD) Regulations at 32 CFR 219

DOD regulations must also be followed when appropriate, i.e. research funding is granted by the DOD for research approved by the VAPORHCS IRB. Under such circumstances, if the DOD requests, a DOD addendum will be added to the FWA for the VAPORHCS. The RAO staff will determine at initial review if a DOD addendum is required. The responsible staff member will add the addendum to the FWA and then notify IRB Analysts, IRB Chair and members, investigators and research staff of any special requirements.

## Authority of the IRB

### Authority of the VAPORHCS IRBs of Record

One VAPORHCS IRB of Record must prospectively review and make a decision concerning all human subjects research that is considered VAPORHCS Research (e.g., conducted at the VAPORHCS or by VAPORHCS employees or agents, or otherwise under the auspices of the VA); this includes VAPORHCS Research funded through the VA nonprofit research corporation (NPC). Further, these IRBs have statutory authority to:

1. Take any action necessary to protect the rights and welfare of human subjects in the research program.
2. Approve, require modifications in, or disapprove the facility’s human research, based on its consideration of the risks and potential benefits of the research, and whether or not the rights and welfare of human subjects are adequately protected.
3. Conduct continuing review of research at intervals appropriate to the degree of risk, but not less than once per year (unless the research meets the criteria described in 2018 Requirements and 38 CFR 16.109; ***NOTE:*** *this does not apply to research when other regulations require continuing review, such as FDA-regulated research.)*
4. Suspend or terminate approval of research that is not being conducted in accordance with the IRB's requirements or that has been associated with unexpected serious harm to subjects (38 CFR 16.113).
5. Observe and/or monitor the VAPORHCS’s conduct of human research, including the informed consent process, to whatever extent it considers necessary to protect human subjects.

Neither the VA facility nor the investigator may engage the services of another IRB for the purposes of avoiding the requirements or determinations of a VAPORHCS IRB of Record.

All VAPORHCS IRBs of record must meet all applicable IRB requirements described in VHA Directive 1200.05.

### Review of Research at Other Institutions

The IRB is responsible for the protection of the rights and welfare of human research subjects at the VAPORHCS and for research conducted under VAPORHCS auspices.

The IRB may be designated for review of research under another institution’s assurance only with the written agreement of the IO and in accordance with applicable ORD, ORO, and OHRP requirements. Such designation must be accompanied by a written agreement specifying the responsibilities of the facility and it’s IRB under the other institution’s assurance. The IRB operated by the VAPORHCS has no authority over or responsibility for research conducted at other institutions in the absence of such a written agreement.

## Review of the SOP

This SOP of the IRB must remain current and in compliance with all applicable regulations. To remain current, this SOP must be reviewed and periodically updated. The Research Administrative Office (RAO) designee, with the assistance of the IRB Co-Chairs, IRB Analysts, ACOS/R&D and AD/R&D, recommends changes to this SOP to comply with the most recent VA and federal regulations. Proposed changes will be presented to the IRB for input. Upon review and approval of a majority of the IRB, the revised version will then be forwarded to the R&DC for approval. Notifications of changes and an updated IRB SOP will be made available electronically to all members and distributed in hard copy to those who request it.

Other documents used by the IRB for its day-to-day functions (including, but not limited to, investigator submission forms, investigators' manual, guidance documents, reviewer forms, checklists, etc.) will also be reviewed and revised as needed.

# Shared Responsibilities of the Institution in Protecting Human Subjects

## VAPORHCS Medical Facility Director

The VAPORHCS Medical Facility Director serves as the Institutional Official (IO) and the legally authorized Signatory Official (SO) to commit an institution to an FWA. An FWA is required prior to conducting non-exempt human subjects research. See 38 CFR 16.103. The IO is responsible for overseeing the VAPORHCS research program. The IO’s responsibilities for the facility’s HRPP are outlined in VHA Directives 1200.05 and 1058.03.

The IO delegates the authority for all respective roles and responsibilities within the HRPP, providing organizational structure and ensuring accountable leadership for oversight activities for all human research at VAPORHCS, to the Associate Chief of Staff/R&D.

## Associate Chief of Staff/Research & Development (ACOS/R&D)

TheACOS/R&Dreports to the IO through the Chief of Staff (COS) and is responsible for the following:

1. Developing, managing and evaluating policies and procedures that ensure compliance with all federal regulations and any applicable state statutes (as determined by Regional Counsel to be more stringent than federal law) governing research. This includes monitoring changes in state, VA and other federal regulations and policies related to human research protection and overseeing all aspects of the HRPP program established for human research protections.
2. Acting as liaison between the VHA ORD and the institution’s R&DC, as well as advising the IO and VISN 20 leadership on key matters regarding research.
3. Implementing the institution’s HRPP policy.
4. Assuring that PIs and other researchers are informed via targeted email when HRPP policies are changed.
5. Submitting, implementing, and maintaining an approved FWA through the IO and the ORO and to OHRP.
6. Managing the facility’s R&D program, including the R&DC and applicable subcommittees.
7. Managing the finances of the facility’s R&D Program.
8. Assisting investigators in their efforts to carry out the VA’s research mission by providing educational opportunities and informing investigators of all changes in federal and applicable state regulations and local policies governing human research.
9. Developing and implementing needed improvements and ensuring follow-up of actions as appropriate for the purpose of managing risk in the research program.
10. Developing training requirements and ensuring that these training requirements for investigators and members of the applicable subcommittees and staff are completed.
11. Reviewing, or designating a reviewer for, all sponsor agreements to assure ethical standards and practices in research are upheld.
12. Suspending or terminating research on an urgent basis if it is not being conducted in accordance with the IRB’s requirements.
13. Assuring research policies prevent billing of research participants for research visits.
14. Fulfilling all other responsibilities delegated by the IO and adhering to the policies and procedures as outlined in the appropriate institutional, HRPP, and R&D Service committee’s SOPs.

## Privacy Officer (PO) and Information System Security Officer (ISSO)

The PO and ISSO serve as consultants to the IRB and are responsible for ensuring proposed human research complies with all applicable requirements for privacy, confidentiality, and information security. They do not have responsibility for approving or disapproving a study, nor the authority to prevent or delay IRB approval of a study. However, to ensure compliance and streamline communication with PIs, any privacy, confidentiality and information security concerns identified by the PO and/or ISSO are included with the IRB contingencies and communicated to the PI by the IRB Analysts. The PO’s responsibilities are outlined in VHA Directive series 1605 and 1200.05 and the ISSO’s responsibilities are outlined in VA Directive 6500 and VA Handbook series 6500 and 1200.05.

## Deputy ACOS/ R&D

At the VAPORHCS, the Deputy ACOS/R&D fulfills all duties and responsibilities delegated by the ACOS/R&D.

## Research & Development Committee

The Research & Development Committee serves in an advisory capacity to the IO through the COS on the professional and administrative aspects of the research program. For specific responsibilities, see the Research & Development Committee SOP at <https://www.va.gov/portlandresearch/documents/rd-sop.pdf>.

## Principal Investigators (including local site investigators in collaborative research)

The IRB recognizes one Principal Investigator (PI) or two co-PIs, if approved, for each project. A PI must have a research appointment, either VA-paid or without compensation (WOC), and the appropriate training, education, expertise and credentials to conduct the research according to the research protocol.

A fellow can serve as PI on their own study or as a co-PI if they are credentialed and privileged as a licensed independent practitioner (LIP) within their specialty at VAPORHCS. Otherwise, individuals in training (e.g., fellows who are not credentialed and privileged as LIPs, residents, students serving internships or externships, etc.), even if they have a license or certification, may not be designated as a PI or co-PI. Such investigators must be mentored by a VA investigator who is sufficiently experienced in the area of the trainee’s research interest. The mentor must serve as the PI and is responsible for ensuring the trainee/student complies with all applicable local, VA and other federal requirements, including those related to research, information security and privacy.

Students/trainees may only participate as a (non-PI/co-PI) member of a VA research team on an approved study if they are enrolled in an institution with an educational affiliation agreement with VAPORHCS or are directly appointed to a VA training program that has no external institutional sponsorship (e.g., VA Advanced Fellowship). ***NOTE:*** *Trainees who do not fulfill the requirements specified above cannot participate in VA research unless the VA medical facility Designated Education Officer seeks a waiver from the Chief Academic Affiliations Officer, or designee, and the CRADO.*

The Pl has ultimate responsibility for his/her research project and must act in accordance with the policies of the HRPP and the IRB and report to the IRB as required.

PIs conducting human research at the VAPORHCS must give first priority to the protection of research subjects, uphold professional/ethical standards and practices, and adhere to all applicable VA and other federal requirements, including the responsibilities, policies and procedures outlined in the IRB SOP and HRPP policies and procedures. Specific responsibilities, when applicable, include:

1. Ensuring research is scientifically sound and minimizing risk to subjects or others.
2. Ensuring compliance with all applicable local, VA, and other Federal requirements.
3. Ensuring adequate resources to carry out the research safely, including but not limited to sufficient investigator time, appropriately qualified research team members, equipment, and space.
4. Ensuring all research staff are qualified (e.g., including but not limited to appropriate training, education, expertise, and credentials) to perform procedures assigned to them during the course of the study.
5. Ensuring that they and all members of their research team are credentialed and privileged as required by current local and VA requirements. Research staff may only perform those activities in a research study for which they have the relevant credentials and privileges. If a PI lacks the requisite credentials and/or privileges for specific procedures in the protocol, a collaborating VA clinician who is appropriately credentialed and/or privileged must be listed on the application as the responsible clinician. The responsible clinician assumes responsibility for the specific procedures in question and all study-related health care decisions.
6. Ensuring that they and all members of their research team complete all required education in the protection of human research participants, as well as all other education and training needed to meet all VHA, federal, and local requirements.
7. Ensuring all investigators and co-investigators are identified on the IRB application and have provided credentials, conflict of interest statements and/or any other documentation required by VA and local facility policies.
8. Submitting only research protocols that are relevant to the health or welfare of the Veteran are scientifically valid; describe the research objectives, background and methodology; provide for fair and equitable recruitment and selection of subjects; minimize risks to subjects and others; and describe a data and safety monitoring plan consistent with the nature of the study. If conducting Collaborative Research, the protocol and other applicable study documents must clearly delineate which research will be conducted as the VA portion of the overall study (e.g., by VA investigators on VA time or VA property). For guidance, see the protocol template at: <https://www.va.gov/PortlandResearch/piservices/rd_forms.asp>.
9. Initiating the study only **after** receiving written final approval from the IRB and all other applicable committees, as well as a written notice from the ACOS/R&D that the research may commence.
10. Adhering to all assurances given to the IRB at the time the project was approved and ensuring that the study is implemented as approved by the IRB and in accordance with the approved protocol and all applicable requirements.
11. For studies involving drugs, devices, or other FDA-regulated test articles, adhering to all requirements in the Investigational Device and/or Drug Usage policy located at: <https://www.va.gov/portlandresearch/documents/hrpp/investigational-device.pdf>
12. Giving a copy of the consent form, when applicable, to each participant. For studies which involve the Research Pharmacy, a copy must also be provided to the Research Pharmacy.
13. Obtaining a HIPAA authorization or an IRB or Privacy Board-approved waiver of HIPAA authorization prior to the use and/or disclosure of the subject’s Protected Health Information (PHI). PHI cannot be used or disclosed without prior authorization or a waiver of authorization unless the PHI constitutes a limited data set and there is an appropriate data use agreement (DUA). The information in the written authorization or approved waiver of authorization or DUA for use or disclosure of a limited data set must not contradict any provisions of the protocol and informed consent documents as applicable
14. Submitting a copy of the signed ICF and HIPAA authorization (when applicable) for each participant enrolled in the research project to the Research Compliance Officer (RCO) per current policy. After auditing, the RCO will shred the copies of the ICF and HIPAA authorization unless otherwise directed by the study team. The PI must ensure that all original signed and dated ICFs and HIPAA authorizations (as applicable) are maintained in the investigator’s research files, readily retrievable, and secured.
15. Creating progress notes for participants in the electronic health record, when appropriate (see Section XVII.P of this SOP).
16. Maintaining a master list of all participants who signed a consent and securing it appropriately in compliance with VA confidentiality and information security requirements in the investigator’s files.
17. Maintaining an Accounting of Disclosures of PHI to all non-VA entities.
18. Submitting all required reports, as outlined in Section XV, to the IRB in a timely manner, consistent with VAPORHCS policy.
19. For studies requiring continuing review, completing and submitting annual review forms for continuing approval of ongoing research in a timely manner to avoid expiration of approval.
20. If the PI is mentoring a student/trainee who does not complete all aspects of the research prior to leaving the VA, the PI must ensure that the protocol is completed or terminated in a timely fashion, and in accordance with all applicable local, VA, and other federal requirements. In such instances, the PI is also responsible for ensuring that all research records are retained by the VA.
21. Following the requirements outlined in the “Presentation and Publication of Research Results” policy.
22. Citing VAPORHCS IRB approval in the methods section of all manuscripts involving human studies.
23. Maintaining research files based on standards of good clinical practice (see Investigator Research Records in the Definitions section of this SOP) and in accordance with the applicable records control schedule. Please refer to VHA RCS 10-1 for a list of local research investigator records that constitute a Federal record in VA research with the applicable specified retention and disposition requirements. Fulfilling all other responsibilities and adhere to the policies and procedures outlined in the appropriate institutional, HRPP, and R&D Service committees’ policies and procedures. ***NOTE:*** *If the PI leaves the VAPORHCS facility, the original research records must be retained at the VAPORHCS for the applicable retention period.*

***For research that is subject to the 2018 Requirements:***

**Posting of Clinical Trial Informed Consent Forms**

Studies that meet the definition of a clinical trial (see Definitions section above) must have one IRB-approved informed consent form (ICF) posted to <https://clinicaltrials.gov>.

1. The responsibility for posting the ICF for a clinical trial is as follows:
   1. Funded or supported by a non-Federal agency or department (e.g. university, industry, private nonprofit organization), or not funded: The Principal Investigator is responsible for posting the ICF.
   2. Any ORD-funded clinical trial: The applicable ORD funding service will be responsible for posting the ICF.
   3. Funded or supported by a Federal agency or department other than VA: The awardee is responsible for posting the ICF.
2. The ICF must be posted after the clinical trial is closed to recruitment and no later than 60 days after the last study visit by the any subject as described in the IRB-approved protocol. For multi-site studies (including collaborative research), this applies when the entire study has closed to recruitment.
3. If the PI is responsible for posting the ICF, it must be the most recently IRB-approved version (i.e. clean copy and unsigned).
4. Any proprietary or personal information (such as names and phone numbers) must be redacted prior to posting the ICF.

***NOTE:*** *more information on posting ICFs is located at:* [*https://prsinfo.clinicaltrials.gov/results\_definitions.html#DocumentUpload*](https://prsinfo.clinicaltrials.gov/results_definitions.html#DocumentUpload)

## All Investigators, Research Staff, Employees and Students

All such personnel are responsible for the following:

1. Holding a current VA appointment to conduct VA research.
2. Completing all applicable, local and national level credentialing and training requirements to conduct the research according to the research protocol.
3. Reporting any events, as described in Section XV, to the IRB.
4. Adhering to all federal regulations and local policies governing human subjects research.
5. Requesting menus and keys in accordance with their VA-IRB approved Scope of Work (SoW), per Clinical Applications Coordinators requirement.  ***NOTE:*** Study personnel will be given access to the electronic health record commensurate with the work they will be performing for the study, which may include submitting orders in the electronic health record.

## IRB Analysts and Other Designated RAO Staff

Full- and part-time IRB Analysts report to the IRB Co-Chairs, the AD/R&D, and ACOS/R&D. The IRB Analysts act as a liaison between the researchers and the IRB. Space for the IRB Analysts and IRB files is under the purview of the RAO. Contact information for the IRB Analysts is located on the Research Service web site at <https://www.va.gov/PortlandResearch/contact/index.asp>.

The IRB Analysts are responsible:

1. Reviewing research proposal submissions and advising PIs about federal, VA, state, and local requirements for conducting research.
2. Maintaining IRB meeting calendars, minutes, membership information, membership education, study documentation and records in accordance with regulatory requirements and reporting change in IRB membership to OHRP.
3. Tracking the progress of submitted research protocols.
4. Generating correspondence to the PI and/or study contact regarding the results of reviews conducted by the IRB and reviews conducted by the PO and ISSO.
5. Determining whether a proposal is ready to be reviewed by the convened board, if applicable.
6. Placing research proposals on the IRB agenda.
7. Creating IRB meeting agendas.
8. Generating IRB minutes.
9. Maintaining databases related to IRB study tracking.
10. Documenting completion of all required training for all researchers before IRB approval is given.
11. Tracking annual completion of required training, including:
12. Notifying PIs and research staff when annual training is due.
13. Informing ACOS or Deputy ACOS/R&D if training is not completed within one month of expiration.
14. Sending a memo from ACOS informing the PI and employee that s/he is no longer approved to work on the research study. Additional action may be needed, depending on the individual’s role in the study. See Section IV, B.6.
15. If a PI fails to complete training, sending a memo from the ACOS administratively suspending the conduct of his/her studies until the training is completed and informing the IRB of the noncompliance.
16. Responding to requests for consultation, (i.e. questions regarding IRB policies and procedures, e.g., questions involving whether or not a project is considered human research and whether it should be submitted to the IRB for review and approval) from investigators, research staff, clinicians, etc., received directly from the individual(s) or from the IRB members and/or Chairs. IRB Analysts may consult with IRB members and Chairs and/or the RAO if necessary to address an individual’s questions.
17. Responding to calls from research participants and other to answer questions about research in general and about VAPORHCS HRPP policies, and, when appropriate forward them to others within the RAO or to specific researchers.
18. Providing notification to OHRP of the IRB’s findings concerning research requiring review by a panel of experts convened in accordance with Subpart D.
19. Assigning the primary and, if applicable, *ad hoc* reviewers to review material submitted to the IRB. The IRB Chairs will assist the IRB Analysts, as necessary, in completing this responsibility.
20. Evaluating each protocol to determine whether a consultant is needed.
21. Obtaining an outside consultant to conduct an in-depth review of a protocol if there is not at least one person on the IRB with appropriate scientific expertise.
22. Fulfilling all other responsibilities and adhere to the policies and procedures outlined in the appropriate institutional, HRPP, and R&D Service committees’ policies and procedures.

Additionally, the IRB Analysts or other designated personnel shall carry out the following responsibilities:

19.

20. Creating a research flag to be activated on patient’s medical records when applicable.

## RAO Designee

The RAO designee is responsible for the following:

1. Attending IRB and R&DC meetings as an *ex officio* non-voting member.
2. Serving as independent contact for research participants to discuss and address problems, concerns and questions and to have their rights explained.
3. Writing, reviewing and revising Research Service-level policies and procedures to assure compliance with all federal regulations and policies, as well as accreditation standards.
4. Providing human research protection education to researchers, IRB members, and IRB Analysts.
5. Receiving and addressing complaints about research at the VAPORHCS. (See the [Complaints and Allegations of Non-Compliance](http://www.portland.va.gov/research/documents/hrpp/complaints-of-non-compliance.pdf) policy located at: <https://www.va.gov/portlandresearch/documents/hrpp/complaints-of-non-compliance.pdf> )
6. Fulfilling other responsibilities as directed by the ACOS/R&D and the IRB.

## Research Compliance Officer (RCO)

The RCO responsibilities are outlined in VHA Directive 1058.01.

## K. VAPORHCS-appointed IRB Co-Chairs

The VAPORHCS-appointed IRB Co-Chairs are responsible for the following:

1. Conduct IRB meetings.

2. Call special meetings when necessary.

3. Consult the IRB Analysts to ensure operation of the IRB is within all applicable regulatory requirements.

4. Review IRB minutes that summarize the actions and reasons for these actions of each presented item reviewed by the IRB.

5. Review and act on requests for exemption from IRB review, i.e. determining if studies qualify for exemption from IRB review.

6. Review requests for expedited review and, if the expedited process is appropriate, either review and approve the study on behalf of the IRB or assign a reviewer to advise them so that they can then act on the request on behalf of the IRB. Requests that do not meet the criteria for expedited review will be considered by a fully convened IRB. A reviewer may not disapprove a study by expedited review.

7. Initially review event reports and determine whether immediate action is necessary to assure participant safety.

8. Work with IRB members, institutional officials, and researchers to ensure that the rights and welfare of research participants are adequately protected.

9. Notify the RAO designee of any research-related complaints and allegations of noncompliance with HRPP institutional policies raised by any individual, review research-related complaints and allegations of noncompliance with HRPP and IRB policies brought forward from the RAO designee and determine if a special meeting of the IRB must be convened to address an immediate participant safety issue or if the issue can be held until the next scheduled meeting.

10. Report to the RAO designee any attempts by investigators or research staff of undue influence toward approval of research.

11. Report to the VAPORHCS Director and appropriate regulatory bodies consistent with VHA policies and procedures. Note: The Co-Chairs may designate any member of their committee or the IRB staff to perform notifications to the VAPORHCS Director.

12. Assist the IRB Analysts, as necessary, in assigning primary and *ad hoc* reviewers to review material submitted to the IRB.

## L. VAPORHCS-appointed IRB Members

The VAPORHCS-appointed IRB members are responsible for the following:

1. Review all applicable human research, assessing the scientific and scholarly validity, and ensure that the rights and welfare of research participants are protected. Such review will assess whether the procedures are consistent with sound research design such that it is likely to yield the expected knowledge.

2. Learn about and remain current on ethical, legal and regulatory issues related to IRB business.

3. Complete appropriate IRB reviewer forms.

4. Verify that all changes required by the IRB were made for research projects contingently approved by the IRB.

5. Maintain the integrity of the IRB review process. In particular, avoid discussing IRB protocols with researchers outside of a convened IRB meeting in a manner that might suggest possible IRB determinations.

6. Maintain confidentiality regarding any information contained in any review.

7. Serve as primary reviewers when assigned, generally within their areas of expertise, and serve as general reviewers on all research discussed at convened meetings.

8. Conduct expedited reviews on behalf of the IRB when so designated by an IRB Co-Chair.

9. Participate in other subcommittees, audits, and/or education, so long as there is no conflict of interest with IRB responsibilities.

10. In addition to completing the education requirements set forth by the IRB Co-Chairs, also successfully complete the education requirement in the protection of human research participants as indicated in the policy Education for Conducting Research at <https://www.va.gov/portlandresearch/documents/Education-for-Research.pdf>.

11. Report to the RAO designee any attempts by investigators or research staff of undue influence toward approval of research.

## M. VAPORHCS-appointed Alternate IRB Members

An alternate IRB member has the same responsibilities as a full time IRB member.

# IRB MEMBERSHIP

## IRB Membership Composition

The IRB membership is selected to assure appropriate diversity, including consideration of race, gender, cultural backgrounds, and sensitivity to community issues and/or attitudes, as well as representation by multiple professions, knowledge and experience with vulnerable subjects and inclusion of both scientific and non-scientific members. The IRB must be sufficiently qualified, through the experience, expertise and diversity of its members, to promote respect for its advice and counsel in safeguarding the rights and welfare of human subjects. The IRB must also possess the professional competence necessary to completely and adequately review research activities commonly conducted by the VAPORHCS, and to ascertain the acceptability of proposed research in terms of institutional commitments (including policies and resources) and regulations, applicable local, VA and other federal requirements, and standards of government ethics and professional conduct and practice. A member of the IRB may fill multiple membership position requirements for the IRB.

Research Administration Office staff including, but not limited to, the ACOS/R&D, Deputy ACOS/R&D, AD for R&D and IRB administrative staff, are prohibited from serving as voting members of the IRB. Facility Directors, their administrative staff, COS, other facility senior administrators (e.g. Associate or Assistant Directors or Chief Nurse, and NPC Administrative Staff) may observe IRB meetings, but they may not serve as voting or non-voting members of the IRB.

In addition to the aspects listed above, each IRB will have at least:

Five members,

One member whose primary area of interest is scientific,

One member whose primary area of interest is non-scientific,

One member who is not affiliated, and is not part of the immediate family of a person who is affiliated, with the VAPORHCS or any of its components or other community-based clinics (Volunteers without a WOC or Veterans whose only relationship is receiving care at the VAPORHCS or benefits from the Veterans Benefits Administration are not considered to be affiliated),

One or more members of more than one profession,

One member from the Research & Development Committee, and

One or more (Co-)Chairs, each with a paid VA appointment.

***NOTE:*** *Members whose training, background, and occupation are within a behavioral or biomedical research discipline should be considered a scientist. Members whose training, background, and occupation are outside of a behavioral or biomedical research discipline should be considered a nonscientist.*

## VAPORHCS-appointed IRB Co-Chairs

1. **Appointment**:The ACOS/R&D nominates two Co-Chairs for the IRB by submitting a resume of each individual to the R&DC. These nominations can occur simultaneously or not. The R&DC reviews the nominations and recommends each individual for formal appointment by the VAPORHCS IO. Each Co-Chair must hold a paid VA appointment.
2. **Voting Status**:Each Co-Chair is a full voting member of the IRB and, when in attendance at a meeting, counts toward the quorum of the committee.
3. **Length of Service**:Each Co-Chair may be appointed to serve for a term not to exceed three years and may be re-appointed indefinitely.

## VAPORHCS-appointed IRB Members

1. Appointment: IRB members are nominated by the ACOS/R&D when the ACOS/R&D submits resumes for member(s) to the R&DC. The R&DC reviews the nomination(s) and recommends the individual(s) for formal appointment by the VAPORHCS IO.
2. Length of Service: Members may be appointed to serve up to a three-year term and may be re-appointed indefinitely. Regular attendance at IRB meetings is expected, and a member may be removed from the IRB on the basis of repeated unexcused absences or non-attention to the functions and responsibilities of the IRB. The R&DC reviews IRB membership annually.

## VAPORHCS-appointed Alternate IRB Members

1. **Identification**: Alternate members are identified and invited to be IRB members based on their professional specialty, qualifications, and experience, which must be comparable to those of the primary member for whom they will serve as alternate. The IRB Roster identifies for which primary member each alternate may serve.
2. **Appointment**:Alternate members may be nominated by the ACOS/R&D, voted on by the R&DC and appointed by the IO. These alternates are nominated with the same criteria of selection as IRB members.
3. **Length of Service**: An alternate IRB member’s length of service may be based upon one of the following:
   1. The individual’s term as an IRB member, if already a changing designation as full time IRB member to alternate member,
   2. The term of the individual s/he is representing, or
   3. A three-year term, if the individual serves as an alternate for multiple full time IRB members.

## VAPORHCS-appointed Ex-Officio Members

Ex-officio members, appointed due to their position at the VAPORHCS, may not vote, deliberate, nor contribute to a quorum. These members must adhere to the same conflict of interest policies and procedures as voting IRB members. Ex-officio members are not nominated and appointed by the IO. They may include the AD/ R&D, ISSO, PO, RAO designee and VA attorney.

