Department of Veterans Affairs
Veterans Health Administration
Washington, DC 20420

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VHA HANDBOOK 1200.05(2)
Transmittal Sheet
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REQUIREMENTS FOR THE PROTECTION OF HUMAN SUBJECTS IN RESEARCH

1. REASON FOR ISSUE: This Veterans Health Administration (VHA) Handbook establishes procedures for the protection of human subjects in Department of Veterans Affairs (VA) research and the operation of the Institutional Review Board (IRB) for VA facilities.

2. SUMMARY OF MAJOR CHANGES: This Handbook was revised extensively to harmonize with the Common Rule as followed by other federal agencies. VA-specific requirements are added as appropriate. The requirements in this Handbook must be implemented no later than March 12, 2015.

3. RELATED ISSUES: VHA Directive 1200, VHA Handbook 1200.01, VHA Handbook 1200.2, VHA Handbook 1200.12, VHA Handbook 1058.01, and VHA Handbook 1058.03.

4. RESPONSIBLE OFFICE: The Office of Research and Development (ORD) (10P9) is responsible for the contents of this Handbook. Questions may be referred to 202-443-5600, or emailed to VHACOORDRegulatory@va.gov.

5. RESCISSIONS: VHA Handbook 1200.05, dated May 2, 2012, and VHA Directive 2008-072, dated Oct. 30, 2013, are rescinded.

6. RECERTIFICATION: This VHA Handbook is scheduled for recertification on or before the last working day of November, 2019.

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REQUIREMENTS FOR THE PROTECTION OF HUMAN SUBJECTS IN RESEARCH

1. PURPOSE: This Veterans Health Administration (VHA) Handbook defines the procedures for implementing the federal policy, known as the "Common Rule" and other applicable federal requirements for the protection of human subjects and must be implemented no later than March 12, 2015. ***NOTE:*** *All sections of rescinded VHA Handbook 1200.05, dated May 2, 2012, must be followed until the VA facility implements the requirements of this new Handbook, but no later than March 12, 2015.* **AUTHORITY:** 38 U.S.C. 501, 7331, 7334; 38 CFR 16.116, 17.32, 17.33.

2. BACKGROUND:

a. The Department of Veterans Affairs (VA) is guided by the ethical principles of respect for persons, beneficence, and justice as set forth in The Belmont Report, Ethical Principles and Guidelines for the Protection of Human Subjects of Research, regardless of who conducts the research or the source of its support. ***NOTE:*** *The Belmont Report may be found at http://www.hhs.gov/ohrp/humansubjects/guidance/belmont.html).*

b. VA is one of the 18 federal departments and agencies that have agreed to follow the Common Rule for the Protection of Human Subjects, effective June 18, 1991. The Common Rule is encoded in Title 38 of the Code of Federal Regulations (CFR) Part 16. This Handbook incorporates Common Rule requirements where applicable.

3. SCOPE:

a. Except as provided in paragraph 3.(d), this policy applies to all VA research (see paragraph 4.ii.) involving human subjects (see paragraph 4.l.).

b. Investigators receiving support from other federal departments or agencies (e.g., the National Institutes of Health (NIH), Department of Defense (DoD)), or from non-Federal sources (e.g., the American Heart Association) must meet the requirements of the funding source, in addition to those of VA and other applicable federal entities. ***NOTE****: When following the requirements of the funding source would cause non-compliance with federal or VA requirements, the federal and VA requirements must be followed.*

c. When FDA-regulated products or test articles are used, FDA regulations apply regardless of funding source.

d. Research activities in which the only involvement of human subjects will be in one or more of the Common Rule categories, outlined in Appendix A, may be exempt from the provisions of this Handbook. ***NOTE:*** *The Common Rule exemptions may not be applied to Food and Drug Administration (FDA)-regulated research (see 21 CFR 56.104 for exemptions applied to FDA-regulated research). The Research and Development (R&D) Committee has oversight for all exempt research (see Handbook 1200.01, Research and Development Committee).*

e. VHA does not conduct planned emergency research (see 21 CFR 50.24) or classified research involving human subjects.

4. DEFINITIONS: The following definitions are intended for use within this Handbook and where appropriate reflect the Common Rule at 38 CFR 16.102 and Department of Health and Human Services (HHS) regulations at 45 CFR 46 Subparts A through D.

a. **Accreditation.** Accreditation is a comprehensive review of the Human Research Protection Program (HRPP) at a VA facility by an independent organization to ensure the program is comprehensive and maintains high ethical and professional standards. VHA selects an accrediting organization to review all VA Human Research Protection Programs.

b. **Adverse Event.** An adverse event (AE) in human subjects research is any untoward physical or psychological occurrence in a human subject participating in research. ***NOTE:*** *AEs are further discussed in VHA Handbooks 1058.01, Research Compliance Reporting Requirements, and 1004.08, Disclosure of Adverse Events to Patients.*

c. **Assurance.** An assurance is a written commitment to protect human research subjects and comply with the requirements of the Common Rule. ***NOTE:*** *Assurances are further discussed in VHA Handbook 1058.03, Assurance for Protection for Human Subjects in Research.*

d. **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 (U.S.C.) 241(d), 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 be compelled in any federal, state, or local civil, criminal, administrative, legislative, or other proceedings to identify such individuals.

e. **Children.** Children are persons who have not attained the legal age to consent to treatments or procedures involved in the research under the applicable law of the jurisdiction in which the research will be conducted.

f. **Clinical Investigation.** The FDA considers the term "clinical investigation" to mean any experiment that involves a test article and one or more human subjects, and that either:

(1) Meets the requirements for prior submission to the FDA under Sections 505(i) or 520(g) of the Federal Food, Drug, and Cosmetic Act, as codified at 21 U.S.C. 355(i) and 360j(g) respectively; or

(2) Does not meet the requirements for prior submission to the FDA under these sections of the Federal Food, Drug, and Cosmetic Act, but the results of which are intended to be submitted later to, or held for inspection by, the FDA as part of an application for a research or marketing permit (21 CFR 56.102(c)).

g. **Collaborative Research.** Collaborative research involves investigators from more than one institution. Collaborative research may include VA and non-VA institutions but does not

include research conducted under a Cooperative Research and Development Agreement (CRADA) with a pharmaceutical company or other non-Federal partners.

h. **Continuing Noncompliance.** Continuing noncompliance is a persistent failure to adhere to the laws, regulations, or policies governing human subjects research. ***NOTE:*** *Continuing noncompliance is further discussed in VHA Handbook 1058.01.*

i. **De-identified Information.** De-identified information is 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 described in the HIPAA Privacy Rule have been removed.

j. **Fetus.** A fetus is the product of conception from the time of implantation until delivery.

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

l. **Human Subject.** A human subject is a living individual about whom an investigator (whether professional or student) conducting research obtains: (1) data through intervention or interaction with the individual or (2) identifiable private information. Individuals who receive test articles or who serve as controls in clinical investigations, including clinical investigations as defined under FDA regulations in 21 CFR 50.3, 312.3(b), and 812.3(h), are also considered human subjects for the purposes of this Handbook.

m. **In Vitro Fertilization.** In vitro fertilization is any fertilization of human ova that occurs outside the body of a female, either through a mixture of donor human sperm and ova or by any other means.

n. **Institutional Official.** The Institutional Official (IO) is the individual legally authorized as signatory official to commit an institution to an assurance. The IO is responsible for ensuring that the institution's HRPP functions effectively and that the institution provides the resources and support necessary to comply with all requirements applicable to research involving human subjects. The Principal Deputy Under Secretary for Health is the IO for VHA Central Office, and VA facility Directors are the IOs for local VA facilities. The IO serves as the official representative of the institution to external agencies and oversight bodies, and provides all written communication with external departments, agencies, and oversight bodies.

o. **Institutional Review Board.** An IRB is a board, committee, or other group formally designated by an institution to review, approve, require modification, disapprove, and conduct

continuing oversight of human subject research in accordance with the Common Rule (38 CFR Part 16) and other applicable regulations. ***NOTE:*** *For the purposes of this Handbook, unless otherwise specified, references to IRB include any IRB which is responsible for approval and monitoring of a particular research project.*

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

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

r. **Investigator.** An investigator is an individual who conducts research, including the principal investigator, co-investigators, sub-investigators, and local site investigators *(see paragraph 29).* ***NOTE:*** *The responsibilities of VA investigators are further discussed in VHA Handbook 1200.01.*

s. **Legally Authorized Representative.** A legally authorized representative (LAR) is 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 procedure(s) involved in the research. ***NOTE:*** *An individual who is qualified as a LAR to provide informed consent on behalf of a prospective research subject may not always qualify as a personal representative for purposes of consent to use or disclose a subject's protected health information (PHI) (i.e., signing a Health Insurance Portability and Accountability Act (HIPAA) authorization). Therefore, in circumstances involving authorization for use or disclosure of a human subject's PHI, the investigator must ensure the LAR meets the requirements of a personal representative under HIPAA and the Privacy Act of 1974 (legal guardian or power of attorney) prior to the LAR's signing a HIPAA authorization (see VHA Handbook 1605.1, Privacy and Release of Information).*

t. **Minimal Risk.** Minimal risk means that the probability and magnitude of harm or discomfort anticipated in the research are not greater in and of themselves than those ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests.

u. **Multi-site Research.** Multi-site research involves more than one research site. Multi-site research may include VA and non-VA institutions, and may include both collaborative research and research conducted under a CRADA with a pharmaceutical company or other non-Federal entity. ***NOTE:*** *See the definition for Collaborative Research at paragraph 4.g.*

v. **Neonate.** Neonate means a newborn within the first 4 weeks of birth.

