

REQUIREMENTS FOR THE PROTECTION OF HUMAN SUBJECTS IN RESEARCH

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

2. SUMMARY OF MAJOR CHANGES:

a. This directive modifies prior VHA Handbook 1200.05 requirements for implementation of the revised Common Rule for the Protection of Human Subjects (the 2018 Requirements) published on January 19, 2017, effective January 21, 2019, to facilitate VA research activities involving multiple institutions and to harmonize VA requirements with those of other Federal agencies. VA-specific requirements are added as appropriate.

b. This directive also incorporates and streamlines requirements previously contained in VHA Handbook 1058.06, Research Conducted by Employees of VHA Program Offices, dated October 28, 2011, which pertained to the review and approval of research conducted by VHA Program Office employees.

c. Amendment dated, March 3, 2020 updated information related to use of IRBs of medical or dental schools and commercial IRBs (see paragraph 5.f.(8)) and human fetal tissue and stem cells (see paragraph 19.c.).

d. Amendment dated January 8, 2021, updates the emergency exemption found in the definition of VA Research (see **NOTE:**) and paragraph 9.b. (see **NOTE:**).

3. RELATED ISSUES: VHA Directive 1200, Research and Development Program dated May 13, 2016; VHA Directive 1200.02(1), Research Business Operations, dated March 10, 2017; VHA Handbook 1200.01, Research and Development Committee, dated June 16, 2009; VHA Handbook 1058.01, Research Compliance Reporting Requirements, dated June 15, 2015; and VHA Handbook 1058.03, Assurance of Protection for Human Subjects in Research, dated November 21, 2014.

4. RESPONSIBLE OFFICE: The Office of Research and Development (ORD) (10X2) is responsible for the contents of this directive. Questions may be referred to 202-443-5600, or emailed to VHACOORDRegulatory@va.gov.

5. RESCISSIONS: VHA Handbook 1200.05, Requirements for the Protection of Human Subjects in Research, dated November 12, 2014; and VHA Handbook 1058.06, Research Conducted by Employees of VHA Program Offices, dated October 28, 2011, are rescinded.

6. RECERTIFICATION: This VHA directive is scheduled for recertification on or before the last working day of January 2024. This VHA directive will continue to serve as national VHA policy until it is recertified or rescinded.

January 7, 2019

VHA DIRECTIVE 1200.05(2)

/s/ Richard A. Stone, M.D.
Executive in Charge

NOTE: *All references herein to VA and VHA documents incorporate by reference subsequent VA and VHA documents on the same or similar subject matter.*

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REQUIREMENTS FOR THE PROTECTION OF HUMAN SUBJECTS IN RESEARCH

1. PURPOSE

This Veterans Health Administration (VHA) directive defines the procedures for implementing the Federal Policy for the Protection of Human Subjects, known as the Common Rule, and other applicable Federal requirements for the protection of human subjects in research. **NOTE:** *This directive will be effective as of January 21, 2019 and must be implemented by that date.* **AUTHORITY:** Title 38 United States Code (U.S.C.) 7334; Title 38 Code of Federal Regulations (CFR) Part 16.

2. BACKGROUND

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

b. VA is one of the 20 Federal departments and agencies that have agreed to follow the Common Rule for the Protection of Human Subjects (the 2018 Requirements) published on January 19, 2017, effective January 21, 2019. The 2018 Requirements are encoded in 38 CFR Part 16. The 2018 Requirements are a major revision of the Common Rule for the Protection of Human Subjects, effective June 18, 1991 (the pre-2018 Requirements), which VA previously agreed to follow. This directive incorporates both the pre-2018 and the 2018 Requirements where applicable.

c. The 2018 Requirements include new or modified regulations that apply to human subjects research activities determined to be exempt or approved by an Institutional Review Board (IRB) on and after January 21, 2019 and human subjects research activities approved by an IRB prior to January 21, 2019 for which a VA facility or IRB has documented that the research will transition to the 2018 Requirements. For purposes of this directive, these regulations will be referred to as the 2018 Requirements. The pre-2018 Requirements apply to human subjects research activities, unless the research is transitioning to comply with the 2018 Requirements as described in this directive, for which such review was waived pursuant to 38 CFR 16.101(i), or for which a determination was made that the research was exempt before January 21, 2019, or to human subject research activities approved by an IRB prior to January 21, 2019.

d. For purposes of this directive, the 2018 Requirements mean the Federal Policy for the Protection of Human Subjects published on January 19, 2017 and further amended by an interim final rule published on January 22, 2018 (83 FR 2885) and a final rule published on June 19, 2018 (83 FR 28497). VA facilities conducting research involving human subjects must comply with the 2018 Requirements in the Federal Policy for the Protection of Human Subjects as described in this directive. If human subjects research

is not required to comply with the 2018 Requirements, it will comply with the pre-2018 Requirements in the Federal Policy for the Protection of Human Subjects as described in this directive.