## Individuals with Special Expertise (Ad Hoc Reviewers/Use of Consultants)

On an as-needed basis, the IRB may, at its discretion, invite individuals with competence in special areas to assist in the review of any issues requiring expertise beyond or in addition to that available on the IRB. This may include the review of a study involving a clinical procedure or specialty not represented on the IRB. The IRB members and/or Chair may determine that the IRB needs additional technical assistance.

Recommendations for consultants may come from the ACOS/R&D, R&DC members, IRB members, and/or medical staff. The *ad hoc* reviewer will be invited to review the research project and will be provided with documented expectations. The IRB Chair and/or Analysts will make the arrangements for such a review. The *ad hoc* reviewer must adhere to the same conflict-of-interest policies and procedures as the IRB members. The *ad hoc* reviewers may attend the IRB meeting when the study is reviewed; however, their presence or absence will not be used in establishing a quorum for an IRB meeting. An *ad hoc* reviewer may not serve as the primary reviewer, nor vote with the IRB. An *ad hoc* reviewer may provide guidance and expertise either in person or through written comment. The qualifications and comments of the *ad hoc* reviewer will become part of the minutes supporting the IRB deliberations.

## Compensation for IRB Service

IRB members are not compensated for serving on the IRB but may receive reimbursement for travel costs.

## Conflict of Interest of VAPORHCS-appointed IRB Members

All IRB members must aim to avoid real or perceived conflicts of interest. Members of the IRB may not work for or hold equity in any outside business interest with which the VA might do business (e.g., pharmaceutical companies or medical device manufacturers).

The IRB Co-Chairs and members may find themselves in any of the following potential conflicts of interest:

1. An IRB Co-Chair or member is listed as a researcher on the study.
2. A researcher must report to or is under the supervision of an IRB Co-Chair or member.
3. An IRB member is a family member of an investigator whose research is scheduled for review.

In cases where a conflict of interest exists, the conflicted member may answer members’ questions during the review process but must step out of the room during the discussion and vote on the study. If the conflicted member is attending by teleconference, the call must be terminated during that portion of the discussion (rather than placed on “hold”), and then re-established when the discussion and vote are complete. If the conflicted member is attending by video conference, they must be placed outside of the meeting (e.g., in the lobby, etc.) and then then returned to the meeting when the discussion and vote are complete. Conflicts of interest of IRB members will be noted in the minutes, and the individual is identified as “recused” during the vote.

## Training and Ongoing Evaluation of VAPORHCS-appointed IRB Co-Chairs and Members

As a condition of the FWA, IRB members are provided education about human subjects protections, ethics and regulatory requirements. The IRB Chairs and members shall meet the educational requirements set forth in the policy, Education Requirements for the Conduct of Research located at: <https://www.va.gov/portlandresearch/documents/Education-for-Research.pdf>

### New IRB Member Training

A Co-Chair of the IRB, the RAO designee and/or a designated IRB Analyst shall provide members with an initial orientation to their committee activities and appropriate continuing education related to the IRB.

Each new IRB member’s training consists of the following:

1. The RAO designee or an IRB Analyst shall schedule a training session with each new member to review their responsibilities, the IRB SOP and other HRPP policies and procedures and offer the opportunity for questions and discussion.
2. An IRB Co-Chair shall discuss with the member(s) the parameters of IRB decision-making and answer any questions the new IRB member(s) may have regarding their responsibilities as IRB member(s) and the functioning of the IRB. The IRB Co-Chair may also assign a mentor to work with the new member.
3. All IRB members are informed of the website link to the VAPORHCS IRB SOP located at <https://www.va.gov/portlandresearch/documents/irb/irb-sop.doc> and all other VAPORHCS HRPP policies and procedures prior to their first meeting with the IRB. They are also given a hard copy of the IRB SOP or any policy if they so request.
4. Once a new member has completed all educational requirements and attended enough meetings to feel competent to carry out their duties and responsibilities, they will be assigned studies to review based on their unique expertise, i.e., strengths, education, and experience levels.

### Continuing IRB Education

The IRB members, including the non-scientist members, are responsible for completing the annual educational requirements as set forth in the policy, Education Requirements for the Conduct of Research located at: <https://www.va.gov/portlandresearch/documents/Education-for-Research.pdf>

## IRB Evaluations

Each year, the RAO designee sends evaluation forms to each IRB member and Co-Chairs for self-evaluation. A separate section of the evaluation form addresses the additional responsibilities of the Chairs. The RAO designee reviews the self-evaluations and compiles a list of areas identified as those in which the IRB members could use additional training, and then presents these findings to the ACOS/R&D and the Chair of the R&DC. In addition, each Chair also evaluates how the IRB functions, as well as the level of service, quality and efficiency of the IRB Analysts, and submits a report to the ACOS/R&D. All evaluations are then included in a report to the R&DC by the RAO designee, through the ACOS/R&D. The RAO designee will work with the IRB Analyst(s) to create trainings that cover the areas of need identified by the IRB members, to be presented at the convened meetings.

# IRB Recordkeeping and Required Documentation

## Record Retention

The IRB shall keep all records in accordance with the applicable records control schedule. Records include electronic and written data. All IRB records collected over the course of the protocol will be maintained by the IRB Analysts in VAPORHCS Research space and/or network location.

## IRB Records

IRB records include the following:

1. IRB membership information
2. Education/training records
3. Credentialing files
4. Standard Operating Procedure
5. Convened IRB meeting minutes
6. Research project files (see item F below)
7. Federalwide Assurance (FWA)

## Access to IRB Records

IRB records are stored securely and in compliance with all applicable regulations. IRB records are accessible to the Research Service staff, IRB Co-Chairs and members, as well as the R&DC Chair and members for committee purposes only. Researchers shall be provided reasonable access to files related to their research. Other authorized individuals, such as accrediting officials and officials of federal and state regulatory agencies, including ORO, OHRP, and FDA, will have access to IRB records for inspection and copying, upon determination of appropriateness and necessity, at reasonable times and in a reasonable manner. Appropriate accreditation bodies shall be provided access and may recommend additional procedures for maintaining security of IRB records.

## IRB Membership Roster

Research Administration Office staff maintain the current VAPORHCS IRB membership roster and report any changes to the OHRP with a copy to the VA ORO. See the IRB roster at <https://www.va.gov/portlandresearch/hrpp/index.asp?tab=0#roster> for the current composition of each IRB. The IRB rosters will include the following information for each member:

1. Name
2. Earned degree(s)
3. Voting and alternate status and representative capacity
4. Representative capacities regarding vulnerable populations (e.g., knowledgeable about or experienced in working with these populations), if any
5. Affiliation status (whether the member or an immediate family member of the member was affiliated with the organization)
6. Indications of experience sufficient to describe each IRB member’s chief anticipated contributions
7. Employment or other relationship between each IRB member and the organization
8. Scientific/non-scientific status
9. The primary member(s) for whom each alternate member may substitute

Copies of the IRB members’ appointment letters and curriculum vitae/resume or equivalent, updated at the time of appointment or reappointments, are kept on file by the RAO.

## Written Standard Operating Procedures

IRB members are provided links to the electronic copy of the VAPORHCS IRB SOP document at the time they join the IRB and each time it is updated. Hard copies are provided upon request, or if a member cannot access electronic copies.

## IRB Research Project Files

The IRB shall maintain a separate file for each research project. Protocols are assigned a unique identification number for internal tracking purposes. The IRB application shall include the IRB forms, as applicable to the protocol. Protocol files shall include all documentation related to the protocol, e.g., submissions, IRB and researcher correspondence, audit reports, IRB forms, etc. The following information must be present, when applicable:

1. Protocols
2. Investigator Brochure
3. Scientific evaluations, when provided by an entity other than the IRB
4. Recruitment materials
5. Consent documents (and/or documentation of waiver or alteration of consent requirements)
6. HIPAA Authorization Documents (and/or documentation of waiver of HIPAA authorization requirements)
7. Progress reports submitted by researchers
8. Reports of injuries to participants
9. Records of continuing review activities
10. Data and safety monitoring reports
11. Amendments
12. Documentation of all reportable events (as described in Section XV), including those of noncompliance
13. Significant new findings and statements of such findings provided to participants
14. Determinations required by the regulations and protocol-specific findings supporting determinations for waiver or alteration of the consent process
15. Audit results and documentation of compliance with remediation requirements when audits are conducted by the RAO designee
16. Participant complaints, unless complaints are filed anonymously
17. Communications with researchers
18. Documentation of relevant approvals including, as applicable, the frequency interval for the next continuing review for initial and continuing review approvals
19. Documentation of waiver of informed consent or waiver of documentation of consent

***For research that is subject to the 2018 Requirements:***

1. The rationale for an expedited reviewer's determination that particular research appearing as a category on the expedited review list is more than minimal risk and therefore is not eligible for expedited review.

## IRB Use of Checklists and Evaluation Aids

The IRB members shall use reviewer checklists when reviewing protocols at the time of initial and continuing review. Checklists are available from IRB Analysts and on the VAPORHCS website and evaluation aids are facilitated through an electronic IRB system. IRB determinations regarding the following are prompted on the applicable checklist(s) and documented in the IRB minutes and/or correspondence:

1. The level of risk of the research.
2. The approval period for the research, including identification of research that warrants review more often than (at least) annually.
3. Whether the medical record of each participant must be flagged to protect the participant’s safety by indicating participation in the study and the source of more information about the study.
4. Justification for approval of research involving pregnant women, neonates, human fetuses, and human in vitro fertilization, addressing each of the criteria specified under 45 CFR 46 Subpart B of the DHHS human subject regulations.
5. Justification for approval of research involving prisoners, addressing each of the categories and criteria specified under 45 CFR 46 Subpart C of the DHHS human subject regulations. Generally, the IRB Analyst is responsible for providing certification of the IRB’s findings to OHRP. **Note:** The VAPORHCS does not review or conduct research with prisoners, except when a waiver is received from the CRADO. If a human participant involved in ongoing research becomes a prisoner during the course of the study, the investigator must promptly notify the IRB and sponsor (if applicable). All research interactions and interventions with, and obtaining identifiable private information about, the now-incarcerated prisoner-participant must be stopped immediately. If immediate cessation of study-related interventions would place the prisoner-participant at risk, the investigator must notify the IRB Chair for additional guidance and communication with VACO.
6. Justification for approval of research involving children, addressing each of the categories and criteria specified under 45 CFR 46 Subpart D of the DHHS and FDA human subject regulations. The IO must approve the facility’s participation in proposed research that includes children as research subjects. For FDA-regulated research, documentation of the IRB findings is required, and notification shall go to the Commissioner of the FDA.
7. The IRB’s consideration of the additional safeguards to protect the rights and welfare of vulnerable subjects. For example, the special protections warranted in specific research projects for groups of individuals who are likely to be vulnerable to coercion or undue influence, such as children, prisoners, individuals who lack decision-making capacity, or economically or educationally disadvantaged persons, regardless of source of support for the research.
8. Justification for approval of emergency use of an investigative or unlicensed article, with specific reference to the criteria specified by DHHS and FDA (see the policy, Investigational Device and/or Drug Usage located at: <https://www.va.gov/portlandresearch/documents/hrpp/investigational-device.pdf>).
9. Rationale for significant or non-significant risk device determinations.
10. Justification for determining when a research activity approved by the IRB, prior to January 21, 2019, can transition to the 2018 Requirements, if applicable.

## Documentation of Expedited Reviews

The review, decision and expedited review eligibility category must be included in the IRB minutes of the next available convened IRB meeting and in the written notification to the investigator and R&DC.

***For research that is subject to the 2018 Requirements:***

Research for which limited IRB review is a condition of exemption may be reviewed by expedited procedures and will be documented in the IRB minutes and presented to the IRB for review as indicated in Section I below.

## IRB Minutes

IRB minutes are completed by the IRB Analysts and must include the following:

1. Attendance by name, also showing when an alternate takes the place of a regular member
2. Documentation that the required quorum was present for each vote, including a non-scientific member
3. Actions taken by the IRB concerning initial or continuing review of research, including: the approval period; specific measures taken to protect vulnerable populations; review of protocol or informed consent modifications or amendments; reportable events; reports from sponsors, cooperative groups, and data and/or safety monitoring entities; waiver or alteration of informed consent process or documentation and/or authorization, including the related justifications and documentation that the IRB determined that all of the criteria for the waiver were satisfied; suspension or termination of research; and other actions, as appropriate
4. For studies approved by the IRB, documentation that the IRB determined that all of the criteria for approval of the research were satisfied
5. The basis for requiring changes in or disapproving
6. Summary of controverted issues (e.g., lack of consensus, etc.) and their resolutions, whether or not there is a split vote
7. If the IRB approves a consent procedure which does not include or alters any of the required elements of informed consent, or which waives the requirement to obtain a signed informed consent document, documentation that all criteria for the waiver have been satisfied
8. Research protocols approved since the last meeting utilizing expedited review procedures and the specific citation for the category of expedited review of each

Minutes shall be available for review as soon as is feasible after the meeting. Once approved by the members at a subsequent IRB meeting, the minutes may not be altered by anyone, including a higher authority, and should be reviewed by the R&DC at the next convened R&DC meeting. After approval by the IRB, an IRB Analyst will enter the date of IRB approval within the minutes document to designate the final approved version of the minutes.

***For research that is subject to the 2018 Requirements:***

Minutes will include the IRB’s rationale for conducting continuing review of research that otherwise would not require continuing review.

## Attendance at IRB Meetings in IRB Minutes

IRB minutes shall list attendance as follows:

1. Names of members present, according to their voting status including members or alternate members who participate through videoconference or teleconference,
2. Names of any alternates attending in lieu of specified (named) excused/absent members. Alternates may substitute for specific excused/absent members only as designated on the official IRB membership roster,
3. Names of any *ad hoc* reviewers present,
4. Names of *ex officio* members present,
5. Names of any RAO staff present and/or excused/absent, and
6. Names of any guests present.

## Quorum Requirements at IRB Meetings

The IRB observes the following rules:

1. A quorum consisting of a majority of the IRB members (or their designated alternates), including at least one member whose primary expertise is non-scientific, must be present to conduct a convened meeting. Research reviewed during an IRB meeting must be approved by a majority of those present at the meeting.
2. Members absenting themselves due to conflicts of interest will be documented as “recused” during the vote. Recusals may not be counted toward quorum requirements.
3. The following individuals will not be considered as part of the quorum and will not vote with the IRB:
4. Any individual not listed on the official IRB membership roster
5. Any ex-officio member of the IRB
6. *Ad hoc* reviewers
7. Consultants
8. Guests
9. Research and Development Service Staff or Administrators
10. When a member and his/her alternate both attend a meeting, only one may vote.
11. If a quorum is lost during a meeting, a quorum must be restored before any discussion of, or action on, issues requiring a vote may occur.

## Documentation of Votes by the Convened IRB

Votes and deliberations on each action reviewed by the convened IRB, including the number of members voting and the names of members who excused themselves during the review of a protocol and when a member leaves the meeting because of conflict of interest, will be documented in the IRB minutes. Votes are categorized as “for”, “against”, “abstained”, “recused”, and “excused” or “absent.”

1. **For** means that the member(s) are voting in favor of the motion to approve, contingently approve, table/defer or disapprove.
2. **Opposed** means that the member(s) are voting in opposition to the proposed motion to approve, contingently approve, table/defer, or disapprove.
3. **Abstained** means a member states that s/he refrains from the vote voluntarily. For example, a member may refrain from a vote if s/he was only present for a portion of the discussion of a particular item.
4. **Recused** applies if a member has a conflict of interest. The member leaves the room and does not participate in the deliberations or vote.

## The Basis for Requiring Changes in or Disapproving Research

The minutes of IRB meetings shall include the basis for requiring changes in or disapproving research. In addition, the IRB will include in its written notification to the investigator, a statement of the reasons for its decision and give the investigator an opportunity to respond in person or in writing (or both).

## IRB Correspondence

Accurate records are maintained of all communications to and from the IRB, including correspondence with researchers, consultants (if applicable), and the R&DC. IRB correspondence, for both full board and expedited reviews, is signed by an IRB Co-Chair, IRB reviewer for the related item or IRB Analyst. Copies of all correspondence are filed in the appropriate research project file located in the RAO, electronic IRB system, or a designated storage area.

The IRB reserves the right to request more information or a change in research procedures. In these cases, the IRB staff will generate a separate memorandum noting whether or not any further action or required changes are needed on the part of the PI or research coordinator in order to approve the continuing review, amendment, etc.

The PI is notified in writing of all IRB decisions regarding each protocol and regulatory criteria upon which decisions are based. All official IRB correspondence is addressed to the PI but may be sent to another study team member, as designated by the PI. If someone other than the PI is designated to receive such correspondence, that individual will be responsible for communicating the results of the review to the PI. The PI is ultimately responsible for the research project and for assuring that the research project and staff comply with IRB requirements. Along with written notification of IRB approval, when relevant, IRB Analysts send the PI/study contact a copy of the IRB-approved ICF(s).

1. **Initial reviews**: If a project receives IRB approval, the R&DC must provide the final approval to the ACOS/R&D before the research can be initiated. Therefore, a copy of the signed final IRB approval letter will be forwarded by an IRB Analyst to the R&DC Coordinator. Once the project is approved by the R&DC, the approval letters from the IRB and any other applicable subcommittees will be sent to the PI and/or designated study contact, along with a letter from the ACOS/R&D notifying them that the research has approval to begin. These letters will be sent as soon as possible after the R&DC meeting.

In cases of contingent approval, or a tabled/deferred decision, an IRB Analyst will notify the PI within three weeks. Responses to tabled/deferred decisions will be reviewed at a convened IRB meeting. Responses to contingent approval may be reviewed by an IRB Co-Chair or designated IRB reviewer. If further clarifications or changes are needed, as determined by the IRB reviewer or convened IRB after the response is received, an IRB Analyst will inform the PI or study contact. Once the reviewer or convened IRB has approved the PI’s response to contingencies, an IRB Analyst will sign the final approval letter and forward a copy to the R&DC Coordinator.

***For research that is subject to the 2018 Requirements:***

For initial approvals, the IRB’s rationale for requiring continuing review when it would not otherwise be required (if applicable), and the continuing review expiration date or the determination that the study does not require continuing review but is still subject to IRB oversight.

1. **Continuing Reviews:** PIs and study contacts will be notified within three weeks of the IRB’s determination (e.g. approved, contingently approved, tabled/deferred) for continuing reviews or modifications.

***For research that is subject to the 2018 Requirements:***

For continuing approvals, the approval letter must include the IRB’s rationale for requiring continuing review when it would not otherwise be required (if applicable), the continuing review expiration date or when the IRB determines that the study no longer requires continuing review, but is still subject to IRB oversight.

Approval letters for initial and continuing reviews will include the expiration date for IRB approval. The IRB shall notify the PI and study contact in writing of expired approvals, suspensions or terminations and shall include a statement of the reasons for the IRB's actions. The terms and conditions of a suspension or termination must be explicit.

Approval letters for any type of review (initial, continuing, modifications, notification, etc.) will only be generated once all required elements are in place. Receipt of an approval letter by the PI/research team indicates that the paperwork on file in the RAO is complete and has all required signatures.

## Dates on Approval Letters and Other Correspondence

All IRB correspondence, including approval letters, are generated from an electronic system. The date of the correspondence is generated by, and included on the correspondence, the system. In the event that the date of a digital signature does not match the date on the memo, the digital signature serves as confirmation by the signer that the date included on the correspondence by the electronic database is appropriate. If an IRB Co-Chair or other member signing any correspondence has concerns regarding the date generated by the database on the correspondence, then they must work with an IRB Analyst to have the correspondence re-generated with an appropriate date. Dates included on the correspondence by the electronic system are the official correspondence dates, and the date of a digital signature itself does not override the date on the correspondence.

## Responses to IRB Correspondence

Any required response to the notifications will be reviewed by the primary reviewer(s). An IRB Co-Chair or IRB voting member may use expedited review procedures to verify that specific minor changes have been addressed by the PI and to authorize approval of material that was contingently approved. If a review was tabled/deferred, the response will be reviewed by both the primary reviewer(s) and the convened IRB. Also see “Appeal of IRB Determinations”.

When the IRB Correspondence includes contingencies requested by the Information System Security Officer (ISSO) and/or Privacy Officer (PO), response materials will be routed to them for review and confirmation that stipulations have been met.

The PI shall be provided with an opportunity to respond in person or in writing to all determinations by the IRB.

Responses should come from the PI or the study coordinator. In cases where a lapse in time could potentially harm human subjects (such as a delay in reporting of an adverse event), co-investigators may communicate directly with the IRB.

## Time Allowed for Submission of Modifications to Secure Initial Approval

In cases where research projects are approved pending minor modification at the time of initial review, PIs are given a three-month deadline to submit the required modifications to the IRB.

If the PI has not replied to the contingencies after three months, the IRB Analysts will contact the PI to remind them about their contingencies and to determine whether or not the PI will be submitting the contingencies or withdrawing the study.

This deadline may be extended up to another three months, for a total of six months, provided that the PI keeps the RAO informed of the status of the protocol. After the six- month period, the PI will receive a warning that, if the requested modifications are not submitted within the next seven days, the protocol will be administratively withdrawn. If the project is administratively withdrawn, the PI must resubmit the study to the IRB for full review as a new protocol.

The IRB will consider exceptions to this policy in extraordinary circumstances that may be out of the PI’s control, e.g., delay in funding or changes to be made by the sponsor.

# EXEMPTION FROM IRB OVERSIGHT/REVIEW

Unless stated otherwise, the R&DC reviews all exempt human research.

Projects meeting the definition of research involving human subjects as defined in this SOP must undergo appropriate review and approval before the research project may begin. If it appears that the study includes human subjects, but may be exempt from IRB oversight, PIs shall submit a written request for exemption to the IRB. The IRB serves as the R&DC’s designee in the review of exempt status based on categories stipulated at 38 CFR 16.101.

***NOTE:*** *Please* *see* ***IRB SOP Appendix 2*** *for further information regarding the exemption categories and requirements, including Limited IRB Review for certain exemption categories.*

Questions regarding whether or not an activity is considered human research should be directed to an IRB Analyst.

If the exempt activity involves PHI, a waiver of HIPAA authorization must be approved by the appropriate authority (IRB or Privacy Board or designated member of the IRB or Privacy Board), a written HIPAA authorization must be obtained from the subject or subject’s LAR or a DUA for use or disclosure of a limited data set must be obtained.

**Limited IRB Review**

The revised Common Rule includes a new process termed “limited IRB review.” Limited IRB review is required for the following exemptions:

* + 2(iii): Educational Tests, Surveys, Interviews, Observations of Public Behavior when information obtained is recorded in an identifiable manner and disclosure of subjects responses could put them at risk.
  + 3(i)(C): Benign behavioral interventions where information obtained is recorded in an identifiable manner and disclosure of subjects responses could put them at risk.

For exemptions 2(iii), and 3(i)(C), limited IRB review involves determining that the research plan makes adequate provision for monitoring the data collected to protect the privacy of subjects and to maintain the confidentiality of data. In Limited IRB review, the IRB does not have to ensure that all of the other IRB approval criteria under 38 CFR 16.111, are met. The 2018 Requirements clarify that IRBs have the authority needed to conduct limited IRB review and that continuing review is not required for research reviewed in accordance with the limited IRB review procedure. The IRB may use the expedited review process when conducting limited IRB review.

Using expedited review procedures, an IRB Co-Chair or a qualified designee (IRB member) will, in a timely manner, determine exempt status. In reviewing the exemption request, the reviewer will assure the research meets the definition of human research and that the research involves no more than minimal risk based on the criteria for exemption as defined by the VA, DHHS and FDA. The convened IRB will be informed of the exempt determination by documentation in the agenda and minutes for the next available convened meeting.

The IRB will notify the PI and the R&DC in writing of its determination that a research project is exempt from IRB approval requirements. The determination may be made by an IRB Co-Chair or qualified designee (IRB member).

If it is determined that a study does not qualify for exemption, then the study team will be contacted to request paperwork for a complete IRB Initial Review submission (New Project), and the study will be evaluated for expedited or convened board review.

The R&DC will review IRB-exempted projects and make a final determination concerning whether to approve the study. The research project may begin once written confirmation from the ACOS/R&D that all applicable approvals have been granted.

If a revision is made to a previously IRB-exempted project, the PI must submit the modification request to the IRB for review. If the change is determined by the IRB reviewer to have affected the previously approved exempt status, the PI must submit applicable forms for review by the IRB of the project as non-exempt human research. If the IRB reviewer determines the project remains exempt, the modification shall be reviewed by the R&DC.

Minor revisions, such as personnel changes, may be acknowledged administratively, rather than voted on by the convened R&DC. The PI will receive an acknowledgement letter signed by the R&D Chair, a qualified voting member of the R&DC, or a member of the Research Administration Office staff. The convened R&DC will be informed of the revision by documentation in the agenda and minutes for the next convened meeting.

Any individual involved in making the determination of exempt status of a proposed research project cannot be involved in the proposed research.

## Documentation of Exemptions from IRB Oversight/Review

Documentation of exempt research rationale for exemption, the category and circumstances for which limited IRB review is a condition of exemption (if applicable), will be completed by the IRB reviewer using the Exempt Reviewer Checklist and Limited-IRB Worksheet (if applicable). This documentation will be included in the applicable review minutes and will be maintained in Research Service records. The basis for the approval of exempt status must be communicated in writing to the PI in a timely manner.

# ROUTINE IRB REVIEW

## Initial Review

Unless determined to be exempt from IRB review, all human research conducted at the VAPORHCS facility by VAPORHCS employees or agents or otherwise under VA auspices must be reviewed and approved based on regulatory criteria by the IRB prior to initiation. No human research may be initiated at the VAPORHCS until all applicable requirements in VHA Directive 1200.05 have been met and the appropriate approvals of the IRB and all other applicable research committees, including the R&DC, have been obtained, as documented by a written notification from the ACOS/R&D.

For convened IRB reviews, primary reviewer(s), will: (1) review and lead discussion on the proposal; (2) provide an assessment of the soundness and safety of the protocol; (3) make recommendations for protocol and ICF revisions; and (4) take appropriate action(s) regarding approval. The PI is invited to attend the portion of the IRB meeting at which his/her initial protocol review occurs and may be invited to attend for reviews of other items related to the research, e.g., major protocol changes or problems involving risk. When the PI attends, s/he may make a brief presentation, answer questions and/or provide clarifications, but they may not be present during IRB deliberations or voting on their proposal.

At the time of initial review, the IRB or reviewer for expedited review will determine the frequency of continuing review of the research, designating an interval not more than one year. Protocols determined to have a higher degree of risk or a higher risk:potential benefit ratio will require a shorter interval for continuing review, e.g., six (6) months. Members will use IRB primary reviewer checklists provided by IRB Analysts to assist in determining the risk level and risk:potential benefit ratio and ensuring the information provided meets appropriate guidelines. Additionally, when determining an appropriate interval for continuing review the following shall be considered:

* The nature of any risks posed by the research project,
* The degree of uncertainty regarding the risks involved,
* The vulnerability of the subject population,
* The experience of the investigators in conducting this type of research,
* The IRB’s previous experience with the investigators (e.g., compliance history, previous problems with the investigator obtaining informed consent, or prior complaints from subjects about the investigator),
* The projected rate of enrollment, and
* Whether the research project involves novel interventions.

