Department of Veterans Affairs **VHA HANDBOOK 1200.05**
Veterans Health Administration **Transmittal Sheet**
Washington, DC 20420 **May 2, 2012**

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 the Department of Veterans Affairs research, which must be implemented no later than May 15, 2012.

2. MAJOR CHANGES. The major change is found in paragraph 64, which reflects changes in Human Research Protection Program accreditation policy.

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

4. RESPONSIBLE OFFICIALS. The Office of Research and Development (ORD)(10P9) is responsible for the contents of this Handbook. Questions may be addressed to (877) 254-3130.

5. RESCISSIONS. VHA Handbook 1200.05, Requirements for the Protection of Human Research Subjects, dated October 15, 2010.

6. RECERTIFICATION. This VHA Handbook is scheduled for recertification on or before the last working day of May 2017.

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REQUIREMENTS FOR THE PROTECTION OF HUMAN SUBJECTS IN RESEARCH

1. PURPOSE

The Department of Veterans Affairs (VA) is one of seventeen Federal departments and agencies that have agreed to follow the Federal Policy for the Protection of Human Subjects (Common Rule), effective June 18, 1991 (56 Federal Register (FR) 28001). This policy is incorporated in title 38 Code of Federal Regulations (CFR) Part 16. This Veterans Health Administration (VHA) Handbook defines the procedures for implementing 38 CFR Part 16 and other applicable Federal requirements for the protection of human subjects, and defines changes to the Human Research Protection Program accreditation policy.

2. AUTHORITY

a. Statutory provisions for protection of VA patient rights title 38 United States Code (U.S.C.) § 501, 7331, and 7334.

b. VA regulations pertaining to protection of patient rights: 38 CFR 16.116, 38 CFR 17.32, and 17.33a.

c. VA regulations pertaining to rights and welfare of human subjects participating in research: 38 CFR Part 16 (Federal Policy for the Protection of Human Subjects).

d. VA regulations pertaining to research related injuries: 38 CFR 17.85.

e. Statutes and regulations pertaining to the release of patient information: 5 U.S.C. 552a, 38 U.S.C. 5701a and 7332, and 45 CFR 160 and 164.

f. VA regulations pertaining to hospital care for research purposes and outpatient care for research purposes: 38 CFR 17.45, 17.85 and 17.92.

g. Department of Health and Human Services (HHS) regulations pertaining to rights and welfare of human subjects participating in research supported by HHS: 45 CFR 46.

h. Food and Drug Administration (FDA) regulations pertaining to rights and welfare of human subjects participating in research involving FDA-regulated products: 21 CFR 11, 50, 54, 56, 312, 314, 812, and 814.

i. Nuclear Regulatory Commission (NRC) regulations pertaining to medical use of byproduct material and protection of human subjects: 10 CFR 20 (Standards for Protection Against Radiation) and 10 CFR 35 (Medical Use of Byproduct Material).

j. VA confidentiality of medical quality assurance records statute: 38 U.S.C. 5705.

3. DEFINITIONS

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

a. **Accreditation.** Accreditation of a Human Research Protection Program (HRPP) is the process of obtaining independent recognition that a HRPP affords protection to human subjects by meeting and exceeding the prevailing ethical, professional, and regulatory requirements, and that the HRPP engages in continuous quality improvement.

b. **Accrediting Organization.** The accrediting organization is an independent body that has developed standards of performance to assess compliance with the prevailing ethical, professional, and regulatory guidelines for the conduct of human subjects research.

c. **Adverse Event (AE).** An AE is any untoward physical or psychological occurrence in a human subject participating in research. An AE can be any unfavorable and unintended event, including an abnormal laboratory finding, symptom, or disease associated with the research or the use of a medical investigational test article. An AE does not necessarily have to have a causal relationship with the research (see subpars. 3w and 3ll and VHA Handbook 1058.01).

d. **Affiliated Institution.** An affiliated institution is an academic institution that has a relationship for the purpose of education, research, or enhanced patient care with a VA medical center documented by a formal Affiliation Agreement in conformance with VA requirements (also referred to as "academic affiliate"). In addition, special purpose agreements documented by a memorandum of understanding (MOU) approved by the Chief Research and Development Officer (CRADO) may be developed in research and development (R&D) areas, such as health services or rehabilitation R&D.

e. **Affiliation Agreement.** An Affiliation Agreement is a written agreement documenting the relationship for the purpose of education, research, or enhanced patient care between a VA medical center and an affiliated institution.

f. **Anonymous.** For the purposes of VA research, anonymous means de-identified (see subpar. 3r) in accordance with both:

(1) The Health Insurance Portability and Accountability Act (HIPAA) Privacy Rule (45 CFR 164.514(b) (see VHA Handbook 1605.1), and

(2) The Common Rule provision that the identity of the subject cannot be readily ascertained by the investigator or associated with the information (38 CFR 16.102(f)).

g. **Assurance (Assurance of Compliance).** For human research, an Assurance is a written commitment to protect human subjects participating in research and to comply with the requirements of 38 CFR Part 16. Assurances are reviewed and approved by the HHS Office for Human Research Protections (OHRP) and various other departments and agencies under the Federal Policy (Common Rule) for the Protection of Human Subjects (56 FR 28001, June 18, 1991) (see VHA Handbook 1058.03). ***NOTE:*** *For the purposes of this Handbook, the terms Assurance, Assurance of Compliance, and Federalwide Assurance (FWA) are synonymous.*

h. **Blinded.** A blinded study design is one comparing two or more interventions in which the research personnel, the subjects, or some combination thereof, do not know the treatment group assignments of individual subjects.

i. **Children.** Children are persons who have not attained the legal age for consent to treatments or procedures involved in the research under the applicable law of the jurisdiction in which the research will be conducted (45 CFR 46.402(a)).

j. **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 § 505(i) or 520(g) of the Federal Food, Drug, and Cosmetic Act; 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 later submitted to, or held for inspection by, the FDA as part of an application for a research or marketing permit (21 CFR 56.102(c)).

k. **Coded Data.** The term "coded data" means "coded private information" as defined in guidance published by HHS entitled Guidance on Research Involving Coded Private Information or Biological Specimens, currently available at: http://www.hhs.gov/ohrp/policy/cdebiol.html (see VHA Handbook 1200.12).

l. **Common Rule.** Common Rule means the Federal Policy for the Protection of Human Subjects adopted by Federal departments and agencies conducting or supporting human subject research. The Common Rule is codified for VA at title 38 CFR Part 16.

m. **Credentialing.** Credentialing is the systematic process of screening and evaluating qualifications and other credentials, including licensure, education, training, and experience, and current competence and health status (see VHA Handbook 1100.19).

n. **Data.** For the purposes of this Handbook, the term data means information derived directly from patients or human research subjects or indirectly through accessing databases. It includes information from Deoxyribonucleic Acid (DNA) sequencing. It does not include information derived from research involving animals or other types of research that do not involve human subjects (see VHA Handbook 1200.12).

o. **Database.** A database is a collection of data or information elements organized in a manner to permit systematic retrieval.

p. **Data Monitoring Committee (DMC), Data and Safety Monitoring Board (DSMB),** or **Data and Safety Monitoring Committee (DSMC).** A DMC, DSMB, or DSMC is group of individuals with relevant expertise that reviews accumulating data from one or more ongoing research studies. The DMC, DSMB, or DSMC independently advises the sponsor or the principal investigator (PI) regarding the continuing safety of the research study's subjects, as

well as the continuing validity and scientific merit of the study. DMC, DSMB, and DSMC are considered synonymous for the purposes of this Handbook.

q. **Data Repository.** A data repository is a database or a collection of databases that have been created or organized to facilitate the conduct of multiple research protocols, including future protocols not yet envisioned. It also may have been created for other purposes such as administrative and clinical purposes (VHA Handbook 1200.12). ***NOTE:*** *For purposes of this Handbook data repository and data warehouse are interchangeable terms.*

r. **De-Identified Data**

(1) For the purposes of VA research, de-identified data are data that have been de-identified in accordance with both:

(a) The HIPAA Privacy Rule (45 CFR 164.514(b) (see VHA Handbook 1605.1), and

(b) The Common Rule provision that the identity of the subject cannot be readily ascertained by the investigator or be associated with the information (38 CFR 16.102(f)).

(2) Such data may also be known as "anonymous" (see subpar. 3f). ***NOTE:*** *Coded data is data identifiable by the individual(s) who has access to the code. Therefore, for the purposes of this Handbook, coded data are not considered to be de-identified or anonymous.*

s. **Delivery.** In the context of pregnancy, delivery means complete separation of the fetus from the woman by expulsion, extraction, or any other means.

t. **Embryo.** An embryo is an organism in the early stages of development, which in humans is the first 6 weeks.

u. **Exempt Research.** Exempt research includes research activities in which the only involvement of human subjects is in one or more of the categories listed in 38 CFR 16.101(b). The exempt status must be determined by the Institutional Review Board (IRB) Chair or an IRB voting member designated by the Chair (see par. 16). ***NOTE:*** *Such an exemption applies only to requirements found in 38 CFR Part 16. All other relevant VA and Federal requirements apply.*

v. **Expedited Review Procedures for Research.** In contrast to a convened IRB review process, the expedited review process consists of a review carried out by the IRB Chair or by one or more experienced voting members of the IRB designated by the IRB Chair in accordance with 38 CFR 16.110(b).

w. **External AE.** In the context of a multi-site study, an external AE is an AE experienced by subjects, research staff, or others at another institution engaged in the trial.

x. **Facility.** For purposes of this Handbook, the term "facility" and "institution" are interchangeable (see subparagraph 3hh).

y. **Federalwide Assurance (FWA).** See subparagraph 3g.

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

aa. **Health Care Agent.** A health care agent is an individual named by the patient in a Durable Power of Attorney for Health Care (38 CFR 17.32(a)(iii)).

bb. **HIPAA Authorization.** The term HIPAA authorization means prior written permission for use and disclosure of protected health information (PHI) from the information's source person, research subject, or legally authorized personal representative, as required under law, including HIPAA. The written authorization must include all elements of a compliant authorization (see VHA Handbook 1605.1) prior to any disclosure of information.

cc. **Human Biological Specimens.** Human biological specimens are defined as materials derived from human individuals, such as blood, urine, tissue, organs, hair, nail clippings, buccal swabs, or any other materials that are either collected specifically for research purposes or as residual specimens from diagnostic, therapeutic, or surgical procedures. Bacteria, fungi, or viruses obtained from human biological specimens are not considered human biological specimens, as long as the human material has been removed.

dd. **Human Research.** Human research is research involving human subjects as defined in this Handbook or one or more identifiable human biological specimens (see par. 53).

ee. **Human Research Protection Program (HRPP).** A HRPP is a comprehensive system to ensure the protection of human subjects participating in research. At a local VA facility, the HRPP consists of a variety of individuals and committees including, but not limited to: the VA facility Director, Associate Chief of Staff (ACOS) for R&D, Administrative Officer (AO) for R&D, Research Compliance Officer (RCO), R&D Committee, IRB, other committees or subcommittees addressing human subjects protection (e.g., Subcommittee on Research Safety (SRS), Institutional Biosafety Committee, Radiation Safety Committee, Radioactive Drug Research Committee, Conflict of Interest Committee), investigators, IRB staff, research staff, health and safety staff (e.g., Biosafety Officer, Radiation Safety Officer) and research pharmacy staff. The objective of this system is to assist the institution in meeting ethical principles and regulatory requirements for the protection of human subjects in research.

ff. **Human Subject.** This definition of human subject includes investigators, technicians, and others assisting investigators, when they serve in a "subject" role by being observed, manipulated, or sampled.

(1) Title 38 CFR Part 16 defines a human subject as a living individual about whom an investigator (whether professional or student) conducting research obtains either:

(a) Data through intervention or interaction with the individual; interaction includes communication or interpersonal contract between the researchers and the subject; or

(b) Identifiable private information (38 CFR 16.102 (f)).

(2) For research covered by Food and Drug Administration (FDA) regulations, human subjects means an individual who is or becomes a participant in a clinical investigation, either as a recipient of the test article or as a control. (21 CFR 50.3(g), 21 CFR 66.102(c)).

(3) For research covered by FDA device regulations, subject means a human who participates in an investigation, either as an individual on whom or on whose specimen an investigational device is used or as a control. A subject may be in normal health or may have a medical condition or disease (21 CFR 812.3(p)).

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

hh. **Institution.** An institution is any public or private entity or agency (38 CFR 16.102(b)). This Handbook distinguishes VA from non-VA institutions (see VHA Handbook 1058.03).

(1) **VA Institution.** A VA institution is any entity that is operated by VA, including but not limited to: VA hospitals, medical centers, clinics, and health care systems; space owned, leased, or rented by VA; and space that is "shared" with a non-VA entity (unless the VA space is leased to a non-VA entity and specifically designated in writing not to be used by VA or VA employees for research). A VA facility may include multiple campuses and satellite components. ***NOTE:*** *For purposes of this Handbook, the terms "facility," "VA facility," and "VA institution" are considered synonymous.*

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

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

(b) Entities operated under a contract with VA including, but not limited to, contract Community-based Outpatient Clinics (CBOCs), contract nursing homes, contract outpatient clinics. ***NOTE:*** *Some entities (e.g., CBOCs) are VA institutions when they are part of the VA facility, but non-VA institutions when they are operated under a contract with VA (e.g., a contract CBOC).*

(c) Academic institutions, including VA–affiliated medical schools, dental schools, and other academic affiliates (see Affiliated Institution).

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

(e) Other Federal, state, or local departments or agencies.

ii. **Institutional Official (IO).** The IO is the individual legally authorized as Signatory Official to commit an institution to an Assurance. 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. 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.

jj. **Institutional Review Board (IRB).** An IRB is a board, committee, or other group formally designated by an institution to review, approve, require modification in, disapprove, and conduct continuing oversight of human research in accordance with 38 CFR Part 16 and other applicable VA and Federal requirements.

kk. **Interaction.** Interaction includes communication or interpersonal contact between investigator and subject (38 CFR 16.102(f)(2)).

ll. **Internal or Local AE.** In the context of a multi-center study, internal AEs are those AEs experienced by subjects, research staff, or others at the reporting individual's own VA facility or VA-approved research site.

mm. **International Research.** VA international research is any VA-approved research conducted at international sites (not within the United States (U.S.), its territories, or Commonwealths); any VA-approved research using either human biological specimens (identified, de-identified, or coded) or human data (identified, de-identified, or coded) originating from international sites; or any VA-approved research sending such specimens or data out of the U.S. (see par. 56). ***NOTE:*** *For the purposes of this Handbook, research conducted at U.S. military bases, ships, or embassies is not considered international research.*

nn. **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 (38 CFR 16.102(f)(2)). Interventional studies are those in which the research subjects are assigned by the investigator to a treatment or other intervention, and their outcomes are measured.

oo. **Investigational Device.** As defined by the FDA, an investigational device is a device that is the object of an investigation (21 CFR 812.3(g)).

pp. **Investigational Device Exemption (IDE).** An IDE is an application to FDA that allows an investigational significant risk device to be used in a clinical investigation to collect safety and effectiveness data. If the device is a non-significant risk device, it is considered to have an approved application for IDE after IRB approval is obtained (see 21 CFR 812).

qq. **Investigational Drug.** According to VHA Handbook 1108.04, an investigational drug is a chemical or biological drug that is used in a clinical investigation. An investigational drug can be:

(1) A new chemical compound, which has not been released by the FDA for general use; or

(2) An approved drug that is being studied for an approved or unapproved use, dose, dosage form, administration schedule, or under an Investigational New Drug (IND) application, in a controlled, randomized, or blinded study (see VHA Handbook 1108.04).

NOTE: *Concurrent medications, comparators, or rescue medications used in the investigational trial that are not the drug(s) being studied are not defined as investigational drugs unless they are not commercially approved or not available through commercial channels. Prescription drugs, over-the-counter drugs, nutritional supplements, herbal preparations, and legend items used for diagnosis or treatment and meeting the definition of "investigational drug" (see subpars. 3pp(1) and 3pp(2)) are considered investigational drugs.*

rr. **Investigational New Drug (IND) Application**. An IND is an application to the FDA that allows an investigational drug or biological product to be studied in humans. An IND must be in effect prior to shipment and administration of investigational drug or biological products (see 21 CFR 312).

ss. **Investigator**. An investigator is any individual who conducts research involving human subjects including, but not limited to, the PI, co-PI, and Local Site Investigator (LSI). The investigator must uphold professional and ethical standards and practices, adhere to all applicable Federal requirements, and comply with applicable local policies and procedures (see par. 9).

(1) **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 employees, without compensation (WOC) employees, and individuals appointed or detailed to VA under the Intergovernmental Personnel Act (IPA) of 1970. In addition, a VA investigator must comply with all applicable VA and VHA requirements, and comply with applicable local VA facility policies and procedures.

(2) **Principal Investigator (PI)**. The PI is a qualified person or persons designated by an applicant institution to direct a research project or program and who usually writes the grant application. The PI oversees scientific, technical, and day-to-day management of the research. In the event of an investigation conducted by a team of individuals, the PI is the responsible leader of that team. ***NOTE:*** *FDA considers Investigator and PI to be synonymous.*

(3) **Co-Principal Investigator (Co-PI).** A Co-PI is when one of two or more PIs share equally in the accountability for a study. A Co-PI must meet the same qualifications of a PI.

(4) **Site Investigator or Local Site Investigator (LSI).** The Site Investigator or LSI is an investigator at a site participating in a multi-site research project. The LSI oversees scientific, technical, and day-to-day management of the research at the local site.

tt. **Legal Guardian.** A legal guardian is a person appointed by a court of competent jurisdiction to maintain and care for the property of an individual, or an individual who the court has declared incompetent due to physical or mental incapacity or age (see VHA Handbook 1605.1).

uu. **Legally Authorized Representative (LAR).** A 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 (38 CFR 16.102(c)).

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 PHI (i.e., signing a 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 in 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).*

vv. **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 (38 CFR 16.102(i)).

ww. **Neonate.** For the purposes of VA research, a neonate is an infant in the first 28 days of life.

xx. **Observational Studies.** Observational studies are non-interventional studies in which individuals are observed and those observations are recorded. Outcomes, including health outcomes, may also be measured by the investigators.

yy. **Office of Research and Development (ORD).** Within VHA Central Office, ORD is the office responsible for the overall policy, planning, coordination, and direction of VA research activities.

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

aaa. **Personal Representative.** A personal representative is a person who, under applicable law, has authority to act on behalf of another individual. This may include power of attorney, legal guardianship of an individual, the executor of an estate of a deceased individual, or someone under Federal, state, local, or tribal law with such authority (e.g., the parent of a minor) (VHA Handbook 1605.1).

bbb. **Pilot Studies.** Pilot studies are full-fledged research studies that must be approved by the IRB(s), when human subjects are involved. They are not considered to be activities preparatory to research.

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

ddd. **Preparatory to Research.** Within VHA, activities "preparatory to research" refer to activities that are necessary for the development of a specific protocol. PHI from data

repositories or medical records may be reviewed during this process without IRB approval, subject authorization, or a waiver of authorization, but only aggregate data may be recorded and used in the protocol application (e.g., potential number of subjects meeting study criteria at each site). Within VHA, an activity preparatory to research does not include the identification of potential subjects and recording of data for the purpose of recruiting these subjects or to link with other data. The preparatory to research activity ends once the protocol has been submitted to the IRB for review (see par. 57 and VHA Handbook 1200.12).

eee. **Prisoner.** A prisoner is any individual involuntarily confined or detained in a penal institution. The term is intended to encompass individuals sentenced to such an institution under a criminal or civil statute, individuals detained in other facilities by virtue of statutes or commitment procedures that provide alternatives to criminal prosecution or incarceration in a penal institution, and individuals detained pending arraignment, trial, or sentencing (see par. 47).

fff. **Privacy Board.** Under HIPAA, a Privacy Board is a board that is established to review and approve requests for waivers or alterations of HIPAA authorizations in connection with use or disclosure of PHI. The Privacy Board:

(1) Consists of members with varying backgrounds and appropriate professional competency, as necessary, to review the effect of the research protocol on the individual's privacy rights and related interests;

(2) Includes at least one member who is not affiliated with the covered entity, not affiliated with any entity conducting or sponsoring the research, and not related to any person who is affiliated with any of such entities; and

(3) Does not have any member participating in a review of any study in which the member has a conflict of interest.

ggg. **Private Information**

(1) Private information must be individually identifiable in order for the information to constitute research involving human subjects (38 CFR 16.102(f)).

(2) Private information includes:

(a) Information about behavior that occurs in a context in which an individual can reasonably expect that no observation or recording is taking place, and

(b) Information which has been provided for specific purposes by an individual and which the individual can reasonably expect will not be made public (e.g., a medical record).

hhh. **Privileging**

(1) For the purposes of this Handbook, the terms "privileging" and "clinical privileging" are the same and are defined as the process by which a practitioner, licensed for independent practice

(i.e., without supervision, direction, required sponsor, preceptor, mandatory collaboration, etc.), is permitted by law and the facility:

(a) To practice independently; and

(b) To provide specified medical or other patient care services within the scope of the individual's license, based on the individual's clinical competence as determined by peer references, professional experience, health status, education, training, and licensure.

(2) Clinical privileges must be facility-specific and provider-specific (see VHA Handbook 1100.19).

iii. **Program for Research Integrity Development and Education (PRIDE).** PRIDE is the program within ORD that is responsible for training, education, and policy development related to VA human subjects protection. Other VA offices, including ORD services (i.e., ORD's Biomedical Laboratory Research and Development (BLR&D), Clinical Science Research and Development (CSR&D), Health Services Research and Development (HSR&D), and Rehabilitation Research and Development (RR&D) Services), may develop policies for research involving human subjects that have requirements in addition to those in this Handbook.

jjj. **Quorum.** A quorum is defined as a majority of the voting members. At meetings of the R&D Committee and its subcommittees, a quorum must be established and maintained throughout the entire meeting in order for business to be conducted. Some committees, such as the IRB have additional requirements for the establishment of a quorum, such as presence of a member whose primary concerns are in nonscientific areas. A member with a conflict of interest cannot:

(1) Contribute to a quorum,

(2) Be present for the discussion of the issue for which they are conflicted, except to answer questions from the committee, or

(3) Be present for the vote on the issue.

kkk. **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 (38 CFR 16.102(d)).

lll. **Research Compliance Officer (RCO).** The RCO is an individual whose primary responsibility is to review research projects relative to requirements for the protection of human subjects, laboratory animal welfare, research safety, research laboratory security, research information protection, and other areas under the jurisdiction of ORO.

NOTE: *Guidance and materials related to RCO responsibilities are provided on ORO's Web site at: http://www.va.gov/oro . Specific guidance for RCO education and the conduct and reporting of required audits is updated annually by ORO and posted prominently on ORO's Web site.*

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

(1) **IRB Records.** IRB records include, but are not limited to: copies of all research proposals and amendments reviewed; scientific evaluations, if any, that accompany the proposals; approved informed consent documents; progress reports submitted by investigators; reports of injuries to subjects; reports of complaints from subjects; minutes of IRB meetings; reports of expedited review activities; records of continuing review activities; copies of all correspondence between IRB and the investigators; reports of deviations from IRB-approved protocol; a list of IRB members; written procedures for IRB in the same detail as described in 38 CFR 16.103(b)(4) and (5); and statements of significant new findings provided to subjects as required by 38 CFR 16.116(b)(5).

(2) **Investigators' Research Records**. Research records include the following when relevant to the study: copies of all IRB-approved versions of the protocol and amendments; case report forms and supporting data (including but not limited to signed and dated informed consent forms and HIPAA authorization forms); documentation on each subject including informed consent, interactions with subjects by telephone or in person, observations, interventions, and other data relevant to the research study; reports of adverse events; data analyses; codes and keys used to de-identify and re-identify subjects' PHI; reports (including, but not limited to abstracts and other publications); all correspondence (including, but not limited to, that with the funding source or sponsor) and with applicable oversight entities (including, but not limited to, IRB, R&D Committee, ORO, and FDA); and a master list of all subjects for whom informed consent has been obtained in the study (see subpar. 9u).

nnn. **Researcher.** A researcher is an investigator (see subpar. 3ss).

ooo. **Sensitive Information**

(1) VA sensitive information is all department data, on any storage media or in any form or format, which requires protection due to the risk of harm that could result from inadvertent or deliberate disclosure, alteration, or destruction of the information.