w. **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&D Committee and education approved by the facility Education Committee is 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 38 U.S.C. Sections 7361-7366).*

x. **Principal Investigator.** A principal investigator (PI) is a qualified individual who directs a research project or research program. The PI oversees scientific, technical, and day-to-day management of the research. In the event of research conducted by a team of individuals, the PI is the responsible leader of the research team.

y. **Pregnancy.** Pregnancy encompasses the period of time from implantation until delivery.

z. **Private Information.** 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 that has been provided for specific purposes by an individual and that the individual can reasonably expect will not be made public (e.g., a health record). Private information must be individually identifiable (i.e., the identity of the subject is provided or may readily be ascertained or associated with the information) in order for obtaining the information to constitute research involving human subjects (38 CFR 16.102(f)).

aa. **Research.** Research means a systematic investigation, including research development, testing and evaluation, designed to develop or contribute to generalizable knowledge. Activities which meet this definition constitute research for purposes of this policy, whether or not they are conducted or supported under a program which is considered research for other purposes. For example, some demonstration and service programs may include research activities. Clinical investigations, including clinical investigations as defined under FDA regulations in 21 CFR 50.3, 312.3(b), and 812.3(h), are considered research for purposes of this Handbook. ***NOTE:*** *Research activities are further discussed in VHA Handbook 1058.05.*

bb. **Research Records.** Research records include, but are not limited to, IRB and R&D Committee records, records of all observations, subject recruitment activities, other data relevant to the investigation, progress notes, research study forms, surveys, questionnaires, and other documentation regarding the study (see VHA Handbook 1907.01, Health Information and Health Records).

cc. **Research and Development Committee.** The R&D Committee 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 Handbook 1200.01).

dd. **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. ***NOTE:*** *The protocol for social or behavioral research is sometimes referred to as the "Research Plan" or "Research Purpose and Methodology."*

ee. **Serious Adverse Event.** A serious adverse event (SAE) is an AE in human subjects research that results in death, a life-threatening experience, inpatient hospitalization, prolongation of hospitalization, persistent or significant disability or incapacity, congenital

anomaly, or birth defect. An AE is also considered serious when medical, surgical, behavioral, social, or other intervention is needed to prevent such an outcome. ***NOTE:*** *SAE's are also discussed at 21 CFR 312.32(a) and in VHA Handbook 1058.01; disclosure of adverse events to patients is discussed in VHA Handbook 1004.08.*

ff. **Serious Noncompliance.** Serious noncompliance is a failure to adhere to the laws, regulations, or policies governing human subjects research that may reasonably be regarded as:

(1) Involving substantive harm, or a genuine risk of substantive harm, to the safety, rights, or welfare of human research subjects, research staff, or others; or

(2) Substantively compromising the effectiveness of a facility's human subjects research protection or human subjects research oversight programs. ***NOTE:*** *Serious noncompliance is further discussed in VHA Handbook 1058.01.*

gg. **Unanticipated or Unexpected.** The terms unanticipated and unexpected refer to an event or problem in VA research that is new or greater than previously known in terms of nature, severity, or frequency, given the procedures described in protocol-related documents and the characteristics of the study population.

hh. **VA Investigator.** A VA investigator is any individual who conducts research approved by the VA R&D committee while acting under a VA appointment on VA time, including full and part-time compensated employees, trainees, without compensation (WOC) employees, and individuals appointed or detailed to VA under the Intergovernmental Personnel Act (IPA) of 1970. ***NOTE:*** *Contractors cannot be VA Investigators.*

ii. **VA Research.** VA research is research that is conducted by VA investigators (serving on compensated, WOC, or IPA appointments) while on VA time. The research may be funded by VA, by other sponsors, or be unfunded. VA research must have R&D Committee approval. ***NOTE:*** *VA research is discussed in VHA Handbook 1200.01 and VHA Handbook 1200.2, Research Business Operations.*

5. ASSURING COMPLIANCE WITH THIS POLICY:

a. Each VA facility engaged in research covered by this Handbook must obtain a Federal-wide Assurance (FWA) prior to conducting any human subjects research. The IO is the individual legally authorized as signatory official to commit an institution to a FWA. ***NOTE:*** *VA facilities filing an FWA and VA Addendum must submit applications and renewals through the Office of Research Oversight (ORO) (see VHA Handbook 1058.03).*

b. **Responsibilities of the Institutional Official.** The IO is responsible for overseeing the facility's research program, and this responsibility cannot be delegated. The IO is responsible for the creation and implementation of an HRPP for research involving human subjects. The exact composition of the HRPP depends on the specific facility, the resources of the facility, and the type, size, and complexity of its research program. The IO's responsibilities for the facility's HRPP include, but are not limited to:

(1) Overseeing the R&D Committee, IRB, and other applicable subcommittees of the R&D Committee, facility research office, and all VA investigators and VA research staff who conduct human subjects research at that facility.

(2) Delegating authority in writing for respective roles and responsibilities for the HRPP. This delegation of authority must provide the organizational structure and ensure leadership for oversight activities for all human subjects research conducted at or by the facility.

(3) Ensuring provision of adequate resources to support the operations of the HRPP.

(4) Ensuring independence of the IRB.

(5) Ensuring that a procedure is in place to review and approve recruiting documents, flyers, and advertisements for research that is not VA research prior to being posted or distributed in any form within or on the premises of a VA facility. Posting or distributing may include announcing, distributing, publishing, or advertising the study either electronically, by hard copy, or other means to anyone, including Veterans, clinicians, or other staff (see ORD guidance at http://www.research.va.gov/resources/policies/default.cfm).

c. All research subject to this Handbook must be reviewed and approved by an IRB designated in the facility's FWA (the IRB of Record), and will be subject to continuing review and oversight by the IRB of Record. ***NOTE:*** *Research that meets the exempt categories are not subject to IRB review but must be reviewed by the R&D Committee (see Appendix A).*

d. The IO is responsible for ensuring that any IRB designated as an IRB of Record for the facility is established in accordance with the requirements of this Handbook and registered through the ORO to the Office for Human Research Protections (OHRP).

(1) The facility's IRB(s) of Record may include the facility's own IRB(s), the VHA Central Office IRB (VA Central IRB), an IRB of another VA facility, the IRB(s) of its affiliated medical or dental school, or an IRB of another federal agency; and

(2) When the facility engages the services of another entity's IRB as its IRB of Record, the IO is responsible for:

(a) Establishing and signing a memorandum of understanding (MOU) or Authorizing Agreement with other VA facilities or external organization(s) providing IRB services (see VHA Handbook 1058.03 and MOU Checklist: http://www.va.gov/ORO/orochecklists.asp); and

(b) Ensuring that at least two VA-compensated (minimum 1/8th full-time employee equivalent) staff from the facility are appointed as voting members to each IRB of Record except for the VA Central IRB (see VA Central IRB Standard Operating Procedures (SOP)) or a central IRB of another federal agency (e.g., National Cancer Institute Central IRB). A small VA facility with fewer than ten active protocols is only required to appoint one voting member and one alternate voting member to ensure consistent representation. ***NOTE:*** *At least one VA voting member of the IRB must be in attendance when their facility's research is discussed at a convened meeting.*

(c) Obtaining approval of the Chief Research and Development Officer (CRADO) if the VA facility wants to establish a new HRPP or change their IRB of Record.

e. A VA facility's own internal IRB cannot serve as an IRB of Record for any non-VA entity except a DoD facility, Department of Energy laboratory, or a VA NPC.

f. Research funded through a VA NPC is considered VA research and the NPC must use the IRB(s) of Record and the R&D Committee of the VA facility that will conduct the research (see VHA Handbook 1200.17).

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

NOTE: *All IRBs regardless of the type described above must meet all the IRB requirements described in this Handbook.*

6. IRB MEMBERSHIP:

a. Each IRB must have at least five voting members with varying backgrounds to promote complete and adequate review of research activities commonly conducted by the institution(s) for which it reviews research. The IRB must be sufficiently qualified through the experience and expertise of its members, and the diversity of the members, including consideration of race, gender, and cultural backgrounds and sensitivity to such issues as community attitudes, to promote respect for its advice and counsel in safeguarding the rights and welfare of human subjects. In addition to possessing the professional competence necessary to review specific research activities, the IRB must be able to ascertain the acceptability of proposed research in terms of institutional commitments and regulations, applicable local, VA and other federal requirements, and standards of government ethics and professional conduct and practice. The IRB shall therefore include persons knowledgeable in these areas. If an IRB regularly reviews research that involves a vulnerable category of subjects, such as children, prisoners, pregnant women, or physically or mentally disabled persons, consideration must be given to the inclusion of one or more individuals on the IRB who are knowledgeable about and are experienced in working with these subjects. IRBs serving VA should also consider including a Veteran or Veteran's representative.

b. Every nondiscriminatory effort should be made to ensure that no IRB consists entirely of men or entirely of women, including the institution's consideration of qualified persons of both sexes, so long as no selection is made to the IRB on the basis of gender. No IRB may consist entirely of voting members of one profession.

c. Each IRB must include at least one voting member whose primary concerns are in scientific areas and at least one member whose primary concerns are in nonscientific areas. Physicians, dentists, nurses, pharmacists, social workers, other clinicians, statisticians, and allied health professionals are considered to be scientists.

d. Each IRB must include at least one voting member who is not otherwise affiliated with the institution and who is not part of the immediate family of a person who is affiliated with the institution. Retired VA employees who are receiving VA retirement benefits are considered to

be affiliated when they are members of a VA IRB. ***NOTE:*** *Veterans who receive their care at the facility, but have never been employed by VA, would not be considered affiliated*.

e. No IRB may have a member participate in the IRB's initial or continuing review of any project in which the member has a conflicting interest, except to provide information requested by the IRB.

f. An IRB may, in its discretion, invite individuals with competence in special areas to assist in the review of issues which require expertise beyond or in addition to that available on the IRB. These individuals may not vote with the IRB.