The primary reviewers conduct a review of the materials provided for initial review, and apply the criteria for approval as noted in this document. Evaluation of the approval criteria is facilitated through the use of primary reviewer checklists located within the electronic protocol management system, which capture VA and other Federal regulations, required elements for informed consent, etc. Evaluation of the study includes distinguishing which activities are VAPORHCS Research and which activities are non-VAPORHCS research. The IRB only approves the components of the research that are conducted at the VAPORHCS, using VAPORHCS resources, or utilizing the VA time of a VA employee.

## IRB Continuing Review

The IRB will conduct substantive and meaningful continuing review based on regulatory criteria of research at intervals appropriate to the degree of risk, but not more than once per year.

PIs and study contacts are notified in writing of the approval date and the expiration date at the time of final initial IRB approval. The PIs and study contacts are additionally notified of which materials to submit in order to allow for a complete continuing review to be conducted. In order to allow adequate time for submission and review of continuing review materials, the IRB continuing review date is set approximately one months prior to the expiration of IRB approval.

The IRB continuing review materials will include all applicable IRB submission materials as noted in Section XI.G.2, Materials for IRB Review. The IRB employs the Primary Reviewer System at the time of continuing review.

1.In addition to reviewing the study to determine whether it continues to meet approval criteria outlined in this document, the IRB reviews the following:

1. Any changes to the research during the last approval period;
2. All reportable events (as per Section XV), sponsor reports and safety reports including IND, IDE and MedWatch reports;
3. Any data and safety monitoring reports received during the last approval period;
4. A summary of any types of AEs, outside safety reports, unanticipated problems, protocol deviations and/or noncompliance that were not required to be reported prior to continuing review (as per Section XV) and that have occurred during the life of the study;
5. Any sponsor-imposed suspensions and device recalls; and
6. Whether or not there have been any significant new findings and, if so, whether those may relate to the participant's willingness to continue participation and, thus, are provided to the subject in accordance with HHS regulations.

3. Studies may meet expedited review criteria for continuing review. An IRB Co-Chair or a qualified designee will determine if criteria are met.

4. A research project that is contingently approved at the time of continuing review may not enroll new participants or access medical records after the research project’s expiration date, unless the contingencies are met and final approval is received from the IRB.

***For research that is subject to the 2018 Requirements:***

The IRB is required to conduct continuing review of non-exempt human subjects research at intervals appropriate to the degree of risk, but not less than once per year, except in the following cases:

***NOTE:*** *This list does not apply to studies when other regulations require continuing review, such as FDA-regulated studies.*

Research subject to the 2018 requirements that meet one of the following categories:

* Research eligible for expedited review
* Research reviewed by the IRB in accordance with the Limited IRB review provisions
* Research that has progressed to the point that it involves only one or both of the following, which are part of an IRB-approved study:
  + Data analysis, including analysis of identifiable private information or identifiable biospecimens; or
  + Accessing follow-up clinical data from procedures that subjects would undergo as part of clinical care

The IRB must document the rationale for conducting continuing review of a research study that is subject to the 2018 Requirements and falls into one of the categories of research that does not require continuing review. The required documentation is included on the continuing review reviewer form that the reviewer completes for both expedited and convened board reviews.

***NOTE:*** *Research not requiring continuing review by an IRB is still overseen by the IRB. Reportable events, such as unanticipated problems involving risks to subjects or others, must be reported as required by the IRB. Any changes in the IRB-approved research must be reported to the IRB and may not be implemented prior to review and approval by the IRB (may be expedited) except when necessary to eliminate apparent immediate hazards to the subject.*

## Process for Continuing Review

Approximately 60 days before the current approval for a research project will expire, the electronic protocol management system will send an email notification to the PI. PIs are asked to submit the materials in time for the next month’s meeting, allowing for review approximately 6 weeks before the protocol’s expiration date. The electronic protocol management system will send an email reminder to PIs who do not respond by the continuing review due date. If the material is not submitted in a timely manner and it is not possible to get the materials to the IRB meeting prior to the approval expiration date, the approval for the study will automatically expire, per the procedures outlined in Section XI.G. No research activities requiring IRB approval may be conducted at any time without a currently valid IRB approval.

1. **Collaborative Research**

VA researchers may collaborate with non-VA institutions. This is encouraged when the VA researchers have a substantive role in the design, conduct, and/or analysis of the research. VAPORHCS may serve as a Coordinating Center for collaborative studies. Each institution involved in the collaboration is responsible for safeguarding the rights and welfare of human subjects and providing oversight of the research activities conducted at their institution.

1. Each collaborating institution engaged in human subjects research must:
   1. Obtain approval from its IRB of Record or utilize a single IRB,
   2. Hold a FWA or another assurance acceptable to VA (e.g., DoD assurance), and
   3. Use the informed consent document and HIPAA authorization required by their respective institutional policies for subjects recruited from that institution, or procedures requiring participation of the subject at that institution. The informed consent document may contain information on the project as a whole as long as the document clearly describes which procedures will be performed under the VAPORHCS’s auspices and which will be performed under another institution’s auspices.
      1. The VAPORHCS informed consent document must clearly state when procedures indicated as occurring at other institutions are part of the VA’s portion of the study,
      2. The informed consent document and HIPAA authorization must be consistent and include information describing the PHI to be collected and/or used by the VA research team, the PHI to be disclosed to the other institutions, and the purpose(s) for which PHI may be used.
2. The protocol, addendum, and/or IRB of Record application must:
   1. Describe the data to be disclosed to collaborators, the entity(ies) to which the data are to be disclosed, and how the data are transmitted, stored, retained, destroyed, and/or further disclosed and to whom. This includes data from individual subjects as well as other data developed during the research such as the analytic data and the aggregate data.
   2. Delineate which research activities will be conducted as the VAPORHCS portion of the overall Collaborative Research study (e.g., on VAPORHCS time or VAPORHCS property).
3. Each VA facility must retain a complete record of all data obtained during the VA portion of the research in accordance with privacy requirements, the Federal Records Act, and VHA Records Control Schedule 10-1.

## Ongoing Review

### Review of Amendments and Changes in IRB Approved Research Procedures and Consent Forms

The IRB must conduct a review of all proposed modifications to IRB approved research projects, including even minor changes and modifications to ICFs. The IRB must approve any changes prior to the implementation of the proposed changes, except when necessary to eliminate apparent immediate hazards to the subject. In the latter case, changes must be submitted for review by the IRB promptly after the change.

Modifications are reviewed by the IRB Analysts to determine potential eligibility for expedited review. Those that appear eligible for expedited review are sent to a primary reviewer with the expedited review checklists and any other applicable checklists for review to occur. Amendments that appear to be more than a minor change to the previously approved research, by either the IRB Analyst or the primary review, will be reviewed by the Primary Reviewer System, presented to and voted on at the full IRB at the convened meeting.

In cases where the amendment is reviewed by the convened IRB, the Primary Reviewer and all IRB members will review all of the documents applicable to the modification request including the most current IRB-approved consent form (if applicable), documents that include the proposed changes or changes made that the PI thought necessary to eliminate apparent immediate hazards to the participant, and the current IRB-approved document that has been changed, if one exists.

If a PI is submitting any changes to the ICF for review, the following should be submitted:

* + - A summary detailing the changes to the ICF; and
    - An electronic copy of the modified ICF with all changes tracked/highlighted.

The date of continuing review of a study is not changed based on the approval date of an amendment, unless the IRB specifies that the continuing review interval must change as a result of the amendment to the study.

If an amendment addresses an issue related to biosafety, PIs are required to submit appropriate paperwork to the Subcommittee on Research Safety as well. Such approval must be received before the amendment is approved by the IRB. In addition, if an amendment addresses an issue related to radiation safety, an IRB Analyst will send it to the Radiation Safety Officer (RSO) for review. The RSO will submit a report to the VAPORHCS Radiation Safety Committee.

### Review of Significant New Findings

The IRB will require that any significant new findings arising from the review process and that might relate to participants’ willingness to continue participation are provided to participants. The IRB will verify at the time of continuing review that no unapproved changes have occurred since the last IRB review, but investigators can notify the IRB at any time of significant new findings.

### Review of Study Finalization Reports

Investigators must submit a notice of study finalization to the IRB upon completion of the research project.

### Absence of a Principal Investigator

When a PI will be absent for a prolonged period (e.g., more than 30 consecutive days) and thus unable to oversee the research and carry out all PI responsibilities, the PI must notify the IRB at least two months prior to their departure, except in the case of an unforeseeable absence due to an emergency. This policy applies to repositories, as well as other human subjects studies.

If a PI is absent without prior notification to the RAO, and the PI and/or other members of the research team are unresponsive to requests from the ACOS, RAO designee or IRB, the study may be administratively terminated, as long as that will not adversely affect any participants. The ACOS/R&D in collaboration with the COS, will verify that the quality of the research being conducted and the safety and treatment of the human subjects involved will not be compromised (i.e. whether or not treatment of the research participants currently enrolled will continue and how these participants will be monitored for safety per protocol). Active recruitment of research participants into the research study must be suspended until the PI returns, or until the PI appoints and the IRB approves a new individual to assume the absent PI’s responsibilities and justifies their credentials to perform the related responsibilities.

If currently enrolled subjects will be undergoing research intervention or follow-up and serious adverse events are possible during the PI’s absence, another qualified investigator with appropriate clinical privileges must be approved by the IRB to assume the absent PI’s responsibilities during that time. Before approval, the individual(s) must complete the required education and credentialing (and if applicable, privileging) requirements, consistent with the policies Credentialing of Personnel in Research & Development Service (located at: <https://www.va.gov/portlandresearch/documents/credentialing.pdf>) and Education Requirements for the Conduct of Research (located at: <https://www.va.gov/portlandresearch/documents/Education-for-Research.pdf>), to perform the absent PI’s responsibilities.

IRB review and approval of a new individual to serve as PI, either for the temporary transfer of PI responsibilities during a PI’s absence or permanently due to the PI’s permanent departure from the position, may be expedited, if it is determined that it meets the criteria for expedited review, such as if a co-investigator will take over as PI in the absence of the original PI. If an individual new to the study team is identified, the IRB may decide that the change is significant enough to warrant review by the convened board. Each change in PI will be evaluated independently to determine appropriateness for expedited review.

If a co-investigator will be absent, active recruitment in the research project may continue, unless the individual’s role in the research is essential and the individual will not be replaced while s/he is absent. If the co-investigator will be replaced, the new co-investigator must complete the required education and credentialing (and if applicable, privileging) requirements, consistent with the policies Credentialing of Personnel in Research & Development Service (located at: <https://www.va.gov/portlandresearch/documents/credentialing.pdf> ) and Education Requirements for the Conduct of Research (located at: <https://www.va.gov/portlandresearch/documents/Education-for-Research.pdf> ), and be approved by the IRB.

### Expiration of Credentials of Research Staff

If the credentials of a member of the research team expire, that member may not continue to work on the research study until such time as the credentials are renewed. If the absence of this individual does not affect that manner in which the study is conducted, and they are not an integral part of the research team, the study may continue without changes. The individual may be administratively removed via a note to the RAO study file. At the time that credentials are renewed, a subsequent note to file may be entered to reactivate their participation in the research.

If credentials of a key individual of the research team expire and their absence will affect how the study is conducted and/or they are identified by name in the research protocol, an amendment must be submitted by the PI to the IRB as soon as possible, taking appropriate action to address the issue. This may include revising the protocol, adding a new member to the research team to replace the one with expired credentials, or other actions to assure that the research may continue.

# EXPEDITED IRB REVIEW OF RESEARCH

The IRB Co-Chairs or a qualified IRB member, designated by an IRB Co-Chair, will make a determination on whether or not a protocol may be reviewed using expedited procedures. IRB members are designated based on their experience and qualifications, which will be determined based on full reviews that they have completed as a primary reviewer and their knowledge and application of ethical principles and regulations demonstrated during discussion of protocols one-on-one and at convened IRB meetings. The IRB member(s) making an expedited review determination may not be involved in the proposed research.

A protocol may be reviewed by expedited procedures if:

1. The research is not greater than minimal risk and falls within the allowable expedited review categories, as listed in Appendix 1 of this SOP and at <http://www.hhs.gov/ohrp/policy/expedited98.html>.
2. A requested change in previously approved research, submitted during the period of one year or less for which approval is authorized, is minor, excluding the addition of procedures that involve more than minimal risk or that did not fall into any of categories 1-7 for expedited procedures.

IRB Analysts will review each submission they regard as possibly eligible for expedited review and may use the expedited reviewer checklist as a guide. The checklist has been designed to capture all eligible components of the expedited review categories referenced above. If it appears that the item(s) is appropriate for expedited review, materials will be sent to the IRB Chair and/or another qualified reviewer(s) The reviewer(s) will receive all materials that the convened IRB would receive. The reviewer(s) may exercise the authority of the IRB using the same criteria for approval as would the convened IRB, but they may not table/defer or disapprove the research. If the IRB Chair and/or qualified reviewer(s) do not approve the research through expedited procedures, then the research project will be reviewed by the convened IRB. The research may only be tabled/deferred or disapproved after non-expedited review by the convened IRB.

The fully convened IRB will be notified of all research approved under expedited procedures, via the agenda and minutes for the next available convened IRB meeting. All correspondence resulting from an expedited review will note that the review was expedited and will be filed with the RAO’s research project file kept in the appropriate Research Service space. The IRB agenda, minutes and correspondence for expedited reviews shall include the expedited review category(ies).

***For research that is subject to the 2018 Requirements:***

Research for which limited IRB review is a condition of exemption may be reviewed by expedited procedures.

For research that is subject to the 2018 Requirements, it is presumed that all activities included on the expedited review list are minimal risk activities and thus eligible for expedited review. If the assigned reviewer believes that a proposed study activity that is found on the expedited review list is greater than minimal risk and thus requires convened board review, the assigned reviewer must document the rationale for determining that the activity is greater than minimal risk on the reviewer form and then inform the IRB Analyst that the study needs to be scheduled for review at the next available convened board meeting.

# Convened IRB Meetings

Unless the research falls into one or more categories appropriate for expedited review, the IRB will conduct initial and continuing reviews of all non-exempt research at convened meetings at which a quorum of the members is present, including a member whose primary interest is non-scientific. **NOTE:** Exempt research requiring limited IRB review may be reviewed at a convened meeting as needed.

## IRB Meeting Schedule

Current IRB meeting schedules and deadlines for IRB submissions are on the Research Service website (<https://www.va.gov/portlandresearch/hrpp/index.asp?tab=0#deadlines>). The IRB agenda, minutes, review materials and all applicable primary reviewer materials are dispersed to the IRB members approximately one week prior to the next convened meeting; this allows time for sufficient review of items so that, during the convened meeting, they may be discussed adequately and have determinations for appropriate action made. IRB review materials include all of the materials as described in Section XI, G.

Meetings may be held in-person in a VAPORHCS conference room, by teleconference, video conference or by a mix of modalities.

## IRB Meeting Procedures

An IRB Co-Chair will call the meeting to order, once a quorum is established. If neither Co-Chair is available to lead a convened meeting, the members present will nominate and elect a Chair pro tempore prior to the Call to Order. The IRB may review and discuss IRB minutes from a previous meeting(s), if available, and determine whether or not any changes to the minutes are necessary. The Co-Chair/Chair pro tempore will call for a vote for approval of the minutes as written or to be amended.

The IRB will review and discuss each agenda item requiring action and vote to approve, contingently approve, table/defer or disapprove each.

Review and determination of approval for a protocol may be deferred when necessary, e.g., if there is not appropriate representational expertise for a particular protocol at the convened meeting or a quorum is lost.

If the IRB is unable to review all agenda items in the allotted time, or if enough members leave or are recused to lose the quorum, the meeting will be reconvened as soon as possible. If necessary, this will occur at a time and date agreed upon by a majority of the members, or the items will go to the next scheduled meeting if a new time and date cannot be found.

PIs may attend meetings to summarize a protocol or give other information as they or the IRB finds necessary. PIs may be present only for the portion of the meeting when they are actually interacting with the board about their protocol and must leave before the IRB continues their discussion and votes.

IRB Analysts will record minutes of each IRB meeting.

## Actions Taken by the Convened IRB

The minutes shall include all applicable actions (listed below) and votes by the convened IRB.

1. **Approved**: Approved means that the study submission was approved with no changes or no additional changes.
2. **Conditionally Approved (i.e. minor changes needed for final approval)**:Contingent approval means to approve the study submission only after described, specific minor changes have been made by the PI and verified by the Primary Reviewer. Appropriate criteria on the applicable checklist have all been met or will be met ***if*** a few specific changes are made.
3. **Tabled/Deferred (i.e. additional substantive information or substantive changes needed to re-consider approval)**: The IRB determines that it lacks sufficient information about the study submission to proceed with its review or that necessary changes are substantive, thus requiring re-review by the full board. **NOTE:** For the purposes of Affiliate University, IRB-3, this is referred to as “Deferred.”
4. **Disapproved**: The IRB determines that the research may not be conducted at the facility or by employees or agents of the facility.
5. **Acknowledged**: Acknowledged is used when one of the actions above does not apply, for example administrative actions not requiring IRB review (e.g., annual check-ins, study closures, etc.).

## Postponement of IRB Review

If the IRB does not take action on an item scheduled for review at a meeting (e.g., because a quorum was lost or the IRB primary reviewer(s) was absent from the meeting), the review of the item will be scheduled for the next available meeting, as appropriate.

## Use of Subcommittees to Support IRB Activities

An IRB Co-Chair may appoint subcommittees on an ad hoc basis to perform non-review functions as needed, such as monitoring compliance with IRB regulations.

## Use of Primary Reviewers

### Assignment of Primary Reviewers

The IRB Analysts will conduct a preliminary review of the IRB application at the time of receipt and generally assign one or two primary reviewers at the time of initial and continuing review to review the protocol for the next IRB meeting, according to consistency with the protocol content and reviewer(s) knowledge and expertise. The IRB Co-Chairs will assist the IRB Analysts, as necessary, in completing this responsibility. Physicians, Pharmacist, Nurses, PhD, and master’s level physical, biological, or social scientists, as well as other biomedical health professionals are considered to have primary concerns in the scientific area. In general, two reviewers will be assigned for initial reviews, but, for more complex research project proposals, additional reviewers may be assigned. In addition, when research involves categories of participants vulnerable to coercion or undue influence, IRB Analysts will consult with an IRB Co-Chair, if necessary, to identify a reviewer or a consultant who is knowledgeable about or experienced in working with such participants.

Amendments and notifications, that are reviewed by the IRB will generally be assigned one primary reviewer, consistent with the protocol content and reviewer knowledge and expertise.

### Responsibilities of Primary Reviewers

The primary reviewers for each item reviewed by the IRB are considered the lead reviewers on the IRB for the research project assigned to them. They are responsible for:

1. Thoroughly familiarizing themselves with all details of the research,
2. Conducting an in-depth review of the research (see applicable checklists, which include criteria for approval of the review as appropriate) and systematically evaluating the protocol to determine whether a consultant is needed,
3. Completing the applicable IRB reviewer forms, and
4. In cases where the items are reviewed at a convened meeting, leading the discussion of the research at the convened meeting, voicing any concerns that arose during their review and identifying any changes that may be required.

### Absentee Primary Reviewer

If a reviewer is absent from the meeting, a new reviewer may be assigned for their items, as long as the new reviewer has reviewed the requisite materials. An absent reviewer may submit their written comments to be read at the meeting, as long as another reviewer is present to serve as a primary reviewer.

## Materials for IRB Review

All IRB members, including alternate members and consultants, when applicable, shall be provided with sufficient information to ensure thorough initial and continuing review of each research proposal. All IRB members shall be afforded full opportunity to discuss each research proposal reviewed during convened meetings.The entire IRB file is also available for review to any IRB member upon request.

### Initial Review Materials include the following:

All Members: for studies reviewed at convened meetings, all IRB members will be provided access to copies of materials listed below before and during IRB meetings at the time of initial review of a research project.

* 1. Initial Review Questionnaire (IRQ) or electronic IRB system equivalent
  2. Copies of specific pages of the protocol referenced in the IRQ (or equivalent)
  3. Any additional attachments. (Attachments include the Human Biological Specimens Questionnaire, IRQ Appendices, Investigational Drug Information Record, etc.)
  4. Abstract
  5. ICF (if applicable)
  6. Any waiver(s) of informed consent and HIPAA authorization (if applicable)

Primary IRB Reviewers: for each study, the assigned primary reviewers will receive the materials listed above, as well as the following for each research project.

* 1. Protocol (complete DHHS-approved protocol and DHHS-approved sample ICF when one exists). The protocol must include a written plan for a research study that includes, at a minimum, a description of the objectives, rationale, design and methods to be used in the conduct of the research.
  2. Investigator’s Brochure(s) and/or equivalent material, if applicable (required if the study involves an investigational drug). This may include the Investigational New Drug (IND) application, and other FDA correspondence. If the investigator is the sponsor of the study, an Investigator’s Brochure and/or equivalent material is required. If a study involves an FDA-approved drug, an Investigator’s Brochure may not exist; for such a study, equivalent information should be provided (package insert) in place of an Investigator’s Brochure.
  3. The sponsor/manufacturer information for any FDA-regulated devices or other articles (including name, description, FDA status and/or correspondence, any previous IRB reports and risks). This may include the Investigational Device Exemption (IDE) application, device manual, package insert, as applicable.

### Continuing Review Materials include the following:

All IRB members: for studies reviewed at convened meetings, all members will be provided access to copies of materials listed below before and during IRB meetings at the time of continuing review of a research project.

* 1. Continuing Review Questionnaire (CRQ) or electronic IRB system equivalent and all items prompted within the form.
  2. ICF(s) (if applicable)
  3. Waiver of Informed Consent Documentation and/or Process and HIPAA authorization (if applicable)
  4. Abstract
  5. IRQ (or equivalent) to provide baseline information and appendices (if applicable)
  6. Any additional applicable forms, based on the enrollment status of the study and/or as prompted by the CRQ

Primary IRB Reviewer(s): for each continuing review of a study, the assigned primary reviewer(s) will receive the above materials, as well as the following for each study.

1. A copy of the complete protocol, including any previously approved modifications.
2. Most recent report capturing all reportable events to date. (If the research is not FDA-regulated, sponsor safety reports are not required.)
3. If research is FDA-regulated, an Investigational Drug Information Record and/or IRQ Appendix E (Investigational Device), and any amended or updated Investigator’s Brochure from the current approval period (if applicable).
4. A summary of safety monitoring reports, if the protocol is greater than minimal risk and/or multi-site (including collaborative research) and therefore includes a data and safety monitoring plan.
5. A summary of any events that were not required to be reported prior to continuing review.

***NOTE****: This list of documents applies to all continuing reviews, whether they are conducted by an expedited procedure, or at a convened IRB meeting. On the IRB meeting agenda, the continuing review events list those items required by the CRQ.*

### Ongoing Review Materials

All members and reviewers will have access to all relevant materials submitted for ongoing review materials (e.g. protocol revisions, reportable events, etc.), as well as previously approved materials necessary to determine that regulatory criteria for approval have been met. This includes all modified documents and related, originally approved documents (e.g., previously approved protocol, ICF(s), and recruitment materials), modification requests, all problem reports, safety reports, etc.

## Individualized IRB Consultations

Individuals who have questions regarding IRB policies and procedures (e.g., questions involving whether or not a project is considered human research and whether it should be submitted to the IRB for review and approval) should direct the question in writing to the IRB Analysts. Once received, the IRB Analysts will consult with the Lead IRB Analyst, the RAO designee and/or the IRB Members and Co-Chairs, as necessary, to address an individual’s questions. Investigators and their staff should not contact the IRB Members or Co-Chairs directly with questions related to IRB policies and procedures. It is not the policy of the VAPORHCS IRB to provide curbside consults (personal consultations) to individual researchers and medical staff.

If an IRB Member or Co-Chair receives a request for consultation, this request should be forwarded to the IRB Analysts for a documented response to the individual’s questions.

## Process for Research Flags

When the IRB determines a study requires a research flag, the RAO will prepare an electronic flag advisory once the study has received initial approval from the IRB. The VA electronic medical record is programmed such that when participants with electronic record flags make scheduled or unscheduled visits to the medical center and clinics, the participant information display will show a screen with the established type of flag advisory highlighted.

The IRB Analyst or RAO staff member will notify the PI and study contact when the flag is ready to be applied. The IRB will determine, based on the PI’s input and study specifics, when the research flag is to be initiated for each participant and when it can be removed. The PI is responsible for activating the research flag according to the IRB determination (i.e., immediately following the informed consent process or immediately following randomization, etc.).

On an annual basis, each flag must be reviewed by the PI or study coordinator and, if the flag is still appropriate, the flag must be marked for continuation. The RAO will prompt research teams to conduct the annual review as each flag’s annual anniversary nears. Researchers are responsible for removing research flags at the appropriate time during each participant’s involvement, as determined by the IRB (i.e., once study intervention is complete).

The RAO is responsible for de-activating the research protocol flag when the study is concluded. However, the PI is responsible for de-activating the research flag if a participant withdraws or when research treatment ends, even if the participant will remain in the study for long-term follow-up or if the study as a whole has not yet been terminated.

### Enrollment of Subject on More than One Study with Research Flag

In general, a participant may only be enrolled in one research study at a time for which the IRB has required a flag advisory in the participant’s electronic medical record. However, the PI can request an exception for dual enrollment of an individual participant(s), who already has another research flag advisory on their record, or for the whole study.

In order to request such an exception, the requesting PI must first contact the PI of any other flagged study for which they wish to be able to dually enroll a participant(s). The other study’s PI may agree to allow this for any participants, or just for a certain participant(s), enrolled into their study, or they may decline to allow this at all.

Once the requesting PI obtains the agreement of the other study’s PI, they must then submit a request for the exception to the IRB. The request should include:

* the applicable modification request form;
* written documentation from the other study’s PI that they agree to allow for the dual enrollment of any of their study’s participants or just for a certain participant(s) (if the latter, the applicable participants should be described without using HIPAA identifiers – e.g. all participants who have completed treatment with study drug, or Participant #0001);
* a copy of the protocol for the other study; and
* any other applicable materials supporting the request and/or requested by the IRB or RAO staff.

If the IRB approves the request, the PI may then enroll the applicable participant(s). A progress note for those participants must be created and include the following:

* the date of IRB approval for the dual enrollment;
* the date that the requesting PI spoke to the other study’s PI; and
* confirmation that the other study’s PI agreed to dual enrollment and whether the agreement was for a certain participant(s) or for the whole study.