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

3. DEFINITIONS

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

a. **Adverse Event.** An adverse event (AE) in human subjects research is any untoward physical or psychological occurrence in a human subject participating in research. **NOTE:** *AEs are further discussed in VHA Handbook 1058.01, Research Compliance Reporting Requirements, dated June 15, 2015, and VHA Handbook 1004.08, Disclosure of Adverse Events to Patients, dated October 2, 2012.*

b. **Assurance.** An assurance is a written commitment to protect human research subjects and comply with the requirements of the Common Rule. **NOTE:** *Assurances are further discussed in VHA Handbook 1058.03, Assurance of Protection for Human Subjects in Research, dated November 21, 2014.*

c. **Certificate of Confidentiality.** A Certificate of Confidentiality is a document issued by a component of HHS pursuant to The Public Health Service Act Section 301(d), 42 U.S.C. 241(d) amended by Section 2012 of the 21st Century Cures Act, Public Law 114-255, to protect the privacy of individuals who are subjects of certain specified research activities by authorizing investigators to withhold from all persons not connected with the conduct of such research the names or other identifying characteristics of such subjects. Persons so authorized to protect the privacy of such individuals may not disclose information in any Federal, State, or local civil, criminal, administrative, legislative, or other proceedings to identify such individuals.

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

e. **Clinical Investigation.** The Food and Drug Administration (FDA) considers the term clinical investigation to mean any experiment that involves a test article and one or more human subjects, and that either:

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

(2) Does not meet the requirements for prior submission to the FDA under these sections of the Federal Food, Drug, and Cosmetic Act, but the results of which are

intended to be submitted later to, or held for inspection by, the FDA as part of an application for a research or marketing permit (21 CFR 56.102(c)).

f. **Clinical Trial.** A research study in which one or more human subjects are prospectively assigned to one or more interventions (which may include placebo or other control) to evaluate the effects of the interventions on biomedical or behavioral health-related outcomes.

g. **Collaborative Research.** Collaborative Research is human subjects research activities involving investigators from VA and at least one non-VA institution. Collaborative Research includes VA and non-VA institutions.

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

i. **De-identified Information.** De-identified information is health information that is presumed not to identify an individual, and with respect to which there is no reasonable basis to believe that the information can be used to identify an individual, because the 18 patient identifiers described in the Health Insurance Portability and Accountability Act (HIPAA) Privacy Rule have been removed or a qualified biostatistician has determined that the health information has been de-identified. De-identified information is no longer covered by the Privacy Act, 38 U.S.C. 5701, 38 U.S.C. 7332, or the HIPAA Privacy Rule (see VHA Directive 1605.01, Privacy and Release of Information, dated August 31, 2016).

j. **Federalwide Assurance.** A Federalwide Assurance (FWA) is an assurance approved for Federalwide use by the Office of Human Research Protections (OHRP) in accordance with Section 103(a) of the Common Rule (see 38 CFR 16.103(a)).

k. **Fetus.** For purposes of this directive and as defined in Subpart B of the Common Rule for the Protection of Human Subjects, a fetus is the product of conception from the time of implantation until delivery.

l. **Human Research Protection Program.** The Human Research Protection Program (HRPP) is a comprehensive system to ensure the protection of human subjects participating in research. The HRPP consists of a variety of individuals and committees such as: the VA facility Director, Associate Chief of Staff for Research and Development (ACOS/R&D), the Administrative Officer (AO) for R&D, the R&D Committee, the IRB, other committees or subcommittees addressing human subjects protection (e.g., Biosafety, Radiation Safety, Radioactive Drug Research, Conflict of Interest), investigators, IRB staff, research staff, health and safety staff (e.g., Biosafety Officer, Radiation Safety Officer), research compliance officers (RCOs), Information System Security Officers (ISSOs), privacy officers (POs), and research pharmacy staff. The objective of this system is to assist the institution in meeting ethical principles and regulatory requirements for the protection of human subjects in research.

m. **Human Subject.** A human subject is a living individual about whom an investigator (whether professional or student) conducts research, and:

(1) Obtains information or biospecimens through intervention or interaction with the individual, and uses, studies, or analyzes the information or biospecimens; or

(2) Obtains, uses, studies, analyzes, or generates identifiable private information or identifiable biospecimens.