(2) The term includes information whose improper use or disclosure could adversely affect the ability of an agency to accomplish its mission; proprietary information; records about specific individuals requiring protection under various confidentiality provisions, such as the Privacy Act and the HIPAA Privacy Rule; and information that can be withheld under the Freedom of Information Act (see VA Directive 6500 and VA Handbook 6500).

ppp. **Serious Adverse Event (SAE).** A local SAE in human research is an AE 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.

qqq. **Sponsor.** For FDA studies, the FDA considers a sponsor to be the person who takes responsibility for and initiates a clinical investigation. The sponsor may be an individual, pharmaceutical company, governmental agency, academic institution, private organization, or other. The sponsor does not actually conduct the investigation unless the sponsor is a sponsor-investigator. A person other than an individual that uses one or more of their own employees to conduct an investigation that it has initiated is a sponsor, not a sponsor-investigator, and the employees are investigators (21 CFR 312.3 and 21 CFR 812.3).

rrr. **Surrogate.** A surrogate is an individual authorized under VHA policy to make decisions on behalf of a subject who lacks decision-making capacity (see par. 36).

sss. **Suspension of IRB Approval.** A suspension of IRB approval is a determination by the IRB Chair, a qualified IRB voting member designated by the IRB Chair, or the convened IRB to temporarily interrupt some or all previously-approved research activities. The suspended activities could include, but not be limited to, recruiting of new subjects for the research. Suspended studies remain open and require continuing review.

ttt. **Termination of IRB Approval.** A termination of IRB approval is a determination by the convened IRB to permanently halt some or all previously approved research activities including, but not limited to, enrollment of new subjects in research.

NOTE: *The terms "suspension" and "termination" apply to interruptions related to concerns regarding the safety, rights, or welfare of human research subjects, investigators, research staff, or others. They do not include interruptions in human research resulting solely from the expiration of the IRB approval period (see VHA Handbook 1058.01).*

uuu. **Test Article.** A test article is any drug for human use, biological product for human use, medical device for human use, human food additive, color additive, electronic product, or any other article subject to regulation under the Federal Food, Drug, and Cosmetic Act or under §§ 351 and 354-60F of the Public Health Service Act (42 U.S.C. 262 and 263b-263n; 21 CFR 50.3(j)).

vvv. **Unanticipated Adverse Event (UAE).** ***NOTE:*** *For the purposes of this Handbook "unanticipated" is the same as "unexpected."* An UAE is an AE that is new or greater than previously known, in terms of nature, severity, or frequency of occurrence, as documented in the protocol or other materials approved by IRB. Such materials may include, but are not limited to: the informed consent form, clinical investigator's brochure, and product labeling (see VHA Handbook 1058.01).

www. **Usual Care.** Usual care is medical or other treatment or services a research subject would receive if not participating in the research study (e.g., the chemotherapy an oncology patient would receive whether or not the patient was participating in a research study).

xxx. **VA Research.** VA research is research that is approved by the R&D Committee and conducted by VA Investigators including PIs, Co-PIs, and Site Investigators on VA time (serving on compensated, WOC, or IPA appointments), utilizing VA resources (e.g., equipment), or on VA property including space leased to, and used by VA. The research may be funded by VA, by other sponsors, or be unfunded.

NOTE: *Research conducted by non-VA investigators that does not utilize VA resources and that occurs on space, or with equipment, leased from VA or covered under a use agreement between VA and a non-VA entity is not considered VA research.*

4. SCOPE

a. **Principles and Policy for the Protection of Human Subjects.** VA is guided by the ethical principles regarding all research involving humans as subjects as set forth in the Belmont Report "Ethical Principles and Guidelines for the Protection of Human Subjects of Research," (at: http://www.hhs.gov/ohrp/humansubjects/guidance/belmont.html) regardless of who conducts the research or the source of support.

b. **Applicability to VA Human Subjects Research.** With the exception of research deemed exempt by IRB, the provisions of this Handbook apply to all VA research involving human subjects, and VA international research (see par. 56). The research may be funded by VA, by other sponsors, or be unfunded (see VHA Handbook 1200.01). ***NOTE:*** *For policy and guidelines regarding off-site VA research, refer to VHA Handbook 1200.16.*

c. **Requirements of Funding Sources.** Investigators receiving support from other Federal departments or agencies (e.g., the National Institutes of Health (NIH)), 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, for the protection of human subjects. ***NOTE:*** *If the funding source's requirements conflict with VA or other Federal requirements, then ORD must be contacted.*

d. **Applicability of FDA Regulations.** When FDA-regulated products are used, FDA regulations apply regardless of funding source.

e. **New Human Research Programs.** The facility Director, or designee, must obtain permission from the CRADO prior to creating a new human research program and applying through VHA Office of Research Oversight (ORO) to OHRP for an FWA.

f. **Protection of the Human Research Subject.** It is imperative that human research subjects receive the highest level of protection possible and that any questions or ethical ambiguities always be resolved in favor of the human research subjects.

g. **Classified Research.** Classified research involving human subjects cannot be approved by a VA IRB or R&D Committee or performed at a VA facility, including space leased to, and used by VA.

h. **Planned Emergency Research.** Planned emergency research must not be granted approval by a VA IRB or R&D Committee and cannot be conducted by VA (see par. 41).

5. FACILITY DIRECTOR GENERAL RESPONSIBILITIES REGARDING HUMAN SUBJECT RESEARCH

The VA facility Director must obtain an FWA in accordance with VHA Handbook 1058.03 prior to conducting any human subjects research. The facility Director (also known as health care system chief executive officer (CEO)) must serve as the institutional official (IO) listed on the FWA for the local VA facility. In addition, the facility Director is responsible for ensuring implementation of the following:

a. **Institutional Culture.** The facility Director is responsible for fostering an institutional culture that supports the ethical conduct of all research involving human subjects.

b. **FWA Signatory Authority.** The facility Director is responsible for serving as signatory authority for the FWA, and thereby making a written commitment to protect human subjects participating in research at the local VA facility and to comply with the requirements of 38 CFR Part 16.

c. **Assurance Training.** The facility Director is responsible for completing assurance training required in VHA Handbook 1058.03 prior to signing the FWA initially, and every 3 years after that.

d. **The VA Facility's HRPP.** The facility Director is responsible for overseeing the creation and implementation of an HRPP for research involving human subjects or human biological specimens. The exact composition of the HRPP depends on the specific facility, the resources of the facility, and the size and complexity of the research program at the facility. The VA facility Director's responsibilities for the facility's HRPP include, but are not limited to:

(1) Overseeing the IRB, R&D Committee, research office, and all investigators and research team members who perform human research at that facility.

(2) Appointing a RCO who reports directly to the Director and is responsible for developing and implementing a research compliance program (VHA Directive 1200 and VHA Handbook 1058.01).

(3) Delegating authority in writing for all respective roles and responsibilities within the local VA facility's HRPP. This delegation of authority must provide the organizational structure and ensure accountable leadership for compliance oversight activities for all human subjects research conducted at the facility.

(4) Creating and implementing initial and continuing education programs.

e. **IRB(s) of Record.** The facility Director is responsible for ensuring that any IRB designated as an IRB of record for a VA facility is established in accordance with the requirements of this Handbook and 38 CFR 16.103(b)(2); registered with OHRP and, if appropriate, FDA; and listed as an IRB of record on the VA facility's FWA. The IRB(s) of record may include the facility's own IRB(s), VA Central IRB, IRB of another VA facility, or an IRB(s) established by an affiliated medical or dental school. Neither the VA facility nor the investigator may engage the services of another IRB for the purposes of avoiding the rulings of the IRB of record.

(1) Under exceptional circumstances, a VA facility may request a waiver from the CRADO to utilize the services of an IRB operated by another Federal department or agency that is signatory to the Common Rule.

(2) A VA facility's own internal IRB cannot serve as an IRB of record for any non-VA entity except a Department of Defense (DOD) facility or a VA nonprofit research and educational foundation. VA nonprofit research and education foundations must have an IRB of record of a VA facility, whether the IRB is the VA facility's own internal IRB, another VA facility's IRB, the VA Central IRB, or its academic affiliate's IRB.

f. **Independence of IRB(s).** The facility Director is responsible for ensuring that the IRB(s) of record functions independently, and that its Chair, or Co-Chairs, and members have direct access to the IO for appeal if they experience undue influence or if they have concerns about the IRB.

NOTE: *Research that has been approved by a VA facility's IRB of record is subject to further appropriate review and approval or disapproval by officials (e.g., the facility Director) and other committees (e.g., the R&D Committee) at that facility. However, officials or committees cannot approve the research if it has been disapproved by the facility's IRB of record (e.g., the VA facility Director cannot approve a study that has been disapproved by IRB) (38 CFR 16.112).*

g. **Resources for HRPP.** The facility Director is responsible for ensuring provision of adequate resources to support the operations of HRPP so that those operations are in compliance with all VA and other Federal requirements that govern human subjects research protection. These resources include, but are not limited to:

(1) **Administrative Resources.** Administrative resources include provisions for meeting space and sufficient staff to support IRB's review and recordkeeping duties (38 CFR 16.103(b)(2)). The meeting space needs to be sufficient to provide privacy for conducting IRB meetings, other sensitive duties, and secure storage of records. The resources also need to include adequate administrative personnel, equipment, and space for the local research office.

(2) **Educational Opportunities.** There is to be appropriate human subjects protection educational opportunities for IRB members, relevant administrative staff, and all members of the research team.

h. **Knowledgeable Staff.** The facility Director is responsible for ensuring that IRB members, relevant administrative staff, and all members of the VA research team are appropriately knowledgeable to fulfill their respective duties in accordance with ethical standards and all applicable local, VA and other Federal requirements.

i. **Human Research Protection Training.** The facility Director is responsible for ensuring that VA human subjects protection training requirements are met (see par. 61).

j. **Correspondence.** The facility Director is responsible for being the point of contact for correspondence addressing human subjects research with OHRP, FDA, and VHA Central Office.

k. **HRPP Accreditation.** The facility Director is responsible for ensuring the VA facility's HRPP is accredited in accordance with paragraph 64.

l. **Credentialing and Privileging.** The facility Director is responsible for certifying that all personnel involved in research including, but not limited to, research office staff, investigators, and other research team members have appropriate credentials and privileges (when applicable) to perform their human research-related duties (see par. 62).

m. **Research Subject Outreach Program.** The facility Director is responsible for ensuring a local Research Subject Outreach Program is implemented to include:

(1) **Communication About the Study.** A reliable mechanism must be provided for research subjects to communicate with research study investigators and with an informed VA representative who is independent of the research study in question (e.g., providing contact information in the informed consent form).

(2) **Information About Volunteering in Research.** Investigators must make every reasonable effort to provide the informational brochure, "Volunteering in Research – Here Are Some Things You Need To Know," (http://www.research.va.gov/programs/pride/veterans/tri-fold.pdf) to potential research subjects in settings where subjects may be recruited (e.g., clinic waiting areas), and to each prospective subject when that individual is approached to take part in a study (see par. 9).

(3) **Venues for Information and Input.** Venues must be provided for research subjects and their designated representatives to obtain information, discuss their questions and concerns, and offer their input.

(4) **Educational Activities.** When appropriate, educational activities must be made available for research subjects and their communities.

n. **Advertising.** The facility Director is responsible for ensuring that recruiting documents, flyers, and advertisements for non-VA research are not posted within or on the premises of a VA facility. Posting of such documents may give the Veteran or visitors to the VA facility the impression that the non-VA study is VA-approved research, the VA supports or endorses the research, or that VA will pay for the research expenses that are incurred. General guidance may be posted within VA indicating that Veterans may speak with their health care providers if they

wish to participate in research and that information on clinical trials is available at: http://clinicaltrials.gov.

o. **Research Compliance Program.** The facility Director is responsible for appointing a RCO.

p. **Audits.** The facility Director is responsible for ensuring appropriate auditing of local human subjects research studies to assess compliance with all applicable local, VA, and other Federal requirements including, but not limited to, ORO requirements. ***NOTE:*** *Human subjects research study audits may be conducted more frequently as deemed appropriate in accordance with ORO requirements.*

(1) **Study Audits.** Each VA-approved human subjects research study must be completely audited in accordance with VHA Handbook 1058.01.

(2) **Informed Consent Audits.** Each study must be audited for compliance with the regulations and policies on informed consent in accordance with VHA Handbook 1058.01.

q. **International Research Site.** The facility Director is responsible for approving the request for permission to conduct international research at the VA facility and ensuring CRADO approval of international research is obtained prior to its initiation at the facility (see subpar. 56e).

6. FACILITY DIRECTOR RESPONSIBILITIES WHEN THE VA FACILITY'S OWN INSTITUTIONAL REVIEW BOARD (IRB) IS AN IRB OF RECORD

In addition to the preceding responsibilities, the facility Director for a VA facility with its own IRB(s) as an IRB(s) of record is responsible for:

a. **Appointing an IRB Chair and IRB Voting Members.** The facility Director is responsible for appointing the IRB Chair (or Co-Chairs, or Chair and Vice Chair), and IRB voting members. ***NOTE:*** *Consideration should be given to the inclusion of a Veteran or a representative of a legally-recognized Veterans Service Organization (VSO).*

(1) If local Standard Operating Procedures (SOPs) call for titles of positions (e.g., Assistant Chief of Staff (ACOS) for R&D, Administrative Officer (AO) for R&D), instead of named individuals, to serve as ex officio, nonvoting members of the IRB, the individuals themselves do not have to be appointed by the IO. They will be considered to be ex officio, nonvoting members of the IRB by virtue of their positions within the local facility.

(2) If the VA facility's own IRB serves as an IRB of record for a second VA facility, the facility Director of the second VA facility must appoint representatives to the first IRB in accordance with subparagraph 7c.

b. **Suspending or Terminating IRB Membership.** The facility Director is responsible for suspending or terminating the IRB membership of any individuals who are not fulfilling their member responsibilities or obligations.

c. **Annual Evaluation.** The facility Director is responsible for ensuring an annual evaluation of the facility's HRPP.

7. FACILITY DIRECTOR RESPONSIBILITIES WHEN AN EXTERNAL IRB OTHER THAN THE VA CENTRAL IRB IS AN IRB OF RECORD

In addition to the preceding responsibilities, the facility Director for a VA facility using an external IRB (e.g., another VA facility's or an academic affiliate's IRB) as an IRB(s) of record is responsible for:

a. **Signing the MOU.** The facility Director is responsible for signing the MOU with the organization(s) providing the IRB(s). This MOU is an agreement delineating the respective roles, responsibilities, and authorities of the VA facility and the external organization providing the IRB(s) (see VHA Handbook 1058.03), including, but not limited to, the external organization's providing unredacted IRB minutes and other relevant documents to the VA facility, and the responsibility for both parties to comply with all applicable VA and other Federal requirements. ***NOTE:*** *The Affiliation Agreement between a VA facility and its academic affiliate does not delineate the IRB-related respective roles, responsibilities, and authorities of VA and academic affiliate providing the IRB. That information is contained in a separate document, an MOU specific for the IRB arrangement. The VA facility must have an Affiliation Agreement with its academic affiliate before entering into an MOU specific for the IRB arrangement.*

b. **Ensuring Compliance by the External IRB.** The facility Director is responsible for ensuring the external IRB of record complies with all applicable VA and other Federal requirements including, but not limited to, the provisions of this Handbook when reviewing VA research. If the terms of the MOU are not met, the VA facility must make alternative IRB arrangements.

c. **Appointing VA Representatives to the External IRB.** The facility Director is responsible for appointing two or more VA-compensated employees who hold a minimum of $5/8^{th}$ VA-compensated appointments as representatives to serve as voting members of each affiliate's IRB or other local VA facility's IRB when that IRB serves as an IRB of record, unless a waiver for such representation is obtained from the CRADO.

(1) These representatives may not include WOCs from the VA facility, or those with IPA appointments.

(2) At least one of these representatives must have scientific expertise.

(3) The representatives must serve as full-voting members of the external IRB; when relevant, this includes reviewing non-VA research matters coming before the IRB.

(4) At least one of the representatives must be present during the review of the VA facility's research at a convened IRB meeting.

***NOTE**: If the affiliated academic institution, other Federal agency, or other external entity has more than one IRB, this provision applies only to the IRB(s) designated to review VA research.*

8. FACILITY DIRECTOR RESPONSIBILITIES WHEN THE VA CENTRAL IRB IS AN IRB OF RECORD

***NOTE:** The local VA facility's IRB of record for some studies is the VA Central IRB.*

In addition to the preceding general responsibilities, the facility Director for a VA facility using the VA Central IRB as an IRB of record is responsible for:

a. Signing and adhering to the MOU between VHA Central Office and the local VA facility delineating the respective roles and responsibilities of each organization (see subpar. 52c).

b. Delegating authority to an individual from the local VA facility to:

(1) **Comment and Respond to VA Central IRB Review.** In this instance, it is to:

(a) Provide comments or suggestions to VA Central IRB, in response to VA Central IRB's initial review considerations; and

(b) Respond to VA Central IRB's approval of the study on behalf of the VA facility as to whether the VA facility chooses to participate or declines to participate in the study.

(2) **Serve as Liaison.** In this instance, it is to serve as the liaison between the facility and both LSI and VA Central IRB.

9. INVESTIGATOR RESPONSIBILITIES

The PI, LSI, and investigator must uphold professional and ethical standards and practices and adhere to all applicable VA and other Federal requirements, including the local VA facility's SOPs, regarding the conduct of research and the protection of human subjects. The responsibilities of the investigator may be defined in the protocol or IRB application. Specifically, the PI's and LSI's responsibilities include, but are not limited to: ***NOTE:** Some of the following responsibilities may be assumed by an investigator working under a PI or LSI.*

a. **Disclosing Conflicts of Interests.** This means disclosing to the IRB any potential, actual, or perceived conflict of interest of a financial, professional, or personal nature that may affect any aspect of the research, and complying with all applicable VA and other Federal requirements regarding conflict of interest.

b. **Ensuring Adequate Resources.** This means ensuring there are adequate resources to carry out the research safely. This includes, but is not limited to, sufficient investigator time, appropriately qualified research team members, equipment, and space.

c. **Ensuring Qualified Research Staff.** This means ensuring research staff are qualified (e.g., including but not limited to appropriate training, education, expertise, credentials and,

when relevant, privileges) to perform procedures assigned to them during the study (see par. 62). In a protocol, study team members are generally identified by name or by title.

(1) If a study team member is identified by name in the IRB-approved protocol, a replacement or termination of their role constitutes a change in the protocol. Such a change requires IRB approval (e.g., if an IRB-approved protocol specifically identified the name of a medical monitor and later another individual was identified to replace the medical monitor, the protocol would require an amendment reflecting the change in the name of the medical monitor. This protocol change would require IRB approval prior to initiation of the change, unless it was necessary to eliminate apparent immediate hazards to the subjects).

(2) If a study team member is replaced by another individual and the IRB-approved protocol identifies the person by title and not name, a replacement by another individual with the same title is not a protocol change. No IRB approval is required (e.g., if a PI appointed a new research study coordinator to replace the original research study coordinator in an IRB-approved protocol when neither is mentioned by name, the replacement in personnel does not require approval by IRB because the protocol remains unchanged).

(3) IRB may also require a specific individual(s) by name to be part of the study team as a condition for IRB approval of the research. In that case, a proposed change in that specific individual would require IRB approval.

d. **Promptly Reporting Changes in PI or LSI.** This means promptly reporting any changes in the PI or LSI to the IRB. Changes in other key research staff, if any, must be reported at time of continuing review, or sooner as required by local SOPs. These changes include, but are not limited to, additions to or loss of staff. Changes in the PI, LSI, Co-PI, or Co-LSI of an IRB-approved project must be evaluated and approved by IRB to ensure the new individual meets the criteria described in 38 CFR 16.111.

e. **Overseeing the Research Staff.** This means overseeing and being responsible for ensuring the research staff under the investigator's direction comply with all applicable requirements including, but not limited to, implementing the research study in accordance with the approved protocol.

f. **Ensuring Complete Information in Research Protocol.** This means ensuring the research protocol contains all required information (see par. 10).

g. **Obtaining Written Approvals.** This means obtaining written approval(s) before initiating research. Before initiating the research study at a given site, IRB approval must be obtained in writing from the Chair or other voting member of the IRB, and all other committees (e.g., R&D Committee), subcommittees, and other approvals according to applicable local, VA, and other Federal requirements.

(1) For a VA multi-site study, not only the PI, but also all LSIs, must obtain such approvals from the relevant local VA facilities' IRBs of record and all other local committees, subcommittees, and other approvals according to the respective applicable local, VA and other Federal requirements.

(2) Research cannot be initiated at any given site until the local investigator has obtained written notification that the research can be initiated from the local ACOS for R&D (see VHA Handbook 1200.01).

h. **Implementing the Study as Approved.** This means ensuring the study is implemented as approved by the IRB and in accordance with other required approvals and with all applicable local, VA, and other Federal requirements including, when applicable, those for research involving investigational drugs (see par. 39) or investigational devices (see par. 40).

i. **Maintaining Investigator's Research Records.** This means maintaining written documentation on file that the protocol is being implemented as approved by IRB and in accordance with other required approvals.

(1) Research records include the following when relevant to the study:

(a) Copies of all IRB-approved versions of the protocol and amendments.

(b) Case report forms and supporting data, including, but not limited to, signed and dated informed consent forms and HIPAA authorizations.

(c) Documentation on each subject including, but not limited to:

1. Informed consent,

2. Interactions with subjects by telephone or in person,

3. Observations,

4. Interventions, and

5. Other data relevant to the research study, including, but not limited to:

a. Progress notes,

b. Research study forms,

c. Surveys, and

d. Questionnaires.

(d) Reports of adverse events.

(e) Data analyses.

(f) Reports including, but not limited to, abstracts and other publications.

(g) All correspondence including, but not limited to, that with the funding source or sponsor, and with applicable oversight entities including, but not limited to, IRB, R&D Committee, ORO, and FDA.

(h) A master list of all subjects for whom informed consent has been obtained in the study (see subpar. 9u).

(2) Documents must be maintained so that they may be audited by the facility RCO or other entities according to applicable sponsor, local, VA and other Federal requirements, and

(3) An Accounting of Disclosure must be maintained for each and every disclosure of information from this study to a non-VA entity. ***NOTE:*** *The facility Privacy Officer can assist in providing a mechanism to account for this disclosure.*

j. **Obtaining Informed Consent.** This means ensuring that no human being is involved as a subject in research covered by this Handbook unless legally effective informed consent of the subject or the subject's LAR has been obtained (38 CFR 16.116). The informed consent must be obtained and documented 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). The only exceptions are if the IRB of record determines the research is exempt (see 38 CFR 16.101(b)), or approves a waiver of informed consent (see 38 CFR 16.116(c) and (d), and par. 35), or approves a waiver of the signed informed consent form (see 38 CFR.117(c) and par. 34).

(1) **Designating Responsibility for Obtaining Informed Consent.** If the PI or LSI does not personally obtain informed consent, the investigator must formally and prospectively designate to another research team member in writing the protocol or the application for IRB approval the responsibility for obtaining informed consent, whether or not a waiver of documentation of informed consent has been approved by the IRB. This designee must be a member of the research team.

(a) Any person designated to obtain informed consent must receive appropriate training and be knowledgeable enough about the protocol to answer the questions of prospective subjects.

(b) The PI or LSI does not have to designate the individual by name, but can designate the position(s) title in the protocol or the application for IRB approval.

(2) **Version of Informed Consent Form.** The most current IRB-approved version of VA Form 10-1086, Research Consent Form, for each study (or the most current IRB-approved electronic version of VA Form 10-1086) must be used as the informed consent form.