## Audits of Research Studies

The Research Compliance Program conducts routine regulatory audits of research studies, signed research ICFs and HIPAA authorization as required by ORO. The RCO reports directly to the IO and receives guidance and direction from him/her and through the VA ORD and ORO. In order to ensure that the research compliance program can fulfill its auditing responsibilities independently, the activities of the RCO may not be determined or managed by the IRB, Research Service, research investigators, or any other research personnel.

The RCO must conduct audits as per written audit plan (per VHA Directive 1058.01). The IRB may require more frequent audits than those conducted by the RCO and will generally request that such audits be conducted by an RAO designee. The requirement to increase the frequency of audits or to audit specific aspects of a study may be based on considerations including, but not limited to:

1. Involvement of vulnerable populations
2. Level of risk
3. Phase I or Phase II studies
4. Involvement of FDA approved drugs for which there has been a new safety warning issued, or change in the labeling that indicates increased risks
5. Issues of noncompliance
6. Data confidentiality or security concerns

When such audits are requested by the IRB, it must be explicit with regard to the timeframe for reporting audit findings to the IRB. Based on the nature of the study and the results of the audit, the IRB may require corrective action and will be explicit with regard to the type of corrective action (such as revising study documents or changing recruitment procedures), who should implement and review the corrective actions and how corrective actions will be evaluated.

# Appeal of IRB Determinations

The IRB shall provide the PI with a written statement of its reasons for disapproving or requiring modifications in proposed research and shall give the PI an opportunity to respond. This correspondence will be provided to the PI within a reasonable time frame for items reviewed outside of a convened meeting. The PI or appropriate designee shall respond electronically. A time frame and format for response, based on the nature of the requested response, will be provided on the IRB correspondence.

When a dispute arises between the IRB and the PI regarding required modifications to the protocol or other parts of the IRB application that cannot be amicably resolved between the parties involved, an appeal may be made by either the PI or the IRB to the R&DC.

The R&DC may organize a meeting with the individuals noted above to discuss the issue at hand and will arrange further meetings with the PI and the IRB or designee, as needed. The R&DC will facilitate the discussion between the PI and the IRB. Final recommendations for approval remain under the purview of the IRB that made the original determinations under appeal, i.e., the appeal will not be reviewed and considered by another IRB. However, the R&DC may want to comment on the process and make recommendations to the IRB for future protocols similar to the one under appeal.

# Determination of Continuing Review Date

## Determination of Continuing Review Date for Studies Reviewed by the Convened IRB

Per federal regulations, the IRB approval period for research may not extend more than 365 days from the time that the convened IRB voted on approval, or approval pending minor modifications (with consideration of leap years). When a study is reviewed by the convened IRB, the continuing review date is determined as follows:

1. Approved with no changes at initial and continuing review: If the convened IRB approves the study with no requirement for modifications, the date of approval is the date of the convened IRB meeting at which approval was granted. The continuing review date is calculated based on that approval date. For example, for a study that was approved outright on 3/2/12 for one year, the approval period would expire on 3/1/13.
2. Approval with minor changes at continuing review: If the convened IRB approved the study contingent on specific minor modifications to the protocol or the ICF(s) (or other study documents), the date of approval will be after the date of the convened meeting. However, the continuing review date is calculated based on the date of convened meeting at which contingent approval was granted. Therefore, a study contingently approved on 3/2/12 may have contingencies addressed by the PI that are subsequently reviewed and approved on 4/1/12; the next approval period for this study would still expire on 3/1/13.
3. Approval with minor changes at initial review: If the convened IRB approved the study contingent on specific minor modifications to the protocol or the ICF(s) (or other study documents) at initial review, the first continuing review date is determined by the date when the IRB Co-Chair, or experienced IRB voting member, grant final IRB approval to the study. For example, if the convened IRB approved the study contingent on specific minor modifications on 3/2/12 and required changes are submitted and subsequently approved for one year on 3/15/12, the next approval period would expire on 3/14/13. ***NOTE:*** *Studies processed through the MIRB system at the time of initial review, will have the continuing review date calculated based on the date of convened meeting at which contingent approval was granted (see item #2 above for example of calculating the continuing review date).*

## Determination of Continuing Review Date for Studies Reviewed by Expedited Procedures

If a study is reviewed and approved by an expedited procedure as outlined in Section X, the date of continuing review is based on the date an IRB Co-Chair, or experienced IRB voting member, grant final IRB approval to the study. For example, if a study receives expedited review on 3/2/12 and required changes are submitted and subsequently approved for one year on 3/15/12, the next approval period would expire on 3/14/13.

Note that the expiration date occurs on the last date that the protocol is approved.

## Expiration of IRB Approval Period

Per VHA ORD policy, if continuing review does not occur within the timeframe set by the IRB, the IRB approval expires. There is no provision for any grace period to extend the conduct of research beyond the expiration date of IRB approval. Once it has been determined that IRB approval of a study has expired, a notification letter to the PI from an IRB Co-Chair, an IRB Analyst or the RAO designee will be generated promptly. In addition, the “IRB Analyst Checklist for Expiration of IRB Approval” will be followed to assure that appropriate individuals at the VAPORHCS, such as the RAO designee and COS (as appropriate), are notified of the expiration of study approval. The checklist prompts for appropriate reporting to outside agencies (such as the FDA, sponsoring agency, private sponsor, or other Federal agencies) as needed.

Once study approval has expired, all research activities (including, but not limited to, enrollment of new subjects, analyses of individually identifiable data, and research interventions or interactions with currently participating subjects) must stop. However, if research participants are currently enrolled in the research project and the suspension of study intervention or interaction will place the participants at risk, the PI must immediately (preferably within 3 business days) submit to an IRB Co-Chair a list of research participants for whom stopping study procedures might cause harm. The IRB Co-Chair must then determine within 2 business days whether or not such interventions or interactions may continue. Continuation of research interventions or interactions with currently enrolled participants should only continue when the IRB or an IRB Co-Chair, as appropriate, finds it is in the best interest of individual participants to do so. IRB review and re-approval must occur prior to re-initiation of the research.

If more than 2 months pass after the approval expiration, the study may be administratively terminated, and the IRB may require the PI to submit a new application to the IRB for review and approval if they wish to continue the study. If less than (or equal to) two months have passed since the expiration date, the items requested at the time of continuing review may be reviewed for consideration of continued IRB approval. The IRB cannot retrospectively grant approval to cover a period of time that did not have IRB approval.

Once the PI submits the required information, it will be reviewed as appropriate by the IRB. PIs who fail to comply with continuing review timelines may be suspended from conducting research. This will be evaluated on a case-by-case basis.

## Criteria for Requiring Review More Often than Annually

The IRB may determine that a protocol should be reviewed more frequently than annually. This may be determined at any time for any reason, including level of risk, nature of adverse events, and study population. The IRB documents in their minutes the determination of risk level and approval period for a research project.

The IRB may consider the following factors in determining the criteria for which studies require more frequent review and what the time frames generally will be:

* 1. Probability and magnitude (degree or risk) of anticipated risks to subjects.
  2. Likely medical condition of the proposed participants.
  3. Overall qualifications of the PI and other members of the research team.
  4. Specific experience of the PI and other members of the research team in conducting similar research.
  5. Nature and frequency of adverse events observed in similar research at this and other facilities.
  6. Vulnerability of the population being studied.
  7. Other factors that the IRB deems relevant.

In specifying an approval period of less than 1 year, the IRB may define the period with either a time interval or a maximum number of participants (e.g., after 3 months or after three participants). Examples of time intervals for IRB approval periods include 3, 6, 9, or 12 months.

# CONTACT WITH SUBJECTS

## Appropriate Contact with Subjects

All recruitment materials referred to below (letters, phone scripts, etc.) and, as applicable, a request for waiver of authorization and/or informed consent process for screening/recruitment purposes must be reviewed and approved by the IRB before contacting any potential participants. For the sections below, the clinician directly involved in the care of a potential research participant is referred to as the treating clinician.

### 1. Initial Contact with Potential Participants

There are multiple methods to recruit participants for research studies. The IRB will evaluate the recruitment plan of the particular study based on the principles of beneficence, justice and respect for persons defined in the Belmont Report and other regulations governing research with human subjects. In addition, in its role as the Privacy Board for the VAPORHCS, the IRB will also evaluate each recruitment plan for compliance with privacy protections described in the HIPAA legislation. Factors that may enter into this evaluation include a) the chance the potential intervention will alter the participants’ clinical treatment, b) the risk of inadvertent disclosure of sensitive information, c) the study design, d) the potential vulnerability of the proposed research participants and e) the rights of the individual guaranteed by HIPAA that protected health information (PHI) will not be disclosed without the subject’s authorization or waiver by the Privacy Board.

The following recruitment options (a, b, or c) are available when initial contact is not initiated by potential participants:

* 1. **WITH THE PERMISSION OF THE POTENTIAL PARTICIPANT:**  
     A treating clinician can ask the potential participant if he/she is willing to discuss a potential study. If the potential participant gives permission, it is up to the PI to explain to the IRB how the permission will be documented. If the potential participant gives permission, he/she can subsequently be contacted by research personnel in person or mailing a paper letter (not e-mail).   
       
     A potential research participant may be contacted initially by phone without first being sent a paper letter only if there is written documentation (in the medical record or appropriately encrypted e-mail) that the treating clinician has discussed with the potential participant that he/she is willing to be contacted by phone.
  2. **WITHOUT THE PERMISSION OF THE POTENTIAL PARTICIPANT BUT WITH THE PERMISSION OF THE TREATING CLINICIAN OR CLINIC/SERVICE DIRECTOR:**   
     A researcher may make initial contact by mail, without first having the potential participant’s permission, through the following steps.
     1. The researcher must first request permission from the treating clinician or clinic/service director, in person, by phone, or by mail (including email, using the required encryption, when sending any sensitive information), to invite an individual to participate. Requests can be batched in one document.
     2. If the treating clinician or clinic/service director gives permission, a copy of a paper letter (not e-mail) from the treating clinician or clinic/service director may be sent by the research team to the potential participant. If the treating clinician or clinic/service director gives permission, it is up to the PI to explain to the IRB how the permission will be documented. Documentation of approval may be batched in one document. The letter to the potential subject may acknowledge information about PHI in order to allow the individual to understand why he/she was identified as a potential participant for the study. In the same envelope, researchers can include a paper letter to introduce the study to potential subjects. The researcher’s form letter should not be individualized (e.g. “Dear Veteran” instead of the potential participant’s name). The letter may include the study title, a copy of the consent form (if applicable) and other relevant information that might infer general knowledge of the potential participant’s PHI.
     3. The letter must allow the individual the ability to opt out, by calling the research team or returning a separate letter indicating that they do not wish to be contacted, or to indicate that he/she may be interested in learning more about the study. The letter must provide a telephone number or other means that the potential participant can use to verify that the study constitutes VA research; it is recommended that the phone number of the Research Assurance Officer or Research Participant line (503-273-5122) be used in such situations. The letter may also state that, if the potential participant does not return a response within two weeks, he/she may be contacted by phone. The PI can appeal the two-week minimum waiting period to the IRB and in certain well justified cases the interval may be adjusted. A letter template is available on the Research Service website.
     4. If no response to the letter is received within two weeks, the research team may contact the potential participant using an IRB-approved phone script. The researcher must identify him/herself, explain why he/she is calling, and ask if the individual is interested in hearing more about the study.   
        If the potential participant is interested in learning about the study, the researcher can proceed. Otherwise, the researcher can ask if the potential participant does not want to participate or would like additional written information. A phone script template is available on the Research Service website.

**WITHOUT THE PERMISSION OF THE POTENTIAL PARTICIPANT, TREATING CLINICIAN, OR CLINIC/SERVICE DIRECTOR:**The IRB may approve studies allowing researchers to contact subjects without the permission of the subjects, treating clinician or clinic director if the subjects were not identified based on their PHI. Examples of studies that may be approved include observational research, surveys, qualitative interviews and studies seeking views of veterans (for example, on how to improve VA services).   
  
If an investigator feels it is justified or necessary to contact potential participants without the permission of the subjects, treating clinician or clinic director, and the subjects will be identified based on their PHI, they may make this request to the IRB. Researchers should address the following concerns in their submission:

1. Why the approaches outlined in a or b (above) may not be necessary or feasible for the study in question (for example, projected number of accruals, number of sites besides VAPORHCS, added risks from or burden of documentation, impacts on scientific rigor, possible selection bias, low risk survey study, etc.).
2. How the potential participant’s safety and confidentiality will be addressed.

If approved by the IRB, the research team will write the letter in place of the treating clinician or clinic/service director described in 2.b.ii to introduce the study and then follow steps 2.b.iii and 2.b.iv (above). In these cases, the letter from the research team should try to avoid mentioning a specific disease. For example, a survey of patients with prostate CA, could be phrased as a study of “patients who may or may not have seen a urologist in the last year.” A study of opiates use could be “for a study of patients who have indicated they might have painful conditions.”

### 2. Contact via Social Media and/or Craigslists

VA-approved studies may be posted on Facebook pages and/or Twitter accounts for a VA facility, and on non-VA-sponsored social media sites. However, in order to assure that sensitive information is not sent in an unencrypted email, any recruitment advertisements placed on social media sites cannot invite communication with prospective participants except by phone, mail or other methods that do not involve personal email or social media messaging.

If a mechanism such as Craigslist is utilized for recruitment and/or contact, the Craigslist posting must be set up to require responses via a phone call or mail, similar to the restrictions placed on Facebook and Twitter accounts. Email is not an acceptable response mechanism for a Craigslist posting.

***NOTE:*** *Recruitment methods that include the use of social media must be clearly described in the research protocol submitted to the IRB for review.*

### 3.Telephone Contact

Telephone use for initial contact is discouraged, unless there is written documentation (e.g., in a progress note in the electronic health record based on a clinician’s conversation with the potential participant) that the individual is willing to be contacted by phone about the study in question or a specific kind of research. When such initial contact occurs by phone, the initial contact must provide a telephone number or other means that the potential participant can use to verify that the study constitutes VA research; it is recommended that the phone number of the RAO designee be used in such situations. In cases where the research team initiates the initial contact by telephone, research team members are prohibited from requesting social security numbers (SSNs) during that contact.

In cases where the potential participant initiates the initial contact by telephone (e.g. in response to a posted advertisement), the research team members may be able to request SSNs during that contact if the IRB approves doing so. For such requests, the IRB will consider the following:

* There is a valid justification provided for needing SSNs at the time of the phone contact. Consideration will be given (but not limited) to whether there is other information (such as date of birth) that could be used instead of SSNs and whether SSNs could be requested at a later point.
* The phone number that potential participants call is a VA number and is clearly indicated as being such when provided to them (e.g. on the advertisement).
* Before providing their SSN, the potential participant is told the reason(s) that it is needed. This information needs to be reflected in the submitted phone script.

The IRB recognizes that there are some cases in which the informed consent document is mailed to the participant, and the informed consent session may occur by telephone. In such cases, if the informed consent document is revised, there is a 30-day grace period (after the date of the IRB approval) before the revised version must be used. This is to allow for the possibility that the previous version of the consent document was sent by mail immediately prior to the approval of a new version and to allow the informed consent session in such cases to move forward. The IRB reserves the right to shorten this grace period, or eliminate it altogether, in cases where the revisions to the consent document affect the health, safety or well-being of the subjects. In cases where expedited review applies, an IRB Co-Chair or primary reviewer may make such as determination to shorten or eliminate the grace period.

### 4. Email Contact

Email contact is not allowed for corresponding with participants, or to use for recruitments, unless VHA privacy and information security requirements are met. Communication of sensitive information by unencrypted email is not permitted.

All research using Azure RMS for participant recruitment and/or contact, must also meet all VHA ORD requirements. Additional information can be accessed on the ORPP&E website: <https://www.research.va.gov/resources/policies/guidance/FAQs-Azure-RMS.pdf> .

***NOTE:*** *Participant recruitment and/or contact methods that include the use of Azure RMS must be clearly described in the research protocol submitted to the IRB for review.*

### 5. Later Contact

When research team members contact enrolled participants by phone, the call must begin by referring to previous contacts and, when applicable, the information provided in the ICF. The IRB generally requires a script for all phone contacts, and the scope of phone contacts with participants must be limited to topics outlined in the IRB-approved protocol and ICF(s).

### 6. Contact via MyHealtheVet

Secure messaging in MyHealtheVet may be used for IRB-approved research in which it is leveraged as part of an intervention (e.g., pre-appointment planning). Secure messaging in MyHealtheVet currently may only be used for other research-related communications after a participant has consented (not for recruitment purposes).

# Reportable Events in Research

Please see VHA Directive 1058.01, Research Compliance Reporting Requirements, for definitions on which events need to be reported and the timeframes associated for each report, please click here: <https://www.va.gov/vhapublications/publications.cfm?Pub=1>.

All researchers conducting research as employees or agents in the VAPORHCS or under VA auspices are required to report events within the timeframes outlined in VHA Directive 1058.01. PIs are also required to report promptly to the IRB and the ACOS/R&D any adverse event (AE) that is reported to OHRP or to the FDA and/or the sponsor, in accordance with FDA requirements.

## How to Submit a Written Report

If any of the events outlined in VHA Directive 1058.01 are identified by members of the research team, they must be reported to the IRB using the required reporting form (reportable event form). If any of the events above are identified by other members of the research community, they may be reported to the IRB in any written format (memo, email, etc.) by that individual via fax to (503) 273-5152 or email to [pvamc-irb@va.gov](mailto:pvamc-irb@va.gov).

## Review after Initial Report is Submitted

Within 5 business days of receipt by the IRB staff, an IRB Co-Chair, a qualified IRB member-reviewer or the convened IRB will review event reports. During this review, the IRB Co-Chair, qualified reviewer or convened IRB will make the required determinations about the event using the appropriate reviewer checklist or tool.

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## Convened IRB Review of a Report

When an event report meets requirements and/or criteria to be reviewed by the convened IRB, an IRB Analyst assigns a primary reviewer to review and present the event report as required at the next scheduled IRB meeting.

1. The primary reviewer, as well as all IRB members, are provided copies of the following and are expected to review this information in advance of the meeting:
2. The related event on the required event reporting form
3. The related reviewer checklist/tool that was completed by the IRB Co-Chair or qualified IRB member-reviewer
4. The results of any investigation, if applicable
5. The currently approved consent document and/or HIPAA authorization, if applicable
6. Any other relevant information, e.g., Investigator’s Brochure for drug studies, medical record progress notes, protocol, etc.
7. Review of reportable events by the convened board will be documented per the requirements in VHA Directive 1058.01.
8. The IRB will also consider the following as potential corrective actions in response to event reports:
9. Modification of information disclosed during consent
10. Providing of additional information to past participants
11. Notification of current participants if new information might affect willingness to continue in research
12. Modification of continuing review schedule
13. Monitoring of the research
14. Monitoring of the consent process
15. Referral to other organizational entities
16. Suspension of research
17. Termination of research
18. Within 5 business days after reviewing events at its convened meeting, the IRB must notify the VA facility Director in writing of determinations.
19. The VA facility Director must then report any such notifications to ORO within 5 business days after receiving the IRB’s notification.
20. Except where remediation requires substantial renovation or fiscal expenditure, hiring, legal negotiations, or other extenuating circumstances, remedial actions must be completed within 120 calendar days after any determination of noncompliance. Where remedial actions cannot be completed in 180 calendar days, the VA facility Director must provide ORO with an acceptable written justification and an acceptable timeline for completion.
21. The IRB must track the determinations for reports of serious and/or continuing noncompliance for use in the VA Medical Facility Director Certification.

## For-Cause Suspension or Termination of IRB Approval of Research

An IRB Co-Chair or a designated reviewer may require an immediate, temporary suspension of enrollment of new participants and/or of continued participation of previously enrolled participants, pending review of the situation by the convened IRB, if research is not being conducted in accordance with the IRB’s requirements or has been associated with unexpected serious harm to subjects. The ACOS/R&D may also suspend or terminate research on an urgent basis if it is not being conducted in accordance with the IRB’s requirements or has been associated with unexpected serious harm to subjects. An IRB Co-Chair or designee or the ACOS/R&D may call an emergency IRB meeting or place the study on the agenda for the next regularly scheduled IRB meeting. ***NOTE:*** *The IO has authority to suspend or terminate IRB approval of research. This authority can be delegated by the IO to the Chief of Staff (COS). ORD has authority to suspend or terminate any research activity it is funding.*

Upon review, if the IRB determines that the research is not being conducted in accordance with the IRB’s requirements or has been associated with unexpected serious harm to subjects, they may vote to suspend or terminate approval of research.

Any suspension or termination of approval must include a statement of the reasons for the IRB’s action and must be reported promptly to the PI, appropriate IO(s), ORO, and appropriate federal agencies according to applicable local, VA and other federal requirements. The PI shall be provided with an opportunity to respond in person or in writing.

In the event of any suspension or termination of approval of research, the IRB, or an IRB Co-Chair or designee (in the case of the need for immediate action), shall consider actions to protect the rights and welfare of currently enrolled participants and whether procedures for withdrawal of enrolled participants take into account their rights and welfare. Possible actions may include one or more of the following:

1. Inform current participants of the suspension/termination
2. Require any resulting adverse event or outcome be reported to the IRB
3. Require arrangements for medical care outside the research study
4. Transfer the research to another investigator
5. Require continuation of the participant in the research under independent monitoring

## Reports from the IRB to other Review Bodies

Prompt written notification will be provided to all persons and oversight agencies as applicable (e.g., FDA, OHRP, etc.). In addition, the following applies:

### Reports to the R&DC

The R&DC is notified of all IRB determinations on reviewed items via review of the IRB meeting minutes.

### Reports to the PO and ISSO

Study teams will notify the PO, Information System and Security Officer (ISSO) and the Records Manager (when applicable) as soon as possible after discovery of any breaches of data security with the potential for loss of privacy of a human subject.

### Reports to and from Outside Agencies

The IRB and IRB records are subject to regulation and inspection by governmental regulatory agencies (e.g., the FDA, OHRP, and VA ORO).

### Report Process

The RAO designee will facilitate the process of reporting to institutional officials and relevant federal agencies through the following steps within the appropriate timeframe:

* 1. Draft a memorandum, addressed to the IO for signature by the IRB Chair.
  2. Draft a memorandum or letter, addressed to each agency, for signature by the IO or other appropriate individual (e.g. ACOS/R&D).
  3. Route the documents through all relevant parties, as applicable.
  4. Send the signed document to the appropriate officials and/or agencies.

## Reporting to organizational offices and external agencies

Reportswill be facilitated by the RAO designee and/or RCO, depending on the report.

### Contents of Reports.

Reports will include all information required by the organizational offices and external agency to which they are reporting. Contents may include the following:

1. Name and any relevant assurance number of facility
2. Title of the research project(s)
3. The number(s) used by the IRB to identify the project
4. Name of any external sponsor(s) of the projects
5. Funding source
6. Name of any external entities to VA that were notified or are to be notified.
7. Detailed description of event
8. Detailed description of actions or proposed actions to address the event including systemic actions when warranted.

The reports to the organizational offices and external agencies must occur in the timeframes outlined those offices and external agencies.

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# Regulatory Criteria Applied During IRB Review

## Required Criteria for IRB Approval of Research

The IRB shall determine the following during initial and continuing review and approval of research, as stated in the VA, DHHS, and FDA regulations. IRB approval of a study means the IRB has determined that the research has satisfied all relevant approval criteria and may be conducted within the constraints set forth by the IRB and by other applicable local, VA and other Federal requirements.

Although the IRB is a subcommittee of the R&DC, neither the R&DC, nor the IO, may approve research involving human subjects that has not been approved by the IRB of record, nor may they alter an adverse report or modifications required by the IRB. For example, the disapproval of a research protocol for ethical or legal reasons by the IRB may not be reversed by the IO or R&DC. However, the R&DC, IO or ORD may disapprove research that the IRB approved.

### Risks to Participants

The IRB must consider the overall level of risk to participants in evaluating proposed research during initial and continuing review of research. The IRB identifies the risks to the participant. These risks must be clearly identified in the ICF. The IRB determines the level of risk of a protocol by evaluating the nature of several types of risk, including but not limited to physical, psychological, and social/economic harms that could result from participation in the research. The IRB also evaluates the probability of the occurrence of a risk, as well as the severity of each potential risk in order to qualify each protocol as less than minimal, minimal, moderate or high risk. The IRB determines the interval for continuing review based on the level of risk of the research project.

The IRB must distinguish research that is greater than minimal risk from research not greater than minimal risk when considering proposals for expedited review and for vulnerable populations. However, the IRB assesses the risk/benefit in all research protocols.

Generally, research projects that may be considered high risk involve high-risk invasive procedures, a Phase 0, I or II clinical trial, investigational drugs, or a significant risk investigational device.

### Risks Minimized

To approve research, the IRB must determine at the time of initial and continuing review that risks are minimized by using procedures (1) consistent with sound research design and (2) that do not expose participants to unnecessary risks. Whenever appropriate, the research should utilize standard care procedures already being performed on participants for diagnostic or treatment purposes.

The IRB examines the research plan, including research design and methodology, to determine that there are no obvious flaws that would place participants at unnecessary risk. This includes the risk that the research is so poorly designed or is so lacking in statistical power that meaningful results cannot be obtained.

### Risks Reasonable Relative to Anticipated Benefits

At initial and continuing review (including amendments, research problems, etc.), the IRB must determine that the risks of the research are reasonable in relation to the anticipated benefits (if any) to participants and the importance of the knowledge that may reasonably be expected to result. This is determined at the time of initial and continuing reviews, as well as on an ongoing basis for other paperwork (such as amendments) submitted for each protocol. The IRB determines the level of physical, psychological, and social/economic risk of the research as well as probable individual and societal benefits of the research.

The IRB analyzes risk/benefit by evaluating the most current information about the risks and benefits of the interventions involved in the research and the reliability of this information. The IRB considers only those risks related to the research, and not the long-range effects (e.g., public policy implications) of applying any knowledge gained from the research.

### Equitable Selection of Participants

The IRB determines by viewing the IRQ, protocol and other research project materials that selection of participants is equitable with respect to gender, age,class, etc. The IRB will not approve a study that does not provide adequately for the equitable selection of participants or has not provided an appropriate scientific and ethical justification for excluding classes of people who might benefit from the research.

In making this determination, the IRB evaluates: the purposes of the research; the setting where the research will be conducted; the scientific and ethical justification for including any categories of populations who are vulnerable to coercion or undue influence such as children, prisoners, impaired decision-making capacity, or economically or educationally disadvantaged persons; the scientific and ethical justification for excluding classes of persons who might benefit from the research; participant recruitment and enrollment procedures; amount and timing of payments; and the inclusion/exclusion criteria.

### Circumstances of Informed Consent Requirements

To approve research, the IRB must determine that legally effective **informed** **consent** shall be sought from each prospective participant or the participant's legally authorized representative (LAR), unless informed consent requirements may be waived or altered under VA regulations or any state statutes that are determined to be applicable by Regional Counsel. Currently, no state or local regulations affect informed consent.