g. VA facilities must maintain accurate membership rosters for their designated IRB(s) of Record and submit the roster(s) to ORO as required by VHA Handbook 1058.03. The roster must list IRB members identified by name, earned degrees, representative capacity, indications of experience such as board certifications, licenses, etc., sufficient to describe each member's primary anticipated contributions to IRB deliberations, and any employment or other relationship between each member and the institution (e.g., full-time employee, part-time employee, member of governing panel or board, paid or unpaid consultant).

h. VA facility research office staff including, but not limited to, the ACOS for R&D, the AO for R&D, and IRB administrative staff may not serve as voting members of the facility's IRB. They may serve as ex officio, non-voting members; however, they and the IRB must be sensitive to any potential, actual, apparent, or perceived conflicts of interest and appropriately manage such conflicts. ***NOTE:*** *Ex officio members are for purposes of this Handbook not allowed to be voting members of the IRB.*

i. Research Compliance Officers (RCOs) may act as consultants to the facility's IRB, but may not serve as voting or non-voting members of the IRB. RCOs may attend IRB meetings when requested by the IRB or as specified by the IRB's standard operating procedures (SOPs). RCO's must be aware of and manage any potential, actual, apparent, or perceived conflicts of interest that arise because of their role. ***NOTE:*** *RCOs are further discussed in VHA Handbook 1058.01*.

j. The Privacy Officer (PO) and the Information Security Officer (ISO) serve in an advisory capacity to the facility's IRB as either non-voting members or as consultants (see paragraph 22 for specific roles and responsibilities).

k. Facility Directors, their administrative staff, COS, other facility senior administrators such as Associate or Assistant Directors or Chief Nurse, and NPC Administrative Staff may observe IRB meetings, but may not serve as voting or non-voting members of the facility's IRB.

l. If alternate members are appointed to the facility's IRB, the IRB's written procedures must describe the appointment and function of alternate members, and the IRB membership roster must identify by name the primary member(s) for whom each alternate member may substitute. The alternate members must have qualifications similar to the member they replace.

m. The IO appoints IRB voting members in writing. Appointment procedures for ex officio, non-voting members are made according to local SOPs and any other applicable VA

requirements. Voting members of VA IRBs and VA representatives to external IRB(s) of Record are appointed for a period of up to 3 years. They may be re-appointed to new terms of up to 3 years without a break in service at the end of each term. ***NOTE:*** *There are not a maximum number of terms for IRB members as long as the composition of the IRB meets all requirements.*

n. The Chair, Co-Chair(s), and Vice Chair(s) of a VA-operated IRB must be paid VA employees (i.e., not holding a WOC or IPA appointment at VA). ***NOTE:*** *This does not apply to IRBs of record external to the VA.*

(1) There may be one IRB Chair, Co-chairs, or a Chair and Vice Chair(s). Each may serve as a voting member of the IRB pursuant to IRB SOPs.

(2) The Chair and, when applicable, Co-chair(s) or Vice Chair(s), are appointed by the IO for a term of up to 3 years, and may be re-appointed indefinitely.

7. IRB FUNCTIONS AND OPERATIONS:

a. **Standard Operating Procedures.** The IRB must establish written SOPs that include, but are not limited to procedures for:

(1) Conducting initial and continuing review of research and reporting findings and actions to the investigator and to the R&D Committee;

(2) Determining which projects require review more often than annually and which projects need verification from sources other than the investigators that no material changes have occurred since previous IRB review;

(3) Ensuring prompt reporting by an investigator to the IRB of proposed changes in a research activity, and ensuring that such changes in approved research, during the period for which IRB approval has already been given, are not initiated without IRB review and approval except when necessary to eliminate apparent immediate hazards to the subject;

(4) Ensuring prompt reporting to the IRB, appropriate institutional officials, and ORO of: (i) any unanticipated problems involving risks to subjects or others or any serious or continuing noncompliance with this policy or the requirements or determinations of the IRB and (ii) any suspension or termination of IRB approval. ***NOTE:*** *Requirements for reporting to ORO are discussed in VHA Handbook 1058.01;*

(5) Determining whether a study meets the criteria in Appendix A for exemption from the requirements of the Common Rule. ***NOTE:*** *The investigator may not self-certify that a study is exempt. The R&D Committee or another subcommittee of the R&D Committee must be responsible for initial and continuing oversight of the exempt research (see VHA Handbook 1200.01);*

(6) Observing, or having a third party observe, research activities, including the informed consent process, when the IRB determines this to be appropriate;

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

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

NOTE: *When the IRB of Record is that of the academic affiliate, the SOPs related to the review of VA research for all affiliate IRBs reviewing VA research must be consistent with this Handbook and all regulations applicable to VA research.*

b. **IRB Functions.** Except when an expedited review procedure is used (see paragraph 9), the IRB must review proposed VA research at convened meetings at which a majority of the voting members (quorum) of the IRB are present, including at least one member whose primary concerns are in nonscientific areas. In order for the research to be approved, it must receive the approval of a majority of those members present at the meeting.

(1) The IRB may vote to approve, require modifications in (to secure approval), or disapprove a protocol.

(2) The IRB determines the approval period (not to exceed 1 year) and whether verification should be required from sources other than the investigators that no substantive modifications have occurred since previous IRB review.

(3) The IRB's review includes a review of the research protocol, the application to the IRB, and all other relevant documents (e.g., informed consent forms, surveys, advertising materials, HIPAA authorization, and investigator's brochure) submitted to the IRB.

(4) A quorum must be present during the review and approval of the study. If the required number and type of voting members are not present at any point during a meeting, a quorum must be restored before any discussion of, or action on, issues requiring a vote may occur.

c. **IRB Minutes.** Minutes of IRB meetings shall be in sufficient detail to show attendance at the meetings; actions taken by the IRB; the vote on these actions including the number of members voting for, against, and abstaining; the basis for requiring changes in or disapproving research; and a written summary of the discussion of controverted issues and their resolution.

(1) For protocols reviewed by the convened IRB, the IRB minutes shall document that the IRB determined that all of the criteria for approval of the research (see paragraph 10) were satisfied.

(2) If the IRB approves a consent procedure which does not include, or which alters, any of the elements of informed consent (see paragraph 15.e.), or waives the requirement to obtain a signed informed consent document (see paragraph 16.c.), it must document that all criteria for the waiver have been satisfied.

(3) IRB minutes must be submitted to the R&D Committee in accordance with local SOPs. When an affiliate IRB is the IRB of Record, the affiliate may either:

(a) Provide VA with unredacted copies of meeting minutes, or

(b) Provide VA with redacted copies of meeting minutes and permit relevant VA personnel (including, but not limited to, ORO staff, local VA Research Office staff, local RCOs, and R&D Committee members) to review the unredacted meeting minutes within two business days of a written request from VA. Such review may occur at the affiliate site during normal business hours, or as otherwise mutually acceptable to VA and the affiliate.

8. IRB REVIEW OF RESEARCH: An institution's IRB of Record shall:

a. Review and have authority to approve, require modifications in (to secure approval), or disapprove all research activities covered by this Handbook;

b. Require that information given to subjects as part of informed consent is in accordance with paragraph 15 of this Handbook. The IRB may require that information, in addition to that specifically mentioned in paragraph 15 of this Handbook, be given to the subjects when in the IRB's judgment the information would meaningfully add to the protection of the rights and welfare of subjects;

c. Require documentation of informed consent or waive documentation in accordance with paragraph 16 of this Handbook;

d. Notify investigators and the R&D Committee in writing of its decision to approve or disapprove the proposed research activity, or of modifications required to secure IRB approval of the research activity. If the IRB decides to disapprove a research activity, it shall include in its written notification a statement of the reasons for its decision and give the investigator an opportunity to respond in person or in writing;

e. Conduct continuing review of research covered by this policy at intervals appropriate to the degree of risk, but not less than once per year; and

f. Have authority to observe or have a third party observe the consent process and the research.

9. EXPEDITED REVIEW:

a. An IRB may use the expedited review process to review either or both of the following:

(1) Any of the categories of research described in Appendix B and found by the reviewer(s) to involve no more than minimal risk; and

(2) Minor changes in previously approved research during the period for which approval is authorized.

b. In the expedited review process, the IRB Chair may carry out the review or delegate the review to one or more experienced reviewers from among voting IRB members.

c. The reviewers may exercise all of the authorities of the IRB except that the reviewers may not disapprove the research. A research activity may be disapproved only after review in accordance with the non-expedited procedure set forth in paragraph 8.

d. The decision and the 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&D Committee.