(3) **Circumstances Under Which Informed Consent is Obtained.** The investigator, or designee, must seek informed consent only under circumstances that:

(a) Provide the prospective subject or LAR sufficient opportunity to consider whether or not to participate, and

(b) Minimize the possibility of coercion or undue influence.

(4) **Usual Care.** The investigator, or designee, must ensure the Informed Consent process clearly defines for the subject which potential risks are related to the research (see subpar. 10g and 38 CFR 16.116(a)(2)) and, therefore, must be discussed with the research team, versus those associated solely with usual care provided by the subject's health care provider. The informed consent process must include language advising subjects to review the risks of the latter with their health care providers.

(5) **Documentation of Informed Consent**

(a) When documentation of informed consent is not waived by IRB, the investigator or designee must ensure the documentation is in accordance with paragraph 33 of this Handbook and includes:

1. The signature and date of the subject or the subject's LAR (see par. 30), and

2. The signature and date of the person obtaining the informed consent, and

3. The signature of the witness and the date of the subject's or LAR's signature was witnessed, when applicable (see subpar. 33c).

(b) If use of facsimile is approved by IRB, the subject may submit the signed and dated informed consent form to the investigator or designee by facsimile.

(6) **Storage of Signed Informed Consent Forms.** The investigator must ensure all original signed and dated forms are in the investigator's research files, readily retrievable, and secure (see subpar. 9i).

k. **Ensuring Consistency of Informed Consent Form, Protocol, and HIPAA Authorization.** This means ensuring the language in the informed consent form is consistent with that in the protocol and, when applicable, in the HIPAA authorization.

l. **Ensuring HIPPA Authorization is Obtained.** This means ensuring that no human being is involved as a subject in research covered by this Handbook, unless the investigator or a designee formally and prospectively designated in writing in the protocol by the investigator (see subpar. 9j(1)) has obtained legally effective HIPAA authorization for the use and disclosure of the subject's PHI, or has obtained Privacy Board or IRB-approved waiver of HIPAA authorization.

(1) If the investigator requires a waiver or alteration of the HIPAA authorization, the investigator must provide the Privacy Board or IRB with information sufficient for the Privacy Board or IRB to find that such waiver or alteration is necessary (VHA Handbook 1605.1).

(2) Investigators can obtain and use real Social Security numbers only when real Social Security numbers are required to meet the specific aims of the research protocol or to enter information into the subjects' health records. The collection and use of real Social Security

numbers must be approved by IRB, and the investigators must follow all applicable VA and other Federal requirements for obtaining and using real Social Security numbers.

m. **Performing Subject Outreach.** This means ensuring that, as part of the local VA facility's Research Subject Outreach Program, the investigator is responsible for:

(1) Making every reasonable effort to make available the informational brochure, "Volunteering in Research – Here Are Some Things You Need To Know," (http://www.research.va.gov/programs/pride/veterans/tri-fold.pdf) to potential research subjects in settings where investigators may recruit subjects (e.g., clinic waiting areas), and to prospective subjects, and their surrogates where applicable, when the individuals are approached to take part in a study.

(2) Ensuring that all informed consent forms provide subjects with required contact information for the VA investigator and relevant study staff. In addition, all informed consent forms must provide a contact independent of the research team in case the research staff cannot be reached, and the subject wish to talk to someone other than the research staff, or the subject wishes to voice concerns or complaints about the research.

(3) Informing the independent contact person who is independent of the research team (e.g., the facility's patient advocate, a member of the research office staff, or IRB staff) of the relevant details of the study; documenting that this independent contact person has been informed; and ensuring the independent contact person's ability to render proper assistance to potential subjects.

n. **Ensuring Appropriate Telephone Contact with Subjects.** This pertains to contacting the subject by telephone. Research team members are prohibited from requesting Social Security numbers by telephone.

(1) **Initial Contact.** During the recruitment process, ensuring the research team makes initial contact with the potential subject 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 (e.g., if the potential subject has diabetes, the subject may indicate a desire to be notified of any diabetes-related research studies). The initial contact must provide a telephone number or other means that the potential subject can use to verify the study constitutes VA research. ***NOTE:*** *One source of information about clinical trials that can be shared with potential subjects is the NIH clinical trials Web site (http://www.clinicaltrials.gov) where VA clinical trials are listed.*

(2) **Later Contact.** Ensuring the research team begins telephone calls to the subject by referring to previous contacts and, when applicable, the information provided in the informed consent form, and ensuring that the scope of telephone contacts with the subject is limited to topics outlined in IRB-approved protocols and informed consent forms.

o. **Obtaining IRB Approval for all Changes.** This means obtaining IRB approval for all changes to the research protocol (e.g., amendments or modifications), including changes to the IRB informed consent form (the IRB informed consent form is unique to each research study),

prior to implementing the changes. The only exception is when it is necessary to change the protocol to eliminate apparent immediate hazards to the subject. The investigator must promptly report these changes to the IRB.

p. **Submitting Continuing Review Materials.** This means ensuring continuing review materials are submitted in a timely manner to provide IRB sufficient time for reviewing and approving the study before IRB approval expires (see subpar. 22e). IRB approval automatically expires if the continuing review and approval does not occur by the expiration date of the current approval (see subpar. 22g for requirements if approval expires).

q. **Reporting Deviations and Complaints.** This means reporting deviations from the protocol and subject complaints to IRB in a time frame specified in local SOPs.

r. **Reporting Problems and SAEs.** This means reporting all unanticipated problems involving risks to subjects or others, and all unanticipated internal (i.e., local) SAEs, whether related or unrelated to the research, in accordance with local SOPs and VHA Handbook 1058.01. ***NOTE:*** *Current guidance on such reporting can be found on the ORO Web site (http://www1.va.gov/oro/).*

s. **Completing Appropriate Actions at Research Project Completion.** This means at completion of the research study, completing all required documentation and storing research records according to all applicable VA and Federal records retention requirements. If appropriate, the investigator communicates the results to subjects or the community from which subjects were recruited.

t. **Transferring of Records.** This means transferring of records by VA upon departure of the investigator**.** If the investigator leaves VA, all research records are retained by the VA facility where the research was conducted. If the grant is ongoing and the investigator leaves one VA facility to go to another VA facility, the investigator must obtain approval for a copy of relevant materials to be provided to the new VA facility's research office. The approval must be obtained from the first VA facility's research office, any other relevant individuals or offices according to VA and local requirements (e.g., compliance, privacy, or Information Security Officers (ISOs)), and the sponsor.

NOTE: *The investigator is not the grantee, nor does the investigator own the data.*

u. **Maintaining a Master List of All Subjects.** This means the investigator must maintain a master list of all subjects from whom informed consent has been obtained whether or not IRB granted a waiver of documentation of informed consent (see 38 CFR16.117(c) and par. 34).

(1) Investigators must not add a subject's name to the master list of all subjects until after:

(a) Informed consent has been obtained from that subject, and

(b) When appropriate, informed consent has been documented using an IRB-approved informed consent form.

(2) IRB may waive the requirement for the investigator to maintain a master list for a given study if both of the following conditions are met:

(a) There is a waiver of documentation of informed consent, and

(b) The IRB determines that including the subjects on such a master list poses a potential risk to the subjects from a breach of confidentiality.

(3) If IRB waives the requirement to maintain such a master list, IRB must provide written documentation in the IRB minutes or IRB protocol file justifying the waiver.

(4) The investigator must secure the master list appropriately in compliance with all VA confidentiality and information security requirements in the investigator's file for each study.

v. **Ensuring Appropriate Research Laboratory Test Reporting.** This means ensuring research laboratories not report laboratory results that are used for diagnosis, treatment, and prevention of disease in patients, unless the research laboratories are properly accredited and meet all requirements of 42 CFR 493 (see VHA Handbook 1106.01).

w. **Ensuring Requirements of Multi-site Studies.** See subpar 52a.

10. RESEARCH PROTOCOL

The investigator is responsible for the research protocol, and therefore, is responsible for:

a. **Ensuring Research is Scientifically Sound.** This means the investigator ensures that the research is scientifically sound.

b. **Ensuring Research Compliance.** This means the investigator ensures that research is in compliance with all applicable local, VA, and other Federal requirements.

c. **Providing a Plan for Recruitment and Selection of Subjects.** The investigator provides a plan for just, fair, and equitable recruitment and selection of subjects. ***NOTE:*** *The requirement for a plan for just, fair, and equitable recruitment and selection of subjects applies to both prospective and retrospective studies, including studies that use clinical or administrative databases or bio-specimens.*

d. **Minimizing Risks.** This means the investigator is responsible for minimizing risks to the subjects or others.

e. **Describing Data and Safety Monitoring Plan for Prospective Studies.** This means the investigator describes the data and safety monitoring plan for prospective studies. This plan must include, but is not limited to, the following:

(1) What safety information will be collected including SAEs (see VHA Handbook 1058.01);

(2) How the safety information will be collected (e.g., with case report forms, at study visits, by telephone calls with subjects);

(3) The frequency of data collection including when safety data collection starts;

(4) The frequency or periodicity of review of cumulative safety data;

(5) If not using a DMC, and if applicable, statistical tests for analyzing the safety data to determine if harm is occurring;

(6) Provisions for the oversight of safety data (e.g., by a DMC); and

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

***NOTE**: The data and safety monitoring plan may vary depending on the potential risks, complexity, and nature of the study. The use of an independent DMC needs to be considered if there are multiple clinical sites, the study is blinded, interventions are high-risk, vulnerable populations are included, or when required by the funding organization, FDA, sponsor, or other relevant entity.*

f. **Describing Data and Safety Monitoring Plan for Retrospective Studies.** This means the investigator describes the safety and monitoring plan for retrospective studies, including studies involving pre-existing data and biological specimens. When applicable, the plan needs to include, but is not limited to, the following:

(1) A discussion with the subject of potential study outcomes that may have an effect on the subject's health or well-being; and

(2) A procedure to determine when and how to notify individual subjects or their health care providers of findings that may affect the subjects' health.

g. **Differentiating Usual Care from Research.** This means the investigator provides for usual care. If the protocol involves "usual care," the protocol must either include a narrative section or there must be a separate document in the IRB application that clearly differentiates the research intervention(s) from "usual care" (whether the "usual care" is limited to one "arm" of the study or is being delivered to all study subjects) (see subpar 9j(4)).

(1) When a study involves "usual care," in the protocol or a separate document in the IRB application the investigator must clearly designate the individual or entity (e.g., the appropriate research personnel versus the subject's health care provider) responsible for relevant aspects of both the research and the usual care.

(2) The subject needs to be able to identify which activity (e.g., treatment or service) is research, and which is usual care, and know who (the researcher or the subject's health care provider) is responsible for:

(a) Explaining potential risks and benefits of the treatment or service to the subject;

(b) Providing the treatment or service;

(c) Monitoring the treatment or service, as applicable;

(d) Defining whether the adverse events result from usual care or research, as applicable;

(e) Alerting the subject if there is a problem with the treatment or service (e.g., a newly discovered risk, a product recall); and

(f) Documenting the subject's clinical course while receiving the treatment or service, as applicable.

NOTE: *The researcher and the subject's health care provider may be the same individual. If they are different individuals, and the subject's health care provider is not involved in the research study, the health care provider is not considered to be a member of the research team.*

h. **Enlisting Clinical Expertise.** This means the investigator provides for clinical expertise. If the investigator is not a clinician, when appropriate, the protocol must have provisions for enlisting the services of a clinician with appropriate expertise and privileges to perform duties that may include, but not be limited to:

(1) Reviewing the data, adverse events, and new study findings; and

(2) Making required decisions to protect the health of the subject (e.g., stopping the participant's involvement in the study or determining when to notify the subject or the subject's health care provider of information that may affect the health of the subject).

i. **Providing for Privacy and Confidentiality.** This means the investigator provides for privacy and confidentiality. To facilitate review of the protocol by the Privacy Officer (see par. 38), the investigator must either dedicate specific sections of the protocol to privacy and confidentiality, or the investigator must develop an additional document that specifically addresses all privacy and confidentiality issues in the protocol; this becomes part of the IRB protocol file. The description needs to be sufficiently specific for the reader to understand how this requirement protects the subject's privacy and the confidentiality of the data. These procedures must be in compliance with all applicable VA and other Federal requirements.

j. **Providing for Information Security.** This means the investigator provides for an information security plan. To facilitate review of the protocol by the ISO (see par. 38), the investigator must either dedicate specific sections of the protocol to information security, or the investigator must develop an additional document that specifically addresses all information security issues in the protocol; it becomes part of the IRB protocol file. The plan must clearly identify and include, but not be limited to:

(1) Whether or not individually identifiable information is to be collected or used;

(2) How the data is to be collected or acquired;

(3) Where the data (original and all copies) is to be stored and corresponding security systems;

(4) How the data is to be transported or transmitted from one location to another;

(5) Who is to have access to the data and how they are to access it (anyone who has access to the data is responsible for its security);

(6) All entities or individuals outside VHA to whom the data is to be disclosed, and the justification for such disclosure and the authority (e.g., the HIPAA authorization);

(7) Who is to have access and be responsible for the security of the information (e.g., the Coordinating Center, the statistician, and PI who has ultimate responsibility);

(8) Mechanisms used to account for the information;

(9) Security measures that must be in place to protect individually identifiable information if collected or used; and

(10) How and to whom a suspected or confirmed loss of VA information is to be reported.

NOTE: *The special sections of the protocol dealing with privacy and confidentiality, and with information security, may be combined.*

k. **Providing Special Safeguards.** This means the investigator provides for special safeguards. When applicable, the protocol includes a narrative section that:

(1) Identifies any circumstances that may warrant special safeguards to protect the rights and welfare of subjects who are likely to be vulnerable including, but not limited to, those subjects who may be susceptible to coercion or undue influence; and

(2) Describes appropriate actions to provide such safeguards.

l. **Providing for Reuse of Data.** This means the investigator, if the data may be reused in other studies, describes the research data repository in which the data is to be stored (see VHA Handbook 1200.12). There must be a research informed consent and a HIPAA authorization associated with the protocol unless these requirements are waived by the IRB. If the IRB does not waive the requirements then the informed consent and HIPAA authorization content must include language on the uses and disclosures of the data as defined in the protocol as well as information on how privacy and confidentiality will be maintained and how the data will be secured. If the creation and operation of the data repository is not included in the data collection protocol, there must be a separate IRB-approved protocol for the creation and operation of the data repository (see VHA Handbook 1200.12).

11. IRB AUTHORITIES

a. **Approval and Disapproval.** IRB must review and have authority to approve, require modifications in (to secure approval), or disapprove all research activities covered by this Handbook, regardless of whether the research is funded by VA, funded from other sources, or unfunded (see 38 CFR 16.109(a) and 38 CFR 16.102(h)).

(1) Any VA research reviewed by IRB must have at least one VA investigator who serves as PI or LSI.

(2) An IRB-approved research activity may be disapproved by the VA facility Director, the R&D Committee, or ORD. If a research activity is disapproved by IRB, the disapproval cannot be overruled by any other authority (e.g., the facility Director or R&D Committee).

b. **Observation.** IRB has authority to observe, or have a third party observe, the consent process and the research (38 CFR 16.109(e)).

c. **Suspension or Termination.** IRB has authority to suspend or terminate approval of research that is not being conducted in accordance with 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 IRB's action and must be reported promptly to the investigator, appropriate IO(s), and the department or agency head, according to applicable local, VA, and other Federal requirements (see 38 CFR 16.113, VHA Handbook 1058.01).

12. IRB COMPOSITION

a. **Member Background.** Each VA IRB of record, whether that of the VA facility or an external organization (e.g., another VA facility, an academic affiliate, or the VA Central 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 (i.e., VA facility and external organization). IRB must be sufficiently qualified through the experience and expertise of its voting members, and the diversity of the voting 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 (38 CFR 16.107(a)). VA IRBs should make every effort to include a Veteran or Veteran representative as part of the fulfillment of the requirement of relevant diversity of experience and expertise.

b. **Understanding of Institutional Commitments and Requirements.** 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 applicable local, VA, and other Federal requirements, and standards of Government ethics and professional conduct and practice. IRB must therefore include persons knowledgeable in these areas (38 CFR 16.107(a)).

c. **Knowledge About Vulnerable Subjects.** If an IRB regularly reviews research that involves a vulnerable category of subjects, such as children, prisoners, pregnant women, or

handicapped or mentally disabled persons, consideration must be given to the inclusion of one or more individuals who are knowledgeable about and are experienced in working with these subjects (38 CFR 16.107(a)).

d. **Gender.** Every nondiscriminatory effort must 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 IRB solely on the basis of gender (38 CFR 16.107(b)).

e. **Profession.** No IRB may consist entirely of voting members of one profession (38 CFR 16.107(b)).

f. **Scientific and Non-Scientific Expertise.** Each IRB must include at least one voting member whose primary expertise is in scientific areas and at least one member whose primary expertise is in non-scientific areas (38 CFR 16.107(c)). Physicians, nurses, pharmacists, social workers, statisticians, and clinical allied health professionals are considered to be scientists.

g. **Nonaffiliated Members.** Each IRB must include at least one voting member who is not otherwise affiliated with VA (38 CFR 16.107(d)) and who is not part of the immediate family of a person who is affiliated with VA. The nonaffiliated voting member must be given a VA WOC appointment if the nonaffiliated voting member is going to be performing the duties and fulfilling the responsibilities of an IRB voting member. The nonaffiliated voting member still would be considered "not otherwise nonaffiliated" with VA if there is documentation that the only reason for the WOC appointment relates to liability coverage for the member's IRB responsibilities.

(1) The requirement for nonaffiliated members to obtain a VA WOC appointment does not apply to members of affiliate IRBs.

(2) Veterans whose only relationship with VA is receiving care at a VA facility or receiving benefits from the Veterans Benefits Administration are not considered to be affiliated for the purpose of being an IRB member. Individuals who perform occasional volunteer activities without a WOC appointment are not considered affiliated. However, those who hold a WOC appointment for volunteer activities other than IRB service are considered to be affiliated.

(3) Individuals who have retired from VA and who are receiving VA retirement benefits are considered affiliated.

(4) Employees of institutions that have formal academic affiliation agreements with VA, and employees of VA nonprofit research and education foundation are considered to be affiliated with VA.

h. **Conflict of Interest.** No IRB may have a member participate in the IRB's initial or continuing review of any study in which the member has a conflicting interest, except to provide information requested by IRB (38 CFR 16.107(e)).

(1) The member with a conflict of interest of a financial, professional, or personal nature must not be present during the vote or during any related IRB discussion except to answer questions; this member cannot be counted toward the quorum (see par. 13).

(2) "Not present" means that an IRB member must leave the room or, if participating in the meeting by conference call or videoconference, must have terminated the connection, not just be placed on "hold."

i. **Consultants or Ad Hoc Advisors.** An IRB may, at its discretion, invite individuals with expertise 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 IRB (38 CFR 16.107(f)). These individuals may be called "consultants" or "ad hoc advisors."

j. **Research Office Staff.** 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 IRB. They may serve as ex officio, non-voting members, but they and IRB must be sensitive to and appropriately manage potential, actual, or perceived conflict of interest.

NOTE: *If local SOPs call for titles of positions (e.g., ACOS for R&D, AO for R&D, ISO, Privacy Officer), instead of named individuals, to serve as ex officio, nonvoting members of IRB, the individuals themselves do not have to be appointed by the IO. They are to be considered to be ex officio, non-voting members of the IRB by virtue of their positions within the local facility.*

k. **RCOs.** RCOs may act as a consultant to the facility's IRB, but may not serve as a member (voting or nonvoting) of the IRB. RCOs may attend IRB meetings when requested by the IRB or as specified by local IRB SOPs.

l. **Facility Directors and Chiefs of Staff.** Facility Directors, their administrative staff, Chiefs of Staff, and other local leadership (e.g., Chief Nurse Executive, members of the management quadrad) may observe IRB meetings, but may not be voting or ex officio, non-voting members of the VA facility's IRB of record.

m. **Privacy Officer and Information Security Officer**

(1) A VA facility Privacy Officer and a VA facility Information Security Officer (ISO) must both be appointed as ex officio, non-voting members to either the facility's IRB or R&D Committee of record in accordance with current VHA policy (see par. 38).

(2) Regardless of whether they are appointed to be ex officio members of IRB or the R&D Committee, the facility Privacy Officer and ISO must be involved in the review of human subjects research to address and mitigate potential concerns regarding privacy and confidentiality, and information security, respectively.

n. **Alternate Members.** If alternate members are appointed to the IRB, IRB's written procedures must describe the appointment and function of alternate members, and the IRB membership roster must identify the primary member(s) for whom each alternate member may substitute. The alternate member's professional specialty, qualifications, and experience must be

comparable to those of the primary member to enable them to adequately fulfill the role of the member to be replaced.

o. **Appointment of Members**

(1) Names of potential new IRB voting members for a VA facility's local IRB must be submitted to the facility Director (the IO) who appoints IRB voting members in writing.

(2) Names of potential new IRB voting members for the VA Central IRB must be submitted to the VHA Central Office IO, or designee, and that IO, or designee, must appoint VA Central IRB voting members in writing.

(3) Appointment procedures for ex officio, non-voting members are to be in accordance with local SOPs and any other applicable VA requirements.

p. **Term of Appointment for Voting Members.** 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 lapse in service at the end of each term.

q. **Chair.** The Chair of a VA IRB must be a paid VA employee (i.e., not have a WOC or IPA appointment at VA).

(1) There may be one IRB Chair, Co-chairs, or a Chair and a Vice Chair. Each is a voting member of IRB.

(2) The Chair and, when applicable, the Co-chair or Vice Chair, are appointed by the IO for a term of up to 1 year, and may be re-appointed after each year indefinitely. For the purposes of this Handbook, the term "Chair" includes Co-chair and Vice Chair.

(3) The requirement for the IRB Chair to be a paid VA employee applies to VA IRBs, not to affiliate IRBs that serve as IRBs of record for VA facilities.

13. IRB CONVENED MEETINGS

IRB must observe the following requirements for convened meetings:

a. **Quorum.** Except when an expedited review procedure is used (see par. 21 and 38 CFR 16.110), a convened meeting at which a majority of the voting members of the IRB are present (i.e., a quorum) is required for IRB to conduct any business including, but not limited to, voting on actions, and reviewing and approving research studies. The quorum must include at least one voting member whose primary concerns are in non-scientific areas (38 CFR 16.108(b)).

(1) **Lack of a Quorum.** 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.

(2) **External IRBs.** For external IRBs that serve as IRBs of record for a VA facility (e.g., affiliate IRBs), one of the officially-designated VA representatives must be present to constitute a quorum for review of VA research.

b. **Scheduling.** Scheduled meetings of the IRB are to occur at intervals appropriate for the quantity, complexity, and frequency of required actions, and to permit adequate IRB oversight of the progress of the research it has approved. Other meetings may be scheduled (e.g., on an as needed basis) in accordance with the facility's SOPs.

c. **Remote Participation in Meetings.** Although it is strongly recommended that IRB members be physically present at the meeting, if physical presence is not possible, some or all members may participate in the meeting by conference call or videoconference, however, voting members cannot participate in the meeting discussions or voting by email.

(1) Any member participating by conference call or videoconference must have received all relevant materials prior to the meeting and must be able to participate actively and equally in all discussions.

(2) Minutes must clearly document which members were present by conference call or videoconference and that the criteria for a member participating by conference call have been satisfied (see subpar. 12h).