Informed consent may only be sought under circumstances that provide the subject (or the LAR) with sufficient opportunity to consider whether or not to participate and that minimize the possibility of coercion or undue influence.

### Documentation of Informed Consent

To approve research, the IRB must determine that informed consent shall be appropriately documented, in accordance with, and to the extent required by, VA, FDA, the Common Rule regulations and applicable (as determined by Regional Counsel to be more stringent than federal law) state and local regulations. Currently, no state or local regulations affect informed consent at the VAPORHCS. Requirements for informed consent and documentation are described in Section XVII.

### Review of Plans for Data and Safety Monitoring

To approve research, the IRB determines that the research plan makes adequate provision for monitoring the data to ensure the safety of participants. A Data and Safety Monitoring Plan may be required for all multi-site research (including collaborative research) and for all research with greater than minimal risk. In general, it is desirable for a Data and Safety Monitoring Board (DSMB) to be established by the study sponsor for research that is blinded, involves multiple sites, involves vulnerable subjects, or employs high-risk interventions. For some studies the National Institutes of Health (NIH) require a DSMB. The IRB may require a DSMB as a condition for approval of research.

When DSMBs are utilized, the IRB conducting continuing review of research may rely on a current statement from the DSMB indicating that it has and will continue to review study-wide AEs, interim findings, and any recent literature that may be relevant to the research, in lieu of requiring that this information be submitted directly to the IRB. However, the IRB shall review all DSMB reports, assess if the risk/benefit ratio has changed and decide independently if any change in the research protocol or informed consent or suspension of research should be required.

1. Review of Safety Monitoring: For studies that are blinded, have multiple sites, recruit vulnerable populations, or employ high-risk interventions, a description of the data and safety monitoring plan must be submitted to the IRB as part of the proposed work. This plan should contain procedures for identification and reporting problems involving previously unrecognized risk and all local serious adverse events. The monitoring provisions must be described in sufficient detail for the IRB to determine whether they are appropriate for the research. All research requires some level of monitoring and PIs are responsible for monitoring their studies. However, the IRB must approve the plan for monitoring data and safety for all research except minimal risk research where the VAPORHCS is the only site. For studies that have a Data and Safety Monitoring Board (DSMB), the research plan must make adequate provisions for monitoring the data collected to ensure the safety of participants.

For research conducted under a DOD Addendum, appointment of a research monitor must be considered by the IRB. A monitor is required for research involving greater than minimal risk, although the IRB can require this for a portion of the research or studies involving no more than minimal risk if appropriate. The independent research monitor must be appointed by name and has authority as follows:

* 1. Stop a research study in progress.
  2. Remove individuals from the study.
  3. Take any steps to protect the safety and well-being of participants until the IRB can assess.

### Privacy of Participants and Confidentiality and Security of Data

The IRB requires that participants’ confidentiality be strictly maintained and privacy protected for all human subjects research, including collaborative research. The IRB serves as the Privacy Board for Research at the VAPORHCS and abides by the Health Insurance Portability and Accountability Act (HIPAA) of 1996 (see HRPP policy, Health Insurance Portability & Accountability Act (HIPAA) in Human Subjects Research located at: <https://www.va.gov/portlandresearch/documents/hrpp/hipaa.pdf>).

All HIPAA authorizations must be approved by the PO, who must review the HIPAA authorization to ensure it contains all required elements and is consistent with all privacy requirements before the PI can begin to use or collect the individual’s information based on an approved research protocol. The IRB does not approve the HIPAA authorization but may review it to verify that it is consistent with the ICF, protocol and other submitted documents.

The IRB may approve a waiver of HIPAA authorization, as appropriate. An investigator requesting a waiver of HIPAA authorization must provide information sufficient to allow the IRB to make the required determination. In accordance with the HIPAA Privacy Rule at 45 CFR 164.512(i)(2), the IRB must document the following:

1. Identification of the IRB of Record;
2. Date of IRB approval of waiver of HIPAA authorization;
3. Statement that the waiver of HIPAA authorization satisfies the following criteria:
   1. The use or disclosure of PHI involves no more than a minimal risk to the privacy of individuals based on the presence of the following elements:
      1. An adequate plan to protect the identifiers from improper use and disclosure;
      2. An adequate plan to destroy the identifiers at the earliest opportunity consistent with conduct of research, unless there is a health or research justification for retaining the identifiers or such retention is otherwise required by law. (e.g., to satisfy records retention requirements).
      3. Adequate written assurances that the PHI will not be reused or disclosed, except as required by law, for authorized oversight of the research study, or for other research for which the use or disclosure of PHI would be permitted by the Privacy Rule;
   2. The research could not practicably be conducted without the waiver; and
   3. The research could not practicably be conducted without access to and use of the requested information.
4. A brief description of the PHI for which the IRB has determined use or disclosure to be necessary;
5. Identification of the IRB review procedure used to approve the waiver of HIPAA authorization (either convened IRB review procedures or expedited review procedures); and
6. Signature of the Chair of the IRB, or a qualified voting member of the IRB designated by the Chair, on the HIPAA authorization waiver document. *NOTE: Signatures may be electronic if they meet VA requirements for electronic signatures.*

***NOTE:*** *If the IRB does not document the waiver of authorization (as required, per VHA Directive 1200.05), the waiver is not valid.*

***NOTE:*** *PHI obtained in research for which the IRB of Record has waived the requirements to obtain a HIPAA authorization and a signed informed consent document may not be disclosed outside VA unless the VA facility PO ensures and documents VA’s authority to disclose the PHI to another institution. NOTE: A waiver of HIPAA authorization is not sufficient to fulfill the requirements of all other applicable privacy regulations, such as the Privacy Act of 1974 (5 USC 552a).*

The IRB also takes into consideration other laws regarding protection of participants’ information, including: the Privacy Act of 1974 (5 USC 552a); VA Claims Confidentiality Statute (38 USC 5701); Confidentiality of Drug Abuse, Alcoholism and Alcohol Abuse, Infection with Human Immunodeficiency Virus (HIV), and Sickle Cell Anemia Medical Records (38 USC 7332); and Confidentiality of Healthcare Quality Assurance Review Records (38 USC 5705). And all disclosures and data transmission must meet privacy and security requirements per VA Directive 6500, VA Handbook 6500, and VHA Directive 1605.01. Laws regarding protection of participants’’ information can be located using the following links:

Privacy Act of 1974 - <http://www.gpo.gov/fdsys/granule/USCODE-2010-title5/USCODE-2010-title5-partI-chap5-subchapII-sec552a/content-detail.html>

VA Claims Confidentiality Statue - <http://www.gpo.gov/fdsys/granule/USCODE-2010-title38/USCODE-2010-title38-partIV-chap57-subchapI-sec5701>

Confidentiality of Drug Abuse, Alcoholism and Alcohol Abuse, Infection with Human Immunodeficiency Virus (HIV), and Sickle Cell Anemia Medical Records - <http://www.gpo.gov/fdsys/granule/USCODE-2011-title38/USCODE-2011-title38-partV-chap73-subchapIII-sec7332/content-detail.html>

Confidentiality of Healthcare Quality Assurance Review Records - <http://www.gpo.gov/fdsys/granule/USCODE-2010-title38/USCODE-2010-title38-partIV-chap57-subchapI-sec5705/content-detail.html>

The IRB recognizes the importance of protecting participant confidentiality, and carefully evaluates each protocol for the confidentiality measures taken. Only those authorized by the IRB (which may include the PI, co-investigators, research assistants, etc.) shall be allowed access to individually-identifiable participant information. Individuals must have prior approval by the IRB before receiving individually identifiable participant data for research purposes. This may include requiring such measures as a set of research codes rather than the use of individually identifiable information, linked to the participant through only one codebook maintained by the PI.

At the time of initial and continuing review, the IRB ensures the privacy and confidentiality of research participants is protected. The IRB evaluates the methods used to obtain information about participants and individuals who may be recruited to participate in studies; the use of personally identifiable records; and the methods to protect the confidentiality and security of research data, including how and where the data will be stored. In some cases, the IRB may also require that a Certificate of Confidentiality be obtained to additionally protect research data as noted in Section XVI, B.7 of this SOP. And, if a study includes information covered under 38 USC 7332 (i.e., drug abuse, alcoholism and alcohol abuse, HIV and/or sickle cell anemia) that will be disclosed outside of VA, the study must include written assurance from the VA researcher (e.g., within the protocol) that the purpose of the data is to conduct scientific research and that no personnel involved in the study will identify, directly or indirectly, any individual patient or subject in any report of such research (e.g., in a manuscript or publication).

The PI will provide the information regarding the privacy and confidentiality of research participants at the time of initial review through the completion of the IRQ (or electronic equivalent), any necessary HIPAA Forms, the research protocol, and/or other submitted materials. The IRB will assure that the HIPAA Authorization (when applicable) is consistent with both the ICF and the protocol.

In reviewing privacy and confidentiality protections, the IRB shall consider the nature, probability, and magnitude of harms that would be likely to result from a disclosure of collected information outside the research. It shall evaluate the effectiveness of proposed de-identifying techniques, coding systems, encryption methods, storage facilities, access limitations, and other relevant factors in determining the adequacy of protections.

Each IRB application specifically identifies where data will be stored. This applies to storage of data during the course of the study. However, research teams may work with the RAO to archive study data (either during or after finalization of study conduct) without submitting a request to the IRB. Therefore, change of storage location, in cases where the research team works with the RAO to archive study records, does not require IRB approval. If study records are archived without the assistance of the RAO after a study is finalized, a note to file should be placed in the researcher’s records, and IRB approval is not required. In the event that study staff and/or their research records need to be moved temporarily (for example, because an office space is being remodeled), a note to file should be included in the researcher’s records to show the temporary move of research records, specifying the new, temporary location, and an explanatory notification (e.g., email) should be sent to the IRB for inclusion in the RAO’s records. All other permanent changes in location of study information, records, data, etc. for active studies must receive prior approval from the IRB.

## Additional Considerations During IRB Review and Approval of Research

### Implementing Flag Advisories in the Electronic Medical Record

An electronic record flag advisory serves as an immediately identifiable alert that promotes safe, appropriate, timely and respectful participant care. Studies that generally should have a flag are moderate or high-risk and invasive, including studies requiring surgery and/or utilizing investigational drugs or significant risk investigational devices. Flags may also be required for studies for which the IRB feels it is important that any medical staff member working with an enrolled participant know that they are participating in a research study, such as research involving interventions that will be used in the medical care of the participant or that could interfere with other care, clinical services that could interfere with other care, or for research involving surveys/interviews that could provoke undue stress or anxiety, unless the IRB determines such a flag is not in the participant’s best interests.

The IRB will decide at initial review whether such a research flag must be activated in the participant’s electronic health record, and require assurance, if applicable, at continuing review that the flag remains activated, unless the requirement was lifted by the IRB. If the risk level of a study changes (e.g. via an amendment or due to new findings), the IRB may consider adding, changing or removing flagging requirements at that time.

When the IRB determines a research flag is appropriate, the board can determine that the flag is to be initiated and removed at designated milestones for each study participant based on the specifics of each study. For example, the IRB may determine that a flag need not be triggered until randomization occurs or intervention begins. The IRB may determine that the research flag can be removed once a participant ceases study intervention while remaining on the study in follow-up. The board will take into consideration the recommendations of the PI; however, for studies in which the use of flags is determined to be appropriate, the IRB has final determination regarding when research flags are initiated and removed for each participant.

### Independent Verification from Sources Other than the Investigator that No Material Changes Have Occurred Since the Previous IRB Review

The IRB recognizes that protecting the rights and welfare of participants sometimes requires that the IRB verify independently, utilizing sources other than the research team, that no material changes have occurred during the IRB-designated approval period.

The IRB shall consider the following factors in determining which studies require such independent verification:

1. Probability and magnitude of anticipated risks to participants.

2. Likely medical condition of the proposed participants.

3. Probable nature and frequency of changes that may ordinarily be expected in the type of research proposed.

4. Prior experience with the PI and research team.

5. Other factors the IRB deems relevant.

In making determinations about independent verification, the IRB may prospectively require that such verification take place at predetermined intervals during the approval period or may retrospectively require such verification at the time of continuing review, review of amendments and/or adverse events.

If any material changes have occurred without IRB review and approval, the IRB will decide the corrective action to be taken.

### Advertisements and Other Recruitment Materials

The IRB is responsible for ensuring that the selection of participants is equitable, and therefore must approve any and all final versions of advertisements and participant recruitment materials (including, but not limited to, flyers, brochures, internet advertisements, social media postings, tapes, CDs, DVDs and other audio/video advertisements) prior to posting and/or distribution for studies conducted under the purview of the VAPORHCS IRB. Recruitment materials should be submitted to the IRB with the initial application or as an addendum to the protocol.

The IRB will review to assure the recruitment material(s) is accurate, is not coercive or unduly optimistic, creating undue influence on individuals to participate. The IRB will also review the mode of advertising/recruiting and evaluate whether the frequency and/or content could be considered coercive or harassment by prospective participants.

Recruitment materials may not include any of the following:

1. Statement or implication of a certainty of favorable outcome or other benefits beyond what is outlined in the consent and the protocol;
2. Exculpatory language;
3. Emphasis on payment or amount to be paid, by such means as larger or bold type; or
4. A promise of free treatment when the intent is only to say that participants will not be charged for taking part in the study.

FDA-regulated study recruitment materials may not include any of the following:

1. Claims inconsistent with FDA labeling, either explicit or implicit, about the drug, biologic or device under investigation;
2. Terms such as "new treatment," new medication" or "new drug" without explaining that the test article is investigational.
3. Statement offering compensation for participation in a trial offered by a sponsor to include a coupon good for a discount on the purchase price of the product once it has been approved for marketing.

Any advertisement or recruitment materials should be limited to the information the prospective participants need to determine their eligibility and interest and which identifies the study. The following items must be included:

1. Study ID number (e.g., eIRB study ID and/or VAIRRS study ID).
2. Include “IRB-approved” somewhere in the text.

Depending on the type of advertisement, the following items must be included when possible:

1. The name and address of the clinical investigator and/or research facility.
2. The condition being studied and/or the purpose of the research.
3. In summary form, the criteria that will be used to determine eligibility for the study (a complete list of eligibility criteria is not required).
4. A truthful and straightforward description of the benefits and burdens to the participant for participating in the study (e.g., payments, no cost treatment, percentage of participants who will receive a placebo).
5. The time or other commitment required of the participants.
6. The location of the research and the person or office to contact for further information.
7. A clear statement that this is research and not treatment.

***NOTE:*** *Advertisements that are intended for informational use only and not for active recruitment (such as studies where participant identification and eligibility requirements are determined Veterans/patients who are hospitalized with specific condition(s) on selected inpatient units) are not required to include all advertisement items a thru g above. However, the IRB is still responsible for ensuring the material meets all applicable criteria in this section.*

The IRB approval date will be documented on printed versions of advertisements and participant recruitment materials, excluding advertisements intended for informational use only as noted above in this section. At initial approval, the approval date on these items is the date of initial IRB approval. If these items are amended during the protocol approval period, the approval date on these items is the date of approval for the related amendment.

See also Section XIV, regarding contact with participants and restrictions on the use of email, and social media.

### Recruitment Incentives

The IRB must approve any and all recruitment incentives to researchers, physicians, and other health care providers for identifying and/or enrolling participants for studies that are conducted under the purview of the VAPORHCS IRB. The PI must disclose this information in the IRB application when a study is initially reviewed by the IRB. The IRB reviews the recruitment incentives to assure that the incentive is not coercive or unduly optimistic, creating undue influence for the researchers to recruit participants into a study overall or by a certain date.

Recruitment Incentives to researchers from a sponsor must not create undue influence to recruit participants for a study and must be reasonable in relation to the work being performed.

For research following a DOD Addendum, when the research involves U.S. military personnel the following additional protections apply:

1. Officers are not permitted to influence the decision of their subordinates.
2. Officers and senior non-commissioned officers may not be present at the time of recruitment.
3. Officers and senior non-commissioned officers have a separate opportunity to participate.
4. When recruitment involves a percentage of a unit, an independent ombudsman is present.

See also Section XIV, regarding contact with participants and restrictions on the use of email, Facebook, Twitter and Craigslist.

### Payment to Research Participants

The IRB reviews any financial or other form of payment to research participants at the time of the initial application to assure that the amount is not coercive given the nature of the research or creates undue influence on an individual to participate. The information is provided in the IRQ, and additional information may be required on an as needed basis.

Payments may not be provided to participants on a schedule that results in coercion or undue influence on the participant’s decision to continue participation. For example, payment may not be withheld as a condition of the participant completing the research. If the participant withdraws early, payment must be prorated to reflect the time and inconvenience of the participant’s participation up to that point. Any bonus for completion must be reasonable and not so large as to unduly induce participants to stay in the study when they would otherwise have withdrawn. The schedule, amount and conditions of payment must be stated in the ICF.

The following are considerations the IRB may take:

1. **No direct participant benefit.** When the study to be performed is not directly intended to enhance the diagnosis or treatment of the medical condition for which the volunteer participant is being treated, and when the standard of practice in affiliated, non-VA institutions is to pay participants in this situation.

2. **Others being paid.** In collaborative research studies, where participants at a collaborating non-VA institution are to be paid for the same participation in the same study at the same proposed rate, the IRB may find that payment is appropriate.

3. **Comparable situations.** In other comparable situations in which, in the opinion of the IRB, payment of participant volunteers is appropriate.

4. **Transportation Expenses.** When transportation expenses are incurred by the participant that would not be incurred in the normal course of receiving treatment and which are reimbursed by another mechanism.

Investigators who wish to pay research participants must indicate in their research project application the justification for such payment which may include consideration of the criteria listed above as well as:

1. Substantiate that proposed payments are reasonable and commensurate with the expected contributions of the participant;

2. State the terms of the participation agreement and the amount of payment in the ICF; and

3. Substantiate that participant payments are fair and appropriate, and that they do not constitute (or appear to constitute) undue pressure on the Veteran participant to volunteer for the research study.

The IRB shall review all proposals involving the payment of participants (in excess of reimbursement for travel) in the light of these guidelines. The RAO must ensure that such payments to participants are made from appropriate funds.

For research under a DOD addendum in which U.S. military personnel are involved, dual compensation is limited:

1. An individual is prohibited from receiving pay or compensation for research during duty hours.
2. U.S. military personnel may be compensated for research if the participant is involved in the research when not on duty.

### Compensation for Injury

Information on compensation for injury must be included in all ICFs for studies involving more than minimal risk, with contact names and telephone numbers, per the requirements of the text of the ICF.

VA medical facilities shall provide necessary medical treatment to a research participant injured as a result of participation in a research project approved by a VA R&DC and conducted under the supervision of one or more VA employees. (VA employee is defined as any person appointed by VA as an officer or employee and acting within the scope of his or her appointment.) The following exceptions apply:

1. If VA medical facilities cannot furnish the care or services required or cannot furnish such care economically, the PI will notify the ACOS/R&D who will work with the VAPORHCS IO to contract for the necessary care.
2. If inpatient care must be provided for a non-Veteran, the VAPORHCS IO may contract for such care.
3. If a research participant needs treatment in a medical emergency for a research-related injury, the VAPORHCS IO shall provide reasonable reimbursement for the emergency treatment in a non-VA medical facility.

However, this requirement does not apply to (1) treatment for injuries due to noncompliance by a participant with study procedures; or (2) research conducted for the VA under a contract with an individual or a non-VA institution.

### Certificates of Confidentiality

Several HHS operating agencies issue Certificates of Confidentiality to protect research subjects. Generally, any Federally-funded research project that involves the use or collection of identifiable, sensitive information will be required to have a Certificate of Confidentiality as required by Section 2012 of the 21st Century Cures Act (42 U.S.C. 241). For purposes of this section and as defined in the 21st Century Cures Act, the term identifiable, sensitive information means information about an individual that is gathered or used during the course of research in which an individual is identified; or there is at least a very small risk, as determined by current scientific practices or statistical methods, that some combination of the, a request for the, and other available data sources could be used to deduce the identity of an individual. An investigator issued a certificate must protect the privacy of individuals involved in the research study and may not disclose or provide to any other person not connected with the research the name of subjects or any informationdocument, or biospecimen that contains identifiable, sensitive information about subjects that was created or compiled for purposes of the research.

For studies that have a Certificate of Confidentiality, disclosure of identifiable information outside of the research team is prohibited, except: (1) when there is a Federal, State or law requiring disclosure of such as for reporting child or elder abuse orcommunicable diseases; (2) when the subject consents for such disclosure; (3) for medical treatment of the individual made with consent of the subject; or (4) when the information is used for other scientific research that is in compliance with applicable Federal regulations governing the protection of human subjects in research.

When VA conducts a study that is protected by a Certificate of Confidentiality, the following apply:

1. For studies in which information about the subject’s participation will be included in the subject’s VHA medical record, information must be given to the prospective subjects as part of the informed process that information regarding study participation will be included in the medical record.
2. For studies in which the IRB requires a written informed consent, the informed consent document approved by the IRB must include a statement that the study has a Certificate of Confidentiality. ***NOTE:*** *The HHS agencies that issue Certificates of Confidentiality usually have guidance specific to the issuing agency on statements that must be included in informed consent documents describing Certificates of Confidentiality.*

***NOTE:*** *Effective Oct. 1, 2017, NIH funded researchers are automatically issued a CoC through their award. Other Department of Health and Human Services (HHS) agencies issue CoCs to researchers they fund. Researchers not funded by HHS can continue to apply to NIH or the FDA as appropriate to request a CoC for HHS-mission relevant research.*

Additional information, regarding CoCs, including the application information necessary for applying for a Certificates of Confidentiality may be obtained on the NIH website at: <http://grants1.nih.gov/grants/policy/coc/index.htm> .

### Compliance with All Applicable Federal, State and Local Laws

The IRB follows and must adhere to all applicable federal, state and local laws in the jurisdictions where the research is taking place. The Research Service and the IRB rely on the Regional Counsel for the interpretation and application of Oregon and Washington State law and the laws of any other jurisdiction where research is conducted as they apply to human research. All consent requirements by the IRB must be consistent with applicable federal, state and local laws.

Currently there are no Oregon or Washington statutes that conflict with or enhance federal requirements on research done at federal facilities. If either state law is amended to require more stringent regulations than are currently required in the federal regulations, the policy is to follow the more stringent state requirements.

Nothing in this SOP is intended to limit the authority of a physician to provide emergency medical care to the extent that the physician is permitted to do so under applicable federal, state or local law.

### IRB Considerations About Ethical Study Design

The IRB takes into consideration the study design to assure that research ethics are being followed. This includes careful consideration of issues such as protection of privacy and confidentiality in epidemiological research, genetic research, and family research. Even studies, which, by their epidemiological nature may not require an ICF, are carefully evaluated to assure that only the information needed is being gathered, that the confidentiality of the information is carefully protected, and that the risk to the participant remains minimal.

### IRB Considerations of Conflict of Interest

Research staff must disclose to the IRB any potential, actual, apparent, or perceived conflict of interest of a financial, professional, or personal nature that may affect any aspect of the research, and comply with all applicable VA and other federal requirements regarding conflict of interest.

With regard to a conflict of interest identified for a researcher, the IRB will review and approve the management plan instituted by the R&DC and assure that the plan includes appropriate disclosure to participants in the ICF before giving final approval to a research project.

### Principal Investigator Expertise

The IRB also considers the professional qualifications and resources of the research team as indicated on the IRB application. The PI must designate all research staff on the IRB application, including co-investigators, collaborators, and study coordinators. In all studies for which the PI is not licensed, credentialed and privileged at the VAPORHCS to perform **all** proposed interventions, the PI must designate a co-investigator with expertise in the relevant medical specialty. In addition, if the PI cannot respond to emergencies experienced by participants, an appropriate clinician must be designated as the “Responsible Clinician” and will be responsible for all participant safety issues, including: checking of all laboratory/study testing in the research; following all laboratory/study results and communicating all moderate or severe results to the study participant, the study participant's primary care and specialty physicians; and assuring the accurate recording of all relevant laboratory/studies in the participant's electronic medical record. This Responsible Clinician will usually be involved in developing the scientific protocol section involving his or her area of expertise and training to assure optimal participant safety and follow-up of abnormal laboratory/study results.

Clinicians must maintain appropriate professional credentials and licensing privileges. The IRB may request additional information from investigators and participating physicians, such as curricula vitae, to assure the qualifications of the research team are appropriate for the proposed study. Research staff working physically at the VA and/or having direct contact with VA participants and/or their identifiable data or human biological specimens, must be credentialed consistent with VA ORD guidelines.

### Credentialing and Education Verification for New Human Research Projects

The IRB staff will verify new human research personnel included on studies as the RAO receives notification they are to be added or as they are appointed. Individuals involved in a study approved by the VA IRB must complete the education and credentialing requirements consistent with the policies Education Requirements for the Conduct of Research (located at: <https://www.va.gov/portlandresearch/documents/Education-for-Research.pdf> ) and Credentialing of Personnel in Research & Development Service (located at: <https://www.va.gov/portlandresearch/documents/credentialing.pdf> ).

### Inclusion of Women and Minorities in Research

The primary goal of VA’s research program is to conduct research that addresses the high-priority health care needs of Veterans. For this reason, the subject population of VA research needs to reflect the demographics of the Veteran population so long as this inclusion does not compromise the scientific integrity of the research. The demographic profile of Veterans is unlike the U.S. population as a whole, and is constantly changing. Special efforts must be made, when scientifically appropriate, to include women Veterans and Veterans who are members of minority groups in studies of diseases, disorders, and conditions that disproportionately affect these Veteran groups. This applies to all VA research activities involving human subjects, human specimens, and/or tissues. When there are insufficient numbers of Veterans to complete a study, every effort must be made to enter non-Veterans subjects who meet the demographic profile of the Veteran population (see below regarding participation of non-Veterans.) The IRB considers the inclusion of women and minorities in research through a question on the IRQ and a corresponding item in the applicable IRB reviewer checklist.

### Relevance to the VA Mission

The investigator must provide information regarding the relevance of the research to the mission of the VA and the Veterans in the study protocol. The IRB will consider the relevance of the research to the mission of VA and the Veteran population that it serves.

### Participation of Non-Veterans as Research Participants

Non-Veterans may be recruited for studies that will generally benefit Veterans and their well-being but would not necessarily include Veterans as subjects. Examples of such studies include those involving surveys of VA providers, Veterans’ family members, or active duty military personnel. Although active duty military personnel are not considered Veterans, they should be included in VA studies whenever appropriate and may be entered into VA research conducted jointly by VA and DoD or within DoD facilities.

If an investigator would like to recruit non-Veterans in a research project, they must provide a justification in the research protocol for including non-Veterans to the IRB, and the IRB consider the justification and provide rationale for any issues with non-Veteran enrollment as part of their review.