10. CRITERIA FOR IRB APPROVAL:

a. In order to approve research covered by this Handbook the IRB must determine that all of the following requirements are satisfied:

(1) Risks to human subjects are minimized in the following ways:

(a) By using procedures that are consistent with sound research design and that do not unnecessarily expose subjects to risk; and

(b) Whenever appropriate, are already being performed on the subjects for diagnostic or treatment purposes. ***NOTE:*** *The IRB must document its determination on the level of risk either in the IRB minutes or the written communication to the investigator*;

(2) Risks to subjects are reasonable in relation to anticipated benefits, if any, and the importance of the knowledge that may be reasonably expected to result. In evaluating risks and benefits, the IRB should consider only those risks and benefits that may result from the research (as distinguished from risks and benefits the subjects would receive even if not participating in the research). The IRB is not to consider possible long-range effects of applying knowledge gained in the research (for example, the possible effects of the research on public policy) as among those research risks that fall within the purview of its responsibility;

(3) Selection of subjects is equitable. In making this assessment, the IRB takes into account the purposes of the research and the setting in which the research is to be conducted and should be particularly cognizant of the special problems of research involving vulnerable populations, such as children, prisoners, pregnant women, physically or mentally-disabled persons, and economically or educationally disadvantaged persons;

(4) Informed consent will be sought from each prospective subject or the subject's legally authorized representative, in accordance with, and to the extent required by paragraph 15;

(5) Informed consent will be appropriately documented, in accordance with, and to the extent required by paragraph 16;

(6) When appropriate, the research protocol makes adequate provision for monitoring the data collected to ensure the safety of subjects; and

(7) When appropriate, there are adequate provisions to protect the privacy of subjects and to maintain the confidentiality of data.

b. When some or all of the subjects are likely to be vulnerable to coercion or undue influence, such as children, prisoners, physically or mentally-disabled persons, or educationally or economically disadvantaged persons, or require special considerations such as pregnant women, the protocol must include additional safeguards to protect the rights and welfare of these subjects.

c. VA also requires the following criteria to be met:

(1) Privacy and confidentiality provisions must take into consideration the requirements of Standards for Privacy of Individually-Identifiable Health Information (HIPAA Privacy Rule), 45 CFR Parts 160 and 164, and other laws regarding protection and use of Veterans' and others information, including the Privacy Act of 1974, 5 U.S.C. 552a; VA Claims Confidentiality Statute, 38 U.S.C. 5701; Confidentiality of Drug Abuse, Alcoholism and Alcohol Abuse, Infection with Human Immunodeficiency Virus (HIV), and Sickle Cell Anemia Medical Records, 38 U.S.C. 7332; and Confidentiality of Healthcare Quality Assurance Review Records, 38 U.S.C. 5705 (see VHA Handbook 1605.1);

(2) Relevance of the research to the mission of VA and the Veteran population that it serves must be considered by the IRB. If non-Veterans will be included, the protocol and related materials must justify the inclusion of non-Veterans; and

(3) The IRB must ensure that mechanisms are implemented to manage, reduce, or eliminate potential, actual, or perceived conflicts of interest related to all aspects of the research, including financial interests, clinical roles (for example, investigator-patient relationships), and other professional or personal roles.

11. REVIEW BY INSTITUTION:

a. Research that has been approved by the IRB may be subject to further appropriate review and approval or disapproval by officials of the institution, but those officials may not approve human subjects research if it has not been approved by the IRB.

b. An IRB-approved research activity may be disapproved by the IO, the R&D Committee, or ORD. If a research activity is disapproved by the IRB, or modifications to the research are required by the IRB, the disapproval or need for modification cannot be overruled by any other authority (e.g., IO or R&D Committee).

c. The R&D Committee must provide the final approval before the research can be initiated in accordance with VHA Handbook 1200.01.

12. SUSPENSION OR TERMINATION OF IRB APPROVAL: The IRB has authority to 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. 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 investigator, appropriate IO(s), ORO (in accordance with VHA Handbook 1058.01), and appropriate federal agencies according to applicable local, VA, and other federal requirements. ***NOTE:*** *The R&D Committee and the IO also have authority to suspend or terminate their approval of research (see Handbook 1200.01).*

13. COLLABORATIVE RESEARCH: This section addresses collaborations between VA and non-VA investigators. Collaboration is encouraged when VA investigators have a substantive role in the design, conduct, and/or analysis of the research. VA may also serve as a Coordinating Center for collaborative studies. ***NOTE:*** *For purposes of this Handbook, collaborative studies do not include studies conducted under a CRADA with pharmaceutical companies or other for-profit entities.*

a. **IRB of Record Approval.** Each institution is responsible for safeguarding the rights and welfare of human subjects and providing oversight of the research activities conducted at that institution.

(1) Each collaborating institution engaged in human subjects research must obtain approval from its IRB of Record and hold a FWA or another assurance acceptable to VA, e.g. DoD assurance.

(2) VA investigators must submit a protocol or other documentation to their VA IRB of Record that delineates which research activities will be conducted by VA.

(3) Each institution engaged in the collaborative research must 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 at VA and which will be performed at other institutions.

(a) The VA informed consent document must clearly state when procedures mentioned at other institutions are part of the VA's portion of the study.

(b) The informed consent document and HIPAA authorization must be consistent and include information describing the following:

1. PHI to be collected and/or used by the VA research team;

2. PHI to be disclosed to the other institutions; and

3. Purpose for which the PHI may be used.

(c) **Waivers.** 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 Privacy Officer ensures and documents VA's authority to disclose the PHI to another institution. A waiver of HIPAA authorization is not sufficient to fulfill the requirements of other applicable privacy regulations such as the Privacy Act of 1974 (5 U.S.C. 552a).

b. **Research Data.** The protocol, addendum, and/or IRB of Record application must describe the data to be disclosed to collaborators, the entity(ies) to which the data are to be disclosed, and how the data are to be transmitted. This includes data from individual subjects as well as other data developed during the research such as the analytic data and the aggregate data.

(1) 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 (RCS) 10-1.

(2) All disclosures and data transmission must meet privacy and security requirements per VA Directive 6500, VA Handbook 6500, and VHA Handbook 1605.1.

c. **Written agreements.** Collaborative research involving non-VA institutions may not be undertaken without a signed written agreement (e.g., a CRADA or a Data Use Agreement (DUA)) that addresses such issues as the responsibilities of each party, the ownership of the data, and the reuse of the data for other research. ***NOTE:*** *Any reuse must be consistent with the protocol, the informed consent document, and the HIPAA authorization.*

14. IRB RECORDS:

a. An institution, or when appropriate an IRB, shall prepare and maintain adequate documentation of IRB activities, including the following:

(1) Copies of all research protocols reviewed, scientific evaluations, if any, that accompany the proposals, approved consent documents, progress reports submitted by investigators, and reports of injuries to subjects;

(2) Minutes of IRB meetings as described in paragraph 7.c.;

(3) Records of continuing review activities;

(4) Copies of all correspondence between the IRB and the investigators;

(5) A roster of IRB members in the same detail as described in paragraph 6.g. IRB records must include a resume or Curriculum Vitae for each voting IRB member that is updated at the time of appointment or reappointment;

(6) Written procedures for the IRB in the same detail as described in paragraph 7.a.; and

(7) Statement of significant new findings provided to subjects, as required by paragraph 15.d.(5).

b. All records must be accessible for inspection and copying by authorized representatives of VA, ORO, OHRP, FDA, and other authorized entities at reasonable times and in a reasonable manner. Records should be disposed in accordance with VHA RCS 10-1.

c. IRB records are the property and the responsibility of the local research office. The local VA facility must designate where the records will be maintained or stored. ***NOTE:*** *Records of an affiliate IRB are addressed in the MOU (see paragraph 5.d.(2)(a) and VHA Handbook 1058.03). The MOU must ensure that all applicable federal and VA regulations are met.*

15. GENERAL REQUIREMENTS FOR INFORMED CONSENT:

a. **General Requirements.** Except as provided elsewhere in this policy, no investigator may involve a human being as a subject in research covered by this policy unless the investigator has obtained the legally effective informed consent of the subject or the subject's legally authorized representative. An investigator shall seek such consent only under circumstances that provide the prospective subject or the representative sufficient opportunity to consider whether or not to participate and that minimize the possibility of coercion or undue influence.

(1) The information that is given to the subject or the representative must be in language understandable to the subject or the representative.

(2) No informed consent process, whether oral or written, may include any exculpatory language through which the subject or the representative is made to waive, or appear to waive, any of the subject's legal rights, or releases or appears to release, the investigator, the sponsor, the institution or its agents from liability for negligence.

b. **Basic Elements of Informed Consent.** Except as provided in paragraph 15.e., in seeking informed consent the following information must be provided to each subject:

(1) A statement that the study involves research, an explanation of the purposes of the research and the expected duration of the subject's participation, a description of the procedures to be followed, and identification of any procedures that are experimental;

(2) A description of any reasonably foreseeable risks or discomforts to the subject;

(3) A description of any benefits to the subject or to others that may reasonably be expected from the research;

(4) A disclosure of appropriate alternative procedures or courses of treatment, if any, that might be advantageous to the subject;

(5) A statement describing the extent, if any, to which confidentiality of records identifying the subject will be maintained;

(6) An explanation as to whether any compensation is available, and an explanation as to whether any medical treatments are available if injury occurs and, if so, what they consist of, or where further information may be obtained (see paragraph 25);

(7) An explanation of whom to contact for answers to pertinent questions about the research and research subjects' rights, and whom to contact in the event of research-related injury to the subject; and

(8) A statement that participation is voluntary, refusal to participate involves no penalty or loss of benefits to which the subject is otherwise entitled, and that the subject may discontinue participation at any time without penalty or loss of benefits to which the subject is otherwise entitled.

c. **Additional Elements Required by VA.** The following additional elements of informed consent are required for VA research:

(1) Any payments the subject is to receive for participating in the study;

(2) Any real or apparent conflict of interest by investigators where the research will be performed; and

(3) A statement that VA will provide treatment for research related injury in accordance with applicable federal regulations (see paragraph 25).

d. **Additional Elements of Informed Consent.** When appropriate, one or more of the following elements of information shall also be provided to each subject:

(1) A statement that the particular treatment or procedure may involve risks to the subject (or to the embryo or fetus, if the subject is or becomes pregnant) that are currently unforeseeable;

(2) Anticipated circumstances under which the subject's participation may be terminated by the investigator without regard to the subject's consent;

(3) Any additional costs to the subject that may result from participation in the research;

(4) The consequences of a subject's decision to withdraw from the research and procedures for orderly and safe termination of participation by the subject;

(5) A statement that any significant new findings developed during the course of the research that may relate to the subject's willingness to continue participation will be provided to the subject;

(6) The approximate number of subjects to be entered in the study; and

(7) When appropriate, a statement that informs VA research subjects that they or their insurance will not be charged for any costs related to the research. ***NOTE:*** *Some Veterans are required to pay copayments for medical care and services specifically related to their medical care provided by VA. These co-payment requirements will continue to apply to medical care and services that are not part of the research procedures or interventions.*

e. **Waiver or Alteration of Informed Consent.** The IRB may approve an informed consent procedure that does not include, or that alters, some or all of the elements of informed consent set forth above, or waive the requirement to obtain informed consent provided that:

(1) The IRB finds and documents that the research or demonstration project is to be conducted by or subject to the approval of state or local government officials and is designed to study, evaluate, or otherwise examine:

(a) Public benefit or service programs (also see Appendix A, paragraph 6); 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; and

(b) The research could not practicably be carried out without the waiver or alteration; **or**

(2) The IRB finds and documents that:

(a) The research involves no more than minimal risk to the subjects;

(b) The waiver or alteration will not adversely affect the rights and welfare of the subjects;

(c) The research could not practicably be carried out without the waiver or alteration; and

(d) Whenever appropriate, the subjects will be provided with additional pertinent information after participation.

f. The informed consent requirements in this Handbook are not intended to preempt any applicable federal, state, or local laws that require additional information to be disclosed in order for informed consent to be legally effective.

g. Nothing in this policy 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.