14. IRB STANDARD OPERATING PROCEDURES (SOP)

The IRB must establish written SOPs that include, but are not limited to:

a. **Initial and Continuing Review.** This refers to IRB's conducting its initial and continuing review of research and for reporting its findings and actions to the investigator (38 CFR 16.103(b)(4)(i)), the ACOS for R&D, and the R&D Committee or, in the case of VA Central IRB, to the IO's designee.

b. **Frequency of Review.** This refers to IRB's determining which projects require review more often than annually (38 CFR 16.103(b)(4)(ii)).

c. **Verification.** This refers to IRB's determining which projects need verification, from sources other than the investigators that no substantive modifications have occurred since previous IRB review (38 CFR 16.103(b)(4)(ii)).

d. **Reporting of Changes in Research Activity.** This refers to the IRB's ensuring prompt reporting to the IRB of proposed changes in a research activity (38 CFR 16.103(b)(4)(iii)) including amendments to the protocol or the informed consent form and ensuring that such changes in approved research are not initiated without IRB's review and approval, except when necessary to eliminate apparent immediate hazard to the subject.

e. **Initiation of Changes.** This refers to the IRB's ensuring that such changes in approved research, during the period for which IRB approval has already been given, may not be initiated

without IRB review and approval except when necessary to eliminate apparent immediate hazards to the subject (38 CFR 16.103(b)(4)(iii)).

f. **Review of Problems and SAEs.** This refers to the IRB's reviewing all unanticipated problems involving risks to subjects or others and all internal or local SAEs reported to IRB in accordance with VHA Handbook 1058.01.

g. **Reporting Requirements.** This refers to the IRB's ensuring prompt reporting to the IRB, and as applicable, to appropriate institutional officials (e.g., the VA facility Director), ORO, and others (e.g., the sponsor) in accordance with applicable local, VA, and other Federal requirements (see VHA Handbook 1058.01), of the following:

(1) Any unanticipated internal or local SAEs, whether related or unrelated to the research.

(2) Any serious or continuing noncompliance with this Handbook or the requirements or determinations of the IRB (38 CFR 16.103(b)(5)(i)), or applicable local, VA and other Federal requirements.

(3) Any suspension or termination of IRB approval (38 CFR 16.103(b)(5)(ii)).

h. **Observing the Informed Consent Process.** This refers to the IRB's observing, or having a third party observe, the informed consent process when the IRB determines it to be appropriate (38 CFR 16.109(e)).

i. **Notifying IRB Members of Expedited Studies.** This refers to the IRB's notifying IRB members of research studies that have been approved under the expedited procedure.

j. **Documenting Expedited Review Eligibility.** This refers to the IRB's documenting in the IRB minutes or the IRB protocol file the expedited review eligibility category the research meets.

k. **Documenting Waiver of Informed Consent and Waiver of Documentation of Informed Consent.** This refers to the IRB documenting in the IRB's minutes or the IRB protocol file the waiver of informed consent (see par. 35) or waiver of documentation of informed consent (see par. 34), and the protocol-specific findings justifying the determination.

l. **Documenting Waiver of HIPAA Authorization.** This refers to the IRB's documenting in the IRB minutes or IRB protocol file the approved waiver of HIPAA authorization and the protocol-specific findings justifying the determination to grant such a waiver.

m. **Audits**

(1) This refers to the IRB's ensuring the performance of periodic and random audits of human subject research studies and requiring investigators to take appropriate and timely corrective actions when deficiencies are identified (see par. 29). These procedures must include, but are not limited to:

(a) Criteria that may prompt increasing the frequency of audits beyond the minimal required frequency;

(b) The timeframe for reporting audit findings to the IRB;

(c) Types of corrective actions the IRB can require based on the audit findings;

(d) Who should implement and review the corrective actions; and

(e) How to evaluate the results of any corrective actions.

(2) These procedures must be consistent with auditing requirements of current VHA policy and those of the Research Auditing Program overseen by the VA facility Director.

(3) The IRB can accept RCO audits to fulfill auditing requirements.

n. **IRB Education.** This refers to the IRB's ensuring that initial and continuing education requirements for the IRB Chair, IRB members, and IRB alternate members are met.

o. **Reporting to Privacy Officer.** This refers to the IRB's reporting to the Privacy Officer any unauthorized use, loss, or disclosure of individually-identifiable subject information.

p. **Reporting to ISO.** This refers to the IRB's reporting violations of VA information security requirements to the appropriate VHA facility ISO, and adhering to the processes and timeframes published in VA incident reporting policies.

q. **IRB Records.** See paragraph 26.

15. IRB RESPONSIBILITIES FOR REVIEW AND APPROVAL OF RESEARCH

a. **IRB Review.** IRB must conduct review by a convened or expedited (i.e., review by the IRB Chair or a qualified IRB voting member designated by the IRB Chair) review procedure of all proposed human subjects research in accordance with local, VA, and other Federal criteria including, but not limited to 38 CFR 16.111 (see pars. 13 and 21, respectively). This review includes a review of the application to the IRB, the research protocol, and all other relevant documents (e.g., informed consent forms, surveys, advertising materials) submitted to IRB. No such study can be initiated until the IRB has determined that the study does not constitute human subjects research, is exempt from IRB approval requirements (see par. 16), or has satisfied all requirements for approval (see par. 17 and 38 CFR 16.101). All research that is determined to be exempt or not to involve human subjects must be reviewed and approved by the R&D Committee. The IRB may consider the following questions in making these determinations:

(1) **Is the Project Research?** The IRB's first responsibility is to determine whether or not the proposed project constitutes a research study (see subpar. 3jjj and 38 CFR 16.102(d)). If the project does not constitute research, the IRB has no responsibilities for review or approval beyond the determination that the project does not constitute research.

(2) **Does the Research Involve Human Subjects?** If the project does constitute a research study, the IRB must determine whether or not it involves human subjects as defined in this Handbook and 38 CFR 16.102(f).

(3) **Is the Human Research Project Exempt?** If the study constitutes research involving human subjects, then the IRB Chair or another IRB voting member designated by the IRB Chair must determine whether or not the study is exempt from IRB review. If the study is exempt from IRB review, the IRB does not have to approve it (see par. 16).

(4) **Non-Exempt Research.** If a proposed human research study does not meet the criteria for exemption from IRB review, the study is considered "non-exempt," and the IRB must:

(a) Conduct initial review using a convened or expedited review procedure,

(b) Determine whether the research has satisfied all relevant criteria for approval, and

(c) Perform subsequent continuing review as appropriate.

b. **Scientific Review.** The IRB is not required to perform a comprehensive scientific review of the study, but is responsible for being sufficiently familiar with the science to perform its review, including a sufficient understanding of the science to carry out its responsibilities including, but not limited to, weighing the potential risks and benefits to the subjects.

c. **IRB Approval.** IRB approval of a study means the IRB has determined that the research has satisfied all relevant approval criteria and may be conducted at an institution within the constraints set forth by the IRB and by other applicable local, VA, and other Federal requirements (38 CFR 16.102(h)).

d. **Initiation of Research.** The investigator must not initiate any research until all applicable requirements of VHA Handbook 1200.01 have been met.

16. EXEMPT RESEARCH

Research activities in which the only involvement of human subjects will be in one or more of the categories outlined in 38 CFR 16.101(b), may be exempt from the provisions of this Handbook and the Common Rule (38 CFR Part 16), including being exempt from IRB-approval requirements. The Common Rule exemptions at 38 CFR 16.101(b) may not be applied to FDA-regulated research (see 21 CFR 56.104 for exemptions applied to FDA-regulated research).

a. **Granting Exemptions.** The investigator must submit the proposed research study and the request for exemption to the IRB. The IRB Chair, or an experienced IRB voting member designated by the Chair, must:

(1) Review all requests for exemption in a timely manner,

(2) Make a determination as to whether or not to grant an exemption based on 38 CFR 16.101(b), and

(3) Record the determination.

b. **Documentation of Exempt Status.** The IRB's determination of exemption must:

(1) Be signed by the IRB voting member who reviewed the research and made the determination that the research was exempt, or denied the exemption.

(2) Include the specific category(ies) from 38 CFR 16.101(b) justifying the exemption from IRB review or, if the request is denied, include the reason for the denial.

NOTE: *The exempt status means the research is exempt from the requirements of 38 CFR Part 16 including reviews by IRB. It does not exempt the research from other required reviews, such as by the R&D Committee.*

17. IRB APPROVAL CRITERIA

To approve research covered by 38 CFR Part 16 and this Handbook, IRB must determine that all of the following requirements are satisfied (38 CFR 16.111). The following criteria must be met before the IRB can grant approval by expedited review, convened initial review, or continuing review. The criteria must also be met, when relevant, before the IRB can grant approval of an amendment to the protocol if the amendment affects any of the following criteria.

a. **Minimization of Risks.** The IRB must determine that risks to human subjects are minimized (38 CFR 16.111(a)(1)) by using procedures that:

(1) Are consistent with sound research design and which do not unnecessarily expose subjects to risk, and

(2) Are already being performed on the subjects for diagnostic or treatment purposes, whenever appropriate.

NOTE*: Consultation with subject matter experts or review by other committees or subcommittees (e.g., Biosafety or Radiation Safety) may be necessary to ensure risks to human subjects are minimized.*

b. **Risks and Benefits.** The IRB must determine that risks to subjects are reasonable in relation to anticipated benefits, if any, and the importance of the knowledge that may reasonably be expected to result. In evaluating risks and benefits, the IRB needs to 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 (38 CFR 16.111(a)(2)).

(1) The IRB must ensure protocols with treatment or services that constitute "usual care" include a narrative section that clearly differentiates the research interventions from usual care, whether usual care is delivered to only some or to all research subjects (see subpar. 10g).

(2) In addition, the IRB must ensure the informed consent process clearly defines for the subject which potential risks are related to the research (38 CFR 16.116(a)(2) and, therefore, needs to be discussed with the research team, versus those associated solely with usual care provided by the subject's health care provider. The informed consent process is to include language advising subjects to review the risks of the latter with their health care providers (see subpar. 17b).

(3) Should an IRB question a protocol's characterization of "usual care," its associated risks, or the person or entity responsible for specific aspects of "usual care," the IRB is to seek clarification from the investigator and, if warranted, from qualified experts (38 CFR 16.107(f)). The IRB must document its determination(s) accordingly.

c. **Equitable Selection of Subjects.** The IRB must determine:

(1) That 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 it needs to be particularly cognizant of the special problems of research involving vulnerable populations, such as: children, prisoners, pregnant women, mentally-disabled persons, and economically or educationally disadvantaged persons (38 CFR 16.111(a)(3)).

(2) If recruitment of non-Veterans is justified and appropriate.

d. **Informed Consent**. The IRB must:

(1) Ensure that informed consent is obtained from each prospective subject or the subject's LAR in accordance with 38 CFR 16.116 (see pars. 30 through 36).

(2) Ensure the informed consent form includes all applicable elements (see pars. 30-33).

(3) Ensure the informed consent form includes appropriate blocks for signatures and dates (see subpar. 33c and subpar. 30d(2)).

(4) Ensure the informed consent form is consistent with the protocol and, when relevant, with the HIPAA authorization.

(5) Determine that informed consent is appropriately documented, in accordance with, and to the extent required by 38 CFR 16.117 (38 CFR 16.111(a)(5)) and in accordance with this Handbook (see par. 33).

e. **Safety Monitoring**. The IRB must determine, when appropriate, that the research plan makes adequate provision for monitoring the data collected to ensure the safety of subjects (38 CFR 16.111(a)(6)). The plan may include establishing a DMC as required by VA or DHHS, and a plan for reporting DMC findings to the IRB and the sponsor. For studies that do not have or are not required to have a DMC and are blinded, have multiple sites, enter vulnerable populations, or employ high-risk interventions, the IRB needs to carefully review the data and safety monitoring plan; it may suggest creation of a DMC.

NOTE: *A sponsor (e.g., ORD or NIH) may require a DMC for a specific study. However, even if a sponsor does not require a DMC, an IRB may determine that a DMC must be established for that study.*

f. **Privacy and Confidentiality**. The IRB must determine, when appropriate, that there are adequate provisions to protect the privacy of subjects and to maintain the confidentiality of data (38 CFR 16.111(a)(7)). Such provisions must take into consideration the requirements of Standards for Privacy of Individually-Identifiable Health Information (HIPAA Privacy Rule), 45 CFR 160 and 164, and other laws regarding protection and use of Veterans' 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. An IRB does not have the authority to approve the HIPAA authorization unless it is incorporated into the informed consent form; however, this Handbook requires the HIPAA authorization and informed consent form to be two separate documents (see par. 38).

g. **Information Security.** The IRB must determine that applicable VHA and VA information security policies pertaining to research are implemented and continually monitored to ensure compliance as set forth in VA Directive 6500 and its Handbooks (see par. 38).

h. **Vulnerable Subjects.** The IRB must assess the individuals or populations being recruited for potential vulnerability to coercion or undue influence, lack of decision-making capacity or increased susceptibility to harm from the research under review. If vulnerability is determined to exist, the IRB must ensure that additional safeguards have been included in the study to protect the rights and welfare of these subjects (38 CFR 16.111(b)). In addition, research involving certain categories of subjects (e.g., pregnant women, prisoners, and children) must adhere to specific requirements (see pars. 45-49).

i. **Conflict of Interest.** The IRB must ensure that steps to manage, reduce, or eliminate potential, actual, or perceived conflicts of interest related to all aspects of the research (financial, role (investigator-patient relationships), and other professional, institutional, or personal roles) have been taken.

j. **Investigator Qualifications.** At the time of initial review, and if there is a change in investigator during the course of the study, the IRB must determine that the investigator(s) has the appropriate background and experience to conduct the research. ***NOTE:*** *The IRB is not responsible for confirming that the investigator or other research team members have met current credentialing, privileging, and training requirements.*

k. **HIPAA Authorization.** The IRB must determine that the protocol, the informed consent form, and the HIPAA authorization are consistent with each other.

18. EXPEDITED REVIEW CRITERIA

The IRB must determine whether or not a study meets expedited review criteria in accordance with the following:

a. An IRB may use the expedited review procedure to review either or both of the following (38 CFR 16.110(b)):

(1) Research in the categories eligible for expedited review (see par. 19 and 38 CFR 16.110(a)) and found by the IRB reviewer(s) to involve no more than minimal risk (38 CFR 16.110(b)(1)); or

(2) Minor changes in previously approved research during the period (of 1 year or less) for which approval is authorized (38 CFR 16.110(b)(2)).

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

c. The IRB must apply the standard requirements for informed consent (or its waiver, alteration, or exception) to all studies that undergo expedited review (see pars. 30-36).

19. EXPEDITED REVIEW ELIGIBILITY

The IRB may use expedited review procedures to review and approve specific categories of research activities as defined in the FR: Volume 63, Number 216, Pages 60364-60367, November 9, 1998. Studies on marketed drugs that significantly increase the risks or decrease the acceptability of the risks associated with the use of the drugs are not eligible for expedited review. The categories of research activities eligible for expedited review are:

a. **Drugs and Devices (Expedited Review Category Number 1, see subpar. 65z).** Clinical studies of drugs and medical devices may undergo expedited review only when the criteria in paragraph 18 and one of the following conditions are met:

(1) The research is on drugs for which an IND application (21 CFR Part 312) is not required.

(2) The research is on medical devices for which:

(a) An investigational device exemption (IDE) application (21 CFR 812) is not required; or

(b) The medical device is cleared or approved for marketing, and the medical device is being used in accordance with its cleared or approved labeling.

b. **Blood Samples (Expedited Review Category Number 2, see subpar. 65aa).** Blood samples are collected by finger stick, heel stick, ear stick, or venipuncture as follows:

(1) From healthy, nonpregnant adults who weigh at least 110 pounds. For these subjects, the amounts drawn may not exceed 550 milliliters (ml) in an 8-week period, and collection may not occur more frequently than two times per week; or

(2) From other adults and children, considering the age, weight, and health of the subjects, the collection procedure, the amount of blood to be collected, and the frequency with which it will be collected. For these subjects, the amount drawn may not exceed the lesser of 50 ml or 3 ml per kilogram (kg) in an 8-week period, and collection may not occur more frequently than two times per week.

c. **Noninvasive Collection of Biological Specimens (Expedited Review Category Number 3, see subpar. 65bb).** Biological specimens for research purposes are to be collected prospectively by noninvasive means. Examples are as follows:

(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 subgingival 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. **Noninvasive Collection of Data (Expedited Review Category Number 4, see subpar. 65cc).** Data must be collected 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 or approved for marketing. ***NOTE:*** *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 of noninvasive collection of data are:

(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 subject's privacy.

(2) Weighing the subject.

(3) Testing sensory acuity.

(4) Magnetic resonance imaging (MRI).

(5) Electrocardiography, electroencephalography, thermography, detection of naturally occurring radioactivity, electroretinography, ultrasound, diagnostic infrared imaging, Doppler blood flow, and echocardiography.

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

e. **Collected Materials(Expedited Review Category Number 5, see subpar. 65dd).** Research involves:

(1) Materials (data, documents, records, or specimens) that have been collected for any purpose, including previous research; or

(2) Materials (data, documents, records, or specimens) that will be collected solely for nonresearch purposes (such as medical treatment or diagnosis).

***NOTE**: Some research in this category may be exempt from the VA regulations for the protection of human subjects (38 CFR 16.101(b)(4)). This listing refers only to research that is not exempt.*

f. **Collection of Data From Voice, Video, or Photographs (Expedited Review Category Number 6, see subpar. 65ee).** See paragraph 55.

g. **Group Characteristics, Surveys, Interviews, and Quality Assurance(Expedited Review Category Number 7, see subpar. 65ff).** Research must be 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 will employ 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 VA regulations for the protection of human subjects (38 CFR 16.101(b)(2) and (b)(3)). This listing refers only to research that is not exempt.*

20. EXPEDITED REVIEW FOR CONTINUING REVIEW

The IRB may use expedited review for continuing review under the following circumstances (Expedited Review Category Number 8, see subpar. 65gg):

a. **Previously-approved Research.** Previously-approved Research is research which has previously been approved by the convened IRB where:

(1) No subjects have been enrolled and no additional risks have been identified; or

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

(a) All subjects have completed all research-related interventions; and/or

(b) The research remains active only for long-term follow-up of subjects; and/or

(c) The remaining research activities are limited to data analysis.

b. **Minimal-risk Research (Expedited Review Category Number 9, see subpar. 65hh).** Minimal-risk research is research not conducted under an IND application or IDE, and where the categories in subparagraphs 19a-19g do not apply, and 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.

21. EXPEDITED REVIEW PROCEDURES

a. In the expedited review process, the review may be carried out by the IRB Chair or by one or more experienced voting members of the IRB designated by the IRB Chair, in accordance with 38 CFR 16.110(b).

b. All of the requirements for IRB approval of research apply to expedited reviews (see par. 17).

c. The reviewers may exercise all of the authorities of the IRB except that the reviewers may not disapprove the research (38 CFR 16.110(b)). A research activity may be disapproved only after review in accordance with the non-expedited procedure set forth in 38 CFR 16.108(b) and 38 CFR 16.110(b) by the convened IRB (see par. 13).

d. The decision and the expedited review eligibility category must be included in the IRB minutes of the next convened IRB meeting (see par. 19), and in the letter conveying the IRB's decision to the investigator.

22. CONTINUING REVIEW

a. **Content of Continuing Review.** The IRB's continuing review of research must be substantive and meaningful, including, but not limited to:

(1) Review of the ongoing level of risks and benefits;

(2) Assessment of the need for special safeguards to protect subjects; and

(3) Review of the adequacy of ongoing protection for potentially vulnerable individuals.

b. **Intervals of Continuing Review.** The IRB must conduct a continuing review of research covered by this Handbook at intervals appropriate to the degree of risk, but not less than once per year (38 CFR 16.109(e)).

c. **Procedures.** The IRB must have written procedures for determining which projects require review more often than annually (38 CFR 16.103(b)(4)(ii)).

d. **Convened IRB.** Continuing review by the convened IRB, with a separate deliberation and recorded vote on each study, is required unless the research is otherwise appropriate for expedited review (see par. 19). Furthermore, the criteria set forth in paragraph 17 must be satisfied for the IRB to approve research.

e. **Investigator Submission for Continuing Review.** The investigator must submit to the IRB a protocol summary (this may be in the form of an abstract) and a written status report that includes:

(1) A brief summary of the research methodology;

(2) The number of subjects entered and withdrawn (including the reason for withdrawal) for the review period and since the inception of the research study;

(3) A summary of complaints regarding the research since the last IRB review;

(4) The gender and minority status of those entered into the protocol, when appropriate;

(5) The number of subjects considered to be members of specific vulnerable populations;

(6) A copy of the current informed consent form (or all current informed consent forms if there is more than one) and any new proposed informed consent form along with a description of changes in the new form;

(7) A copy of the current HIPAA authorization document;

(8) A list of all amendments to the protocol since the last IRB initial or continuing review and approval;

(9) Information that may impact on the risk benefit ratio, such as SAEs and complaints regarding the research;

(10) Summaries, recommendations, or minutes of the DMC meetings (if applicable) or findings based on information collected by the data and safety monitoring plan submitted in the initial proposal;

(11) An assurance that all identified unanticipated internal or local SAEs, whether related or unrelated to the research, have been reported as required to the IRB of record (see VHA Handbook 1058.01);

(12) A summary of all unanticipated problems involving risks to subjects or others, and all internal or local SAEs;

(13) Research findings to date, if available;

(14) Any relevant multi-center trial reports;

(15) New scientific findings in the literature, or other relevant findings, that may impact on the research; and

(16) A statement signed by the PI certifying that all subjects entered onto the master list of subjects for the study signed an informed consent form prior to undergoing any study interactions or interventions, unless the IRB has granted a waiver of informed consent (38 CFR 16.116(c) and (d)), or a waiver of the signed informed consent form (38 CFR 16.117(c)).

f. **IRB Review.** All IRB members (both voting and nonvoting, ex officio) need to, at a minimum, receive, and review a protocol summary and a status report on the progress of the research. At least one voting member of the IRB (i.e., a primary reviewer) also needs to receive a copy of the complete protocol, including any modifications previously approved by the IRB. Furthermore, upon request, any IRB member also needs to have access to the complete IRB protocol file and relevant IRB minutes prior to or during the convened IRB meeting.

(1) The IRB must ensure that all approval criteria as described in paragraph 17 are satisfied.

(2) The IRB must ensure that the currently approved or proposed informed consent document remains accurate and complete and contains all required elements including appropriate blocks for signatures and dates (see subpar. 30d(2)) and, if applicable, that the informed consent form and the HIPAA authorization are consistent with each other and with the protocol.

(3) The IRB must ensure that any significant new findings that may affect the subject's willingness to continue participation are provided to the subjects.

(4) When reviewing continuing research under an expedited review procedure, the IRB Chair or designated voting IRB member(s) should receive and review all the preceding referenced documentation, including the complete protocol.

(5) The IRB must ensure that the master list of subjects entered into the study contains only those subjects who have signed an informed consent form unless the IRB has granted a waiver of informed consent (38 CFR 16.116(c) and (d)), or a waiver of the signed informed consent form (38 CFR.117(c)). The IRB may rely on assurances from the PI and audits conducted by the RCO.

g. **Expiration of IRB Approval.** When continuing review occurs annually and the IRB performs continuing review within 30 days before the IRB approval period expires, the IRB may retain the anniversary date as the date by which the continuing review must occur. 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:

(1) The local research office is responsible for promptly notifying the investigator.

(2) The investigator must:

(a) Stop all research activities including, but not limited to, enrollment of new subjects; continuation of research interventions or interactions with currently participating subjects; and data analysis.

(b) Immediately submit to the IRB Chair a list of research subjects who could be harmed by stopping study procedures.

(3) The IRB Chair, with appropriate consultation with the facility Chief of Staff, determines if subjects on the list may continue participating in the research interventions or interactions.

(4) Once the study approval has expired, IRB re-review and re-approval must occur before the study can resume. The IRB cannot retrospectively grant approval to cover a period of lapsed IRB approval.