All the regulations pertaining to the participation of Veterans as research participants, including requirements for indemnification in case of research-related injury, pertain to non-Veteran participants enrolled in VA-approved research. Once approval from the IRB to enroll non-Veterans has been received, non-Veteran participants must be treated in the same manner as Veterans. However, in addition to signing the ICF and HIPAA authorization (as applicable), each non-Veteran participant, as well as Veterans not enrolled in VHA health care, must also be provided with a copy of the VA Notice of Privacy Practices, as well as sign VA Form 10-0483: Acknowledgement of the Notice of Privacy Practices (<https://www.va.gov/portlandresearch/documents/irb/10-0483-fill.pdf>).

### Ionizing Radiation

All studies involving Radiological devices or procedures are reviewed by the RSO, who is a member of at least one IRB. Studies reviewed by the other IRB that include a radiation component are also sent to the RSO for review. The RSO reviews the science of the radiation dose absorbed, performs an additional risk assessment particular to the use of radiation, and assures that the use of radioactivity and the conduct of procedures are appropriate.

The PI must clearly indicate on the IRQ (or electronic equivalent), whether the research project involves any x-ray or radioactive materials and provide additional information as appropriate on an IRB appendix, including the procedures, frequency and purpose. The PI must also determine if the procedures are those which the participant would receive even if they were not enrolled in the study, i.e. which procedures are standard of care.

In reviewing the study, the RSO will determine whether the planned exposure is within the allowable limit and whether or not the ICF adequately reflects the risks to participants. The RSO will utilize the following guidelines when evaluating overall risk and the risk-benefit ratio:

1. Radiation exposure being done for the standard of care and uses routine procedures: The IRB may request review or consultation by the RSO. The ICF will frequently make only general mention of the exposure.
2. Radiation exposure exceeds the standard of care, using routine procedures, and offers the prospect of direct benefit to the participant: The ICF must differentiate which procedures are being done for standard of care and which are being done solely for research. The ICF must state that the total dose exceeds standard care, and what risks may occur versus standard care. When radiation exposure is research-related, the ICF should clearly describe in lay language the quantity, significance, and risk, if any, of the radiation absorbed dose. The ICF must include the boilerplate information in the VA ICF Template.
3. Radiation exposure exceeds the standard of care, using routine procedures, and offers no prospect of direct benefit to the participant: When radiation exposure is research-related, the ICF should clearly describe in lay language the quantity, significance, and risk, if any, of the radiation absorbed dose. The ICF must include the boilerplate information in the VA ICF Template.

### Research Involving Deception or Withholding of Information

Sometimes in psychological or educational research, deception is necessary to prevent participant bias. Whenthe IRB reviews research projects involving incomplete disclosure or deception, it must apply both common sense and sensitivity to the review. The IRB must be satisfied that any deception is necessary and that, if appropriate, the participants will be debriefed. Debriefing may sometimes be inappropriate, e.g., if the debriefing itself would present an unreasonable risk of harm without a corresponding benefit. The IRB must also assure the proposed participant population is suitable.

Deception may only be permitted where the IRB documents that an alteration of informed consent (i.e. alteration of the usual informed consent requirements) is justified under the criteria present in VA regulations and the Common Rule and 38 CFR 16.116(d). Specifically, the IRB must find and document that all four of the following criteria have been satisfied:

* + 1. The research presents no more than minimal risk to participants.
    2. The alteration shall not adversely affect the rights and welfare of the participants.
    3. The research could not practicably be carried out without the alteration.
    4. Where appropriate, the subjects shall be provided with additional pertinent information after

participation.

In making the determination to approve the use of deception under an alteration of informed consent, the IRB should consider each criterion in turn, and document specifically (in the minutes of its meetings and/or in the IRB protocol file) how the proposed research satisfies that criterion.

### Evaluations of Adequacy of the Research Site and Institutional Commitments

The protocol (or protocol) should include a statement about the resources available to conduct the research, including information about the research space. Based on the protocol and other study documents provided by the investigator, the IRB should consider whether the research location will have a negative impact on the research, and whether the research site is adequate. The consideration is documented by the primary reviewer(s) on a reviewer checklist or equivalent tool. Special attention to this issue should be given in cases that the research site is not at the VAPORHCS; for example, if the research will be conducted at a community based outpatient clinic, a Vet Center, or some other site that is under the IRB’s purview.

### Review of Proposed International Research

International research (as defined in Section III) includes multi-site trials involving non-US sites where VA is the study sponsor, a VA investigator is the overall study-wide PI, VA holds the Investigational New Drug (IND), or the VA manages the data collection and the data analyses. International research does not include studies in which VA is only one of multiple participating sites (e.g., collaborative research) where the overall study-wide PI is not a VA investigator (i.e., the PI for the study as a whole is not a VA investigator).

Before approving international research involving human subjects research, the IRB must ensure that human subjects outside of the US who participate in research projects in which VA is a collaborator receive equivalent protections as research participants inside the US.

Guidance on the requirements for approving international research can be found here: <https://www.research.va.gov/resources/policies/guidance/intl-research.pdf>.

# Informed Consent Requirements and Documentation

## Purpose of Informed Consent

Researchers must obtain the legally effective informed consent of the participant or the participant’s legally authorized representative **before** conducting any procedures required by the protocol, unless the informed consent requirements are waived by the IRB or the study is exempt from IRB review. Informed consent is an ongoing process of information exchange between the prospective research participant and a trained individual conducting the consent process. Informed consent presumes two simultaneous concepts: informed decision-making and voluntary participation. Prospective participants must be given sufficient information about the research and its risks and potential benefits to reach an **informed decision** as to whether they will **voluntarily participate.**

The consenting process begins during participant recruitment and includes any oral instructions and/or explanations, presentation of the written ICF and any other materials approved by the IRB, the opportunity for the individual to ask questions and receive satisfactory answers, signing of the written agreement by the participant or legal representative and, in some cases, a witness. If a potential participant or LAR seems hesitant about participating in a study or feels they should discuss participation with any family members, the investigator or his/her representative must allow the participant ample time to consider and make his/her decision. The participant may contact the researcher at a later time to agree to participate in the study and sign the formal document. Throughout the study, the PI and other research staff should encourage the participant to ask questions at any time during procedures or study visits or to contact a researcher if a question arises between visits.

## Circumstances of Informed Consent Requirements

To approve research, the IRB must determine that legally effective **informed** **consent** shall be sought from each prospective participant or the participant's LAR, unless informed consent requirements can be waived or altered under VA regulations.

As part of the informed consent process, there should be an assessment of the prospective research participant’s capacity to consent to the research protocol, prior to consenting the individual, to ensure that s/he is able to understand the study procedures and all risks and benefits in order to make an informed decision. The IRB may determine that, for a high-risk study, specific procedures should be put in place to assess the research participant’s capacity to consent. If the individual does not have capacity to consent, surrogate consent may be obtained from an LAR, as described in Section XIX.

The General Requirements for Informed Consent include:

1. Presenting and ensuring the informed consent information is presented in a language that is understandable to the participant (or the participant’s LAR).
2. Excluding any exculpatory language from the informed consent process:
3. Through which the participant or their LAR is made to waive, or appear to waive, any of the participant’s legal rights, or
4. Through which the researchers, sponsor, VAPORHCS, or VAPORHCS’s employees or agents are, or appear to be, released from liability for negligence.
5. Obtaining legally effective informed consent from the participant or their LAR prior to initiation of any procedures that are performed for the purposes of research, unless the IRB approves allowing screening procedures to occur prior to consent, as allowable per applicable requirements.
6. Providing the prospective participant or the LAR with sufficient opportunity to discuss and consider whether or not to participate.
7. Ensuring that participants or their LARs provide consent without coercion or undue influence.

***For research that is subject to the 2018 Requirements:***

1. The prospective participant or the LAR must be provided with the information that a reasonable person would want to have in order to make an informed decision about whether to participate, and an opportunity to discuss that information.
2. Informed consent must begin with a concise and focused presentation of the “key information” that is most likely to assist a prospective participant or LAR in understanding the reasons why one might or might not want to participate in the research.
3. Informed consent as a whole must present information in sufficient detail relating to the research and must be organized and presented in a way that does not merely provide lists of isolated facts, but rather facilitates the prospective participant’s or LAR’s understanding of the reasons why one might or might not want to participate.

***For research that is subject to the 2018 Requirements:***

Screening, Recruiting or Determining Eligibility: The IRB may approve a research proposal in which an investigator will obtain information or biospecimens for the purposes of screening, recruiting, or determining the eligibility of prospective subjects without the informed consent of the prospective subject or the subject’s LAR if either of the following conditions is met:

* + 1. The investigator will obtain information through oral or written communication with the prospective subject or LAR; OR
    2. The investigator will obtain identifiable private information or identifiable biospecimens by accessing records or stored identifiable biospecimens.

***NOTE:*** *A waiver of HIPAA authorization must be approved prior to accessing any PHI for screening, recruiting, or determining the eligibility. Informed consent is required before any research interventions occur after eligibility is determined.*

## Consent after Anxiolysis, Sedation or Anesthesia Care

Care must be given to evaluate a research participant’s capacity to consent after they have had anxiolysis, sedation or anesthesia care. This includes taking into account the following:

1. The ideal informed consent process occurs no sooner than 18-24 hours after anxiolysis, sedation, or anesthesia care, regardless of the type or amount of sedative(s) used.)
2. No informed consent process shall occur sooner than 12 hours after anxiolysis, sedation, or anesthesia care, regardless of type or amount of sedative(s) used.
3. If the 12-hour post-sedation time frame occurs during the hours of 10 pm-6 am, the informed consent process shall occur after participants have rested overnight.
4. No informed consent shall be obtained from a legally authorized representative if the participant is an otherwise competent person and will be able to provide adequate informed consent after the effects of sedation subside.
5. Researchers who foresee logistical difficulties meeting these guidelines may ask the IRB for consideration of exceptions for a particular study. The ACOS/R&D will also review any concerns raised by researchers.

## Documentation of Informed Consent

Unless the IRB determines that the applicable criteria are met to waive the requirement for an informed consent process and/or for documentation of informed consent, informed consent shall be documented by the use of a written consent form approved by the IRB. VA regulations, the Common Rule, and FDA regulations provide two methods for documenting informed consent:

1. **Written Informed Consent Document**

In cases that consent must be documented, the IRB must determine that the ICF embodies all of the required elements of informed consent (these elements are discussed in detail in Section XVII, K-M). The most current IRB-approved version must be used for consenting participants. IRB approval of the consent form will be documented on the ICF, indicating the date of IRB approval.[[1]](#footnote-1)

The form must be signed and dated by the participant or the participant’s LAR. A copy must be given to the person signing the form.

The person obtaining consent must also sign the ICF, unless the IRB waives this requirement (even when the signature of the participant or their LAR continues to be required). This requirement may be waived by the IRB when the study involves no physical contact with the subject (e.g., where the only contact with the subject is by telephone or mail).

With prior IRB approval, consent may be obtained electronically so long as the informed consent process meets all of the requirements outlined in Section XVII.K-M and as per VA regulations. In addition, authentication controls on electronic consent must provide reasonable assurance that such consent is rendered by the proper individual, and the participant or their LAR must date the electronic consent as is typical or the software must provide the current date when signed.

When applicable, a copy of the signed ICF must also be forwarded to the Research Pharmacy prior to dispensing any investigational drug. FDA regulations require that the signature be dated. This form may be read to the potential research participant or his/her LAR. The potential participant/LAR must be given adequate time to read the document and make a decision regarding participation prior to signing the ICF.

a. **Additional Considerations Regarding Written Informed Consent**

If a photograph, video recording or audio recording of a human participant for research purposes, the ICF for research must include information describing any photographs, video, and/or audio recordings to be taken or obtained for research purposes, how they will be used for the research, and whether they will be disclosed outside the VA. An informed consent to take a photograph, video, and/or audio recording cannot be waived by the IRB. ***NOTE:*** *The consent for research does not give legal authority to disclose the photographs, video, and/or audio recordings outside VA. A HIPAA authorization is needed to make such disclosures.*

For research following a DOD Addendum, the IRB must determine that the ICF includes provisions for research-related injury that follow the requirements of the DOD component. The most recent DOD ICF may be employed for active duty personnel participating in VA research.

If approved by the IRB, the participant may submit the signed and dated ICF to the investigator or designee by facsimile.

1. **Short Form Written Informed Consent**

Consent may also be documented through use of a “short form” written consent document, which states that the required elements of informed consent have been presented orally to the participant or their LAR in a language understandable to the participant or LAR. The oral presentation must contain all of the information that is contained in the “short form” written consent document. When this method is used, the following is necessary:

* 1. The IRB must approve the “short form” written consent document and a written summary of what is to be presented orally. The written summary must embody the basic and required additional elements of consent.
  2. There must be a witness to the oral presentation; the witness must speak both English and, if applicable, the language of the participant.
  3. The “short form” must be signed by the participant (or LAR) and the witness.
  4. The written summary must be signed the witness and the person actually obtaining consent.
  5. If the research is FDA-regulated, the participant or LAR must date the “short form”.
  6. A copy of the summary and the “short form” must be given to the participant (or the LAR).
  7. The original signed “short form” and summary must be filed in the PI’s research file for that participant.

***NOTE:*** *The IRB cannot waive the requirement for a witness or witness signature when the short form consent is used.*

***For research that is subject to the 2018 Requirements:***

The “short form” written consent document must also state that key information, as described in Section XVII.K, was presented first to the participant or their LAR before any other information, if any, was provided.

## Approval Date on Informed Consent Documents

The IRB approval date will be documented on the ICF or “short form.” At initial approval, the approval date on the consent document(s) is the date of initial IRB approval. If the consent document(s) is amended during the protocol approval period, the approval dated on the consent document(s) is the approval date of the amendment. At continuing review, the ICF and/or “short form” must be documented with the new approval date, even if no changes have been made to the document(s).

## Individuals Authorized to Conduct the Informed Consent Process

The PI is authorized to conduct the informed consent process. If the PI may not personally obtain informed consent from all participants, they must delegate these responsibilities in writing to properly trained individuals.

The PI is responsible for ensuring that the individuals whom they authorize to conduct the informed consent process are sufficiently knowledgeable of the research project and procedures, as well as the informed consent process. The designee must be able to adequately answer questions or concerns raised by the potential research participant or legally authorized representative during the consent process.

If the PI wishes to contract with a firm (e.g., a survey research firm) that will obtain consent and/or collect private individually identifiable information from human subjects, and/or will be involved in activities that would institutionally engage the firm in human subjects research, the firm must have its own IRB oversight of the activity. In addition, the Privacy Officer must determine that there is appropriate authority to allow the disclosure of individual names and other information to the contracted firm.

## Observation of the Informed Consent Process

The IRB has the authority to observe the informed consent process of any currently active research study. Situations where the IRB might consider such observation might include reports of a complaint or possibility of undue influence or coercion, or an audit that raises doubts about the adequacy of the informed consent process. An IRB member or designee may observe a consent session as an impartial observer or conduct structured interviews of research participants.

In addition, informed consent documentation is reviewed by the RCO or designee to assure that it was correctly completed and that all required signatures are in place.

## Witnesses of Informed Consent Process

A witness must be present as follows:

1. The IRB may require a witness to be present during the signing of the written informed consent document. Unless specified otherwise by the sponsor or IRB, the witness does not need to witness the entire informed consent process, only the signing of the document. The witness must also sign and date the written informed consent document. The witness may not be the person obtaining consent but may be another member of the study team or a family member of the participant or LAR.
2. If the sponsor or IRB requires a witness to the consenting process, a witness must be present during the entire informed consent process. If this requirement is in addition to the witness to the participant’s signature and the same person is to serve in both capacities, a note to that effect must be placed under the witness’ signature line.
3. When a “short form” written consent document is used, a witness is always required to be present during the informed consent process, as well as the signing. The witness must sign and date both the short form written consent document and the summary of the oral presentation given to the participant or the participant’s LAR. Again, the witness may not be the person obtaining consent. Ideally, the witness would be a family member or friend of the research participant, but may also be a staff member or member of the study team.

## Informed Consent Reading Level and Language

VA regulations, the Common Rule, and FDA regulations require that informed consent documentation be written at the appropriate reading level of the potential participant population and be obtained in a language that is understandable to the participant (or the participant’s legally authorized representative).

In cases where informed consent must be obtained from non-English speakers, the PI is responsible for working with the IRB to determine that an effective and appropriate method is in place. This may include the use of a reliable, certified translator or a certified translation of the informed consent document.

## Exculpatory Language

The informed consent, written or oral, may not contain any exculpatory language through which the participant or the LAR is made to waive or appear to waive any of the participant’s legal rights, or releases or appears to release the researchers, sponsor, and/or the institution or its agents from liability for negligence.

## Required Basic Elements of Informed Consent

To ensure an effective informed consent process, VA regulations, the Common Rule, and FDA regulations mandate the inclusion of the fundamental informed consent elements and additional elements when appropriate. Depending on the nature of the research, an may request elimination of any of the elements.

The following information will be provided to each participant:

1. Name of the Study
2. The name of the PI
3. A statement that the study involves research
4. An explanation of the purposes of the research
5. The expected duration of the subject’s participation
6. A description of the procedures to be followed
7. Identification of any procedures which are experimental
8. Description of any reasonably foreseeable risks or discomforts and possible unforeseeable risks to the participant:Risks may include physical, psychological, social or economic risks.A statement must be included that the particular treatment or procedure might involve risks to the participant that are currently unforeseeable.
9. Reasonably expected benefits to participants or others: Care must be taken not to overstate the benefits and create an undue influence on participants. Payment for subject's participation in a research project is not to be considered as a benefit of the research.
10. Appropriate alternatives to participation that might be advantageous to the participant.
11. Extent of privacy and confidentiality: Research often poses the risk of loss of confidentiality to participants. Many persons who would not otherwise have access to identifiable, private information about the participant may be involved in the research process. Consent information should describe any procedures that the research team will use to protect participants' confidential records. In some research, loss of privacy and confidentiality may be the greatest risk of participation. For FDA-regulated studies, consent forms must include a statement that the FDA may inspect research records. *NOTE: All potential disclosures of protected health information to a non-VA entity must be listed within the HIPAA authorization (when use of a HIPAA authorization is applicable).*
12. Compensation or treatment for injury:Informed consent information must include explanations regarding the following:
13. For studies that are greater than minimal risk: Whether any compensation is available, whether any medical treatments are available if injury occurs and if so, what they consist of or where further information may be obtained.
14. In accordance with Federal law, a statement that VA will provide necessary medical treatment to a research participant injured by participation in a research project approved by the VAPORHCS R&DC and conducted under the supervision of one or more VA employees. ***NOTE:*** *This does not apply to injuries due to noncompliance by a subject with study procedures or to research conducted for VA under a contract with an individual or a non-VA institution (although Veterans injured as a result of participation in such research may nevertheless be eligible for care from VA under other statutory and regulatory provisions). Information on the responsibility for research-related injury under such circumstances must be included in the consent form.*
15. Contact information must include details, including telephone numbers, about whom to contact for the following types of information:
    1. For answers to questions or to voice concerns about a specific research project, the PI and other members of the research team are appropriate contacts.
    2. For answers to questions about participants' rights, contact the RAO designee or VA Regional Counsel.
    3. In the event of a research-related injury, the VA Regional Counsel, the RAO designee and the researchers are all appropriate contacts.
    4. To speak with someone unaffiliated with a specific research project to ask questions or voice concerns about participant’s rights, offer input, or to voice complaints about any VA research, participants should be given contact information for the Research Service, the RAO designee, and the VA Regional Counsel.
16. Voluntary participation statement: It is particularly important at the VA for participants and prospective participants to understand and have complete confidence that failure to participate will not jeopardize their VA-provided care. Informed consent information must contain the following statements:
    1. Participation in the research is voluntary.
    2. Refusal to participate will involve no penalty or loss of benefits to which the participant is otherwise entitled and the participant may discontinue participation at any time without penalty or loss of benefits to which they are entitled.

***For research that is subject to the 2018 Requirements:***

In addition to the required elements listed above, the informed consent must include a statement indicating that identifiers might be removed and the de-identified information or biospecimens used for future research without additional informed consent from the subject or their LAR.

## Additional Elements of Informed Consent, Required Where Appropriate

In accordance with regulations, the following information will be provided to each participant, when appropriate.

1. Unforeseeable risks to participants, embryos, or fetuses:A statement that the particular treatment or procedure may involve currently unforeseeable risks to the participant (or to the embryo or fetus if the participant is or may become pregnant).
2. Investigator-initiated termination of participation:The informed consent information must specify anticipated circumstances (e.g., participant noncompliance with research, participant not benefiting from research) under which the subject’s participation may be terminated by the investigator without regard to the participant’s consent.
3. Additional costs**:** Any additional costs to the participant that may result from participation in the research with consideration of Federal laws concerning Veterans’ eligibility for medical care and treatment.
4. Early withdrawal/procedures for termination:Participants have the right to withdraw from the research. However, some studies involve medications or procedures that would be dangerous for participants to discontinue abruptly. For studies of this nature, the informed consent documentation must inform participants of the possible consequences of a decision to withdraw. Note also the following:
5. If there are procedures regarding how to withdraw safely from the research, these must also be described.
6. It is not appropriate for research staff to administer any additional research-oriented questionnaires or interventions to participants who have decided to withdraw unless required for the safety of the participant.
7. The consent document cannot give the participant the option of having data removed if they withdraw. The data already collected remains part of the study database. Researchers may also consult public records, e.g., records establishing survival status.
8. If a participant chooses to withdraw only from the interventional portion of a study and wishes to continue to be followed for associated clinical outcome information, informed consent must be obtained for this as described in the original approved ICF. The IRB must approve a new consent form for this purpose.
9. Significant new findings: The participant must be informed that any significant new knowledge or findings developed during the course of the research that might affect the risks or benefits and therefore the participant’s willingness to continue participation will be provided to the participant. The ICF must detail the procedures for contacting participants regarding this new information and for affirming their continued participation.
10. Approximate number of participants to be involved in the study.
11. FDA-regulated studies: Research involving an FDA-regulated test article requires a statement that the FDA may choose to inspect research records that includes the participant’s individual medical records. In addition, there must be a statement in the ICF that the study will be registered on [www.Clinicaltrials.gov](http://www.Clinicaltrials.gov).
12. Payment for participation:Ifappropriate, the informed consent information should include a clear statement describing any payment the participant is to receive for participation, the required conditions for payment, and the payment schedule. Since VA regulations, the Common Rule, and FDA regulations all state that participants may withdraw from research at any time without penalty of loss of benefits to which they are otherwise entitled, completing the research may not be made a condition of payment. Therefore, the informed consent information should be a description of how payment will be prorated and calculated for participants who withdraw early.
13. If the research will involve taking photographs or making voice or video recordings, a discussion of the fact that they are being taken for the research, who will have access to them, and what their disposition will be after the research is completed.
14. Any real or apparent conflict of interest by investigators where the research will be performed.
15. Costs:Informed consent information must indicate to VA research subjects that neither they nor their insurance will be charged for any costs related to the research. Researchers should note, however, that certain Veterans are subject to co‑payments for medical care, pharmaceutical, and services provided by VA that are not part of the research procedures or interventions.

***For research that is subject to the 2018 Requirements:***

Informed consent must include the following *additional* information, when appropriate:

* biospecimens, even if identifiers are removed, may be used for commercial profit and whether the subject will share in the profit
* whether clinically relevant research results will be disclosed to subjects or their LAR and, if so, under what conditions
* whether the research project will or might include whole genome sequencing

## Human Biological Specimen Consent Elements

If human biological specimens will be obtained as part of a research study, the following information should be included as part of informed consent.

1. A statement of whether or not the specimen will be used for future research, and options for how the specimen may be used (any research, research by the PI, or other researchers, genetic analysis, research related to specific area, etc.).
2. If the specimens may be used for future studies, information regarding where the specimens will be retained, who will have access to them, and how long they will be retained.
3. Whether or not the participant will be re-contacted after the original study is completed.
4. As applicable, a statement that, if the participant requests, the specimen and all links to the clinical data will be destroyed.

## Routing of Signed Informed Consent Forms

VHA policy requires a copy of the signed consent documents and the signed HIPAA authorizations for all research participants be submitted to the RCO, for auditing purposes per their current policy, as soon as possible, preferably within 3 business days of consenting the participant. If ICFs are signed by participants at home and then returned by mail, they must be stamped with a “received date” prior to submission to the RCO for auditing.

## Medical Records

The PI is responsible for assuring that a medical record is created in the electronic health record for all research participants who do not already have such a record and are admitted as in-patients, treated as outpatients, and/or have research procedures or interventions that are used in or may impact their medical care at a VA medical facility or at facilities contracted by VA to provide services to Veterans. Creation of a medical record requires identifiable information, such as the participant’s name, social security number, date of birth and address. Informed consent and HIPAA authorization documents are not required to be in the medical record.

Individual participants that don’t have electronic health records are not required to have one created, if the Principal Investigator has determined the study doesn’t require progress notes (e.g. subjects are not admitted as in-patients, treated as outpatients, or have research procedures or interventions that re used in or may impact their medical care). ***NOTE:*** *See Section V, Principal Investigator responsibilities and Section XVII.P, Progress Notes.*

When access to patient health records is no longer required, the study has been completed, or when authorization is revoked, the Principal Investigator, or designee, must notify the facility Health Information Management System (HIMS) professional and, if applicable, the ISSO. Instructions for notifications will be provided by HIMS, and when applicable the ISSOs. ***NOTE:*** *See VHA Directive 1907.01 and/or VAPORHCS facility HIMS professional for guidance.*

## Progress Notes

Progress notes must be entered for individual participants as noted below. The PI is responsible for ensuring that the progress notes are created for each individual participant as soon as possible and no later than 24 hours after a research visit. Progress notes must be identified as research notes to differentiate from other clinic visits. A progress note must be created for all research subjects (Veterans or non-Veterans) who receive research procedures or interventions as inpatients or outpatients at VA medical facilities that are either used in or may impact the medical care of the research subject at a VA medical facility or at facilities contracted by VA to provide services to Veterans (e.g., Community-Based Outpatient Clinics or community living centers). ***NOTE:*** *See Section V, Principal Investigator responsibilities.*

1. Encounters and/or procedures for research must be coded as non-billing events.
2. A progress note must also be entered, or included in the other progress notes, for the following:
3. For drug studies, the researcher must enter a progress note when a participant is enrolled and list any drug interactions and/or toxicities, e.g. in the target participant population, that are not included or are not listed in sufficient detail on VA Form 10-9012 or directing attention to the 10-9012 if no additional information is needed. VA Form 10-9012 or superseding forms as defined in VHA Handbook 1108.04 per VHA Directive 1907.01 are entered by the Research Pharmacy.
4. A copy of any research results used for medical care.
5. For documentation of capacity to consent (as described in Section XI.D., Determining Capacity to Consent).
6. For documentation of surrogate consent from a Legally Authorized Representative (LAR) (as described in Section XIX.E., Legally Authorized Representative).
7. For documentation of IRB approval to dual enroll an individual in two research studies that have required research flags (as described inSection XI.I., Process for Research Flags).