16. DOCUMENTATION OF INFORMED CONSENT:

a. Except as provided in paragraph 16.c., informed consent shall be documented by the use of a written consent form approved by the IRB and signed by the subject or the subject's LAR. A copy shall be given to the person signing the form.

b. Except as provided in paragraph 16.d., the informed consent document may be either of the following:

(1) A written consent document that embodies the elements of informed consent described in paragraph 15. This form may be read to the subject or the subject's legally authorized representative, but in any event, the investigator shall give either the subject or the representative adequate opportunity to read it before it is signed; or

(2) A short form written consent document stating that the elements of informed consent required in paragraph 15 have been presented orally to the subject or the subject's legally authorized representative. When this method is used, there shall be a witness to the oral presentation. Also, the IRB shall approve a written summary of what is to be said in the oral presentation to the subject or the representative. Only the short form itself is to be signed by the subject or the representative. However, the witness shall sign both the short form and a copy of the summary, and the person actually obtaining consent shall sign a copy of the summary. A copy of the summary shall be given to the subject or the representative, in addition to a copy of the short form. ***NOTE:*** *The IRB cannot waive the requirement for a witness or witness signature when the short form consent is used.*

c. The IRB may waive the requirement for the investigator to obtain a signed consent document for some or all subjects if it finds either:

(1) That the only record linking the subject and the research is the consent document and the principal risk is potential harm resulting from a breach of confidentiality. Each subject will be asked whether the subject wants documentation linking the subject with the research, and the subject's wishes will govern; or

(2) That the research presents no more than minimal risk of harm to subjects and involves no procedures for which written consent is normally required outside of the research context.

d. In cases in which the documentation requirement is waived, IRB may require the investigator to provide subjects with a written statement regarding the research.

e. **VA-specific Requirements.**

(1) The consent form must be the most recent IRB-approved consent form that includes all the required elements and, as appropriate, additional elements. The IRB approval must be documented on the consent form indicating the date of approval.

(2) The informed consent document must be signed and dated by:

(a) The subject or the subject's LAR; and

(b) The person obtaining the informed consent. However, the IRB may waive this requirement for the signature of the person obtaining consent (even where the signature of the subject or the LAR continues to be required) where there is no physical contact with the subject (e.g., where the only contact with the subject is by telephone or mail).

(c) Consent may be obtained electronically so long as the informed consent process meets all requirements in paragraph 16 of this Handbook and VA requirements; and:

(1) Authentication controls on electronic consent provide reasonable assurance that such consent is rendered by the proper individual; and

(2) The subject dates the consent as is typical or that the software provides the current date when signed.

f. **Photography, Video and/or Audio Recording for Research Purposes.** The informed consent for research must include information describing any photographs, video, and/or audio recordings to be taken or obtained for research purposes, how the photographs, video, and/or audio recordings will be used for the research, and whether the photographs, video, and/or audio recordings will be disclosed outside VA.

(1) An informed consent to take a photograph, video and/or audio recording cannot be waived by the IRB.

(2) 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.

17. RESEARCH INVOLVING PREGNANT WOMEN, HUMAN FETUSES, AND NEONATES AS SUBJECTS:

a. Research that involves provision of in vitro fertilization services cannot be conducted by VA investigators while on official duty, or at VA facilities, or at VA-approved off-site facilities. ***NOTE:*** *Prospective and retrospective studies that enroll or include pregnant subjects who conceived through in vitro fertilization or other artificial reproductive technologies are permitted.*

b. Research in which the focus is either a fetus, or human fetal tissue, in-utero or ex-utero (or uses human fetal tissue), cannot be conducted by VA investigators while on official 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.

c. VA investigators cannot conduct interventions in research that enroll neonates while on official duty, or at VA facilities, or at VA-approved off-site facilities. Prospective observational and retrospective record review studies that involve neonates or neonatal outcomes are permitted.

d. Women who are known to be pregnant and/or their fetuses may be involved in research if all of the requirements of 45 CFR 46.204 are met including informed consent requirements and the following ethical and scientific criteria:

(1) Where scientifically appropriate, preclinical studies, including studies on pregnant animals, and clinical studies, including 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. 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; and

(4) The VA medical facility Director certifies that the medical facility has sufficient expertise in women's health to conduct the proposed research (see guidance at http://www.research.va.gov/resources/policies/default.cfm).

18. RESEARCH INVOLVING PRISONERS AS SUBJECTS:

a. 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. ***NOTE:*** *Refer to the ORD Web site at*

http://www.research.va.gov/resources/policies/default.cfm for details on the procedures for waiver applications.

b. If such a waiver is granted, the research must comply with the requirements of 45 CFR 46.301 - 46.306. ***NOTE:*** *A link to these requirements is provided on the ORD Web site at: http://www.research.va.gov/resources/policies/default.cfm.*

19. RESEARCH INVOLVING CHILDREN AS RESEARCH SUBJECTS:

a. VA is authorized to care for Veterans and to conduct research that supports the mission of VHA and that enhances the quality of health care delivery to Veterans. Therefore, research involving children must be reviewed carefully by the IRB for its relevance to VA and must not be greater than minimal risk. The VA 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: *For purposes of this Handbook, research involving biological specimens or data obtained from children is considered to be research involving children even if de-identified. If the biological specimens or data were previously collected, they must have been collected under applicable policies and ethical guidelines.*

b. 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:*** *A link to these requirements is provided on the ORD Web site at: http://www.research.va.gov/resources/policies/default.cfm.*

20. SUBJECTS LACKING DECISION-MAKING CAPACITY:

a. **Criteria for Enrollment.** Individuals who lack decision-making capacity may be enrolled in VA research where:

(1) The IRB determines that the proposed research entails:

(a) No greater than minimal risk to the subject; or

(b) Presents a greater probability of direct benefit to the subject than harm to the subject; or

(c) Greater than minimal risk and no prospect of direct benefit to individual subjects, but 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 to satisfying the conditions above, the IRB determines that:

(a) 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**

(b) 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).

b. **Determination of Capacity.** When planning to enter subjects with impaired decision-making capacity, investigators must address in the protocol how they will determine when surrogate consent (i.e., a LAR) will be required. In general, the research staff must perform or obtain and document a clinical assessment of decision-making capacity for any subject suspected of lacking decision-making capacity. However, the IRB must review and approve the plan to ensure that it is appropriate given the population and setting of the research. ***NOTE:*** *Individuals ruled incompetent by a court of law are considered to lack decision-making capacity.*

c. **Surrogate consent.** When the potential subject is determined to lack decision-making capacity, investigators must obtain consent from the LAR of the subject (i.e., surrogate consent). ***NOTE:*** *Investigators and IRBs have a responsibility to consult with the Office of General Counsel (OGC) regarding state or local requirements for surrogate consent for research that may supersede VA requirements.*

d. **Authorized Person.** The following persons are authorized to consent on behalf of persons who lack decision-making capacity in the following order of priority in accordance with VA regulations at 38 CFR 17.32(e), (g)(3). ***NOTE:*** *Consent for research is required in addition to the consent that is obtained for the patient's non-research related treatments and procedures.*

(1) Health care agent (i.e., an individual named by the subject in a Durable Power of Attorney for Health Care);

(2) Legal guardian or special guardian;

(3) Next of kin: a close relative of the patient 18 years of age or older, in the following priority: spouse, child, parent, sibling, grandparent, or grandchild; or

(4) Close friend.

NOTE: *The persons authorized to consent on behalf of persons who lack decision-making capacity for participation in the research may not necessarily be the same as the persons authorized to provide permission for the use and disclosure of information on a HIPAA authorization on behalf of persons who lack decision-making capacity (see VHA Handbook 1605.1).*

e. **Dissent or Assent.** If feasible, the investigator must explain the proposed research to the prospective research subject even when the surrogate gives consent. Although unable to provide informed consent, some persons may resist participating in a research protocol approved by their representatives. Under no circumstances may a subject be forced or coerced to participate in a research study even if the LAR has provided consent.

f. **Responsibilities of LARs.** LARs are acting on behalf of the potential subjects, therefore:

(1) LARs must be told that their obligation is to try to determine what the subjects would do if able to make an informed decision.

(2) If the potential subjects' wishes cannot be determined, the LARs must be told they are responsible for determining what is in the subjects' best interest.