NOTE: *Individuals who receive test articles or who serve as controls in clinical investigations, including clinical investigations as defined under FDA regulations in 21 CFR 50.3, 312.3(b), and 812.3(h), are also considered human subjects for the purposes of this directive.*

n. **Identifiable Private Information.** Identifiable private information is information for which the identity of the subject is or may readily be ascertained by the investigator or associated with the private information.

o. **Identifiable Biospecimen.** An identifiable biospecimen is a biospecimen for which the identity of the subject is or may readily be ascertained by the investigator or associated with the biospecimens.

p. **Institutional Official.** The Institutional Official (IO) is the individual legally authorized as Signatory Official to commit an institution to an FWA. The Signatory Official assures that human subjects research to which the FWA applies is conducted in accordance with the terms of the assurance (see VHA Handbook 1058.03). The Principal Deputy Under Secretary for Health or designee is the IO for VHA Central Office, and VA facility Directors are the IOs for local VA facilities.

q. **Institutional Review Board.** An IRB is a board, committee, or other group formally designated by an institution to review, approve, require modification, disapprove, and conduct continuing oversight of human subject research in accordance with the Common Rule (38 CFR Part 16) and other applicable regulations. ***NOTE:*** *For the purposes of this directive, unless otherwise specified, references to IRB include any IRB which is responsible for approval and monitoring of a research project.*

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

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

t. **Investigator.** An investigator is any individual who conducts research including, but not limited to, the Principal Investigator (PI), sub-investigator or co-investigator, and Site Investigator or Local Site Investigator (LSI). All VA investigators on a VA research study or program must hold a VA appointment.

(1) **Principal Investigator.** The Principal Investigator (PI) is a qualified person who directs a research study or program. The PI oversees scientific, technical, and day-to-day management of the research. If a study is conducted by a team of individuals, the PI is the responsible leader of that team.

(2) **Sub-Investigator or Co-Investigator.** A sub-investigator or co-investigator is a qualified person designated by the PI or LSI to perform critical research procedures and/or to make important research-related decisions. Both terms are interchangeable but are key personnel on a research study or program.

(3) **VA Investigator.** A VA investigator is any individual who conducts research while acting under a VA appointment, including full and part-time employees, without compensation (WOC) employees, or individuals appointed or detailed to VA under the Intergovernmental Personnel Act (IPA) of 1970 (5 U.S.C. 3371 et seq.). Individuals working under a contract with VA cannot conduct research as VA Investigators under a WOC appointment while simultaneously working as a contractor. **NOTE:** *Trainees can serve as a co- or sub-investigator but must have a VA PI sufficiently experienced in the area of the trainee's research interest to serve as the PI. Trainee research activities are further discussed in VHA Directive 1200.02(1), Research Business Operations, dated March 10, 2017.*

u. **Legally Authorized Representative.** A legally authorized representative (LAR) is an individual or judicial or other body authorized under applicable law to consent on behalf of a prospective subject to the subject's participation in the procedure(s) involved in the research. If there is no applicable law addressing this issue, LAR means an individual recognized by institutional policy as acceptable for providing consent in the non-research context on behalf of the prospective subject to the subject's participation in the procedure(s) involved in the research.

v. **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.

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

x. **Nonprofit Research and Education Corporations.** VA-affiliated nonprofit research and education corporations (NPC) are authorized by Congress under 38 U.S.C. 7361-7366 to provide flexible funding mechanisms for the conduct of research and education at one or more VA facilities. Research approved by a facility R&D Committee and education approved by the facility Education Committee are considered to be a VA research project or a VA education activity respectively, regardless of the source of funding, the entity administering the funds, or the research or education site (*see VHA Handbook 1200.17, Department of Veterans Affairs Nonprofit Research and Education Corporations Authorized by Title 38 U.S.C. Sections 7361 Through 7366, dated April 27, 2016 and revised May 9, 2017*).

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

z. **Private Information.** Private information includes information about behavior that occurs in a context in which an individual can reasonably expect that no observation or recording is taking place, and information that has been provided for specific purposes by an individual and that the individual can reasonably expect will not be made public (e.g., a medical record). (See 38 CFR 16.102(e)(4)).

aa. **Program Office.** A Program Office is any office within the VHA Office of the Under Secretary for Health. A Program Office includes all of its component offices and subdivisions, regardless of physical location. **NOTE:** *The organization chart for the VHA Office of the Under Secretary for Health may be found on the VHA Web site.*

bb. **Program Office Employee.** A Program Office employee is any individual working under a VA appointment in a VHA Program Office, regardless of duty station, including (but not limited to) full and part-time employees, WOC employees, and employees under the IPA.