23. AMENDMENTS TO STUDIES

All amendments to the protocol or changes in the informed consent form must be reviewed, and approved in writing by the IRB prior to the investigator's initiating the changes, except when necessary to eliminate immediate hazard(s) to the subject(s).

a. **Submission of Amendments.** The amendment, a justification for the amendment, and when relevant, a copy of the protocol with the amendment incorporated, a copy of the amended informed consent form, and documentation of HIPAA authorization or waiver of HIPAA authorization must be submitted to the IRB.

b. **Expedited IRB Review.** Amendments may be reviewed and approved by expedited procedures if the amendment represents a minor change in previously-approved research during the period (of 1 year or less) for which approval is authorized (see par. 21).

c. **Convened IRB Review.** When amendments are substantive modifications or clarifications directly relevant to the determinations required by the IRB and do not fall within the list of categories of research that may be entitled to expedited review according to 38 CFR 16.110(b), the amendment must be reviewed by the convened IRB. IRB SOPs must define "substantive." The IRB must ensure that all approval criteria as described in paragraph 17 are satisfied to approve the amendment.

(1) Because the protocol and the informed consent form must be consistent with each other, if there is an amendment or modification to the protocol that affects the informed consent form, there must be an analogous amendment or modification to the informed consent form.

(2) Similarly, if there is an amendment of modification of the informed consent form that affects the protocol, there must be an analogous amendment or modification to the protocol.

(3) Both the protocol and informed consent form must be consistent with the HIPAA authorization. If an amendment to the protocol or the informed consent form is not relevant to uses or disclosures of PHI, the HIPAA authorization does not have to be modified.

d. **Date of Continuing Review.** The date of continuing review is not changed based on the approval date of the amendment unless the IRB specifies that the date of continuing review is changed.

24. IRB APPROVAL DATE

The date of IRB approval of a study is used to determine when continuing review must be performed.

a. **Convened IRB Review.** If the convened IRB procedure is employed, the continuing review date is determined by the date the convened IRB reviewed and approved the study.

(1) **No Conditions.** If the convened IRB approves the study with no requirement for modifications, the date of approval is the date of the convened IRB meeting at which approval was granted.

(2) **Minor Conditions.** If the convened IRB approves the study contingent on specific minor modifications to the protocol or the informed consent form, the study cannot proceed until subsequent review and approval of the materials submitted in the investigator's response to the minor conditions specified by the convened IRB. The IRB Chair, or an experienced IRB voting member designated by the Chair, may use expedited review procedures to verify that the specific minor conditions were met. The date of approval for the purpose of determining the date of continuing review is the date the study was approved by the convened IRB contingent on minor conditions being addressed.

(a) Investigators must be notified in writing when the IRB Chair or designated IRB voting member has approved the minor conditions.

(b) The approval of minor conditions by the Chair or designated IRB voting member must be documented in the minutes of the first IRB meeting that takes place after the date of the approval of the minor conditions.

(3) **Substantive Conditions.** If the convened IRB defers approval of a study contingent on substantive modifications or clarifications to the protocol or the informed consent form, the convened IRB must review and approve the investigator's modifications. The date of approval is the date the substantive modifications or clarifications were approved by the convened IRB.

b. **Expedited Review.** If the expedited review procedure is employed, the date of continuing review of the research study is based on the date the IRB Chair, or experienced IRB voting member(s) designated by the IRB Chair, gives IRB approval to the research study (see subpar. 22g).

25. IRB COMMUNICATION WITH INVESTIGATORS

a. **Initial Review.** An IRB must notify the investigator, the R&D Committee, and the local research office or, in the case of the VA Central IRB, the individual designated by the IO, in writing of the IRB's decision to approve or disapprove a proposed research activity or of modifications required to secure IRB approval in accordance with 38 CFR 16.109(d).

(1) The notification by the IRB must be signed by the Chair, or the voting member of the IRB who reviewed the research.

(2) After the IRB has approved a study, it must not be initiated until the investigator has been notified in writing by the ACOS for R&D that all applicable approvals have been obtained and the study may be initiated (see subpar. 9g).

b. **Approved Informed Consent Form.** Along with written notification of IRB approval, when relevant, IRB staff must send the investigator a copy of the IRB-approved informed consent form.

c. **Amendments or Modifications.** The IRB must approve all amendments or modifications to research activities or informed consent forms that previously have been approved by the IRB. The IRB must notify in writing the investigator and the local research office or, in the case of the VA Central IRB, the individual designated by the IO, of the IRB's decision to approve, disapprove, or require changes to approve the amendments or modifications. The notification by the IRB must be signed by the Chair, a voting member of the IRB, or a member of the IRB staff, before the investigator may initiate any changes or modifications to the protocol or informed consent form, except when necessary to eliminate immediate hazard(s) to the subject(s).

d. **Continuing Review.** The IRB must notify the investigator, the R&D Committee, and the local research office or, in the case of the VA Central IRB, the individual designated by the IO, in writing of its determination to approve, disapprove, or require changes to approve the continuing review. The notification by the IRB must be signed by the IRB Chair, another voting member of the IRB, or a member of the IRB staff.

e. **Reasons for Disapproval.** If the IRB disapproves a research activity, it must 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 (38 CFR 16.109(d)). The IRB must send the notification to the investigator and the local research office or, in the case of the VA Central IRB, the individual designated by the IO. The notification by the IRB must be signed by the Chair or another voting member of the IRB.

f. **Exemptions.** The IRB must notify the investigator, the R&D Committee, and the local research office or, in the case of the VA Central IRB, the individual designated by the IO, in writing of its determination that a research project is exempt from IRB approval requirements. The notification by the IRB must be signed by the IRB Chair, or another voting member of the IRB, or a member of the IRB staff.

26. IRB RECORDS

The IRB must have SOPs in place to ensure preparation and maintenance of adequate documentation of its activities in accordance with 38 CFR 16.115, including:

a. **IRB Protocol File.** See paragraph 27.

b. **IRB Minutes.** See paragraph 28.

c. **Continuing Review.** There must be records of continuing review activities (38 CFR 16.115(a)(3)).

d. **Correspondence.** There must be copies of all correspondence between the IRB and the investigators (38 CFR 16.115(a)(4)) including the IRB's requirement for modifications to the protocol or informed consent form, the IRB's approval, and any other relevant correspondence about the study (e.g., with the VA facility Director, ACOS for R&D, R&D Committee, and between the reviewers and the investigator).

e. **IRB Roster.** There must be a list of IRB members identified by name; earned degrees; representative capacity; indications of experience such as board certifications, licenses, etc., sufficient to describe each member's chief anticipated contributions to IRB deliberations; and any employment or other relationship (affiliated or non-affiliated) between each member and the institution (e.g., full-time employee, part-time employee) (38 CFR 16.103(b)(3) and 38 CFR 115(a)(5)). When applicable, the list must include alternate members and the IRB member or class of member for whom each alternate member can substitute. The IRB must maintain all previous membership rosters.

f. **IRB Member Resume.** There must be a resume or Curriculum vitae for each voting IRB member.

g. **IRB SOPs.** There must be written SOPs for the IRB in the same detail as described in paragraph 14, 38 CFR 16.103(b)(4)-(5), and 38 CFR 16.115(a)(6).

h. **Record Retention**. The required records, including the investigator's research records, must be retained until disposition instructions are approved by the National Archives and Records Administration (NARA) and are published in VHA's Records Control Schedule (RCS 10-1).

(1) All records must be accessible for inspection and copying by authorized representatives of VA, OHRP, FDA, and other authorized entities at reasonable times and in a reasonable manner in accordance with 38 CFR 16.115(b).

(2) 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.

(3) Complete (non-redacted) minutes, whether from the VA or affiliate IRB reviewing VA research, must be submitted to the R&D Committee.

27. IRB STUDY FILE

The IRB records consist of all copies of all: research proposals reviewed; scientific evaluations, if any, that accompany the protocols; approved informed consent forms; progress reports submitted by investigators; and reports of injuries to subjects (38 CFR 16.115(a)(1)). The IRB protocol file must contain copies of all items reviewed including, but not limited to, all versions of:

a. Research protocols.

b. Investigator's brochures, if any.

c. Recruitment materials, if any.

d. Scientific evaluations. Scientific evaluations, if any, that accompany the protocols.

e. IRB-Approved Informed Consent Forms.

f. HIPAA authorization documents (or documentation of waiver of HIPAA authorization).

g. Any proposed amendments and the IRB action on each amendment.

h. Progress reports submitted by investigators for continuing review.

i. Reports of internal or local SAEs.

j. Documentation of protocol deviations.

k. Documentation of non-compliance with applicable requirements.

l. Audit results and documentation of compliance with remediation requirements.

m. Significant new findings. Statements of significant new findings provided to subjects as required in 16.116(b)(5) (38 CFR 16.115(a)(7)).

n. Subject complaints.

o. Summaries of DMC findings.

p. Communications with the investigator, including, but not limited to applicable:

(1) Documentation of all relevant approvals,

(2) Documentation of waiver of HIPAA authorization, and

(3) Documentation of waiver of informed consent or waiver of documentation of informed consent.

28. IRB MINUTES

Draft minutes of IRB meetings must be written and available for review within 3 weeks of the meeting date. Once approved by the voting members at a subsequent IRB meeting, the minutes must be signed by the IRB Chair, or a qualified voting member of the IRB designated by the Chair. The final minutes cannot be altered by anyone, including other authorities or committees (e.g., the VA facility Director, RCO, Privacy Officer or ISO, or the R&D Committee). Minutes of IRB meetings must be in sufficient detail to document:

a. **Attendance.** Attendance at the meetings includes those members or alternate members who participated through videoconference or teleconference (see subpar. 13c); and documentation that those who attended through videoconferencing or teleconferencing received all relevant material prior to the meeting and were able to actively participate in all discussions.

b. **Quorum.** There must be the presence of a quorum for each vote, including the presence of one voting member whose primary concern is in a non-scientific area. ***NOTE:*** *This quorum, including the presence of one voting member whose primary concern is in a non-scientific area, could be indicated in the minutes by tracking attendance. It does not have to be indicated with each vote.*

c. **Alternate Members.** If applicable, document the presence of alternate members attending the meeting and for whom they are substituting.

d. **IRB Actions.** Document actions taken by the IRB.

e. **Vote.** Document the vote on these actions including the number of voting members voting for, against, and abstaining.

f. **IRB Member Conflict of Interest.** When an IRB member has a potential, actual, or perceived conflict of interest relative to the proposal under consideration, document the IRB member was not present during the deliberations or voting on the proposal, and that the quorum was maintained. ***NOTE:*** *"Not present" means that an IRB member must leave the room or, if participating in the meeting by conference call or videoconference, must have terminated the connection.*

g. **IRB Determinations and Justifications**

(1) Document determinations made by the convened IRB when those determinations are required by applicable VA and other Federal requirements.

(2) Document protocol-specific findings justifying those IRB determinations for:

(a) Waiver or alteration of the informed consent process in accordance with 38 CFR 16.116(c) and (d)), or 38 CFR 16.117(c) (see pars. 34 and 35);

(b) Research involving pregnant women;

(c) Research involving prisoners; and

(d) Research involving children.

NOTE: *The minutes must specifically document that the IRB determined that all criteria for waiver or alteration of the informed consent process were met.*

(3) If an IRB uses an expedited review process, these determinations and protocol-specific findings justifying those IRB determinations must be documented in either the IRB protocol file or the minutes.

h. **Vulnerable Populations.** Document any review of additional safeguards to protect vulnerable populations if entered as study subjects (see pars. 45-49) and findings related to the use of surrogate consent.

i. **Subjects Susceptible to Coercion or Undue Influence.** Document that safeguards are adequate to protect the rights and welfare of subjects who are likely to be susceptible to coercion or undue influences (see pars. 45-49).

j. **Risk and Rationale.** Document the IRB's determination of the level of risk (e.g., whether or not the research constitutes minimal risk) and the rationale for the IRB's determination of the level of risk.

k. **Informed Consent Requirements.** Document the IRB's determination that all appropriate elements were included in the informed consent form, and are included in the informed consent process. In studies using an informed consent form, the form must include appropriate blocks for signatures and dates (see subpar. 30d(2)).

l. **Frequency of Continuing Review.** Document the IRB's determination of the frequency of continuing review of each study.

m. **Changes or Disapproval.** Document the basis for requiring changes in or disapproving research.

n. **Controverted Issues.** Provide a summary of the discussion of controverted issues and their resolution.

o. **Significant New Findings.** Provide statements of significant new findings.

p. **Non-Veteran Subjects.** Provide a summary of the justification for including non-Veterans as subjects (see par. 56).

q. **Real Social Security Numbers.** Provide a summary of the discussion when real Social Security Numbers (SSNs), scrambled SSNs, or the last four digits of SSNs will be used in the study. The summary needs to include the security measures that are in place to protect the SSN

instances embedded in the study. ***NOTE:*** *This does not apply if the only use of SSNs is on the informed consent form or the HIPAA authorization as required by VHA Handbook 1907.01).*

29. AUDITS

The IRB may require more frequent audits by the RCO or other means than those required in VHA policy (see subpar. 5p and VHA Handbook 1058.01). The IRB also may require the RCO to conduct more focused audits of one or more aspects of the study. The requirement to increase the frequency of audits or to audit specific aspects of the study may be based on considerations including, but not limited to:

a. Involvement of vulnerable populations;

b. Level of risk;

c. Phase I or Phase II studies;

d. Involvement of FDA approved drugs for which there has been a new safety warning issued, or change in the labeling that indicates increased risks;

e. Issues of noncompliance; or

f. Data confidentiality or security concerns.

30. GENERAL REQUIREMENTS FOR INFORMED CONSENT

Except as provided in paragraph 35 of this Handbook, no investigator may involve a human being as a subject in research covered by this Handbook unless the investigator has obtained the legally effective informed consent of the subject or the subject's LAR (38 CFR 16.116). An individual who is qualified to be a LAR for research purposes may not always qualify as a personal representative for purposes of consenting to use or disclose a living subject's PHI (i.e., signing a HIPAA authorization). Therefore, in circumstances involving authorization for use or disclosure of a subject's PHI, the investigator must ensure the LAR meets the requirements of a personal representative in 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).

a. **Circumstances Under Which Informed Consent May Be Sought.** The Common Rule requires (38 CFR 16.116):

(1) The investigator to seek informed consent only under circumstances that:

(a) Provide the prospective subject or the subject's LAR sufficient opportunity to read the informed consent document when applicable,

(b) Provide the prospective subject, or the subject's LAR, sufficient opportunity to consider whether or not to participate, and

(c) Minimize the possibility of coercion or undue influence.

(2) The information that is given to the subject or the subject's LAR must be in language understandable to the subject or the subject's LAR.

(3) No informed consent, whether oral or written, may include any exculpatory language through which the subject or the subject's LAR:

(a) Is made to waive, or appear to waive, any of the subject's legal rights; or

(b) Releases, or appears to release, the investigator, the sponsor, the institution, or its agents from liability for negligence

b. **Person Obtaining Informed Consent.** If someone other than the investigator conducts the informed consent process and obtains informed consent from a subject or the subject's representative, the investigator must formally and prospectively designate, in writing in the protocol or the application for IRB approval, the individual who will have this responsibility (see subpar. 9j(1)). The person so designated must have received appropriate training to perform this activity. This person must be knowledgeable about the research to be conducted and the consenting process, and must be able to answer questions about the study.

c. **Observing the Process.** The IRB has the authority to observe or have a third party observe the informed consent process.

d. **Informed Consent Form.** The most current IRB-approved version of VA Form 10-1086, Research Consent Form, for each study (or the most current IRB-approved electronic version of VA Form 10-1086) must be used as the informed consent form.

(1) All required elements must be completed (see par. 31) as well as any additional elements required by the IRB which may include, but not be limited to those in paragraph 32.

(2) The informed consent form must contain a designated block for each required signature (e.g., subject, person obtaining the informed consent, and witness when applicable) and for the date of each signature (see subpar. 33c). ***NOTE:*** *For the purposes of the informed consent form, a "block" may be a labeled line, window of a table, or other format that clearly indicates what type of signatures and dates the IRB specifically requires for that study's informed consent form.*

31. REQUIRED ELEMENTS OF INFORMED CONSENT

a. **Elements of Informed Consent Required by the Common Rule.** Except as provided in paragraphs 34, 35, and 36 of this Handbook, 38 CFR 16.116(a) requires the following elements of informed consent be provided to each subject:

(1) **A Statement That the Study Involves Research.**

(2) **An Explanation of the Purposes of the Research.**

(3) **The Expected Duration of the Subject's Participation.** A description of the expected length of the subject's commitment to active participation in the interventions or interactions of the study, including long-term follow-up. This does not include the time after all interventions and interactions with the subject have ended and the study activities include only analysis of specimens and/or data, and/or preparations for publication of results.

(4) **A Description of the Procedures to be Followed.**

(5) **Experimental Procedures.** Identification of any procedures that are experimental (38 CFR 16.116(a)(1)).

(6) **Risks or Discomforts.** A description of any reasonably foreseeable risks or discomforts to the subject (38 CFR 16.116(a)(2)).

(a) This description is to include, but not be limited to, physical, social, legal, economic, and psychological risks.

(b) Risks that do not result from the research, but that result solely from treatments or services that have been designated in the IRB-approved protocol to be the responsibility of the health care provider, should not be described in the consent form. The informed consent process is to include language advising subjects to review the risks of such clinical treatments or services with their health care provider(s).

(7) **Benefits.** A description of any benefits to the subject or to others that may reasonably be expected from the research (38 CFR 16.116(a)(3)).

(8) **Alternatives.** A disclosure of appropriate alternative procedures or courses of treatment, if any, that might be advantageous to the subject (38 CFR 16.116(a)(4)).

(9) **Confidentiality.** A statement describing the extent to which confidentiality of records identifying the subject will be maintained (38 CFR 16.116(a)(5)). If appropriate, a statement that Federal agencies including, but not limited to, the FDA, OHRP, ORO, and the VA Office of the Inspector General (OIG) may have access to the records. If an FDA-regulated test article is involved, FDA requires a statement that the FDA may choose to inspect research records that include the subject's individual medical records.

(10) **Research-Related Injury**

(a) For research involving more than minimal risk, a statement that includes:

1. An explanation as to whether any compensation is available if injury occurs, and

2. 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 (38 CFR 16.116(a)(6) and see par. 59).

(b) Although the Common Rule at 38 CFR 16.116(a)(6) only requires that the informed consent contain information on research-related injury if the study is more than minimal risk, VA regulations (38 CFR 17.85) require VA to provide care for all research-related injuries including those studies that are considered minimal risk.

(11) **Contact Information.** 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 (38 CFR 16.116(a)(7) is to be provided. There must be at least one contact other than the investigator or study personnel.

(12) **Participation is Voluntary.** A statement that participation is voluntary, refusal to participate involves no penalty or loss of benefits to which the subject is otherwise entitled, and the subject may discontinue participation at any time without penalty or loss of benefits to which the subject is otherwise entitled (38 CFR 16.116(a)(8)).

b. **Other Elements of Informed Consent Required by VA.** In addition to the elements for informed consent required by the 38 CFR Part 16, VA requires the following elements of informed consent:

(1) **The Name of the Study.**

(2) **The Name of the PI.** The name of the PI and, in multi-site studies, the name of the LSI.

(3) **The Sponsor of the Study.**

32. ADDITIONAL ELEMENTS OF INFORMED CONSENT

a. **Additional Elements of Informed Consent Required by the Common Rule.** When appropriate, the Common Rule requires one or more of the following elements of information be provided to each subject (38 CFR 16.116(b)). Also, when any of these additional elements are appropriate, VA requires them to be documented in the IRB-approved informed consent form unless documentation of informed consent is waived.

(1) **Unforeseeable Risks.** 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) which are currently unforeseeable (38 CFR 16.116(b)(1)).

(2) **Termination of Subject's Participation.** Anticipated circumstances under which the subject's participation may be terminated by the investigator without regard to the subject's consent (38 CFR 16.116(b)(2)).

(3) **Additional Costs.** Any additional costs to the subject that may result from participation in the research (38 CFR 16.116(b)(3)).

(a) Pursuant to 38 CFR 17.102, subjects in VA-approved research cannot be charged, nor can their insurance be billed, for research-related interventions or procedures (e.g., tests, drugs, clinic visits, hospital admissions, transportation) that are required by the protocol. If medical

services are furnished to a person who is not eligible for medical services as a Veteran, the medical care appropriation will be reimbursed from the research appropriation.

(b) When appropriate for the informed consent for VA-approved research to include information on additional costs to the subject that may result from participation in the research, the informed consent must contain a statement that a Veteran subject or a non-Veteran subject will not be required to pay for medical services received as a subject in an approved VA research study. The only exception is that certain Veterans are required to pay applicable co-payments for medical care and services provided by VA that are not rendered as part of the VA-approved research study (see 38 U.S.C. 1710(f) and 1710(g)). An example of language that may be appropriate for the informed consent form is "Some Veterans are required to pay co-payments for medical care and services provided by VA. These co-payment requirements will continue to apply to VA-provided medical care and services that are not part of this study."

(4) **Consequences of Withdrawal From Study.** The consequences of a subject's decision to withdraw from the research and procedures for orderly and safe termination of participation by the subject (38 CFR 16.116(b)(4)).

(5) **New Findings.** A statement that any significant new findings which may relate to the subject's willingness to continue participation, developed during the course of the research, will be provided to the subject (38 CFR 16.116(b)(5)).

(6) **Number of Subjects.** The approximate number of subjects involved in the study (38 CFR 16.116(b)(6)).

b. **Additional Elements of Informed Consent Required by VA.** When appropriate, VA requires one or more of the following elements of information be provided to each subject. Also, when any of these additional elements are appropriate, VA requires them to be documented in the IRB-approved informed consent form, unless documentation of informed consent is waived.

(1) **Commercial Product.** If applicable, that the investigator believes that the human biologic specimens obtained could be part of, or lead to the development of, a commercially valuable product.

(2) **Future Use of Specimens.** If the specimens are to be retained after the end of the study for future research, where the specimens will be retained, who will have access to them, and how long they will be retained. Current applicable institutional, VA, and other Federal requirements must be met for handling, use, and storage of biologic specimens and data (see VHA Handbook 1200.12).

(3) **Future Use of Data.** If any of the data will be retained after the study for future research, where the data will be stored, and who will have access to the data (see VHA Handbook 1200.12). Current applicable institutional, VA and other Federal requirements must be met for use and storage of data (see VHA Handbook 1200.12).

(4) **Re-contact.** If the subject will be re-contacted for future research whether within VA or outside VA.

(5) **Payment for Participating in the Study.** If appropriate, a statement regarding any payment the subject is to receive for participating in the study and how the payment is to be made (see par. 59).

(6) **Disclosure of Results.** If the subject will receive a report of the aggregate results or any results specific to the subject.

33. DOCUMENTATION OF INFORMED CONSENT

Informed consent must be documented prospectively by the use of a written consent form approved by the IRB (38 CFR 16.117(a), unless documentation of informed consent has been explicitly waived by the IRB (38 CFR 16.117(c)). ***NOTE:*** *Email communications do not constitute documentation of informed consent.*

a. **Consent Form.** VA Form 10-1086, must be used as the consent form for VA research. The only exception is that a DO(D informed consent form may be employed for active duty military personnel participating in VA research at DOD sites when VA-specific language is not necessary (e.g., when language for treatment of research related-injury is not needed because active duty military personnel are covered by DOD). The informed consent form must be the most recent IRB-approved informed consent form that includes all the required elements and, as appropriate, additional elements (see pars. 31 and 32).

(1) The requirement to utilize VA Form 10-1086 to document informed consent applies to all VA-approved research including, but not limited to, studies in which VA investigators working on VA research enroll subjects at the affiliate hospital or other sites outside VA (e.g., community centers or shopping malls).