***NOTE:*** *For additional guidance and progress notes requirements related to informed consent/refusal, capacity to consent and/or surrogate consent from a LAR, please see VHA Handbook 1004.01.*

## Waiver of Documentation of Consent

An IRB may waive the requirement to obtain written documentation of informed consent for some or all of the participants based on criteria below. ***NOTE:*** *This provision can be used only for the waiver of documentation of consent, not for waiver or alteration of consent itself.*

To approve such a waiver, the IRB will review a written description of the information that will be provided to participants. The IRB may also require the investigator to provide participants with a written statement regarding the research. The IRB also must find and document **either** of the following conditions:

1. The only record linking the participant and the research would be the consent document and the principal risk would be potential harm resulting from a breach of confidentiality. In this case, each participant may be asked whether the participant wants documentation linking the participant with the research, and the participant's wishes will govern. (This waiver provision is **not** applicable to FDA-regulated research.)

**OR**

1. The research presents no more than minimal risk of harm to participants and involves no procedures or activities for which written consent is normally required outside of the research context. (This waiver provision is allowable for both FDA and non-FDA regulated research.)

IRB minutes shall clearly reflect this waiver provision and the justification for its use. The IRB may also waive the Health Insurance Portability and Accountability Act of 1996 (HIPAA) requirements for an authorization for research purposes. In these cases, the IRB must additionally document the justification for its use. Please see HRPP policy, Health Insurance Portability & Accountability Act (HIPAA) in Human Subjects Research located at: <https://www.va.gov/portlandresearch/documents/hrpp/hipaa.pdf>.

***For research that is subject to the 2018 Requirements:***

The IRB may also waive the requirement to obtain a signed informed consent form for some or all participants if the IRB finds and documents that the participants or LARs are members of a distinct cultural group or community in which signing forms is not the norm, the research presents no more than minimal risk of harm to subjects, and an appropriate alternative mechanism for documenting that informed consent was obtained will be used.

## Waiver or Alteration of Informed Consent Requirements (Waiver of Consent Process)

VA regulations permit the IRB to approve a consent procedure that does not include or that alters some or all of the required elements of informed consent, or to waive the requirement to obtain informed consent altogether. To approve such a waiver or alteration, the IRB must find and document the following:

1. The research or demonstration project is to be conducted by, or is subject to, the approval of state or local government officials and is designed to study, evaluate, or otherwise examine:
2. Public benefit or service programs,
3. Procedures for obtaining benefits or services under those programs,
4. Possible changes in or alternatives to those programs or procedures, or
5. Possible changes in methods or levels of payment for benefits or services under those programs; and
6. The research could not practically be carried out without the waiver or alteration.

**OR**

1. The research involves no more than minimal risk to the participants, and
   1. The waiver or alteration will not adversely affect the rights and welfare of the participants,
   2. The research could not practically be carried out without the waiver or alteration, and
   3. Whenever appropriate, the participants will be provided with additional pertinent information after participation.
   4. For research subject to the 2018 Requirements, in addition to 2.a-c above: If the research involves using identifiable private information or identifiable biospecimens, the research could not practicably be carried out without using such information or biospecimens in an identifiable format

For an alteration of the consent requirements, an IRB may not omit or alter any of the requirements described in Section XVII.B.1-9.

These findings and their justifications shall be clearly documented in IRB minutes. The IRB may not approve such alterations or waivers for FDA-regulated research. The waiver or alteration of informed consent requirements for FDA-regulated articles is applicable only for emergency use (see the HRPP policy, Investigational Device and/or Drug Usage located at: <https://www.va.gov/portlandresearch/documents/hrpp/investigational-device.pdf>)

The IRB may also waive the Health Insurance Portability and Accountability Act of 1996 (HIPAA) requirements for an authorization for research purposes and must also document justification of this waiver. See the HRPP policy, Health Insurance Portability & Accountability Act (HIPAA) in Human Subjects Research located at: <https://www.va.gov/portlandresearch/documents/hrpp/hipaa.pdf>

For research conducted under a DOD Addendum, if the research participant meets the DOD definition of “experimental subject,” (see Section III. Definitions) a waiver of the consent process may not be granted unless a waiver is obtained from the Secretary of Defense. If the research participant does not meet the definition of “experimental subject,” a waiver may be approved based on the criteria above.

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## Exceptions from Informed Consent for Emergency Use of a Test Article

Please see the HRPP policy, Investigational Device and/or Drug Usage, for exceptions to informed consent during emergency use of a test article located at: <https://www.va.gov/portlandresearch/documents/hrpp/investigational-device.pdf>.

## Activities Preparatory to Research

VA investigators may use individually-identifiable health information to prepare a research protocol prior to submission of the protocol to the IRB for approval without obtaining a HIPAA authorization or waiver of authorization. Activities preparatory to research only encompass the time to prepare the protocol and ends when the protocol is submitted to the IRB. Contacting potential research subjects and conducting pilot or feasibility studies are not considered activities preparatory to research.

Investigators may not arbitrarily review PHI and must document the following information as Preparatory to Research:

1. Access to PHI is only to prepare a protocol,
2. No PHI will be removed from VHA, and
3. Access to PHI is necessary for preparation of the research protocol.

The RAO designee will review and approve written requests for Preparatory to Research activities and instruct the investigator to retain the determination for purposes of audit documentation.

Non-VA researchers may not obtain VA information for preparatory to research activities without appropriate VA approvals (see Directive 1605.01).

During preparatory to research activities, the VA investigator:

* + - 1. Must only record aggregate data, which may only be used for background information to justify the research or to show that there are adequate numbers of potential subjects to allow the investigator to meet enrollment requirements for the research study;
      2. Must not record any individually identifiable health information; and
      3. Must not use any individually identifiable information to recruit research subjects.

***NOTE****: Preparatory activities can include reviewing database output (computer file or printout) containing identifiable health information generated by the database owner, if the investigator returns the database output to the database owner when finished aggregating the information.*

# Review of Research Involving Subject Groups Requiring Special Protections

As listed in the Federal regulations, some subject populations may be vulnerable to coercion or undue influence, including:

* Prisoners
* Persons with impaired decision-making capacity
* Children
* Economically or educationally disadvantaged persons

The IRB must be cognizant of the vulnerable nature of the groups listed above, as well as other groups that may be vulnerable to coercion or undue influence. However, Veterans as a whole should not be considered an inherently vulnerable population. The IRB must carefully evaluate each protocol to determine whether vulnerable subjects are included in the study population and what measures have been taken to protect them.

## Elements to Consider in Reviewing Research Involving Vulnerable Subjects

VA regulations and FDA regulations require the IRB to give special consideration to protecting the welfare of particularly vulnerable subjects, such as children, prisoners and economically or educationally disadvantaged persons.

The IRB is required to consider the scientific and ethical reasons for including vulnerable populations in research. The IRB is also required to have adequate representation on the IRB to consider specific kinds of research involving these vulnerable populations in a satisfactory manner.

The IRB must pay special attention to specific elements of the research plan when reviewing research involving vulnerable subjects. These IRB should:

1. Consider strategic issues, such as inclusion and exclusion criteria for selecting and recruiting participants; informed consent and willingness to volunteer; coercion and undue influence; and confidentiality of data.
2. Consider group characteristics, such as economic, social, physical, and environmental conditions, to ensure that the research incorporates additional safeguards for vulnerable subjects.
3. Ensure that certain groups are not over-selected or excluded, based on perceived limitations or complexities associated with those groups. For example, it is not appropriate to target prisoners as research subjects merely because they are a readily available "captive" population.
4. Ensure that, just as in providing regular medical care, research studies that plan to involve any potentially vulnerable populations must have adequate procedures in place for assessing and ensuring subjects' capacity and understanding, and for obtaining informed consent or assent. When weighing the decision whether to approve or disapprove research involving vulnerable subjects, the IRB shall look to see that such procedures are a part of the research plan. In certain instances, it may be possible for researchers to enhance understanding for potentially vulnerable subjects (for example: requiring someone not involved in the research to obtain the consent; the inclusion of a consent monitor, a subject advocate, and/or an interpreter for hearing-impaired subjects; translation of ICFs into languages the subjects understand; and reading the consent form to subjects slowly and ensuring their understanding, paragraph by paragraph).
5. Consider when it may be appropriate to require additional safeguards to protect potentially vulnerable populations. For example, the IRB may require that someone other than the primary care provider conduct the informed consent session, that someone from the IRB oversee the consent process, that additional measures for evaluating capacity to consent are utilized and/or that a waiting period be established between initial contact and enrollment in order to allow time for family discussion and questions.
6. Utilize their access to legal counsel at the VAPORHCS for assistance in interpreting laws for the protection of research participants, e.g., in the case of determining whether a person is competent to consent.

## Pregnant Women, Neonates and Fetuses

The DHHS regulations detail special protections for research involving pregnant women, neonates, fetuses, and human *in vitro* fertilization. Under these regulations, the IRB is required to document specific findings to minimize the potential for risk or harm to the neonate or fetus, and additional attention must be given to the conditions for obtaining informed consent.

Unilateral exclusion of non‑pregnant women of reproductive potential from research is not permitted by the IRB. However, given compelling scientific justification, this type of exclusion may be considered by the IRB, as well as whether it may also be appropriate to exclude men of reproductive potential.

Per VHA Directive 1200.05, research that uses human fetal tissue or that focuses on either a fetus, or focuses on either a fetus, or human fetal tissue, in-utero or ex-utero cannot be conducted by VA investigators while on official VA duty, at VA facilities, or at VA-approved off-site facilities. Use of stem cells shall be governed by the policy set by NIH for recipients of NIH research funding (<https://stemcells.nih.gov/policy/2009-guidelines.htm> ).

For research in which the focus is human stem cells (<https://stemcells.nih.gov/policy/2009-guidelines.htm> ) shall be governed by the policy set by NIH for recipients of NIH research funding.

For research that involves neonates or neonatal outcomes, prospective observational and retrospective record review studies are permitted. VA investigators cannot conduct interventions in research that include neonates while on official VA duty, at VA facilities, or at VA-approved off-site facilities. VA investigators may conduct research involving noninvasive monitoring of neonates if the research is determined by the IRB to be minimal risk. The reviewing IRB must have the appropriate expertise to evaluate any VA research involving neonates and must comply with the requirements of 45 CFR 46.205. The VA medical facility Director must certify that the medical facility has sufficient expertise in neonatal health to conduct the proposed research.

For research that involves of *in vitro* fertilization services, studies involving provision of or the enhancement of FDA-approved methods of *in vitro* fertilization for studies involving consenting subjects, both male and female, undergoing or who have undergone *in vitro* fertilization for the treatment of certain forms of human infertility are permitted. Prospective and retrospective studies that enroll or include pregnant subjects who conceived through in vitro fertilization or other artificial reproductive technologies are also permitted.

***NOTE:*** *Research involving the creation of a human embryo or embryos solely for research purposes or research in which a human embryo or embryos are destroyed, discarded, or knowingly subjected to risk of injury or death greater than that allowed for research on fetuses in utero under 45 CFR 46.208(a)(2) and Section 498B of the Public Health Service Act (42 U.S.C. 289g(b)) cannot be conducted by VA Investigators at VA facilities, or at VA approved off-site facilities*

Women who are known to be pregnant and/or their fetuses may be involved in research if all of the following requirements are met and the VA medical facility Director certifies that the VA medical facility has sufficient expertise in women’s or reproductive health to conduct the proposed research if the research includes interventional studies or invasive monitoring of pregnant women as subjects (see guidance at <https://www.research.va.gov/resources/policies/default.cfm> ), including informed consent requirements and the following ethical and scientific criteria:

1. Where scientifically appropriate, preclinical studies on pregnant animals, and clinical studies on non-pregnant women, have been conducted and provide data for assessing potential risks to pregnant women and fetuses;
2. The risk to the fetus is caused solely by interventions or procedures that hold out the prospect of direct benefit for the woman or fetus, or, if there is no such prospect of benefit, then the risk to the fetus is not greater than minimal and the purpose of the research is the development of important biomedical knowledge that cannot be obtained by any other means;
3. Any risk is the least possible for achieving the objectives of the research;
4. If the research holds out the prospect of direct benefit to the pregnant woman, the prospect of a direct benefit both to the pregnant woman and the fetus, or no prospect of benefit for the woman nor the fetus when risk to the fetus is not greater than minimal and the purpose of the research is the development of important biomedical knowledge that cannot be obtained by any other means, her consent is obtained in accord with the informed consent provisions of this SOP;
5. Each individual providing consent under (2) or (4) of this section is fully informed regarding the reasonably foreseeable impact of the research on the fetus or neonate;
6. For children who are pregnant, assent and permission are obtained in accordance with the provisions of 45 CFR Part 46, Subpart D. Research involving clinical interventions with the potential of greater than minimal risk cannot be conducted by VA for children who are pregnant;
7. No inducements, monetary or otherwise, will be offered to terminate a pregnancy;
8. Individuals engaged in the research will have no part in any decisions as to the timing, method, or procedures used to terminate a pregnancy; and
9. Individuals engaged in the research will have no part in determining the viability of a neonate.

## Collecting Pregnancy Information or Information about Newborns

If a female subject becomes pregnant while participating in VA research, and pregnancy is not the focus of the research, the majority of the time the female subject will no longer receive the clinical intervention described in the IRB-approved protocol once the Investigator is made aware of the pregnancy. If such a female subject is withdrawn entirely from the study, no additional information may be collected about the subject or the pregnancy, as participation is considered to have ended. However, a subject can be withdrawn solely from receiving the intervention and remain in the study, allowing the Investigator to continue data collection and other follow-up activities. Note that the data collection and follow-up activities must be described in the protocol and informed consent approved by the IRB, the HIPAA authorization, and the subject must not revoke that portion of the consent and HIPAA authorization.

If the female partner of a male Veteran research participant becomes pregnant during the period that he is participating in a VA research study, no data may be collected about or from the female or her pregnancy until the IRB-approved protocol includes provisions for collecting information from the pregnant female partner of a male subject enrolled in the research. In addition, informed consent must be obtained from the female partner prior to the collection of any data about her unless the IRB has waived informed consent. The female partner must also provide written authorization for the use of her protected health information.

During the review of the request to collect data about pregnancy and pregnancy outcomes, the IRB must ensure that:

1. The IRB-approved protocol addresses the data collection procedures for obtaining data about the progress of the pregnancy and pregnancy outcomes (live birth with or without birth defects, stillborn, or aborted fetus);

2. Informed consent has been obtained from the adult subject to obtain information about the progress of the pregnancy and pregnancy outcomes, unless the IRB has waived informed consent in accordance with applicable criteria;

3. The data collection involving the pregnant female subject described in the protocol must comply with current VA policies (see guidance at

<https://www.research.va.gov/resources/policies/default.cfm>; and

4. The data collection involving the newborn infant described in the IRB-approved protocol meets 45 CFR 46 subpart D requirements for research activities not involving greater than minimal risk.

## Prisoners as a Vulnerable Population in Research

Research involving prisoners cannot be conducted by VA investigators while on official VA duty, at VA facilities, or at VA-approved off-site facilities unless a waiver has been granted by the CRADO. If such a waiver is granted, the research must comply with the requirements of 45 CFR 46.301 – 46.306.

Waiver requests must be submitted electronically to the CRADO by the VA medical facility Director with the following documents:

1. A letter from the VA medical facility Director supporting the conduct of the VA study involving prisoners;
2. Rationale for conducting the research involving prisoners to include additional ethical protections taken by the proposed research for prisoners to make voluntary and uncoerced decisions whether or not to participate as subjects in research;
3. Documentation of the VA investigator’s qualifications to conduct the research involving prisoners, such as a biosketch and a list of all research team members;
4. Location of institutions where the research is proposed to be conducted;
5. A copy of the IRB approval letter specifically documenting its review determinations according to 45 CFR 46.305(a);
6. A copy of the IRB minutes approving the research with documentation that at least one member of the IRB included a prisoner or a prisoner representative for the review of the research;
7. A copy of the IRB-approved research study;
8. A copy of the IRB-approved informed consent document; and
9. A copy of the written HIPAA authorization.

**Incarceration During a Study** - If a subject becomes incarcerated during the course of their participation in a study:

1. Researchers must notify the IRB as soon as they become aware that the subject has been incarcerated.
2. The researcher must make a determination as to whether or not it is the best interests of the subject to remain in the study, or if the subject can be safely withdrawn from the study.
3. If the researcher determines it is in the best interest of the subject to remain in the study, the subject’s continued participation in the study is contingent on the IRB’s reviewing and approving such participation. The IRB approval must comply with all applicable VA and Federal regulations for including prisoners in research.
4. After IRB and other relevant approvals (e.g., from the penal system) for the incarcerated subject’s continued participation in the study have been obtained, a waiver must also be obtained from the CRADO.
5. The researcher must comply with all applicable requirements including, but not limited to, applicable court, penal system, and local, VA, and other Federal requirements.

## Children (Minors) as a Vulnerable Population in Research

Research involving children must be reviewed carefully by the IRB for its relevance to VA and must not present greater than minimal risk to the children. The VAPORHCS Medical Facility Director must approve participation in the proposed research that includes children (see guidance at: <http://www.research.va.gov/resources/policies/default.cfm>). ***NOTE:*** *Research involving biological specimens or data, even if de-identified, that are obtained from children is considered to be research involving children. If the biological specimens or data were previously collected, they must have been collected under applicable Federal policies and ethical guidance.*

The IRB must have the appropriate expertise to evaluate any VA research involving children and must comply with the requirements of 45 CFR 46.401 – 46.404 and 46.408. ***NOTE****: Per VHA Directive 1200.05, research involving children does not include neonates.*

# Review of Research on Human Subjects Likely to Need Surrogate Consent

Research involving individuals who may have impaired decision-making capacity warrants special attention, as members of this population may be vulnerable to coercion. Such individuals must be protected from exploitation and harm, while allowing the conduct of essential research on problems that are unique and/or relevant to this population.

In cases where research involving individuals who have impaired decision-making capacity is approved, surrogate consent from a Legally Authorized Representative (LAR) will need to be obtained for such individuals (as per section XIX.E). And, the IRB may require additional safeguards (e.g., involvement of subject advocates, independent consent monitoring, formal capacity assessment, waiting periods, etc.) as part of the research plan to protect subjects.

No individual who lacks decision-making capacity may participate in VA Research until the IRB has reviewed and approved participation of that individual, or that class of individuals, in a given study. Such approval may be sought with the initial IRB application, as a subsequent study modification, or as needed on a case-by-case basis.

When planning to enroll subjects with impaired decision-making capacity, investigators must address in the protocol how they will determine when surrogate consent will be required. The investigator and research staff must have adequate procedures in place for assessing and ensuring a potential subjects’ capacity and understanding, unless they have already verified that the potential subject has been ruled incompetent by a court of law. The IRB must review and approve these procedures to ensure that they are appropriate, given the population and setting of the research.

For research that poses greater than minimal risk, the IRB may require investigators to use independent and qualified professionals to assess whether potential subjects have the capacity to give voluntary, informed consent. Even in research involving only minimal risk, the IRB may require that the study include a capacity assessment if there are reasons to believe that potential subjects’ capacity may be impaired. It is not necessary to require a formal capacity assessment by an independent professional for all potential research subjects with mental disorders.

It is often possible for researchers and others to enable persons with some decisional impairments to make voluntary and informed decisions to consent or refuse participation in research. Potential measures include repetitive teaching, group sessions, audiovisual presentations, and oral or written recall tests. Other measures might include follow-up questions to assess subject understanding, videotaping or audio-taping of consent interviews, second opinions, use of independent consent observers, interpreter for hearing-impaired subjects, allowing a waiting period before enrollment, or involvement of a trusted family member or friend in the disclosure and decision making process.

## Criteria for Enrollment of Individuals with Impaired Decision-Making Capacity

Individuals who lack decision-making capacity may be enrolled in protocols if:

1. The proposed research entails:
   1. No greater than minimal risk to the subject, as determined by the IRB, or
   2. A greater probability of direct benefit to the subject than harm to the subject, or
   3. Greater than minimal risk and no prospect of direct benefit to individual subjects, but is likely to yield generalizable knowledge about the subject’s disorder or condition that is of vital importance for the understanding or amelioration of the subject’s disorder or condition.
2. In addition, the IRB must determine that:
3. The research cannot be performed solely with persons who possess decision-making capacity, and the focus of the research is the disorder leading to the subjects’ lack of decision-making capacity, whether or not the lack of decision-making itself is being evaluated (e.g., an individual who lacks decision-making capacity as the result of a stroke can participate in a study of cardiovascular effects of a stroke), or
4. The subject of the research is not directly related to the subjects’ lack of decision-making capacity but the investigator has presented a compelling argument for including such subjects (e.g., transmission of methicillin-resistant staphylococcus aureus infections in a nursing home where both individuals with and without decision-making capacity are affected).

## IRB Review of Studies Involving Surrogate Consent

When reviewing studies that include subjects likely to need surrogate consent, the IRB membership must include at least one member who has experience working with those who need surrogate consent and/or conducting research with such populations. When potential subjects may be vulnerable to coercion or undue influence, an individual who is knowledgeable about or experienced in working with such participants may be invited to attend the IRB meeting as a consultant. Consideration may be given to adding another member who is a member of the population, such as a family member of such a person or a representative of an advocacy group for that population. The IRB may utilize ad hoc reviewers as necessary to ensure appropriate expertise.

The IRB may approve the inclusion of individuals who lack decision-making capacity in research studies when appropriate provisions are made for surrogate informed consent to be obtained from LARs (as outlined in section XIX.E). In order to approve the inclusion of such individuals in a study, the IRB must:

1. Ensure the study includes appropriate procedures for respecting dissent of those individuals;
2. Consider whether or not the study needs to include procedures for obtaining assent from those individuals; and
3. Determine whether any additional safeguards need to be used for the study (e.g., consent monitoring).

In the IRB minutes or IRB protocol file, the IRB must document its deliberations and the criteria, from section XVIII, that were met in order to allow approval of inclusion of individuals who lack decision-making capacity.

## Temporary or Fluctuating Decision-Making Capacity

Both researchers and IRB members must be aware that lack of decision-making capacity may be temporary (e.g., due to head trauma) or fluctuate (e.g., due to schizophrenia) for some individuals. Such individuals must be evaluated by a qualified practitioner (who may be a member of the research team), to determine the individual’s ability to provide informed consent. This evaluation must be performed as described in the IRB-approved protocol. If the individual is deemed to lack decision-making capacity at the time of the time of informed consent, a LAR must provide surrogate informed consent (as described in section XIX.E). If the subject regains decision-making capacity, the PI or designee must repeat the informed consent process with the subject and obtain the subject’s consent to continue with the study.

For research protocols involving subjects who have a temporary or fluctuating lack of decision-making capacity, the IRB should ensure that the study researchers establish and maintain ongoing communication with involved caregivers. Periodic re-consent should be considered in some cases, to accommodate fluctuating capacity in which a participant may be able to consent for themselves, and re-consent by a LAR when capacity is lost. Third party consent monitors may be used during the recruitment and consenting process, or waiting periods may be required to allow more time for the subject and/or their LAR to consider the information that has been presented.

## Determining Capacity to Consent

Decision-making capacity should usually be evaluated on an individual basis in order to avoid incorrect assumptions as to an individual's ability to make decisions. An individual ruled incompetent by a court of law is considered to lack decision-making capacity.

The decisional capacity of a potential research subject should be evaluated when there are reasons to believe that they may not be capable of making voluntary and informed decisions about research participation.

Decisional capacity in the research context has been interpreted by the American Psychiatric Association as requiring: (1) ability to evidence a choice; (2) ability to understand relevant information; (3) ability to appreciate the situation and its likely consequences; and (4) ability to manipulate information rationally. A range of professionals and methods may be utilized to assess capacity to consent. In general, the consent assessor should be a researcher or consultant who is familiar with dementias or the other underlying cause of lack of capacity and is qualified to assess and monitor capacity to consent in such subjects on an ongoing basis. The IRB will consider the qualifications of the proposed individual(s) and whether s/he is sufficiently independent of the research team and/or institution.

For studies that have been approved for enrolling vulnerable populations, when there is reason to believe that the individuals may lack decision-making capacity, a qualified practitioner must assess capacity of each potential subject to consent or a legal determination must be made (the VAPORHCS legal counsel may be consulted). If feasible, the practitioner must explain the proposed research to the prospective participant, even when surrogate consent is to be obtained. The PI, using an assessment tool or process approved by the IRB, must determine whether a potential subject lacks decision-making capacity and is unlikely to regain it within a reasonable period of time. The determination must be documented in the person’s medical record in a signed and dated progress note (See Section XVII.P. Progress Notes) as described in VHA Handbook 1004.01.

## Legally Authorized Representative (LAR)

If it has been verified that a potential subject lacks capacity to consent for themselves and the IRB has approved the inclusion of such individuals in the study, consent must be obtained from the potential subject’s LAR on behalf of the potential subject before the subject may participate in the research. The definition of Legally Authorized Representative, consistent with VA policy, is in the Definitions section of this SOP. If the potential subject objects to participating, this objection must be heeded.

An individual who has been determined to lack capacity to consent must be notified of that determination before permission may be sought from their LAR to enroll that individual in the study. The individual should also be informed about the research to the extent compatible with their understanding and, whenever possible, the individual should provide their assent to participate and also sign and date a separate assent form. If permission is given to enroll such an individual in the study, the potential subject must then be notified of that permission. Some individuals may resist participating in a study for which their LAR provided consent. Under no circumstances may individuals be forced or coerced to participate in a study.

An LAR must be fully informed of the study and have sufficient opportunity to consider what the wishes of the potential subject would be and whether or not to consent on behalf of the subject. The LAR must receive all of the information that a regular potential subject would receive, in language that is understandable to them. The LAR must also be told that their obligation is to try to determine what the prospective subject would do if able to make an informed decision and that, if the prospective subjects’ wishes cannot be determined, the LAR is responsible for determining what is in the subjects’ best interest.

Surrogate consent will be accepted from individuals in the order identified in this SOP (see DEFINITIONS: Legally Authorized Representative). If the potential subject indicates that they do not wish to participate, then the surrogate consent cannot be honored.

When surrogate consent is to be used, the researcher must:

1. Provide the IRB with a description of the procedures to ensure that subjects’ LARs are well informed regarding their roles and obligations to protect individuals who lack decision-making capacity, and
2. Provide information (i.e., informed consent process and HIPAA authorization) to the subjects’ LARs that would ordinarily be required to be made to the subjects themselves if they had decision-making capacity.