21. CERTIFICATES OF CONFIDENTIALITY:

a. Several HHS operating agencies issue Certificates of Confidentiality to protect research subjects. Generally, any research project that collects personally identifiable, sensitive information and that has been approved by an IRB operating under either an approved FWA issued by the OHRP or the approval of the FDA is eligible for a Certificate of Confidentiality. Sensitive information for purposes of a Certificate of Confidentiality includes (but is not limited to) information relating to sexual attitudes, preferences, or practices; information relating to the use of alcohol, drugs, or other addictive products; information pertaining to illegal conduct; information that, if released, might be damaging to an individual's financial standing, employability, or reputation within the community or might lead to social stigmatization or discrimination; information pertaining to an individual's psychological well-being or mental health; and genetic information or tissue samples.

b. Some types of research projects that are eligible for a Certificate of Confidentiality include:

(1) Research on HIV, Acquired Immune Deficiency Syndrome, and other sexually transmitted diseases;

(2) Studies that collect information on sexual attitudes, preferences, or practices;

(3) Studies on the use of alcohol, drugs, or other addictive products;

(4) Studies that collect information on illegal conduct;

(5) Studies that gather information that if released could be damaging to a participant's financial standing, employability, or reputation within the community;

(6) Research involving information that might lead to social stigmatization or discrimination if it were disclosed;

(7) Research on participants' psychological well-being or mental health;

(8) Genetic studies, including those that collect and store biological samples for future use; and

(9) Research on behavioral interventions and epidemiologic studies.

c. Investigators and IRBs are urged to consider the use of Certificates of Confidentiality when appropriate.

d. When VA conducts a study that is protected by a Certificate of Confidentiality, the following health record documentation provisions apply:

(1) For studies that do not involve a medical intervention (e.g., observational studies, including interview and questionnaire studies), no annotation may be made in the health record.

(2) For studies that involve a medical intervention, a progress note entry should indicate that an individual has been enrolled in a research study, any details that would affect the subject's clinical care, and the name and contact information for the investigator conducting the study. Subjects' informed consent forms and HIPAA authorization documents are not to be included in the health record.

e. Investigators should work with the research office in their facility to assure that when Veterans are enrolled in a study protected by a Certificate of Confidentiality, they are not simultaneously enrolled in other interventional studies unless it is absolutely clear that this enrollment does not raise safety issues.

22. PRIVACY OFFICER AND INFORMATION SECURITY OFFICER DUTIES: The PO and the ISO serve in an advisory capacity to the IRB as either non-voting members or as consultants. The facility PO and ISO are responsible for:

a. Ensuring that the proposed research complies with all applicable local, VA, and other Federal requirements for privacy and confidentiality, and for information security, by identifying and addressing potential concerns about proposed research studies.

b. Reviewing the proposed study protocol, study specific privacy and security information, and any other relevant materials submitted with the IRB application.

c. Identifying deficiencies in the provisions for privacy and confidentiality or information security, respectively, of the proposed research, and making recommendations to the investigator and/or the IRB of options available to correct the deficiencies.

d. Following up with the investigator and/or the IRB, in a timely manner, to ensure the proposed research is in compliance with relevant privacy and confidentiality and information security requirements, respectively, before the investigator initiates the study.

e. A final review is required only after the IRB has approved the study to ensure no further changes impact the privacy and security requirements of this study.

***NOTE**: If a study includes information covered under 38 U.S.C. 7332 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. manuscript or publication.*

23. HIPAA AUTHORIZATION:

a. **Written Authorization.** In accordance with the HIPAA Privacy Rule at 45 CFR 164.508, a written authorization signed by the individual to whom the information or record pertains, is required when VA medical facilities need to access, collect, develop, use, or disclose individually-identifiable health information for a purpose other than treatment, payment, or health care operations (e.g., research) unless there is legal authority (e.g., waiver, limited data set with data use agreement, etc.) to disclose such information (see VHA Handbook 1605.1).

(1) VA Form 10-0493, Authorization for Use & Release of Individually Identifiable Health Information for VHA Research, must be used to document the authorization. The authorization may not be embedded in the consent form;

(2) The information in the authorization must not contradict any provisions of the protocol, informed consent, or other documents submitted for IRB approval;

(3) All potential disclosures to a non-VA entity must be listed within the authorization;

(4) The PO 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 (see VHA Handbook 1605.1);

(5) Data disclosed under a properly executed HIPAA authorization must be securely transferred according to VA information security requirements;

b. **Waiver of HIPAA Authorization.** An investigator requesting a waiver of HIPAA authorization must provide information sufficient to allow the IRB or Privacy Board 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:

(a) The use or disclosure of the requested information involves no more than minimal risk to the privacy of individuals based on, at least, 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 the research, unless there is a health or research justification for retaining the identifiers or such retention is otherwise required by law. ***NOTE:*** *Records, including identifiers, must be retained until disposition instructions are approved by the National Archives and Records Administration (NARA) and are published in VHA RCS 10-1. Once the disposition schedule is determined, records should be disposed in accordance with VHA RCS 10-1;* and

3. Adequate written assurances that the PHI will not be reused or disclosed to any other person or entity, except as required by law, for authorized oversight of the research study, or for other research for which the use or disclosure of the requested information is permitted by the Privacy Rule;

(b) The research could not practicably be conducted without the waiver; and

(c) 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).

(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, the waiver is not valid. If the IRB of record cannot provide a waiver of authorization, a properly constituted Privacy Board may be used to review and approve the waiver request in accordance with 45 CFR 164.512(i) (see VHA Handbook 1605.1).*

c. **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.

(1) VA investigators must not arbitrarily review PHI based on their employee access to PHI until the investigator documents the following required information as "Preparatory to Research" in a designated file that is readily accessible for those required to audit such information (e.g., Health Information Manager or PO):

(a) Access to PHI is only to prepare a protocol;

(b) No PHI will be removed from the covered entity (i.e., VHA); and

(c) Access to PHI is necessary for preparation of the research protocol.

(2) Non-VA researchers may not obtain VA information for preparatory to research activities without appropriate VA approvals (see VHA Handbook 1605.1).

(3) During the preparatory to research activities the VA investigator:

(a) Must only record aggregate data. The aggregate data 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;

(b) Must not record any individually identifiable health information; and

(c) 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.*

(4) Contacting potential research subjects and conducting pilot or feasibility studies are not considered activities preparatory to research.

(5) Activities preparatory to research only encompass the time to prepare the protocol and ends when the protocol is submitted to the IRB.

24. PARTICIPATION OF NON-VETERANS AS RESEARCH SUBJECTS:

a. Non-Veterans may be entered into a VA-approved research study that involves VA outpatient or VA hospital treatment (38 CFR 17.45, 17.92), but only when there are insufficient Veteran patients suitable for the study. The investigator must justify including non-Veterans and the IRB must review the justification and provide specific approval for recruitment of non-Veterans.

(1) **Outpatient Care for Research Purposes.** Any person who is a bona fide volunteer may be furnished outpatient treatment when the treatment to be rendered is part of an approved VA research study and there are insufficient Veteran patients suitable for the study (38 CFR 17.92).

(2) **Hospital Care for Research Purposes.** Any person who is a bona fide volunteer may be admitted to a VA hospital when the treatment to be rendered is part of an approved VA research study and there are insufficient Veteran patients suitable for the study (38 CFR 17.45).

b. Non-Veterans may be recruited for studies that will generally benefit Veterans and their well-being but would not include Veterans as subjects. Examples include surveys of VA providers, studies involving Veterans' family members, or studies including active duty military personnel. Although active duty military personnel are not considered Veterans, they should be included in VA studies whenever appropriate.

c. In addition to the non-Veterans referenced above, active duty military personnel may be entered into VA research conducted jointly by VA and DoD or within DoD facilities.

d. All VA regulations and policies related to Veterans as research subjects apply to non-Veterans entered into VA research.

e. Non-Veterans may not be entered into VA studies simply because a non-Veteran population is easily accessible to the investigator.

f. Investigators must follow VHA Handbook 1605.04, Notice of Privacy Practices, to provide notice of privacy practices and acknowledgement for any non-Veteran enrolled in the approved protocol.

25. TREATMENT OF RESEARCH-RELATED INJURIES:

a. VA medical facilities, including joint VA-DoD federal health care centers, must provide necessary medical treatment (i.e., not just emergency treatment) to a research subject injured as a result of participation in a research study approved by a VA R&D Committee and conducted under the supervision of one or more VA employees (38 CFR 17.85). This requirement does not apply to:

(1) Treatment for injuries due to non-compliance by a subject with study procedures; or

(2) Research conducted for VA under a contract with an individual or a non-VA institution.

b. Care for VA research subjects under this paragraph must be provided in VA medical facilities, except in the following situations:

(1) If VA facilities are not capable of furnishing economical care or are not capable of furnishing the care or services required, VA medical facility Directors shall contract for the needed care;

(2) If inpatient care must be provided to a non-Veteran under this paragraph, VA medical facility Directors may contract for such care; or

(3) If a research subject needs treatment in a medical emergency for a condition covered by this paragraph, VA medical facility Directors must provide reasonable reimbursement for the emergency treatment in a non-VA facility.

26. INTERNATIONAL RESEARCH:

a. VA international research is defined 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 out of the U.S. This definition applies regardless of the funding source (funded or unfunded) and to research conducted through any mechanism of support including MOUs, CRADAs, grants, contracts, or other agreements. ***NOTE:*** *For the purposes of this Handbook, research conducted at U.S. military bases, ships, or embassies is not considered international research.*

(1) Sending specimens or data to individuals with VA appointments at international sites (e.g., a WOC appointment, a VA investigator on sabbatical at an international site) is considered international research. 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.

(2) International research includes multi-site trials involving non-U.S. sites where VA is the study sponsor, a VA investigator is the overall study-wide PI, VA holds the Investigational New Drug (IND), or the VA manages the data collection and the data analyses.