(2) The "most recent" IRB-approved version of the informed consent form contains the date of the version of the informed consent form most recently approved by the IRB (e.g., in a header or footer). For instance, if the most recent version of the informed consent sent for approval by the IRB was the June 14, 2009, version, and the IRB approved it on July 1, 2009, the investigator must ensure the informed consent form contains the date June 14, 2009, on each page. The June 14, 2009, version would continue to be the most recent version even after approved by the IRB during the continuing review process (i.e., if there is no change in the informed consent form at the time of continuing review, it is not considered a new version).

b. **IRB Approval Date.** The IRB approval must be documented in the IRB minutes or IRB protocol files for those studies reviewed by the expedited process. IRB correspondence with the investigator must clearly indicate which version of the informed consent form has been approved (e.g., see the example in subpar. 33a(2)). The IRB approval date must be documented by the use of a stamp or preprinted box on each page of the informed consent form. This stamp or preprinted box must indicate the most recent date of IRB approval of the informed consent form. The IRB must maintain a copy of the approved informed consent form in its records.

c. **Signatures and Dates.** The informed consent form must be signed and dated by:

(1) The subject or the subject's LAR (38 CFR 16.117(a)),

(2) The person obtaining the informed consent, and

(3) A witness, if required by IRB (e.g., the IRB may require a witness if the study involves an invasive intervention or an investigational drug or device). A witness is always required when a short form consent is employed (see subpar. 33f(2)).

(a) The witness is required to witness only the subject's or subject's LAR's signature, not the informed consent process (e.g., if the subject does not want the witness to know the nature of the research study), unless the sponsor or IRB requires the witness to witness the informed consent process.

(b) The witness cannot be the person who obtained informed consent from the subject, but may be another member of the study team or may be a family member.

d. **Original Signed Consent Form.** The original signed and dated informed consent form (see subpar. 30d(2)) must be filed in the investigator's research file for that subject so that it is readily accessible for auditing. If the subject submits the signed and dated informed consent form to the investigator or designee by facsimile, the person who obtains informed consent must sign and date the facsimile, and then the facsimile can serve as the original informed consent document. If facsimile is used for the informed consent document, measures must be employed to ensure the confidentiality of the information, and the privacy of the subject.

e. **Copies of Signed Consent Form**

(1) A copy of the signed and dated informed consent form must be provided to the subject or the subject's LAR (38 CFR 16.117(a)).

(2) Where applicable, a copy of the signed and dated informed consent form must be placed in the medical record in accordance with VHA Handbook 1907.01.

f. **Consent Documents.** Except as provided in paragraph 34 the informed consent form may be either of the following (38 CFR 16.117):

(1) **Written Informed Consent With All Required Elements**. The consent may be in the form of a written consent document that embodies the elements of informed consent required by 38 CFR 16.116. This form may be read to the subject or the subject's LAR, but in any event, the investigator must give either the subject or the representative adequate opportunity to read it before it is signed (38 CFR 16.117(b)(1)); or

(2) **Short Form Consent.** The consent may be in the form of a short form written consent document stating that the elements of informed consent required by 38 CFR 16.116 have been presented orally to the subject or the subject's LAR (38 CFR 16.117(b)(2)). When this method is used:

(a) There must be a witness to the oral presentation (38 CFR 16.117(b)(2)).

(b) The IRB must approve a written summary of what is to be said to the subject or the LAR (38 CFR 16.117(b)(2)).

(c) Signatures are to be obtained as follows:

1. The short form is to be signed by the witness, and the subject or LAR (38 CFR 16.117(b)(2)).

2. The copy of the summary is to be signed by the witness and the person actually obtaining consent (38 CFR 16.117(b)(2)).

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

(d) A copy of the summary and a copy of the short form are to be given to the subject or the LAR (38 CFR 16.117(b)(2)).

(e) The original signed short form and summary must be filed in the investigator's research file for that subject.

(f) Where applicable (see VHA Handbook 1907.01), a copy of the signed short form informed consent form must be placed in the medical record in accordance with VHA Handbook 1907.01.

(g) The investigator must file all original, signed and dated, short form informed consent forms in the investigator's research file for that subject, so that they are readily accessible for auditing.

34. WAIVER OF DOCUMENTATION OF INFORMED CONSENT

a. **Criteria for Waiver.** The IRB may waive the requirement for the investigator to obtain a signed consent form for some or all subjects if it finds and documents either (38 CFR 16.117(c)):

(1) That the only record linking the subject and the research would be the consent document and the principal risk would be 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 (38 CFR 16.117(c)(1)); 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 (38 CFR 16.117(c)(2)).

b. **Written Statement.** In cases in which the documentation requirement is waived, IRB may require the investigator to provide subjects with a written statement regarding the research (38 CFR 16.117(c)(2)).

c. **IRB Documentation.** IRB must document its determinations regarding a waiver of documentation of informed consent in the IRB minutes or in the protocol file (see par. 28).

d. **Informed Consent Process.** Unless IRB has granted a waiver of informed consent (see par. 35), even if IRB has granted a waiver of documentation of informed consent, the investigator, or designee, must still perform an adequate informed consent process (see pars. 30-33).

35. WAIVER OF INFORMED CONSENT

a. **Government Research and Informed Consent is Not Practicable.** The IRB may approve a consent procedure which does not include, or which alters, some or all of the elements of informed consent; or waive the requirement to obtain informed consent, provided the IRB finds and documents that (38 CFR 16.116(c)):

(1) The research is to be conducted by, or is subject to, the approval of state or local government officials and is designed to study, evaluate, or otherwise examine (38 CFR 16.116(c)(1)):

(a) Public benefit of 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.

(2) The research could not practicably be carried out without the waiver or alteration (38 CFR 16.116(c)(2)).

b. **Minimal Risk Research.** The IRB may approve a consent procedure that does not include, or that alters, some or all of the elements of informed consent; or the IRB may waive the requirements to obtain informed consent, provided the IRB finds and documents that (38 CFR 16.116(d)):

(1) The research involves no more than minimal risk to the subjects (38 CFR 16.116(d)(1));

(2) The waiver or alteration will not adversely affect the rights and welfare of the subjects (38 CFR 16.116(d)(2));

(3) The research could not practicably be carried out without the waiver or alteration (38 CFR 16.116(d)(3)); and

(4) Whenever appropriate, the subjects are provided with additional pertinent information after participation (38 CFR 16.116(d)(4)).

c. **Other Applicable Federal, State, or Local Laws.** The informed consent requirements in this Handbook are not intended to preempt any applicable Federal, state, or local laws which require additional information to be disclosed in order for informed consent to be legally effective (38 CFR 16.116(e)).

d. **IRB Documentation.** The IRB must document its determinations regarding a waiver of informed consent in the IRB minutes or in the protocol file (see par. 28).

36. SURROGATE CONSENT

Under appropriate conditions, investigators may obtain consent from the LAR of a subject (i.e., surrogate consent). ***NOTE:*** *Check with Regional Counsel for state or local requirements for surrogate consent for research that may supersede VA requirements.*

a. **Assessment of Capacity.** Before persons who lack decision-making capacity may be considered for participation in any VA research, the IRB must find that the proposed research meets all of the conditions contained in paragraphs 17 and 49 of this Handbook.

b. **Investigators' Responsibilities for Surrogate Consent.** Investigators must:

(1) Provide the IRB with a description of the procedures to ensure that subjects' LARs are well informed regarding their roles and obligations to protect persons who lack decision-making capacity.

(2) Provide information (i.e., informed consent process and HIPAA authorization) to the subjects' LARs that would ordinarily be required by this Handbook to be made to the subjects themselves if they had decision-making capacity.

c. **LARs**

(1) **Authorized Person.** The following persons are authorized to consent on behalf of persons who lack decision-making capacity in the following order of priority (38 CFR 17.32(e)) (see subpar. 3aaa for personal representative for the purposes of signing a HIPAA authorization):

(a) Health care agent (i.e., an individual named by the individual in a Durable Power of Attorney for Health Care (38 CFR.17.32(a)(iii));

(b) Legal guardian or special guardian;

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

(d) Close friend.

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 human subject's PHI (i.e., signing a 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 (legal guardian or power of attorney) in HIPAA and the Privacy Act of 1974 prior to the LAR's signing a HIPAA authorization (see VHA Handbook 1605.1).

(2) **Responsibilities of LARs.** LARs are acting on behalf of the potential subjects, therefore:

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

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

(c) LARs generally assume the same rights and responsibilities as the individuals who lack decision-making capacity in the informed consent process (see 38 CFR 17.32(e)).

d. **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 (i.e., if they dissent) 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.

e. **Fluctuating Capacity.** Investigators, IRB members, and LARs must be aware that decision-making capacity may fluctuate in some subjects. For subjects with fluctuating decision-making capacity or those with decreasing capacity to give consent, a re-consenting process with surrogate consent may be necessary (see subpar. 49c).

37. HIPAA AUTHORIZATION

a. **Written Authorization.** A written HIPAA authorization signed by the individual to whom the information or record pertains is required when VA health care facilities need to utilize individually-identifiable health information for a purpose other than treatment, payment, or health care operations (e.g., research) (VHA Handbook 1605.1).

(1) In accordance with 45 CFR 164.508(b)(3)(ii), an authorization for a use or disclosure of psychotherapy notes may not be combined with any other authorization for a use or disclosure unless the other authorization is also for a use or disclosure of psychotherapy notes.

(2) The HIPAA authorization for the use or disclosure of individually-identifiable health information for a VA research study must be a standalone document (i.e., not combined with any other type of written permission for the same research study, including the research informed consent form).

(3) An IRB does not have the authority to approve a HIPAA authorization unless it is incorporated into the informed consent document. Since this Handbook requires the HIPAA authorization and the informed consent form to be separate documents, the IRB cannot approve a

HIPAA authorization for a VA research study. However, the IRB may waive the requirement for a HIPAA authorization (see subpar. 37b).

(4) The IRB must ensure the protocol and informed consent form are consistent with the HIPAA authorization.

NOTE: *Research involving limited data sets may be performed in accordance with VHA Handbook 1605.1 A limited data set may not be de-identified information or data. VHA may disclose a limited data set for research pursuant to a data use agreement.*

b. **Waiver of HIPAA Authorization (see 45 CFR 164.512(i)(2)).** A request from an investigator for the IRB to waive the HIPAA authorization must be accompanied by sufficient information to allow the IRB to make the required determination. The IRB must document its findings and this documentation must include, but is not limited to, all of 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 mandated by applicable VA or other Federal requirements; and

3. Adequate written assurances that the requested information 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 would be 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) The specific findings on which the IRB based its decision to grant the waiver of HIPAA authorization.

(6) Identification of the IRB review procedure used to approve the waiver of HIPAA authorization (either convened IRB review procedures (see par. 13 and 38 CFR 16.108(b)) or expedited review procedures (see par. 21 and 38 CFR 16.110).

(7) Signature of Chair of the IRB, or qualified voting member of the IRB designated by the Chair, on the HIPAA authorization waiver document.

***NOTE**: The documentation of the IRB's findings may be in the IRB minutes or the IRB protocol file. If IRB does not document the waiver of authorization as required, the waiver is not valid.*

38. PRIVACY OFFICER AND INFORMATION SECURITY OFFICER (ISO) RESPONSIBILITIES

The Privacy Officer and the ISO are responsible for:

a. Ensuring the proposed research complies with all applicable local, VA, and other Federal requirements for privacy and confidentiality, and for information security, respectively, by identifying, addressing, and mitigating potential concerns about proposed research studies, and by serving in an advisory capacity to the IRB or R&D Committee as a nonvoting member.

b. Reviewing the proposed study protocol and any other relevant materials submitted with the IRB application.

***NOTE:** It is not sufficient for the Privacy Officer or ISO to review a checklist completed by the investigator, and not the study protocol and related materials themselves. To facilitate the review of the proposal by the Privacy Officer and the ISO, the investigator must either dedicate specific sections of the protocol to privacy and information security, respectively, or the investigator must develop an additional document that specifically addresses all privacy and information security issues in the proposal, and that additional document will become part of the IRB protocol file (see subpars. 10i and 10j).*

c. Completing their respective reviews of the proposed research and informing IRB of all their findings related to privacy and confidentiality, and to information security, respectively.

***NOTE:** They are not responsible for approving or disapproving a study, nor do they have the authority to prevent or delay IRB approval of a study. The IRB is responsible for approving all non-exempt human research studies. Exempt studies should be approved in accordance with VHA Handbook 1200.01.*

d. Identifying deficiencies in their respective reviews of the proposed research, and making recommendations to the investigator of options available to correct the deficiencies.

e. Following up with the investigator, 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.

f. Providing summary reports of their review and assessment of each study according to the requirements of this paragraph. The summary report must clearly:

(1) Indicate either that all applicable local, VA, and other Federal requirements for privacy and confidentiality, and for information security, respectively, have been met; or

(2) Identify specific deficiencies and suggest available options for correcting those deficiencies.

g. Providing their summary reports on each study to the IRB staff (whether VA or affiliate IRB) within a time frame that does not prolong the study approval process. They must provide their summary reports prior to, or at, the convened IRB meeting at which the study is to reviewed or, in the case of expedited review, prior to, the IRB approval determination of the IRB Chair, or designee. For exempt studies, they must submit their summary reports to the ACOS for R&D, and ensure the study is in compliance before the study is initiated.

h. Providing their final reports on each study to the IRB staff (whether VA or affiliate IRB) in a timely manner.

39. INVESTIGATIONAL DRUGS IN RESEARCH WITH HUMAN SUBJECTS

VA human research involving investigational drugs must be conducted in accordance with all applicable VA and other Federal requirements including, but not limited to this Handbook, VHA Handbook 1108.04, and FDA regulations. This applies to investigator conduct and IRB review and approval of investigational drug studies, as well as storage and security procedures for investigational drugs. If the research involves FDA-regulated drugs, both VA requirements and FDA regulations apply. FDA regulations supersede VA requirements for human subjects research under FDA jurisdiction unless VA requirements are more restrictive than applicable FDA regulations.

a. **Investigational New Drug (IND) Application.** An IND application must be submitted to FDA for a clinical investigation on products that are subject to section 505 of the Food, Drug, and Cosmetic Act or to the licensing provisions of the Public Health Service Act (58 Stat. 632, as amended (42 U.S.C. 201 et seq.)) unless the clinical investigation meets the exemption criteria set forth in 21 CFR 312.2(b).

b. **Investigator Responsibilities.** To receive an investigational drug as defined by VHA Handbook 1108.04, in addition to FDA regulations for the conduct of research under an IND and investigator responsibilities identified in paragraph 9 of this Handbook, the investigator must:

(1) Provide the Pharmacy Service or Research Investigational Pharmacy information on each subject receiving an investigational drug through the electronic medical record or other locally approved means. Documentation is to include allergies, toxicities, or adverse drug events related to the investigational drug, or the potential for interaction with other drugs, foods, or dietary supplements, i.e., herbals, nutriceuticals (see VHA Handbook 1108.04).

(2) Ensure the local Pharmacy Service or Research Service Investigational Pharmacy receives:

(a) Documentation of IRB and any other relevant approvals;

(b) A copy of VA Form 10-9012, Investigational Drug Information Record, when applicable;

(c) A copy of the current approved protocol;

(d) A copy of the informed consent form for each participating subject with all appropriate signatures;

(e) Documentation of the IRB continuing review approval;

(f) Copies of sponsor-related correspondence specific to the drug(s) as appropriate; and

(g) Copies of all correspondence addressed to the investigator from the FDA (and other involved authorities) specific to the investigational drug(s) as appropriate.

(3) Inform the Chief of the Pharmacy Service, the research pharmacy when applicable, and the IRB in writing when a study involving investigational drugs has been suspended, terminated, or closed.

(4) Comply with all dispensing requirements.

(5) Comply with all documentation requirements and make relevant records accessible to the investigational drug pharmacist when requested (VHA Handbook 1108.04).

(6) Comply with all VHA pharmacy requirements regarding receiving, dispensing, storing, and record-keeping for investigational drugs.

c. **IRB Review**. When an IRB reviews a study involving a drug, whether or not the drug has been approved by the FDA, the IRB's review and approval of the study must comply with applicable FDA, VA, and other Federal requirements including, but not limited to, this Handbook, 21 CFR 56, and 21 CFR 312.2(b)(1).

40. INVESTIGATIONAL DEVICES IN RESEARCH WITH HUMAN SUBJECTS

IRB review and approval and investigator conduct of all investigational device studies must be in accordance with all applicable VA and other requirements including, but not limited to this Handbook and FDA regulations (e.g., 21 CFR Parts 50 and 56, and Investigational Device Exemptions (IDE) (21 CFR 812)). If the research involves FDA-regulated devices, both VA requirements and FDA regulations apply. FDA regulations supersede VA requirements for human subjects research under FDA jurisdiction unless VA requirements are more restrictive than applicable FDA regulations.

a. **IDE Status.** No research involving an investigational device can be approved by the IRB if it is unclear whether the device requires an IDE, or if the IDE status for an investigational device is unknown.

b. **Investigator Responsibilities.** The investigator must ensure the procedures, in the conduct of research involving an investigational device, are in accordance with all applicable local, VA and other Federal requirements, including FDA regulations.

c. **IRB Review.** When an IRB reviews a study involving a device, whether or not the device has been approved by the FDA, the IRB's review and approval of the study must comply with all applicable local, VA, and other Federal requirements including, but not limited to, this Handbook, 21 CFR 50, 21 CFR 56, 21 CFR 812.60, 21 CFR 812.62, 21 CFR 812.64, and 21 CFR 812.66. If the research involves FDA-regulated devices, both VA requirements and FDA regulations apply. FDA regulations supersede VA requirements for human subjects research under FDA jurisdiction, unless VA requirements are more restrictive than applicable FDA regulations.

NOTE: *Although certain clinical investigations of devices are exempt from IDE regulations (21 CFR 812.2(c)), exemption from IDE regulations does not necessarily mean the study is exempt from IRB review and approval (see par. 16) and informed consent.*

(1) **Written Procedures**

(a) The IRB reviewing investigational medical device studies must have written procedures for conducting the reviews; determining and documenting if the device studies represent a "significant risk" (SR) or a "nonsignificant risk" (NSR); reporting findings to the investigator; and, when appropriate, reporting findings to the sponsor (21 CFR 812.66) if the IRB determines the device to be significant risk.

(b) If an NSR determination is made, the IRB follows procedures in accordance with the criteria the IRB would use in considering approval of any research involving an FDA-regulated product, including all applicable local, VA, and other Federal requirements including, but not limited to this Handbook and 21 CFR 56.111.

(2) **Risk Determination.** Unless the study is exempt from IDE regulations, the IRB must categorize a nonsignificant device study as either SR or NSR. The IRB must document its determination of SR or NSR in the IRB minutes.

(a) For SR device studies, investigators must provide the IRB with copy of the FDA's approval of the IDE application (see 21 CFR 812.20).

(b) NSR device studies do not require submission of an IDE application before starting the study. FDA considers an NSR device study to have an approved IDE application after obtaining and maintaining IRB approval. Sponsors and investigators must meet the abbreviated requirements at 21 CFR 812.2(b). ***NOTE:*** *An NSR device study may represent greater than minimal risk depending on the research.*

d. **Humanitarian Use Device.** A Humanitarian Use Device (HUD) is a medical device intended to benefit patients in the treatment or diagnosis of a disease or condition that affects or is manifested in fewer than 4000 individuals in the U.S. per year (21 CFR 814.3(n)). ***NOTE:*** *If a physician uses a HUD as defined and described in FDA regulations, the physician must follow FDA regulations.*

41. EMERGENCY USE OF A TEST ARTICLE

a. **Emergency Medical Care.** Nothing in this Handbook or the Common Rule is intended to limit the authority of a physician to provide emergency medical care, to the extent the physician is permitted to do so under applicable local, state, VA, and other Federal requirements (38 CFR 16.116(f)). ***NOTE:*** *Emergency medical care is not research and does not need to be approved by an IRB.*

b. **Emergency Use of a Test Article.** FDA regulations describe specific instances when a test article (e.g., an investigational drug, device, or biologic) may be used on a human subject when there is not sufficient time to obtain IRB approval (21 CFR 56.102(d)). All FDA regulations for emergency use of a test article must be met including, but not limited to, obtaining informed consent from the subject or the subject's LAR unless FDA regulations are met for an exception from informed consent (21 CFR 50.23(a)). Within VA, emergency use of a test article is not considered to be research. Therefore, the patient is not a research subject, the emergency care cannot be claimed as research, and the outcome of such care cannot be included in any report of research activity subject to 38 CFR Part 16.

c. **Planned Emergency Research**. "Planned emergency research" differs from "emergency use" situations because planned emergency use involves IRB approval of a research study before the emergency arises (21 CFR 50.24). Planned emergency research cannot be conducted by VA.

42. SERIOUS ADVERSE EVENTS (SAE)

a. **SAE Reporting.** The investigator must report all unanticipated internal or local SAEs, whether related or unrelated to the research, to the IRB as specified under local SOPs and VHA Handbook 1058.01.

b. **IRB Responsibilities for SAEs.** A qualified IRB voting member reviewer (or alternatively, the convened IRB) must review the reports of internal or local SAEs, and must determine and document whether the event is serious, whether it is anticipated or unanticipated, and whether it is related, possibly related, or probably related to the research in accordance with VHA Handbook 1058.01.

(1) **Documentation of Whether or Not Action is Warranted.** After taking into account considerations including, but not limited to, whether or not the study still meets IRB approval criteria under 38 CFR 16.111 and 38 CFR 16.116 (such as whether or not the risks to subjects have changed; whether or not the risk to benefit ratio has changed; and whether or not this constitutes new information that needs to be given to the subjects), the qualified IRB voting member-reviewer (or the convened IRB) must document whether or not one of the following applies in accordance with VHA Handbook 1058.01:

(a) Immediate Action Warranted. Immediate action (e.g., suspension of activities; notification of subjects) is necessary to prevent an immediate hazard to subjects in accordance with VA regulations at 38 CFR 16.103(b((4)(iii), and review by the convened IRB is needed; or

(b) No Immediate Action Warranted. Review by the convened IRB is needed, but immediate action to prevent an immediate hazard to subjects is not warranted.

(2) **Reporting to Convened IRB.** If the preceding determinations are made by a qualified IRB voting member reviewer, the determinations must be reported to the IRB at the IRB's next convened meeting in accordance with VHA Handbook 1058.01.

(3) **Reporting to the Facility Director.** If the qualified IRB voting member reviewer (or the convened IRB) determines that the AE is serious, unanticipated, and related, or possibly related, to the research, the IRB Chairperson must report the event to the VA facility Director as soon as possible, but no later than 5 business days after the determination (VHA Handbook 1058.01). The VA facility Director then has an additional 5 business days to report the event to ORO (VHA Handbook 1058.01).

(4) **Informed Consent Modifications.** If it is determined that an informed consent modification is warranted, the convened IRB must determine and document in its records whether or not previously enrolled subjects must be notified of the modification and, if so,

(a) When such notification must take place, and

(b) How such notification must be documented (see VHA Handbook 1058.01).

c. **AEs of Research-Related Clinical Care.** When subjects experience AEs while undergoing clinical care that is part of a research study, the clinical care AEs must be disclosed to subjects in accordance with current VHA policy.