It must be documented in writing by the researcher that:

1. The LAR:
   1. Is named,
   2. Made aware of their responsibilities,
   3. Has been informed about the risks and benefits of the study,
   4. Is aware that the subject had consented to participate, if they did so before losing decision-making capacity,
   5. Is aware of their rights to withdraw the subject from the study and to contact the PI or RAO regarding questions or problems, and
   6. That the surrogate will be informed of future information that is needed to be informed as would a regular study subject, and
2. The subject, if possible, has given their assent to participation in the study.

Progress notes (See Section XVII.P. Progress Notes) during the period of surrogate consent should note that subject himself/herself demonstrates no dissent from participation in the study as described in VHA Handbook 1004.01.

# SPECIAL CONSIDERATIONS FOR SPECIAL TYPES OF RESEARCH

## Behavioral and Social Sciences Research

This type of research generally involves surveys, observational studies, or personal interviews.

### Social and Psychological Harms

The primary concerns when evaluating behavioral and social science research are the risk of harm to participants with respect to social or psychological harm. Therefore, the IRB should pay particular attention to the following:

1. The potential for participants to experience stress, anxiety, guilt, or trauma that could result in genuine psychological harm.
2. The risks of criminal or civil liability or other risks that could result in serious social harms, such as damage to financial standing, employability, insurability, or reputation; stigmatization; and damage to social or family relationships.
3. If information is to be collected on living individuals other than the consented participants, e.g., participant’s family members, the IRB should consider the risk of harm to those individuals.

To mitigate such risks, the IRB shall review the proposal for appropriate preventive protections and debriefings, adequate disclosure of risks in the informed consent information, and mechanisms to protect the confidentiality and privacy of persons participating in or affected by the research.

### Privacy and Confidentiality Concerns

The use of confidential information is an essential element of much social and behavioral research. Methods used to identify potential research participants or to gather information about participants must not compromise the privacy of the individuals. In general, identifiable information may not be obtained from private (non‑public) records without the approval of the IRB and the informed consent of the participant, even for activities intended to identify potential participants who will later be approached to participate in research.

## Research with Existing Materials/Data

Planning to use materials or data that will exist separate from the research, but are not currently in existence, as well as research that proposed to use materials or data already in existence, each have special considerations. These types of studies often use or create data repositories.

### Prospective Use of Existing Materials

Prospective studies are designed to observe outcomes or events (e.g., diseases, behavioral outcomes, or physiological responses) that occur subsequent to identifying the targeted group of participants, proposing the study, and initiating the research.

Prospective studies using materials (data, documents or records) that will "exist" in the future because they will be collected for some purpose unrelated to the research (e.g., routine clinical care) do not qualify for **exemption** under VA regulations because the materials in these studies are not in existence at the time the study is proposed and initiated.

***For research that is subject to the 2018 Requirements:***

See Appendix 2 for existing materials that qualify for exemption.

### Retrospective Use of Existing Materials

Retrospective studies involve research conducted by reviewing materials (data, documents or records) collected in the past (e.g., medical records, school records, or employment records) and existing at the time the research is proposed and initiated.

1. Such research may be exempt under VA regulations if the information is publicly available or if the information is recorded in such a manner that participants cannot be identified, either directly or through identifiers linked to the participants.
2. If not exempt, the IRB may review such research utilizing expedited procedures, provided that the research involves no more than minimal risk to participants.
3. However, retrospective studies using existing materials occasionally entail significant, greater than minimal risks and require review by the convened IRB (e.g., where the research reveals previously undisclosed illegal drug use and the expedited review raised concerns about invasion of participants' privacy and/or the adequacy of confidentiality protections proposed by the investigators).

When researchers will access data directly from the facility in which participants were seen, then IRB approval is needed from each researcher’s IRB of record. If the records will be accessed from the Austin data center or through a network database or access point, then documentation of IRB approval from the IRB of record for each researcher is required. However, facilities who release data are not necessarily engaged in research; only facilities where researchers are accessing data are considered to be engaged in research and therefore require IRB approval.

### Research Utilizing Large, Existing Data Sets

The use of large, existing data sets (i.e. data that is “on the shelf” at the time the protocol is initiated) requires IRB review when the data to be obtained will contain individually-identifiable private information about individuals. In such cases, the IRB must determine whether the information may be used without additional informed consent from the participants.

1. In making this determination, the IRB should first examine the conditions of informed consent under which the data were originally obtained. It may be that the proposed research is permissible under the original terms of consent.
2. If this is not the case, then the IRB should consider whether it is permissible to waive the usual informed consent requirements.
3. In other cases, the IRB may determine that the research can proceed only if the researcher obtains and uses de-identified data. Under this scenario, codes and other identifiers are permanently removed from the data set before the data are sent to the researcher, and the removal is accomplished in such a manner that neither the researcher nor the source maintaining the data set can reestablish participants' identities.
4. An alternative to de-identifying data is to maintain the data set as a data repository under the guidelines established by OHRP and VA.

### Research Utilizing Research Data- and/or Bio-Repositories (Banks)

Research repositories are often established over in order to allow the use of research data and/or human biological specimens for future research.

Repository activities involve three components: (a) the **collection** of data and/or human biological specimens; (b) the **bank/repository** storage and data management center; and (c) the **receipt** of data and/or specimens from the repository byinvestigators. Under a repository arrangement, the IRB formally oversees all elements of repository activity, setting the conditions for collection, secure storage, maintenance, and appropriate sharing of the data with external investigators. Specifically, the IRB determines the parameters for sharing data and/or specimens (which may be identifiable within the repository) in a manner such that additional informed consent of participants is, or is not, required.

Typically, these parameters may involve formal, written agreements between the investigator and the repository, stipulating conditions as follows:

1. The repository shall not release any identifiers to the investigator.
2. The investigator shall not attempt to recreate identifiers, identify participants, or contact participants.
3. The investigator shall use the data only for the purposes and research specified.
4. The investigator shall comply with any conditions determined by the repository IRB to be appropriate for the protection of participants.

Repositories of human biological specimens that will be maintained at the Portland VAMC must meet the requirements outlined in the IRB Review of Use of Research Repositories policy located at: <https://www.va.gov/portlandresearch/documents/irb/repository-policy.doc>. If human biological specimens will be maintained outside the VAPORHCS for future research purposes, they must be kept either in a VACO-approved tissue bank, or a waiver must be obtained from the VAPORHCS ACOS/R&D.

## Epidemiological Research

Epidemiological research often makes use of sensitive, individually identifiable, private information (usually obtained from medical or other private records), and links this information with additional information obtained from other public or private records, such as employment, insurance, or police records. Epidemiological research may also combine historical research with survey and interview research. Epidemiological studies often present significant problems regarding both privacy and confidentiality.

* + 1. The IRB must first consider privacy issues and satisfy that the research does not constitute an unwarranted invasion of the participants' privacy. In doing so, the IRB shall seek to establish that the investigator has legitimate access to any individually-identifiable information to be utilized. Regional Counsel will be consulted if questions arise whether state laws might apply to a specific instance.
    2. Once the IRB's privacy concerns have been resolved, the IRB will examine mechanisms for maintaining the confidentiality of data collected. The IRB shall seek to establish that confidentiality protections are appropriate to the nature and sensitivity of the information that has been obtained. Confidentiality protections will be in accordance with HIPAA.
    3. Because epidemiological research typically requires large numbers of subjects, investigators almost always request that the IRB waive the usual requirements for informed consent and authorization. To approve such a waiver in epidemiological research, the IRB must find and document that the criteria for a waiver of informed consent have been met.

## Family History Research

Family history research is a common technique used in bio‑social and bio-behavioral research. Family history research typically involves obtaining information from one family member about other family members (third parties).

* + 1. It is important to recognize that VA regulations include in the definition of human subject a living individual about whom a researcher obtains "identifiable private information." Thus, the family members (third party) identified and described by their family member may be human subjects under the regulations if a researcher obtains identifiable private information about them.
    2. The IRB must determine whether family members (third parties) are human subjects in such research, and if so, consider the possible risks involved, and determine whether their informed consent and authorization is required or can be waived under the conditions specified at 38 CFR 16.116(d). There is not total consensus in the available guidance on this issue. OHRP representatives have advised that "third parties" about whom identifiable and private information is collected in the course of research are human subjects. Confidentiality is a major concern in determining if minimal risk is involved. The IRB may consider if informed consent from third parties may be waived in accordance with Section 45 CFR 116 (d) and if so, document that in the IRB minutes. In many cases, a waiver of consent may be appropriate.

## Research Involving Potentially Addictive Substances

Research involving potentially addictive substances often involves the use of what may be termed "abuse‑liable" substances. Abuse-liable substances are pharmacological substances that have the potential for creating abusive dependency. Abuse-liable substances include both legal and illicit drugs. The following are among the issues that the IRB should consider when reviewing research involving potentially addictive substances:

1. When this type of research is proposed, the IRB must consider the participants' capacity to provide continuous informed consent, ensuring that participants are competent and are not coerced.

2. If such research involves institutionalized participants, the participants' ability to exercise autonomy could be impaired.

3. The IRB must also consider requirements for equitable selection of participants and protections for maintaining confidentiality, since such a population may be at risk for discrimination or over-selection.

4. The IRB must be sensitive to the ethical context of the research, in that there may be moral dilemmas associated with the use of placebos, or in cases where addicts are presented with alcohol and/or drugs.

5. It is critical that the IRB focus on the considerations of risk and benefits of such research.

## Research Involving VAPORHCS Employees, Students and Trainees

The IRB upholds all ethical standards in approving research involving VAPORHCS employees, students and/or trainees. The IRB takes into consideration undue influence an employee may experience when approached to participate in a research project. The IRB ensures that no employees, students, or trainees feel obligated to participate in research to avoid loss of employment or privileges. VA employees may participate during work time with supervisor approval if the research is directly related to their duties and responsibilities. For research that is not related to their employee duties, employees may participate only on their own time outside their normal tour of duty (such as during a 15-minutes break, during a lunch break, or before or after work). VA employees are eligible for the same participation incentives as non-VA employees.

## Research Involving Deceased Persons

In the rare cases of proposed research involving deceased persons, the IRB may evaluate the nature of the research and determine if consent of family members is necessary or whether the deceased may be treated in the same manner as that of donated tissue.

Investigators who propose research involving decedent’s protected health information must complete the HIPAA Research on Decedents' Information Application located within the electronic protocol management system. The researchers will be expected to adhere to the provisions of HIPAA. Additional guidance regarding research on decedent’s information is detailed in VHA Directive 1605.01 located at: https://www.va.gov/vhapublications/publications.cfm?Pub=1.

# FOOD AND DRUG ADMINISTRATION (FDA) REGULATED RESEARCH

## Investigational Drugs, Devices, and Biologics

Drugs, devices and biologics utilized in research or utilized for expanded access and/or emergency use, and humanitarian use devices, are covered in the HRPP policy, Investigational Device and/or Drug Usage located at: <https://www.va.gov/portlandresearch/documents/hrpp/investigational-device.pdf>. That document outlines responsibilities for all parties, as well as definitions and procedures for the IRB review of studies with drugs, devices and/or biologics.

### FDA Requirements in Relation to VA, Common Rule, and DHHS Requirements

In addition to regulations governing the use of investigational drugs and devices, the FDA has regulations governing human subjects protections. The human subject protection requirements found in FDA regulations are substantively the same as the VA and Common Rule requirements. However, there are important differences:

1. The FDA has different definitions for "human subject" and "clinical investigation” (research). See Definitions in this SOP for “Research”, “Human Subject”, and “Investigational New Drug”.
2. Conditions for exemption, exception, and waiver of IRB review and informed consent requirements differ.
3. FDA regulations require specific determinations for the IRB review of device studies.
4. FDA regulations include specific reporting requirements that are not found in VA regulations, the Common Rule, or DHHS regulations. See 21 CFR 312.32 and 312.33, 21 CFR 812.150 and 21 CFR 814.126, as applicable.
5. DHHS regulations include specific additional protections, which are not contained in the VA and Common Rule requirements, for: pregnant women, fetuses, and human in vitro fertilization; prisoners; and children.

### Additional VA Requirements

VA policy requires that all research comply with the VA human subject regulations, as well as with all applicable regulations and requirements regarding storage and security procedures for investigational agents (including VHA Handbook 1108.04). The following applies to studies using an investigational drug, an approved drug used for an unapproved indication or an approved drug used as a comparator in a study.

1. A VA Investigational Drug Information Record (VA Form 10‑9012) must be completed by the PI and submitted to the RAO.
2. Upon approval of the research by the IRB, a copy of the final approval notification and the Form 10-9012, both signed by an IRB Co-Chair or IRB reviewer, must be forwarded to the PI/study contact and to the Research Pharmacy by the research team.

### FDA and Pharmacy Benefits Management Warnings

**Drug Warnings:** The Research Pharmacy is aware of all investigational drugs currently in use in active research studies.

1. Pharmacy will email Pharmacy Benefits Management (PBM) warnings, based on FDA warnings, to the ACOS/R&D, ADR&D and RAO designee.
2. The RAO designee (or ACOS/R&D or AD/R&D) will ask the Research Pharmacy to determine if any research studies are using the relevant drug(s).
3. Research Pharmacy will email the names of relevant PIs to the ACOS/R&D, AD/R&D and RAO designee. No action will be required if no investigator is using the drug.
4. The ACOS/R&D or a RAO designee, will contact any PI using the drug, IRB Chairs, and, if necessary, all IRB members. PIs will be requested to submit a report of the event within five business days (see Section XV of this SOP).
5. The IRB Chair or designated IRB voting member will review the submitted report and determine if immediate action is required, if an emergency meeting of the IRB is warranted, or if the issue may wait until a convened IRB meeting.
6. PIs will notify study participants of the warning, if directed so by the warning (based on level) or by the IRB.
7. A file containing correspondence, as well as all PBM/FDA warnings, will be maintained by the Research Pharmacy.

**Device warnings:** When the FDA issues an alert/warning, the RAO designee or an IRB Analyst will generate a report. No action will be required if no investigator is using the device.

1. The ACOS/R&D or an R&D staff member designated by the ACOS/R&D will contact the relevant PIs, IRB Chairs, and all IRB members. PIs will be requested to submit a report of the event within 5 business days (see Section XV of this SPO).
2. An IRB Co-Chair will review the submitted report and determine if immediate action is required, if an emergency meeting of the IRB is warranted, or if the issue can wait until a convened IRB meeting.
3. PIs will notify study participants of the alert/warning if directed by the alert/warning (based on level) or by the IRB.

**REFERENCES:**

5 USC 552, Public information; agency rules, opinions, orders, records, and proceedings

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21 CFR 312, Investigational New Drug Application

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21 CFR 814, Premarket Approval of Medical Devices

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**CONCURRENCES:** Endorsed by the R&DC ##/##/####.

**RESCISSION:** IRB SOP endorsed by the R&DC 6/1/2020

**FOLLOW-UP RESPONSIBILITY:** ACOS, Research & Development Service (R&D)

David M. Cohen, M.D.

ACOS, Research & Development Service

# Appendix 1: Categories of Research That May Be Reviewed by the IRB Through Expedited Procedures

The following categories are used to evaluate studies for possible expedited review. This list is directly from OHRP at <http://www.hhs.gov/ohrp/policy/expedited98.html>

These categories are also used to evaluate the minimal risk levels referenced in the protocol deviation reporting policy included in this SOP.

1. Clinical studies of drugs and medical devices only when condition (a) or (b) is met.
   1. Research on drugs for which an investigational new drug application (21 CFR Part 312) is not required. (Note: Research on marketed drugs that significantly increases the risks or decreases the acceptability of the risks associated with the use of the product is not eligible for expedited review.)
   2. Research on medical devices for which (i) an investigational device exemption application (21 CFR Part 812) is not required; or (ii) the medical device is cleared/approved for marketing and the medical device is being used in accordance with its cleared/approved labeling.
2. Collection of blood samples by finger stick, heel-stick, ear stick, or venipuncture as follows:
   1. From healthy, non-pregnant adults who weigh at least 110 pounds. For these subjects, the amounts drawn may not exceed 550 ml in an 8-week period and collection may not occur more frequently than 2 times per week; or
   2. From other adults and children, considering the age, weight, and health of the subjects, the collection procedure, the amount of blood to be collected, and the frequency with which it will be collected. For these subjects, the amount drawn may not exceed the lesser of 50 ml or 3 ml per kg in an 8-week period and collection may not occur more frequently than 2 times per week.
3. Prospective collection of biological specimens for research purposes by noninvasive means.  
   Examples: (a) hair and nail clippings in a nondisfiguring manner; (b) deciduous teeth at time of exfoliation or if routine patient care indicates a need for extraction; (c) permanent teeth if routine patient care indicates a need for extraction; (d) excreta and external secretions (including sweat); (e) uncannulated saliva collected either in an unstimulated fashion or stimulated by chewing gumbase or wax or by applying a dilute citric solution to the tongue; (f) placenta removed at delivery; (g) amniotic fluid obtained at the time of rupture of the membrane prior to or during labor; (h) supra- and sub-gingival dental plaque and calculus, provided the collection procedure is not more invasive than routine prophylactic scaling of the teeth and the process is accomplished in accordance with accepted prophylactic techniques; (i) mucosal and skin cells collected by buccal scraping or swab, skin swab, or mouth washings; (j) sputum collected after saline mist nebulization.
4. Collection of data through noninvasive procedures (not involving general anesthesia or sedation) routinely employed in clinical practice, excluding procedures involving x-rays or microwaves. Where medical devices are employed, they must be cleared/approved for marketing. (Studies intended to evaluate the safety and effectiveness of the medical device are not generally eligible for expedited review, including studies of cleared medical devices for new indications.)  
   Examples: (a) physical sensors that are applied either to the surface of the body or at a distance and do not involve input of significant amounts of energy into the subject or an invasion of the subject’s privacy; (b) weighing or testing sensory acuity; (c) magnetic resonance imaging; (d) electrocardiography, electroencephalography, thermography, detection of naturally occurring radioactivity, electroretinography, ultrasound, diagnostic infrared imaging, doppler blood flow, and echocardiography; (e) moderate exercise, muscular strength testing, body composition assessment, and flexibility testing where appropriate given the age, weight, and health of the individual.
5. Research involving materials (data, documents, records, or specimens) that have been collected, or will be collected solely for non-research purposes (such as medical treatment or diagnosis). (NOTE: Some research in this category may be exempt from the HHS regulations for the protection of human subjects. 45 CFR 46.101(b)(4) located at: <http://www.hhs.gov/ohrp/humansubjects/guidance/45cfr46.html> This listing refers only to research that is not exempt.)
6. Collection of data from voice, video, digital, or image recordings made for research purposes.
7. Research on individual or group characteristics or behavior (including, but not limited to, research on perception, cognition, motivation, identity, language, communication, cultural beliefs or practices, and social behavior) or research employing survey, interview, oral history, focus group, program evaluation, human factors evaluation, or quality assurance methodologies. (NOTE: Some research in this category may be exempt from the HHS regulations for the protection of human subjects. 45 CFR 46.101(b)(2) and (b)(3) located at: <http://www.hhs.gov/ohrp/humansubjects/guidance/45cfr46.html> . This listing refers only to research that is not exempt.)
8. Continuing review of research previously approved by the convened IRB as follows:
   1. Where (i) the research is permanently closed to the enrollment of new subjects; (ii) all subjects have completed all research-related interventions; and (iii) the research remains active only for long-term follow-up of subjects; or
   2. Where no subjects have been enrolled and no additional risks have been identified; or
   3. Where the remaining research activities are limited to data analysis.

Continuing review of research, not conducted under an investigational new drug application or investigational device exemption where categories two (2) through eight (8) do not apply but the IRB has determined and documented at a convened meeting that the research involves no greater than minimal risk and no additional risks have been identified.

# Appendix 2: Exemption from IRB Oversight/Review

1. FDA - Studies involving the use of FDA regulated articles may **not** be considered for an exemption from the Basic HHS Policy for Protection of Human Research Subjects Subpart A of 45 CFR 46 unless the sponsor or sponsor-investigator receives a written waiver from the FDA *[21 CFR 56.105].*
2. Department of Veterans Affairs policy requires that research involving children is approved by the Facility Director and research involving prisoners must receive a **waiver** from the Chief Research and Development Officer (VHA Directive 1200.05
3. Exempt research activities involving interacting or obtaining information by education tests, survey or interview procedures, or behavioral interventions requires the following information about the research be given to subjects orally or in writing (VHA Directive 1200.05):
   1. The activity is research;
   2. Participation is voluntary;
   3. Permission to participate can be withdrawn;
   4. Permission for use of data can be withdrawn for exempt research activities involving the collection and use of identifiable data; and
   5. Contact information for the VA Investigator

**For research subject to the 2018 Requirements (Common Rule): 38 CFR 16.104:**

For research subject to the 2018 Requirements:

* + Each of the exemptions may be applied to research involving pregnant women if the conditions of the exemption are met.
  + The exemptions do not apply to research involving prisoners.
  + The exemptions for Categories 1, 4, 5, and 6, may be applied to research subjects who are children if the conditions of the exemption are met. Exempt category 2(a) and (b) of this section may only apply to research subject to 45 CFR 46, Subpart D involving educational tests or the observation of public behavior when the investigator(s) do not participate in the activities being observed. Paragraph 2.b.(3) of this section may not be applied to research subject to 45 CFR 46, Subpart D.
  + ***NOTE:*** *Guidance regarding exemption categories 7 and 8 is not included in this SOP.* ***Exemption category 7 and category 8*** *for storage and maintenance for secondary research, for which broad consent is required, are not being implemented at VAPORHCS.*

**Categories of Exempt Research**

(1) Research, conducted in established or commonly accepted educational settings, that specifically involves normal educational practices that are not likely to adversely impact students' opportunity to learn required educational content or the assessment of educators who provide instruction. This includes most research on regular and special education instructional strategies, and research on the effectiveness of or the comparison among instructional techniques, curricula, or classroom management methods.

(2) Research that only includes interactions involving educational tests (cognitive, diagnostic, aptitude, achievement), survey procedures, interview procedures, or observation of public behavior (including visual or auditory recording) if at least one of the following criteria is met:

(i) The information obtained is recorded by the investigator in such a manner that the identity of the human subjects cannot readily be ascertained, directly or through identifiers linked to the subjects;

(ii) Any disclosure of the human subjects' responses outside the research would not reasonably place the subjects at risk of criminal or civil liability or be damaging to the subjects' financial standing, employability, educational advancement, or reputation; or

(iii) The information obtained is recorded by the investigator in such a manner that the identity of the human subjects can readily be ascertained, directly or through identifiers linked to the subjects, and an IRB conducts a limited IRB review to make the determination required by §16.111(a)(7).

(3) Research involving benign behavioral interventions in conjunction with the collection of information from an adult subject through verbal or written responses (including data entry) or audiovisual recording if the subject prospectively agrees to the intervention and information collection and at least one of the following criteria is met:

(i) The information obtained is recorded by the investigator in such a manner that the identity of the human subjects cannot readily be ascertained, directly or through identifiers linked to the subjects;

(ii) Any disclosure of the human subjects' responses outside the research would not reasonably place the subjects at risk of criminal or civil liability or be damaging to the subjects' financial standing, employability, educational advancement, or reputation; or

(iii) The information obtained is recorded by the investigator in such a manner that the identity of the human subjects can readily be ascertained, directly or through identifiers linked to the subjects, and an IRB conducts a limited IRB review to make the determination required by §16.111(a)(7).

For the purpose of this provision, benign behavioral interventions are brief in duration, harmless, painless, not physically invasive, not likely to have a significant adverse lasting impact on the subjects, and the investigator has no reason to think the subjects will find the interventions offensive or embarrassing. Provided all such criteria are met, examples of such benign behavioral interventions would include having the subjects play an online game, having them solve puzzles under various noise conditions, or having them decide how to allocate a nominal amount of received cash between themselves and someone else.

If the research involves deceiving the subjects regarding the nature or purposes of the research, this exemption is not applicable unless the subject authorizes the deception through a prospective agreement to participate in research in circumstances in which the subject is informed that he or she will be unaware of or misled regarding the nature or purposes of the research.

(4) Secondary research for which consent is not required: Secondary research uses of identifiable private information or identifiable biospecimens, if at least one of the following criteria is met:

(i) The identifiable private information or identifiable biospecimens are publicly available;

(ii) Information, which may include information about biospecimens, is recorded by the investigator in such a manner that the identity of the human subjects cannot readily be ascertained directly or through identifiers linked to the subjects, the investigator does not contact the subjects, and the investigator will not re-identify subjects;

(iii) The research involves only information collection and analysis involving the investigator's use of identifiable health information when that use is regulated under 45 CFR parts 160 and 164, subparts A and E, for the purposes of “health care operations” or “research” as those terms are defined at 45 CFR 164.501 or for “public health activities and purposes” as described under 45 CFR 164.512(b); or

(iv) The research is conducted by, or on behalf of, a Federal department or agency using government-generated or government-collected information obtained for non-research activities, if the research generates identifiable private information that is or will be maintained on information technology that is subject to and in compliance with section 208(b) of the E-Government Act of 2002, 44 U.S.C. 3501 note, if all of the identifiable private information collected, used, or generated as part of the activity will be maintained in systems of records subject to the Privacy Act of 1974, 5 U.S.C. 552a, and, if applicable, the information used in the research was collected subject to the Paperwork Reduction Act of 1995, 44 U.S.C. 3501 et seq.

(5) Research and demonstration projects that are conducted or supported by a Federal department or agency, or otherwise subject to the approval of department or agency heads (or the approval of the heads of bureaus or other subordinate agencies that have been delegated authority to conduct the research and demonstration projects), and that are designed to study, evaluate, improve, or otherwise examine public benefit or service programs, including procedures for obtaining benefits or services under those programs, possible changes in or alternatives to those programs or procedures, or possible changes in methods or levels of payment for benefits or services under those programs.

(i) Such projects include, but are not limited to, internal studies by Federal employees, and studies under contracts or consulting arrangements, cooperative agreements, or grants. Exempt projects also include waivers of otherwise mandatory requirements using authorities such as sections 1115 and 1115A of the Social Security Act, as amended.

(ii) Each Federal department or agency conducting or supporting the research and demonstration projects must establish, on a publicly accessible Federal Web site or in such other manner as the department or agency head may determine, a list of the research and demonstration projects that the Federal department or agency conducts or supports under this provision. The research or demonstration project must be published on this list prior to commencing the research involving human subjects.

(6) Taste and food quality evaluation and consumer acceptance studies:

(i) If wholesome foods without additives are consumed, or

(ii) If a food is consumed that contains a food ingredient at or below the level and for a use found to be safe, or agricultural chemical or environmental contaminant at or below the level found to be safe, by the Food and Drug Administration or approved by the Environmental Protection Agency or the Food Safety and Inspection Service of the U.S. Department of Agriculture.

1. In order to allow for administrative delay from the date the IRB approves an informed consent document and when the PI receives the most recently approved document, the previously approved informed consent is valid until 5 business days after the date on the most recently approved document. This timeline might be extended per section XIV.A.3 when consent is obtained via telephone contact. [↑](#footnote-ref-1)