(3) International research does not include studies in which VA is only one of multiple participating sites 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).

b. Before approving international research involving human subjects research, the IRB must ensure that human subjects outside of the U.S. who participate in research projects in which VA is a collaborator receive equivalent protections as research participants inside the U.S. (see OHRP guidance at http://www.hhs.gov/ohrp/international/index.html). ***NOTE:*** *The VA medical facility Director must approve participation in the proposed international research (see guidance at: http://www.research.va.gov/resources/policies/default.cfm).*

c. All international research must also be approved explicitly in a document signed by the VA medical facility Director, except for Cooperative Studies Program activities which must be approved by the CRADO.

27. ACCREDITATION OF HUMAN RESEARCH PROTECTION PROGRAMS: Any VA facility with a FWA must obtain accreditation of its HRPP by the accrediting organization specified by ORD. This HRPP accreditation must be obtained in accordance with a schedule determined by ORD based on the facility's HRPP accreditation status and history. ***NOTE:*** *Refer to the ORD Web site for details on accreditation procedures: http://www.research.va.gov/pride/accreditation/default.cfm.*

a. Maintenance of HRPP accreditation must be in accordance with ORD HRPP accreditation requirements including those relating to academic affiliates or other Federal agencies providing IRB services to the VA facility.

b. Academic affiliates may be required to cooperate with the accrediting organization specified by ORD or to maintain their own accreditation with another accrediting organization recognized by ORD.

28. STUDENT AND OTHER TRAINEE RESEARCH:

a. Trainees (e.g., students, residents, or fellows of any profession) may serve as participants, but not PIs within a VA facility, use VA human subjects data, or use human biological specimens that have been collected within VA for clinical, administrative, or research purposes only when:

(1) The study has been approved by the local VA medical facility and IRB, if appropriate; and

(2) Either they are:

(a) Enrolled in an institution with an educational affiliation agreement with that VA facility; or

(b) Directly appointed to a VA training program that has no external institutional sponsorship (e.g. VA Advanced Fellowship). ***NOTE:*** *A waiver may be obtained from the CRADO under special circumstances.*

b. A VA investigator sufficiently experienced in the area of the trainee's research interest must serve as PI and is responsible for oversight of the research and the trainee/student. The PI 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.

(1) If the trainee does not complete all aspects of the research prior to leaving VA, the VA investigator must ensure the protocol is completed or terminated in an orderly fashion, and in accordance with all applicable local, VA, and other federal requirements.

(2) When the trainee leaves VA, the VA investigator is responsible for ensuring that all research records are retained by VA.

29. VA INVESTIGATOR RESPONSIBILITIES: The investigator must give first priority to the protection of research subjects, uphold professional and ethical standards and practices, and adhere to all applicable VA and other federal requirements, including the local VA facility's policies and procedures, regarding the conduct of research and the protection of human subjects. The investigator must hold a current VA appointment to conduct VA research.

a. **Qualifications to Conduct Human Subjects Research.** VA investigators must have the appropriate training, education, expertise, and credentials to conduct the research according to the research protocol.

(1) PIs must ensure that 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.

(2) Investigators and their staff conducting human subjects research must be credentialed and privileged as required by current local and VA requirements (see VHA Handbook 1100.19 and VHA Directive 2012-030, Credentialing of Health Care Professionals, or successor policy). Investigators and their research staff may only perform those activities in a research study for which they have the relevant credentials and privileges.

(3) Investigators and co-investigators must be identified on the IRB application and must provide credentials, conflict of interest statements or other documentation required by VA and local facility policies.

(4) All individuals involved in conducting VA human subjects research are required to complete training in ethical principles on which human subjects research is to be conducted. Specific requirements regarding the type and frequency of training are found on ORD's Web site at: http://www.research.va.gov/pride/training/options.cfm. All other applicable VA and VHA training requirements at the local and national level must be met (e.g., privacy and information security training).

b. **Research Protocol.** The investigator must develop and submit a research protocol that is scientifically valid, describes the research objectives, background and methodology, provides for fair and equitable recruitment and selection of subjects, minimizes risks to subjects and others, and describes a data and safety monitoring plan consistent with the nature of the study. The research must be relevant to the health or welfare of the Veteran population. When relevant, the protocol must include the following safety measures:

(1) The type of safety information to be collected including AEs;

(2) Frequency of safety data collection;

(3) Frequency or periodicity of review of cumulative safety data;

(4) Statistical tests for analyzing the safety data to determine if harm is occurring; and

(5) Conditions that trigger an immediate suspension of the research, if applicable.

c. **Approvals.** The investigator must submit the protocol for initial review and obtain written approvals from the IRB, other applicable committees, and from the R&D Committee. In addition, the investigator must receive written notice from the ACOS/R&D that the research may commence before initiating the research.

(1) Once approved by the IRB, the protocol must be implemented as approved. All modifications to the approved research protocol or consent form must be approved by the IRB prior to initiating the changes except when necessary to eliminate apparent immediate hazards to the subject.

(2) The investigator must also obtain continuing review and approval at a frequency established by the IRB, but not less than once every year and is expected to submit all materials required for continuing review in sufficient time to assure approval prior to the expiration date. No research activities may be conducted at any time without a currently valid IRB approval.

d. **Conflict Of Interest.** The investigator 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.

e. **Initial Contact.** During the recruitment process, members of the research team must make initial contact with potential subjects in person or by letter prior to initiating any telephone contact, unless there is written documentation that the subject is willing to be contacted by telephone about the study in question or a specific kind of research as outlined in the study. ***NOTE****: If a research repository from a previous study is used to identify subjects, there must be an IRB approved HIPAA waiver for this activity in the new protocol.*

(1) Any initial contact by letter or telephone must provide a telephone number or other means that the potential subject can use to verify that the study constitutes VA research.

(2) If a contractor makes the initial contact by letter, the VA investigator must sign the letter.

NOTE: *This paragraph does not apply to situations where a Veteran calls in response to an advertisement.*

f. **Informed Consent for Research.** The investigator must obtain and document legally effective informed consent of the subject or the subject's LAR prospectively (i.e., no screening or other interaction or intervention involving a human subject can occur until after the IRB-approved informed consent requirements have been met) that is in alignment with ethical principles that govern informed consent for research. The only exceptions are if the IRB determines the research is exempt, or approves a waiver of the informed consent process, or approves a waiver of the signed informed consent document (see paragraphs 15 and 16).

(1) If the investigator does not personally obtain informed consent, the investigator must delegate this responsibility in writing (e.g., by use of a delegation letter) to research staff sufficiently knowledgeable about the protocol and related concerns to answer questions from prospective subjects, and about the ethical basis of the informed consent process and protocol.

(a) If the investigator contracts with a firm, e.g., a survey research firm, to obtain consent from subjects, collect private individually identifiable information from human subjects, or are 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 PO must determine that there is appropriate authority to allow the disclosure of individual names and other information to the contracted firm.

(b) The investigator must ensure that all original signed and dated informed consent documents are maintained in the investigator's research files, readily retrievable, and secure.

g. **HIPAA Authorization.** The investigator or designee must obtain HIPAA authorization for the use and disclosure of the subject's PHI, or obtain an IRB-approved waiver of HIPAA authorization (see paragraph 23 in this Handbook and VHA Handbook 1605.1) unless there is a limited data set and appropriate DUA.

h. **Reporting.** The investigator is responsible for reporting unanticipated problems involving risks to subjects or others, serious unanticipated problems involving risks to subjects or others, local unanticipated serious adverse events, apparent serious or continuing noncompliance, any termination or suspension of research; and privacy or information security incidents related to VA research, including: any inappropriate access, loss, or theft of PHI; noncompliant storage, transmission, removal, or destruction of PHI; or theft, loss, or noncompliant destruction of equipment containing PHI, in accordance with local facility or IRB SOPs and VHA Handbook 1058.01. ***NOTE:*** *Current guidance on such reporting can be found on the ORO Web site at: http://vaww.vha.vaco.portal.va.gov/sites/ORO/RCO/Memoranda%20and%20Clarifications/Forms/AllItems.aspx. This is an internal VA Web site not available to the public.*

i. **Research Records.** All written information given to subjects must be in the investigator's research file along with the consent form(s). The investigator's research records are not yet scheduled in VHA RCS 10-1 and therefore must be retained until disposition instructions, as approved by NARA, are published in VHA RCS 10-1. ***NOTE:*** *Once the disposition schedule is determined, records should be disposed in accordance with VHA RCS 10-*

1. If the investigator leaves VA, all research records must be retained by the VA facility where the research was conducted.

j. **VHA Health Record.** A VHA health record must be created or updated, and a progress note created, for all research subjects (Veterans or Non-Veterans) who are admitted to VA medical facilities as in-patients, treated as outpatients at VA medical facilities, or when research procedures or interventions are 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 nursing homes) (see VHA Handbook 1907.01). Informed consent documents are not required to be in the health record.

k. **Investigational Drugs and Devices.** The investigator must conduct VA human subjects research involving investigational drugs and devices in accordance with all applicable VA policies and other federal requirements including, but not limited to: this Handbook, VHA Handbook 1108.04, and applicable FDA regulations. The storage and security procedures for test articles used in research must be reviewed and approved by the IRB and follow all applicable federal rules.

l. **Initiation of Research Projects.** IRB approval is for a specified time period based on the degree of risk of the study, not to exceed 1 year. The IRB determines the expiration date based upon its date of review and communicates that date to the investigator in the written approval letter. The investigator must not initiate the IRB approved research protocol until all applicable requirements in VHA Handbook 1200.01 have also been met including obtaining R&D Committee approval.

m. **Expiration of IRB Approval.** There is no provision for any grace period to extend the conduct of research beyond the expiration date of IRB approval. Therefore, continuing review and re-approval of research must occur on or before the date when IRB approval expires. If approval expires, the investigator must:

(1) Stop 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, except where stopping such interventions or interactions could be harmful to those subjects; and

(2) Immediately submit to the IRB Chair a list of research subjects who could be harmed by stopping specified study interventions or interactions. The IRB Chair must determine within 2 business days whether or not such interventions or interactions may continue.