43. 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 facilities as in-patients, treated as outpatients at VA facilities, or when research procedures or interventions are used in the medical care of the VA research subject at a VA facility or at facilities contracted by VA to provide services to Veterans (e.g., contract CBOCs or contract nursing homes) (see VHA Handbook 1907.01).

a. **When a Health Record is Required.** A record must be created:

(1) When the research requires use of any clinical resources, such as: radiology, cardiology (e.g., electrocardiogram, stress test, etc.), clinical laboratory, and pharmacy; or

(2) If the research intervention may lead to physical or psychological AEs (see VHA Handbook 1907.01).

b. **What a Health Record Must Include.** At a minimum, the health record must include the following information for an approved research study:

(1) The name of the study;

(2) The person obtaining the subject's informed consent;

(3) A statement that the subject or the subject's LAR was capable of understanding the informed consent process;

(4) A statement that the study was explained to the subject or the subject's LAR;

(5) A statement that the subject or the subject's LAR consented before participation in the study began;

(6) A statement that the subject or the subject's LAR was given the opportunity to ask questions;

(7) A copy of the signed and dated research informed consent form (i.e., VA Form 10-1086) in accordance with VHA Handbook 1907.01;

(8) A copy of the HIPAA authorization for data use or disclosure (see VHA Handbook 1907.01);

(9) A copy of the initial enrollment progress note and other applicable progress notes (see VHA Handbook 1907.01);

(10) Information on possible drug interactions and/or toxicity of the pharmaceutical agents that are being administered to the subject because of the research (i.e., investigational drugs) (see VHA Handbook 1907.01);

(11) VA Form 10-9012, Investigational Drug Information Record, or superseding forms for investigational drugs as defined in VHA Handbook 1108.04 (see VHA Handbook 1907.01);

(12) A copy of any research results that are used for medical care (see VHA Handbook 1907.01);

(13) Information on all research and experimental interventions including potential risks, indications, and applicable progress notes see (see VHA Handbook 1907.01); and

(14) VHA Form 10-3203, Consent for Use of Picture and/or Voice, if applicable (see par. 54).

c. **Identifying Research Clinic Visits.** A method to identify clinic visits solely for research (such as a note title) must be used to differentiate those visits from any other clinic visits. The research titled note may be included in the Crisis, Warnings, Allergies and/or Adverse Reactions, and Directives (CWAD) alerts (see VHA Handbook 1907.01).

d. **Non-Billing Events.** Clinic visits and inpatient care for research purposes must be coded as non-billing events (see VHA Handbook 1907.01).

e. **When Access to Patient Health Records is No Longer Required for a Study.** When access to patient health records is no longer required for a study, the study has been completed, or when authorization is revoked, the investigator or designee, must notify the facility HIM program manager and, if applicable, the ISO (see VHA Handbook 1907.01).

44. FLAGGING A VHA HEALTH RECORD

The IRB may determine that the patient health record must be flagged to protect the subject's safety by indicating the subject's participation in the study (see VHA Handbook 1907.01).

a. **Mandatory Flagging**

(1) The patient health record must be flagged if the subject's participation in the study involves:

(a) Any invasive research procedure (e.g., muscle biopsy or bronchoscopy);

(b) Interventions that will be used in the medical care of the subject, or that could interfere with other care the subject is receiving or may receive (e.g., administration of a medication, treatment, or use of an investigational device);

(c) Clinical services that will be used in the medical care of the subject (e.g., orders for laboratory tests or x-rays ordered as a part of the study), or that could interfere with other care the subject is receiving or may receive; or

(d) The use of a survey or questionnaire that may provoke undue stress or anxiety unless the IRB determines that mandatory flagging is not in the best interests of the subject (e.g., an interview study of victims of sexual assault).

(2) In other situations, the IRB determines if flagging is necessary.

b. **Flagged Health Record Contents.** If IRB determines and documents that the patient health record must be electronically flagged in Computerized Patient Record System (CPRS) as participating in a research study then, in accordance with VHA Handbook 1907.01, the health record must:

(1) Identify the investigator, as well as contact information for a member of the research team that would be available at all times. ***NOTE:*** *The research team must have an appropriate member available (on-call) at all times.*

(2) Contain information on the research study or identify where this information is available.

c. **Duration of Flagging.** The duration of flagging is determined by local policy.

45. VULNERABLE SUBJECTS

a. **VA Requirements.** Whenever VA has more stringent requirements than DHHS for protection of vulnerable individuals or vulnerable populations as research subjects, all VA requirements must be met.

b. **Documentation of Vulnerability.** Where relevant, the IRB needs to document why it considers an individual or population to be vulnerable, and that adequate safeguards have been included in the study to protect the rights and welfare of subjects who are likely to be vulnerable. Individuals or populations that may be temporarily or permanently vulnerable include, but are not limited to, those who:

(1) Are susceptible to coercion or undue influence (e.g., the homeless, prisoners, students, patients with limited or no treatment options, socially and economically disadvantaged).

(2) Lack comprehension of the research and its potential risks (e.g., educationally disadvantaged, dementia, schizophrenia, depression) (see par. 49).

(3) Have increased susceptibility to harm from the procedures of the specific study under review (e.g., individuals who would have to answer study survey questions about their sexual assault).

(4) Are at risk for economic, social, or legal consequences from the study (e.g., individuals who would have to answer study survey questions about their drug use or HIV status).

c. **Populations Considered to be Categorically Vulnerable.** This subparagraph defines populations that are considered categorically vulnerable and specifies VA requirements for the inclusion of any of these categories of subjects in research. While all protocols need to be assessed for vulnerability of subjects within the context of the specific protocol (see subpar. 17h), the populations named in this subparagraph must always have the additional protections specified in this paragraph applied. VA considers the following populations to be categorically vulnerable:

(1) **Fetuses.** Research in which the focus is either a fetus, or human fetal tissue, in-utero or ex-utero (or uses human fetal tissue), must not be conducted by VA investigators while on official duty, or at VA facilities, or at VA approved off-site facilities.

(2) **Neonates.** Research related to neonates including, but not limited to, observational or interventional research, must not be conducted by VA investigators while on official duty, or at VA facilities, or at VA approved off-site facilities.

(3) **Pregnant Women.** See paragraph 46.

(4) **Prisoners.** See paragraph 47.

(5) **Children.** See paragraph 48.

(6) **Subjects who Lack Decision-making Capacity.** See paragraph 49.

d. **In Vitro Fertilization.** Research related to in vitro fertilization is not to be conducted by VA investigators while on official duty, or at VA facilities, or at VA-approved off-site facilities.

46. RESEARCH INVOLVING PREGNANT WOMEN

This paragraph applies to women who are pregnant at the time they are entered into a study. It does not preclude entering women of child bearing potential into studies including studies whose interventions include FDA's Categories for Drug Use in Pregnancy's Category C drugs. Women of child bearing potential may not be entered into studies involving the use of FDA Categories for Drug Use in Pregnancy's Category D or X drugs unless a waiver is obtained from the CRADO. Pregnant women may be the focus of the research if all of the following conditions are met (45 CFR 46.204):

a. **Prior Studies Have Been Performed.** Where scientifically appropriate, preclinical studies, including studies on pregnant animals, and clinical studies, including studies on nonpregnant women, have been conducted and provide data for assessing potential risks to pregnant women and fetuses (45 CFR 46.204(a)).

b. **Prospect of Direct Benefit.** The risk to the fetus is caused solely by interventions or procedures that hold out the prospect of direct benefit for the woman or the fetus; or, if there is no such prospect of benefit, the risk to the fetus is not greater than minimal and the purpose of the research is the development of important biomedical knowledge which cannot be obtained by any other means (45 CFR 46.204(b)).

c. **Minimization of Risks.** Any risk is the least possible for achieving the objectives of the research (45 CFR 46.204(c)).

d. **Monitoring Risks.** Adequate provision has been made to monitor the risks to the subject and the fetus.

e. **Informed Consent.** If the research holds out the prospect of direct benefit to the pregnant woman, the prospect of a direct benefit both to the pregnant woman and the fetus, or no prospect of benefit for the woman nor the fetus when risk to the fetus is not greater than minimal and the purpose of the research is the development of important biomedical knowledge that cannot be obtained by any other means, the pregnant woman's informed consent is obtained in accord with the informed consent provisions of 38 CFR 16.116 (see pars. 30-35 and 45 CFR 46.204(d)).

f. **Impact on Fetus.** Each individual providing informed consent, under subparagraph 46e, is fully informed regarding the reasonably foreseeable impact of the research on the fetus (45 CFR 46.204(f)).

g. **No Inducements to Terminate Pregnancy.** No inducements, monetary or otherwise, are to be offered to terminate a pregnancy (45 CFR 46.204 (h)).

h. **Decisions to Terminate Pregnancy.** Individuals engaged in the research have no part in any decisions as to the timing, method, or procedures used to terminate a pregnancy (45 CFR 46.204(i)).

i. **Determining Viability of Fetus.** Individuals engaged in the research have no part in determining the viability of a fetus (45 CFR 46.204 (j)).

47. RESEARCH INVOLVING PRISONERS

a. **Vulnerable Population.** Prisoners are considered a vulnerable population and may be under constraints because of their incarceration which could affect their ability to make a truly voluntary and uncoerced decision whether or not to participate as subjects in research (45 CFR 46.302).

b. **Waiver From CRADO.** Research involving prisoners cannot be conducted by VA investigators while on official VA duty, using VA resources, completely or partially in a VA facility or at a VA-approved off-site facility unless a waiver has been granted by the CRADO. If such a waiver is granted by the CRADO, the research must be in accordance with applicable Federal regulations pertaining to prisoners as research subjects (see 45 CFR 46, Subpart C 46.301–46.306, Additional Protections Pertaining to Biomedical and Behavioral Research Involving Prisoners as Subjects). ***NOTE:*** *Requirements for requesting a waiver may be obtained by contacting ORD.*

c. **Incarceration During a Study.** If a subject becomes incarcerated during the course of a study:

(1) Investigators must notify the IRB as soon as they become aware that the subject has been incarcerated.

(2) The investigator must make a determination as to whether or not it is the best interests of the subject to remain in the study, or if the subject can be safely withdrawn from the study.

(3) If the investigator determines it is in the best interest of the subject to remain in the study, the subject's continued participation in the study is contingent on the IRB's reviewing and approving such participation. The IRB approval must comply with 45 CFR 46.301-306.

(4) After IRB and other relevant approvals (e.g., from the penal system) for the incarcerated subject's continued participation in the study have been obtained, a waiver must also be obtained from the CRADO (see subpar. 47b).

(5) The investigator must comply with all applicable requirements including, but not limited to, applicable court, penal system, and local, VA, and other Federal requirements.

48. RESEARCH INVOLVING CHILDREN

a. **Waiver From CRADO.** 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 cannot be conducted by VA investigators while on official VA duty, using VA resources, completely or partially in a VA facility or at a VA-approved off-site facility unless a waiver has been granted by the CRADO. ***NOTE:*** *For purposes of this Handbook, research involving biological specimens or data obtained from children is considered to be research involving children.*

b. **Criteria for Waiver.** Prior to requesting a waiver, the following criteria must be met:

(1) The study represents no greater than minimal risk as determined by the IRB.

(2) The study meets all requirements in 45 CFR 46, Subpart D, Additional Protections for Children Involved as Subjects in Research, Sections 46.401 through 46.404, and 46.408.

(3) The IRB reviewing the study has appropriate membership to represent children's interests and pediatric expertise.

(4) The IRB reviewing the study has specific SOPs regarding children in research.

(5) The VA facility Director certifies that the facility is able to respond to pediatric emergencies if the study includes interactions with children at the VA facility.

(6) If the sponsor of the research is not VA, the facility Director makes certain that the sponsor of the research has procured appropriate liability insurance.

c. **Waiver Application.** To request a waiver, the following information must be submitted to ORD for each protocol:

(1) A cover letter signed by the VA facility Director that contains the following information:

(a) Certification by the VA facility Director that the facility is able to respond to pediatric emergencies if the study includes an interaction with children at the VA facility.

(b) Any additional safeguards that have been incorporated into the clinical site where children will be studied.

(c) Information on the study's funding source and on liability coverage if the sponsor is not VA.

(d) Certification that the IRB has determined the study to be of no greater than minimal risk and has approved the study.

(e) A statement that the required elements of 45 CFR 46 Subpart D have been met.

(f) A description of the relevance to Veterans' health of both the study and the inclusion of children in the study.

(2) A copy of the study protocol, the informed consent form, the assent document, and HIPAA authorization. The informed consent document signed by the parent or guardian is the vehicle for parent or guardian permission. Provisions for permission by parents or guardians must be documented in accordance with, and to the extent required by, 38 CFR 16.117.

(3) Minutes of the IRB meeting approving the study. The IRB minutes need to reflect the discussion regarding level of risk, the informed consent and assent forms, the investigators' qualifications to conduct research involving children, and any additional safeguards incorporated into the protocol.

(4) If the study involves biological specimens or data collected from children, in addition to the preceding requirements, the following must be submitted:

(a) A discussion of how the biological specimens or data were, or will be, obtained and under what consents or authorization.

(b) If the biological specimens or data were, or will be, collected for research purposes, the IRB approval, the informed consent form, and the HIPAA authorization for the research.

(c) If biological specimens or data were, or will be, collected from an international site, a waiver from the CRADO for international research (see par. 54).

(d) Plans for future use of biological specimens or data.

49. RESEARCH INVOLVING PERSONS WHO LACK DECISION-MAKING CAPACITY

This Handbook is designed to protect human subjects from exploitation and harm and, at the same time, make it possible to conduct essential research on problems that are unique to persons who lack decision-making capacity (e.g., a study of treatment options for comatose persons can only be performed with persons who lack decision-making capacity). Persons who lack decision-making capacity are not to be subjects in research simply because they are readily available.

a. **IRB Review and Approval.** No individual who lacks decision-making capacity may participate in VA Research until the IRB has reviewed and approved that individual's, or that class of individuals', participation in a given study.

b. **Criteria for Decision-Making Capacity**

(1) An individual is presumed to have decision-making capacity unless any one or more of the following apply:

(a) It has been documented by a qualified practitioner in the individual's medical record in a signed and dated progress note that the individual lacks capacity to make the decision to participate in the proposed study. ***NOTE:*** *The qualified practitioner may be a member of the research team.*

(b) The individual has been ruled incompetent by a court of law.

(2) If there is any question as to whether or not a potential adult subject has decision-making capacity, and there is no documentation in the medical record that the individual lacks decision-making capacity, and the individual has not been ruled incompetent by a court of law, the investigator must consult with a qualified practitioner (who may be a member of the research team) about the individual's decision-making capacity before proceeding with the informed consent process.

c. **Temporary or Fluctuating Lack of Decision-Making Capacity.** Individuals, who because of a known condition, are at high risk for temporary (e.g., head trauma) or fluctuating (e.g., schizophrenia) lack of decision-making capacity must be evaluated by a qualified practitioner (who may be a member of the research team), to determine the individual's ability to provide informed consent. This evaluation must be performed as described in the IRB-approved protocol. If the individual is deemed to lack decision-making capacity at the time of their participation in the study, a LAR must provide informed consent (see par. 36). If the subject regains decision-making capacity, the investigator or designee (see subpar. 9j(1)) must repeat the informed consent process with the subject, and obtain the subject's permission to continue with the study.

d. **Criteria for Enrollment.** Individuals who lack decision-making capacity may be enrolled in protocols if:

(1) The proposed research entails:

(a) No greater than minimal risk to the subject as determined by the IRB; or

(b) If the research presents some probability of harm, there must be at least a greater probability of direct benefit to the subject; or

(c) Greater than minimal risk and no prospect of direct benefit to individual subjects, but is likely to yield generalizable knowledge about the subject's disorder or condition that is of vital importance for the understanding or amelioration of the subject's disorder or condition.

(2) The disorder (e.g., Alzheimer's) leading to the individual's lack of decision-making capacity is being studied, 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), but only if the study cannot be performed with only persons who have decision-making capability.

(3) The subject of the study is not directly related to the individual's lack of decision-making capacity, but the investigator can make a compelling argument for including individuals who lack decision-making capacity in the study (e.g., transmission of methicillin-resistant *Staphylococcus aureus* (MRSA) infections in a nursing home where both individuals with, and those without, decision-making capacity are affected).

e. **IRB Determination.** If the criteria in subparagraph 49d are met, the IRB may approve the inclusion of individuals who lack decision-making capacity in research studies on the basis of informed consent from LARs as defined in paragraph 36.

(1) Before approving the study, the IRB must:

(a) Ensure the study includes appropriate procedures for respecting dissent;

(b) Consider whether or not the study needs to include procedures for obtaining assent; and

(c) Determine whether any additional safeguards need to be used (e.g., consent monitoring).

(2) The IRB must document its deliberations and the criteria in subparagraph 49d it used to approve inclusion of individuals who lack decision-making capacity in the IRB minutes or IRB protocol file.

50. ENGAGEMENT IN HUMAN SUBJECTS RESEARCH

a. In general, a VA facility is considered "engaged" in a particular non-exempt human subjects research study when an individual with a VA appointment (including full and part-time employees, WOC employees, and employees under the Intergovernmental Personnel Act (IPA) of 1970) at that facility obtains for the purposes of the research study:

(1) Data about the subjects of the research through intervention or interaction with them;

(2) Identifiable private information about the subjects of the research; or

(3) The informed consent of human subjects for the research.

b. When a VA facility is engaged in human subject research, it must:

(1) Hold an FWA;

(2) Have a VA PI or LSI for that study; and

(3) Have the facility's IRB of record approve the study.

51. NOT ENGAGED IN HUMAN SUBJECTS RESEARCH

a. If a VA facility is not engaged in any human research then the VA facility does not need to have an FWA.

b. If a VA facility is not engaged in research for the purposes of an individual study, then its IRB of record does not need to approve that study.

c. If a VA facility is not engaged in research for the purposes of a given study, it has no jurisdiction over that study, except the facility Director may determine that the study cannot be conducted on its premises.

NOTE: *See OHRP Guidance on Engagement of Institutions in Human Subjects Research, October 16, 2008, for examples and additional guidance.*

52. MULTI-SITE STUDIES

If conducting human research studies involving more than one engaged institution (see par. 50), each institution is responsible for safeguarding the rights and welfare of human subjects entered at its site, and for complying with all applicable local, VA, and other Federal requirements.

a. **Investigator Responsibilities.** In addition to the requirements in paragraph 9 of this Handbook:

(1) The PI of the overall study in a VA multi-site study must submit a protocol to the IRB of record for the PI's facility that includes the following:

(a) A method for ensuring that all engaged participating sites have the most current version of the protocol, the most current version of the informed consent form, and the most current version of the HIPAA authorization.

(b) A method for ensuring that all required approvals have been obtained at each engaged participating site (including approval by the site's IRB of record) before the study is implemented at that site.

(c) A method for notifying the Director of any facility deemed by the PI's IRB of record not to be engaged in the research, but on whose premises research activities will take place, before initiating the study (e.g., the PI conducts a survey of employees at a facility that is not engaged in the research) (see subpar. 51c). The facility Director has the authority to disapprove the conduct of these research activities on that facility's premises (see subpar. 5f).

(d) A method for confirming that all amendments and modifications to the protocol, the informed consent form, and the HIPAA authorization have been communicated to engaged participating sites, and that all required local facility approvals (including approval by the local facility's IRB of record) have been obtained before the amendment or modification is implemented.

(e) A method for ensuring that all engaged participating sites safeguard VA data as required by VA information security policies.

(f) A method for communicating to engaged participating sites SAEs that have the potential to affect implementation of the study.

(g) A method of communicating regularly with engaged participating sites about study events and interim results (if appropriate).

(h) A method for ensuring all LSIs conduct the study appropriately.

(i) A method to ensure all non-compliance with the study protocol or applicable requirements is reported in accordance with VHA Handbook 1058.01.

(j) A method for notifying local facility directors and LSIs when a multi-site study reaches the point that it no longer requires engagement of the local facility (e.g., all subsequent follow-up of subjects will be performed by the PI from another facility).

(2) When the investigator is a LSI for a multi-site study (whether the LSI is also a PI or solely a LSI), the LSI must:

(a) Conduct the study according to the most recently approved version of the protocol, the most recently approved version of the informed consent form, the most recently approved version of the HIPAA authorization, and all applicable local, VA, and other Federal requirements;

(b) Ensure that all amendments and modifications to the protocol and the informed consent form are submitted to and approved by the local IRB of record prior to initiating any changes;

(c) Report any unanticipated internal or local SAEs, whether related or unrelated to the research, in accordance with VHA Handbook 1058.01;

(d) Report study events and interim results (if available) to the local IRB of record as required by local IRB policies; and

(e) Oversee all aspects of the study at their local site.

b. **Local VA Facility's IRB of Record's Responsibilities for Multi-Site Research When the VA Facility's Investigator is the Multi-Site Study PI for All Participating Facilities and the VA Central IRB is Not Being Used .** In addition to other IRB responsibilities delineated in this Handbook, when the VA facility's investigator is the multi-site study PI or study sponsor for all participating facilities, and VA Central IRB is not being used, the PI's or study sponsor's local VA facility's IRB of record is responsible for:

(1) When a participating site is added to the study, determining:

(a) Whether or not that site will be engaged in human subjects research.

(b) If the site will be engaged in research, then reviewing and confirming that it:

1. Has an active FWA, and

2. Has provided documentation of all relevant approvals, including approval of its IRB of record.

(2) Approving the study-wide protocol and sample informed consent document to be provided to each LSI at engaged facilities.

(3) Ensuring the study-wide protocol contains a mechanism for ensuring that any differences in the protocol or informed consent at engaged local participating sites are justified by the LSI, and that they are approved by the PI before being implemented.

(4) Ensuring there are clear AE reporting requirements, a data monitoring committee if applicable (or other reliable monitoring mechanism) with clear procedures and requirements, and a clearly defined feedback loop to the PI's or study sponsor's IRB.

(5) Reviewing the PI's plan for communicating appropriate critical information (e.g., reports of data and safety monitoring) to engaged participating sites.

(6) Ensuring, when relevant, confidentiality and information security requirements are met for information storage at and transmission to statistical or coordinating centers.

(7) Reviewing reports from applicable DMCs.

c. **Local VA Facility's Responsibilities When Using the VA Central IRB as an IRB of Record.** The facility Director, when using the VA Central IRB as an IRB of Record, is responsible for:

(1) Entering into an MOU with the VHA Central Office that stipulates the respective authorities, roles, and responsibilities of VHA Central Office, the VA Central IRB, and the local VA facility when the local VA facility elects to use the VA Central IRB as an IRB of record.

NOTE: *A new MOU must be executed when there is a change in the FWA signing official (e.g., when there is a new facility Director or acting facility Director).*

(2) Modifying its FWA to list the VA Central IRB as an IRB of record.

(3) Maintaining SOPs for using the VA Central IRB as an IRB of record.

(4) Retaining responsibility for oversight of its local HRPP.

53. RESEARCH INVOLVING HUMAN BIOLOGICAL SPECIMENS

All activities involving the collection of human biological specimens for research purposes, as well as the research use of specimens collected for clinical care, must be conducted under the terms of an approved research protocol. The collection and use of human biological specimens (either identifiable or de-identified) must comply with all applicable VA and other Federal requirements including, but not limited to: 21 CFR 50, 21 CFR 312, 38 CFR 16, 45 CFR 46 D (if research involves specimens from children), 45 CFR 160 and 164 (HIPAA), VHA Handbook

1200.8, and current VA requirements for research involving human biological specimens or superseding requirements. ***NOTE:*** *ORD can be contacted for questions regarding research involving stem cells or cord blood.*

54. RESEARCH INVOLVING HUMAN DATA

Use of VA or non-VA human data and data repositories (whether developed for health care, administration of VA programs, or research) for research purposes must be consistent with the mission of VA including:

a. Having relevance to the health of Veterans,

b. Protecting the privacy of the individuals from whom the data were collected, and

c. Being consistent with all applicable ethical and regulatory standards, and all applicable VA and other Federal requirements (see VHA Handbook 1200.12).

NOTE*: The information from DNA sequencing is considered human subjects data (see subpar. 3n and VHA Handbook 1200.12).*

55. RESEARCH INVOLVING COLLECTION OF DATA FROM VOICE, VIDEO, OR PHOTOGRAPHS MADE FOR RESEARCH PURPOSES

a. **Informed Consent for Research**

(1) Informed consent for research must be obtained from each research subject before taking photographs or making voice or video recordings that will be used for research purposes.

(2) Unless IRB grants a waiver of documentation of informed consent for research, the informed consent form for research (i.e., VA Form 10-1086) must include a discussion of why photographs, or voice or video recordings are being taken for the research, who will have access to them, and what their disposition will be after the research is completed (see subpar. 55b for VA Form 10-3203 requirements, and subpar. 55c for VA Form 10-5345, Request for and Authorization to Release Medical Records or Health Information, requirements).

b. **VA Form 10-3203, Consent for Use of Picture and/or Voice.** VA Form 10-3203 documents permission for pictures, video, and voice recordings to be made or taken. In the conduct of research, VA Form 10-3203 must be used in accordance with applicable VA and VHA policy.