30. REFERENCES:

a. 5 U.S.C. 552a, The Privacy Act of 1974.

b. 21 U.S.C. 321-60, Federal Food, Drug, and Cosmetic Act.

c. 38 U.S.C. 501, Rules and Regulations.

d. 38 U.S.C. 1710, Eligibility For Hospital, Nursing Home, and Domiciliary Care.

e. 38 U.S.C. 5701, Confidential Nature of Claims.

f. 38 U.S.C. 5705, Confidentiality of Medical Quality-Assurance Records.

g. 38 U.S.C. 7331, Informed Consent.

h. 38 U.S.C. 7332, Confidentiality of Drug Abuse, Alcoholism and Alcohol Abuse, Infection with Human Immunodeficiency Virus (HIV), and Sickle Cell Anemia Medical Records.

i. 38 U.S.C. 7334, Regulations.

j. 42 U.S.C. 262, Regulation of Biological Products.

k. 10 CFR Part 20, Standards for Protection Against Radiation.

l. 10 CFR Part 35, Medical Use of Byproduct Material.

m. 21 CFR Part 11, Electronic Records; Electronic Signatures.

n. 21 CFR Part 50, Protection of Human Subjects.

o. 21 CFR Part 56, IRBs.

p. 21 CFR Part 312, Investigational New Drug Application.

q. 21 CFR Part 812, Investigational Device Exemptions.

r. 38 CFR Part 16, Protection of Human Subjects.

s. 38 CFR Part 17, Medical.

t. 45 CFR Part 46, Protection of Human Subjects, Subpart A – Basic HHS Policy for Protection of Human Subjects; Subpart B – Additional Protections for Pregnant Women, Human Fetuses and Neonates Involved in Research; Subpart C – Additional Protections Pertaining to Biomedical and Behavioral Research Involving Prisoners as Subjects; and Subpart D – Additional Protections for Children Involved as Subjects in Research.

u. 45 CFR Part 160, General Administrative Requirements.

v. 45 CFR Part 164, Security and Privacy, Subpart E –Privacy of Individually Identifiable Health Information.

w. Expedited Review Categories, 63 FR 60364, Nov. 9, 1998.

x. VA Directive 6500, Managing Information Security Risk: VA Information Security Program.

y. VHA RCS 10-1.

z. VHA Directive 1200, VHA R&D Program.

aa. VHA Directive 2012-030, Credentialing of Health Care Professionals.

bb. VHA Handbook 1004.01, Informed Consent for Clinical Treatments and Procedures.

cc. VHA Handbook 1058.01, Research Compliance Reporting Requirements.

dd. VHA Handbook 1058.03, Assurance of Protection for Human Subjects in Research.

ee. VHA Handbook 1058.05, VHA Operations Activities That May Constitute Research.

ff. VHA Handbook 1100.19, Credentialing and Privileging.

gg. VHA Handbook 1108.04, Investigational Drugs and Supplies.

hh. VHA Handbook 1200.01, R&D Committee.

ii. VHA Handbook 1200.08, Safety of Personnel Engaged in Research.

jj. VHA Handbook 1200.12, Use of Data and Data Repositories in VHA Research.

kk. VHA Handbook 1200.16, Off Site Research.

ll. VHA Handbook 1200.17, VA NPC Authorized By Title 38 U.S.C. §§ 7361-66.

mm. VHA Handbook 1200.2, Research Business Operations.

nn. VHA Handbook 1605.1, Privacy and Release of Information.

oo. VHA Handbook 1605.02, Minimum Necessary Standard for Protected Health Information.

pp. VHA Handbook 1605.04, Notice of Privacy Practices.

qq. VHA Handbook 1907.01, Health Information Management and Health Records.

rr. VA Handbook 6500, Risk Management Framework for VA Information Systems - Tier 3: VA Information Security Program.

CATEGORIES OF EXEMPT RESEARCH

1. Research activities in which the only involvement of human subjects will be in one or more of the following categories may be exempt from this policy (38 CFR 16.101(b)):

2. Research conducted in established or commonly accepted educational settings, involving normal educational practices, such as:

a. Research on regular and special education instructional strategies; or

b. Research on the effectiveness of or the comparison among instructional techniques, curricula, or classroom management methods.

3. Research involving the use of educational tests (cognitive, diagnostic, aptitude, achievement), survey procedures, interview procedures or observation of public behavior, unless:

a. Information obtained is recorded in such a manner that human subjects can be identified, directly or through identifiers linked to the subjects; and

b. Any disclosure of the human subjects' responses outside the research could reasonably place the subjects at risk of criminal or civil liability or be damaging to the subjects' financial standing, employability, or reputation.

NOTE: *The exemption for research involving survey or interview procedures or observations of public behavior does not apply to research involving children, except for research involving observation of public behavior when the investigator(s) do not participate in the activities being observed.*

4. Research involving the use of educational tests (cognitive, diagnostic, aptitude, achievement), survey procedures, interview procedures, or observation of public behavior that is not exempt under paragraph 3 of this Appendix, if:

a. The human subjects are elected or appointed public officials or candidates for public office; or

b. Federal statute(s) require(s) without exception that the confidentiality of the personally identifiable information will be maintained throughout the research and thereafter.

5. Research involving the collection or study of existing data, documents, records, pathological specimens, or diagnostic specimens, if these sources are publicly available or if the information is recorded by the investigator in such a manner that subjects cannot be identified, directly or through identifiers linked to the subjects.

6. Research and demonstration projects which are conducted by or subject to the approval of department or agency heads, and which are designed to study, evaluate, or otherwise examine:

a. Public benefit or service programs;

b. Procedures for obtaining benefits or services under those programs;

c. Possible changes in or alternatives to those programs or procedures; or

d. Possible changes in methods or levels of payment for benefits or services under those programs.

NOTE: *The determination of exempt status for research and demonstration projects meeting the criteria in paragraph 6 in this Appendix must be made by the Under Secretary for Health on behalf of the Secretary of VA, after consultation with Office of Research and Development (ORD), Office of Research Oversight (ORO), Office of General Counsel (OGC), and other experts, as appropriate.*

7. Taste and food quality evaluation and consumer acceptance studies,

a. If wholesome foods without additives are consumed; or

b. 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 (FDA) or approved by the Environmental Protection Agency or the Food Safety and Inspection Service of the U.S. Department of Agriculture.

ACTIVITIES APPROPRIATE FOR EXPEDITED REVIEW

Source: 63 FR 60364-60367, Nov. 9, 1998.

1. APPLICABILITY: Research activities that: (1) present no more than minimal risk to human subjects, and (2) involve only procedures listed in one or more of the following categories, may be reviewed by the Institutional Review Board (IRB) through the expedited review procedure authorized by Title 45 Code of Federal Regulations (CFR) 46.110 and 21 CFR 56.110. The activities listed should not be deemed to be of minimal risk simply because they are included on this list. Inclusion on this list merely means that the activity is eligible for review through the expedited review procedure when the specific circumstances of the proposed research involve no more than minimal risk to human subjects.

a. The categories in this list apply regardless of the age of subjects, except as noted.

b. The expedited review procedure may not be used where identification of the subjects and/or their responses would reasonably place them at risk of criminal or civil liability or be damaging to the subjects financial standing, employability, insurability, reputation, or be stigmatizing, unless reasonable and appropriate protections will be implemented so that risks related to invasion of privacy and breach of confidentiality are no greater than minimal.

c. The expedited review procedure may not be used for classified research involving human subjects.

d. IRBs are reminded that the standard requirements for informed consent (or its waiver, alteration, or exception) apply regardless of the type of review--expedited or convened--utilized by the IRB.

e. The below research categories, 2.a. through 2.g., pertain to both initial and continuing IRB review.

2. RESEARCH CATEGORIES:

a. Clinical studies of drugs and medical devices only when the following conditions are 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.

b. 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 (as defined under 45 CFR 46.402(a)), 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.

c. Prospective collection of biological specimens for research purposes by noninvasive means. Examples include, but are not limited to:

(1) Hair and nail clippings in a non-disfiguring manner;

(2) Deciduous teeth at time of exfoliation or if routine patient care indicates a need for extraction;

(3) Permanent teeth if routine patient care indicates a need for extraction;

(4) Excreta and external secretions (including sweat);

(5) 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;

(6) Placenta removed at delivery;

(7) Amniotic fluid obtained at the time of rupture of the membrane prior to or during labor;

(8) 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;

(9) Mucosal and skin cells collected by buccal scraping or swab, skin swab, or mouth washings;

(10) Sputum collected after saline mist nebulization.

d. 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 include, but are not limited to:

(1) 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 subjects' privacy;

(2) Weighing or testing sensory acuity;

(3) Magnetic resonance imaging;

(4) Electrocardiography, electroencephalography, thermography, detection of naturally occurring radioactivity, electroretinography, ultrasound, diagnostic infrared imaging, doppler blood flow, and echocardiography; and

(5) Moderate exercise, muscular strength testing, body composition assessment, and flexibility testing where appropriate given the age, weight, and health of the individual.

e. Research involving materials (data, documents, records, or specimens) that have been collected, or will be collected solely for nonresearch 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)). This listing refers only to research that is not exempt.*)

f. Collection of data from voice, video, digital, or image recordings made for research purposes.

g. 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), (b)(3)). This listing refers only to research that is not exempt*.)

h. Continuing review of research previously approved by the convened IRB as follows:

(1) Where:

(a) The research is permanently closed to the enrollment of new subjects;

(b) All subjects have completed all research-related interventions; and

(c) 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.

i. Continuing review of research, not conducted under an investigational new drug application or investigational device exemption where research categories 2.b. through 2.h. 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.