(1) When the research subject is a patient (either an inpatient or outpatient), the subject must sign VA Form 10-3203 to permit photographs or video and voice recordings that will be used for research purposes even if the IRB has waived the requirement for documentation of informed consent for research (VA Form 10-1086). Photography or recordings cannot occur prior to the patient's granting such permission (VHA Handbook 1907.01).

(2) When the research subject is a patient, the subject's signed and dated VA Form 10-3203 must be placed into the medical record along with, if applicable, the signed and dated research informed consent form (i.e., VA Form 10-1086). The signed VA Form 10-3203 must be obtained and placed in the subject's medical record, even if the IRB has waived documentation of informed consent for research.

c. **VA Form 10-5345, Request for and Authorization to Release Medical Records or Health Information.** VA Form 10-5345 documents permission for the disclosure of medical records or health information, including pictures, video, and voice recordings to another individual. In the conduct of research, VA Form 10-5345 must be used in accordance with applicable VA and VHA policy.

56. INTERNATIONAL RESEARCH

NOTE: *For the purposes of this Handbook, research conducted at U.S. military bases, ships, or embassies is not considered international research.*

All individuals who participate as subjects in research at international sites must be provided appropriate protections that are in accord with those given to research subjects within the U.S., as well as protections considered appropriate by local authority and custom at the international site (38 CFR 16.101(g)).

a. **Definition of VA International Research.** VA international research is defined as any VA-approved research conducted at international sites (not within the U.S., its territories, or Commonwealths); any VA-approved research using either human biological specimens (identified, de-identified, or coded) or human data (identified, de-identified, or coded) originating from international sites; or any VA-approved research that entails sending such specimens or data out of the U.S. ***NOTE:*** *This includes sending such 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). It also includes a VA's serving as a coordinating center for an international research project.*

b. **Multi-Site Trials.** Multi-site trials are covered under this definition if any of the following apply:

(1) VA is a sponsor;

(2) VA functions as the coordinating center;

(3) VA subcontracts to a foreign site;

(4) The PI for the total study is a VA investigator; or

(5) The VA investigator is specifically collaborating with an international investigator and the VA investigator sends data or human biological specimens outside the U.S., or receives them from outside the U.S.

NOTE: *This requirement does not apply if VA is only one of the participating sites and the trial does not meet the preceding conditions.*

c. **CRADO Permission.** Permission must be obtained from the CRADO, or designee, prior to initiating any VA-approved international research. This applies regardless of the funding source (funded or unfunded) and to research conducted through any mechanism of support including agreements, MOU, Cooperative Research and Development Agreements (CRADA), grants, or contracts. The CRADO, or designee, will not grant permission for an international research study involving prisoners as research subjects.

d. **FWA and Approval.** All international sites must hold an international FWA, and the research must be approved by the IRB or Research Ethics Board of the participating site(s) that are listed on the international FWA.

e. **VA Facility Director's Responsibilities.** In addition to VA facility Director responsibilities delineated elsewhere in this Handbook, the facility Director is responsible for:

(1) Approving the request for permission to conduct international research prior to forwarding it to the CRADO for action.

(2) Ensuring permission has been obtained from the CRADO, or designee, for the international research prior to its initiation by an investigator at the facility. ***NOTE:*** *Information on how to request permission may be references at: http://www.research.va.gov/resources/policies/docs/instructions-intl-research.pdf .*

f. **PI Responsibilities.** In addition to the PI responsibilities delineated elsewhere in this Handbook, the PI is responsible for:

(1) Obtaining approval from the facility Director.

(2) Obtaining permission from the CRADO, or designee, in writing before initiating an international research study.

(3) Conducting research in compliance with this Handbook, and all other applicable VA and other Federal requirements including those for protecting human subjects, tissue banking, use of databases, Federal criminal laws, and the Standards of Ethical Conduct for Employees of the Executive Branch.

57. USE PREPARATORY TO RESEARCH

Data repositories (including VA medical records) may be used (i.e., accessed) by VA investigators for activities that are preparatory to VA research without the requirement to obtain either a HIPAA authorization from the subject or a waiver of HIPAA authorization by an IRB or Privacy Board. This includes use of PHI for the preparation of a research protocol prior to submission to the IRB(s). "Preparatory to research" activity is the only instance of access for research purposes allowed in VHA without a written HIPAA authorization signed by the individual, a waiver of HIPAA authorization by an IRB or Privacy Board, or approval by the

IRB(s). This access is granted only to VHA researchers. Non-VHA researchers may not access VHA data for reviews preparatory to research. Additionally, the following holds true:

a. **Representations by the Investigator.** The investigator must make the representations necessary for preparatory access as required by the HIPAA Privacy Rule and document it in the investigator's research files. The representations required by the HIPAA Privacy Rule are:

(1) The access to PHI is only to prepare a protocol;

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

(3) The PHI accessed is necessary for preparation of the research proposed.

b. **Aggregate Data.** Only aggregate data may be recorded in the researcher's files, and these aggregate data may be used only 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 targets or sample size requirements.

c. **No Recording of Individually Identifiable Health Information.** Individually identifiable health information may not be recorded.

d. **No Recruiting From Data.** Data or information reviewed may not be used for contacting or recruiting subjects.

e. **Repository Requirements.** Investigators must comply with all other access requirements set by the repository of interest.

f. **Agreements.** See VHA Handbook 1200.12 regarding requirements for Data Use Agreements (DUA) or Data Transfer Agreements (DTA).

NOTE: *Pilot studies are full-fledged research studies that must be approved by the IRB(s), when human subjects are involved. Pilot studies are not considered to be "activities preparatory to research."*

NOTE: *No formal IRB determination of exemption from human subject protection requirements is needed if all of the conditions listed in paragraph 57 are satisfied.*

58. PARTICIPATION OF NON-VETERANS AS RESEARCH SUBJECTS

VA research needs to be relevant to Veterans or active duty military personnel. The investigator must justify including non-Veterans in a VA research protocol, and the IRB must review the justification for inclusion of non-Veterans and specifically approve entering non-Veterans into the study before any non-Veterans can be recruited. The IRB must appropriately document in the IRB minutes or IRB protocol file its determinations regarding participation of non-Veterans in the study.

a. **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).

b. **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).

c. **Other Research.** Non-Veterans may be entered into an approved VA research study when the investigator can present a compelling argument to the IRB for the inclusion of non-Veterans (e.g., insufficient number of Veterans; survey of VA employees; study of active duty military; study involving Veterans' family members), and the research is relevant to the care of Veterans or active duty military personnel.

59. PAYMENT TO SUBJECTS

a. **Payment Permitted.** Payment to subjects may be permitted, with IRB approval, in the following circumstances:

(1) **No Direct Subject Benefit**. When the study to be performed is not directly intended to enhance the diagnosis or treatment of the condition for which the volunteer subject is being treated, when the standard of practice in affiliated non-VA institutions is to pay subjects in this situation.

(2) **Others Being Paid**. In multi-institutional studies, when human subjects at a collaborating VA or non-VA institution are to be paid for the same participation in the same study, subjects may be paid at a rate comparable to that proposed at the other sites, if deemed reasonable by the local IRB.

(3) **Comparable Situations**. In other comparable situations in which, in the opinion of the IRB, payment of subjects is appropriate.

(4) **Transportation Expenses**. When transportation expenses are incurred by the subject that would not be incurred in the normal course of receiving treatment and that are not reimbursed by any other mechanism.

NOTE: *Investigators must not pay human subjects to participate in research when the research is integrated with a patient's medical care and when it makes no special demands on the patient beyond those of usual care.*

b. **Protocol Provisions for Payment.** Prospective investigators who wish to pay research subjects must include in the protocol:

(1) Substantiation that proposed payments are reasonable and commensurate with the expected contributions of the subject;

(2) The terms of the payment and the amount of payment are in the informed consent form.

(3) Substantiation that subject payments are fair and appropriate, and that they do not constitute (or appear to constitute) undue pressure or influence on the prospective research subjects to volunteer for, or to continue to participate in, the research study. In addition, the payments do not constitute (or appear to constitute) coercion to participate in, or continue to participate in, the research study.

c. **IRB Review.** The IRB must review all proposals for payment of subjects to ensure conformity with VA requirements.

d. **Source of Funding.** The VA facility research office must ensure IRB-approved payment to subjects is made from a VA-approved source for funding research activities.

***NOTE**: Due to limitations in the Financial Management System, payments to subjects made through Austin Financial Services Center generate Internal Revenue Service (IRS) Form 1099 regardless of amount. This information, and the fact that the SSN will be used for this purpose, must be included in the informed consent form. Gift cards are not subject to these reporting requirements.*

60. TREATMENT OF RESEARCH-RELATED INJURIES TO HUMAN SUBJECTS

a. **VA Facilities' Responsibilities.** VA medical facilities must provide necessary medical 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 does not apply to:

(1) Treatment for injuries due to non-compliance by a subject with study procedures (38 CFR 17.85(a)(1)); or

(2) Research conducted for VA under a contract with an individual or a non-VA institution (38 CFR 17.85(a)(2)).

b. **Provision of Care Outside VA Facilities.** 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. Under these circumstances, VA facility Directors may contract for such care (38 CFR 17.85(b)(1)).

(2) If inpatient care must be provided to a non-Veteran under this paragraph, VA facility Directors may contract for such care (38 CFR 17.85(b)(2)).

(3) The sponsor cannot bill the injured subject's insurance company for the injury; however, the sponsor is responsible for reasonable and customary costs incurred for treatment of injury reasonably related to the subject's participation in the study described in the scope of work except to the extent that:

(a) The injury is attributable to the negligence or willful misconduct of an indemnitee; or

(b) The injury is attributable to failure to administer the test article as required in the protocol or to otherwise substantially follow the protocol.

(4) If a research subject needs treatment in a medical emergency in a non-VA facility for a condition covered by this paragraph, VA facility directors must provide reasonable reimbursement for the emergency treatment in a non-VA facility (38 CFR 17.85(b)(3)).

61. HUMAN SUBJECTS PROTECTION TRAINING

a. **Required Training**

(1) All individuals involved in conducting VA human research are required to successfully complete training in ethical principles on which human research is to be conducted and accepted good clinical practices (GCP), although VA does not formally endorse International Committee on Harmonisation (ICH) GCP (see the VA ORD Web site at: http://www.research.va.gov/pride/training/default.cfm, for a current listing of courses that fulfill these requirements, including courses at academic affiliates). All other applicable VA and VHA training requirements at the local and national level must be met (e.g., privacy training).

(2) Training provided by some VA facilities and by some VA facilities' academic affiliates has been approved by ORD to meet the training requirement for GCP and the ethical principles on which human research should be conducted. For example, if investigators with dual appointments at VA and those academic affiliates take the affiliates' training in GCP and the ethical principles on which human research should be conducted, the investigators do not have to take the VA's version of the same kind of training, but they must present documentation that they have completed this training to their VA Research Office. A list of approved alternative training sources is posted on the ORD Web site at http://www.research.va.gov/programs/pride/training/options.cfm. ORD will review other training upon request to determine whether or not it meets the requirements of this Handbook.

b. **When Training is Required.** All individuals who are subject to this Handbook are required to:

(1) Complete training in GCP and the ethical principles on which human research is to be conducted before they may participate in human subjects research, and

(2) Update such training every 2 years thereafter. Local facilities have the option of defining "every 2 years" as within 730 days after the previous training, within the second full calendar year after the previous training, or within the second full fiscal year after the previous training. Each facility must specify which definition of "every 2 years" it uses in its policies and procedures for this training requirement.

NOTE: *Other kinds of training (e.g., Privacy, Information Security) may be required more frequently (e.g., on an annual basis).*

c. **VA Facilities' Responsibilities.** It is the responsibility of the VA facility Director, or designee, to develop local SOPs, to provide documentation that the biennial requirements are

met for GCP, and to conduct training the ethical principles in which human studies research is conducted. It is at the discretion of the VA facility Director, or designee, to determine whether its SOPs call for tracking the biennial requirement by fiscal year, calendar year, or on a 365-day cycle.

d. **Applicability**

(1) This training requirement applies to all individuals involved in the conduct of VA human subjects research regardless of pay status, appointment type (title 38, title 5, IPA, or WOC), and length of time at the VA facility, including, but not limited to:

(a) Investigators;

(b) Study coordinators;

(c) Research assistants;

(d) Other members of the research team;

(e) Trainees, such as house officers and students;

(f) All members of the research office whose responsibilities include involvement with human research (e.g., the ACOS for R&D and the AO for R&D);

(g) All VA IRB staff, all VA IRB voting members, and all ex officio, nonvoting members of VA IRBs;

(h) VA representatives to external IRBs (e.g., affiliated academic institutions);

(i) All voting, and ex officio, nonvoting members of R&D Committees; and

(j) Members of other research committees or subcommittees that review research involving human subjects.

(2) This training requirement also applies to investigators and research team members conducting studies involving human subjects that are exempt from IRB review, as well as those conducting human research for which the IRB has granted a waiver of informed consent or a waiver of documentation of informed consent.

NOTE: *Nonscientist members (e.g., clergy, lawyers, community representatives, subject advocates) may require individualized training to ensure comprehension of their responsibilities as an IRB member. If a local facility provides such training, it needs to be included in its SOPs.*

e. **Exceptions to Applicability.** This training requirement does not apply to:

(1) Secretarial support staff,

(2) Research office staff whose responsibilities do not involve human research (e.g., those who deal only with research involving animals), or

(3) Community members of the IRB. However, community members of the IRB must complete specific training for IRB members as defined in the facilities' SOPs.

NOTE: *Facility Directors are not required to complete this training, but are required to complete the required Assurance training (see subpar. 5c and VHA Handbook 1058.03).*

f. **Academic Affiliate.** If the IRB of an affiliated academic institution or other external organization serves as the IRB of record for a VA facility, the external IRB members are to be encouraged to complete VA required human subjects protection training or its equivalent. The local VA facility is not required to track such training.

g. **DMC.** Members of a DMC for a VA research study are encouraged to complete VA required human subjects protection training or its equivalent. The local VA facility is not required to track such training.

h. **Individuals Outside VA.** Individuals outside VA (e.g., phlebotomists, x ray, and laboratory technicians) who are not VA employees (paid, WOC, or IPA), and whose work occurs exclusively outside the VA facility (e.g., at affiliated academic institution), must meet their own institutions' requirements for training, but the local VA facility is not required to track such training.

NOTE: *All members of the research team for a VA research study must be VA employees (paid, WOC, or IPA). The only individuals outside VA who do not need a VA appointment or VA-specific training are those who perform a service for the research study in the course of their usual clinical duties.*

i. **Clinical Service Providers.** Individuals who provide services for the research study in the course of their routine clinical duties (e.g., an x-ray technician who performs a chest x-ray, or clinical laboratory technician who performs a routine blood count), but have no other role or responsibility for the research study, are not required to complete VA human research protection training.

62. CREDENTIALING AND PRIVILEGING

All VA research staff (clinical and non-clinical) conducting human research (exempt or non-exempt) must be credentialed and privileged (if applicable) as required by current local, VA, VHA (see VHA Handbook 1100.19), and ORD requirements. Research staff (including volunteers) may only perform those activities in a research study for which they have the relevant:

a. **Credentials.** Each member of the research staff must be appropriately credentialed, except individuals providing secretarial support who should undergo the Human Resource Management (HRM) process for administrative personnel.

b. **Privileges**

(1) If the local facility where the research is to be performed requires privileging to perform a given duty (e.g., a procedure) in the clinical setting, the individual must be privileged at that facility to perform the duty before the individual can perform that duty in the research setting.

(2) If the local VA facility requires privileging to perform a given procedure, it is not sufficient for only the supervisor of the person performing the research procedure to be privileged for that procedure. The person actually performing the research procedure must be privileged for the procedure.

c. **Research Scope of Practice or Functional Statement.** Except as specified in subparagraph 62c(2), each member of the research team must have a research scope of practice statement or functional statement that has been approved by the individual's immediate supervisor and the ACOS for R&D, and that defines the duties the person is allowed to perform for research purposes. A research scope of practice statement or functional statement must be developed for all research personnel (clinical and non-clinical) who are not privileged for all the duties the person is allowed to perform for research purposes. The research scope of practice statement or functional statement must be consistent with the occupational category under which the individual was hired, and it must not include any duties for which the individual is not qualified. Current scopes of practice for all non-privileged research personnel must be retained by the Research Office.

NOTE: *A duty (e.g., a procedure) cannot be added to a scope of practice statement or functional statement, unless the individual meets all criteria to perform the duty in the clinical setting (e.g., the individual must be privileged for a procedure if privileging is required for that procedure in the local clinical setting).*

(1) If research personnel are involved in more than one study, the research scope of practice statement or functional statement may be written to cover multiple studies (i.e., personnel do not need a research scope of practice statement for each protocol).

(2) If an employee's clinical privileges, clinical scope of practice statement, or clinical functional statement includes all of the duties necessary for a specific research study (e.g., taking a medical history, drawing blood, performing a muscle biopsy, ordering and interpreting laboratory tests), a separate research scope of practice statement or functional statement does not need to be developed. However, if there are additional duties, these need to be included in the research scope of practice statement along with a copy of the clinical privileges, clinical scope of practice statement, or clinical functional statement.

d. **License, Registration, and Certification.** The employee must have all required licenses, registrations, or certifications to perform a given procedure, intervention, or other activity in the research setting and practice only within the scope allowed by such licenses, registrations, or certifications.

63. STUDENT AND OTHER TRAINEE RESEARCH

a. **Research Conducted by Students and Other Trainees to Fulfill Academic Requirements.** Only students and other trainees (including residents and fellows), including VA employees, from schools with an academic affiliation agreement consistent with current VHA policy, may serve as investigators within a VA facility, or use data, or human biological specimens that have been collected within VA for clinical, administrative, or research purposes. ***NOTE:*** *A waiver may be obtained from the CRADO under special circumstances.*

(1) A VA investigator sufficiently experienced in the area of the trainee's research interest must serve as PI or co-PI and is responsible for oversight of the research and the trainee. The PI or co-PI is responsible for ensuring the trainee complies with all applicable local, VA, and other Federal requirements.

(2) In conducting the research, the trainee must comply with all VA and other Federal and local institutional requirements, including those related to research, information security, and privacy.

(3) If the trainee does not complete all aspects of the research prior to leaving VA, the VA employee serving as the PI or co-PI must ensure the protocol is completed or terminated in an orderly fashion, and in accordance with all applicable local, VA, and other Federal requirements.

(4) When the trainee leaves VA, the VA employee serving as the PI or co-PI is responsible for ensuring all research records are retained by VA.

64. ACCREDITATION OF HUMAN RESEARCH PROTECTION PROGRAMS

Any VA facility with a Federalwide Assurance must obtain accreditation of its HRPP by the Accrediting Organization under contract with VA. This HRPP accreditation must be obtained in accordance with a schedule to be determined by the ORD based on the facility's HRPP accreditation status and history. Maintenance of HRPP accreditation must be in accordance with ORD HRPP accreditation requirements including those relating to academic affiliates providing IRB services to the VA facility. Academic affiliates may be required to cooperate with the Accrediting Organization under contract with VA or to maintain their own accreditation with another accrediting organization recognized by VA. ***NOTE:*** *The HRPP accreditation requirements are posted on the ORD web site at: http://www.research.va.gov/pride/accreditation/default.cfm.*

65. REFERENCES

a. Title 5 U.S.C., Chapter 5, Administrative Procedure, Section 552a, The Privacy Act of 1974.

b. Title 37 U.S.C., Chapter 57, Records and Investigations, Section 5701, Confidential nature of claims.

c. Title 37 U.S.C., Chapter 57, Records and Investigations, Section 5705, Confidentiality of medical quality-assurance records.

d. Title 38 U.S.C., Chapter 5, Authorities and Duties of the Secretary, Section 501, Rules and regulations.

e. Title 38 U.S.C., Chapter 17, Hospital, Nursing Home, Domiciliary, and Medical Care, Section 1710. Eligibility for hospital, nursing home, and domiciliary care.

f. Title 38 U.S.C., Chapter 73, Veterans Health Administration, Organization and Functions, Section 7331, Protection of Patient Rights, Informed consent.

g. Title 38 U.S.C., Chapter 73, Veterans Health Administration, Organization and Functions, Section 7334, Protection of Patient Rights, Regulations.

h. Title 42 U.S.C., Chapter 6a, Public Health Service, Section 262 Regulation of biological products.

i. Title 42 U.S.C., Chapter 6a, Public Health Service, Section 263 Preparation of biological products by Service

j. Title 10 CFR Chapter I, Nuclear Regulatory Commission, Part 20, Standards for Protection Against Radiation.

k. Title 10 CFR Chapter I, Nuclear Regulatory Commission, Part 35, Medical Use of Byproduct Material.

l. Title 21 CFR Chapter I, Food and Drug Administration, Department of Health and Human Services, Part 11, Electronic Records; Electronic Signatures.

m. Title 21 CFR Chapter I, Food and Drug Administration, Department of Health and Human Services, Part 50, Protection of Human Subjects.

n. Title 21 CFR Chapter I, Food and Drug Administration, Department of Health and Human Services, Part 54, Financial Disclosure by Clinical Investigators.

o. Title 21 CFR Chapter I, Food and Drug Administration, Department of Health and Human Services, Part 56, Institutional Review Boards.

p. Title 21 CFR Chapter I, Food and Drug Administration, Department of Health and Human Services, Part 312, Investigational New Drug Application.

q. Title 21 CFR Chapter I, Food and Drug Administration, Department of Health and Human Services, Part 812, Investigational Device Exemptions.

r. Title 21 CFR Chapter I, Food and Drug Administration, Department of Health and Human Services, Part 814, Premarket Approval of Medical Devices.

s. Title 38 CFR Chapter I, Department of Veterans Affairs, Part 16, Protection of Human Subjects.

t. Title 38 CFR Chapter I, Department of Veterans Affairs, Part 17, Medical.

u. Title 45 CFR Subtitle A, Department of Health and Human Services, Part 160, General Administrative Requirements.

v. Title 45 CFR Subtitle A, Department of Health and Human Services, Part 164, Security and Privacy, Subpart E – HIPAA Privacy and Research.

w. Title 45 CFR Subparts A, B, C, and D, Department of Health and Human Services, Part 46, Protection of Human Subjects.

x. Federal Food, Drug and Cosmetic Act, Section 505, New Drugs.

y. Federal Food, Drug and Cosmetic Act, Section 520, General provisions respecting control of devices intended for human use.

z. Expedited Review Category Number 1, 63 FR 216: 60364-60367, November 9, 1998.

aa. Expedited Review Category Number 2, 63 FR 216: 60364-60367, November 9, 1998.

bb. Expedited Review Category Number 3, 63 FR 216: 60364-60367, November 9, 1998.

cc. Expedited Review Category Number 4, 63 FR 216: 60364-60367, November 9, 1998.

dd. Expedited Review Category Number 5, 63 FR 216: 60364-60367, November 9, 1998.

ee. Expedited Review Category Number 6, 63 FR 216: 60364-60367, November 9, 1998.

ff. Expedited Review Category Number 7, 63 FR 216: 60364-60367, November 9, 1998.

gg. Expedited Review Category Number 8, 63 FR 216: 60364-60367, November 9, 1998.

hh. Expedited Review Category Number 9, 63 FR 216: 60364-60367, November 9, 1998.

ii. VA Directive 6500, Information Security Program.

jj. VHA's Record Control Schedule (RCS 10-1).

kk. VHA Directive 1200, Veterans Health Administration Research and Development Program.

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

mm. VHA Handbook 1058.01, Reporting Adverse Events in Research to the Office of Research Oversight.

nn. VHA Handbook 1058.2, Research Misconduct.

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

pp. VHA Handbook 1100.19, Credentialing and Privileging.

qq. VHA Handbook 1108.04, Investigational Drugs and Supplies.

rr. VHA Handbook 1200.01, The Research and Development Committee Handbook.

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

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

uu. VHA Handbook 1200.09, Inclusion of Women and Minorities in Research.

vv. VHA Handbook 1200.16, Offsite Research.

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

xx. VHA Handbook 1605.2, Minimum Necessary Standard for Protected Health Information.

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