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

(1) Scholarly and journalistic activities (e.g., oral history, journalism, biography, literary criticism, legal research, and historical scholarship), including the collection and use of information, that focus directly on the specific individuals about whom the information is collected.

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

(3) Collection and analysis of information, biospecimens, or records by or for a criminal justice agency for activities authorized by law or court order solely for criminal justice or criminal investigative purposes.

(4) Authorized operational activities (as determined by each agency) in support of intelligence, homeland security, defense, or other national security missions.

dd. **Research Records.** Research records include, but are not limited to, IRB and R&D Committee records, records of all observations, subject recruitment activities, other data relevant to the investigation, progress notes, research study forms, surveys, questionnaires, and other documentation regarding the study (see VHA Records Control Schedule (RCS) 10-1, Chapter 8).

ee. **Research and Development Committee.** The R&D Committee is a committee responsible, through the Chief of Staff (COS) to the VA facility Director, for oversight of the facility's research program and for maintenance of high standards throughout that program (see VHA Handbook 1200.01, Research and Development (R&D) Committee, dated June 16, 2009).

ff. **Research Protocol.** A research protocol details the aims and objectives of a research study, scientific rationale, the methods used to carry out the research, and how data will be analyzed. For human subjects research it also entails how subjects will be accessed/recruited, any foreseeable risks, and how these risks will be mitigated. ***NOTE: The protocol for social or behavioral research is sometimes referred to as the Research Plan or Research Purpose and Methodology.***

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

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

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

hh. **Signatory Official.** The Signatory Official is the individual legally authorized to commit an institution to the requirements of an FWA.

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

jj. **VA Research.** VA research is research that is conducted by investigators (serving on VA compensated, WOC, or IPA appointments) while on VA time or on VA property. The research may be funded by VA, by other sponsors, or be unfunded. VA

research must have R&D Committee approval before it is considered VA Research and before it can be initiated. All research activities approved by the R&D Committee are considered VA Research. **NOTE:** Any emergency use of a test article does not require R&D Committee approval but is VA research under this policy.

4. POLICY

It is VHA policy that all VA facilities that conduct research involving human subjects must have or obtain the services of a functional IRB as part of its HRPP, and that such research and IRB reviews be conducted in accordance with this directive and applicable Federal laws and regulations. It is VHA policy that all research involving human subjects must adhere to the 2018 Requirements, except that research which is subject to the pre-2018 Requirements need not comply with standards which are specifically stated in this directive to be "subject to the 2018 Requirements."

5. RESPONSIBILITIES

a. **Under Secretary for Health.** The Under Secretary for Health is responsible for ensuring overall VHA compliance with this directive.

b. **Principal Deputy Under Secretary for Health.** The Principal Deputy Under Secretary for Health or designee is responsible for serving as the Institutional Official (IO) for VHA Central Office.

c. **Deputy Under Secretary for Health for Operations and Management.** The Deputy Under Secretary for Health for Operations and Management is responsible for:

(1) Communicating the contents of this directive to each of the Veterans Integrated Service Networks (VISNs); and

(2) Ensuring that each VISN Director has the sufficient resources to fulfill the terms of this directive in all of the VA medical facilities within that VISN.

d. **Chief Research and Development Officer, VA Central Office.** The Chief Research and Development Officer (CRADO), VA Central Office, is responsible for ensuring that the Office of Research and Development (ORD) develops human subjects research policies for VA research using the standards in this directive defining and describing how VA human subjects research can be conducted within the Common Rule for the Protection of Human Subjects.

e. **Veterans Integrated Services Network Director.** Each VISN Director is responsible for ensuring that VA research programs at facilities within the VISN comply with current VA policies and guidelines relating to human subjects research.

f. **VA Medical Facility Director.** Each VA medical facility Director is responsible for:

(1) Serving as the IO for the medical facility. The IO is the individual legally authorized as SO to commit an institution to an FWA. An FWA is required prior to

conducting any human subjects research subject to the 2018 Regulations. See 38 CFR 16.103. **NOTE:** *VA facilities filing an FWA and VA Addendum must submit applications and renewals through the Office of Research Oversight (ORO) (see VHA Handbook 1058.03);*

(2) Overseeing the facility's research program. The IO is responsible for the creation and implementation of an HRPP for research involving human subjects. The exact composition of the HRPP depends on the specific facility, the resources of the facility, and the type, size, and complexity of its research program. For additional information see VHA Directive 1200.02(1). The IO's responsibilities for the facility's HRPP include, but are not limited to:

(a) Ensuring that the institution's HRPP functions effectively and that the institution provides the resources and support necessary to comply with all requirements applicable to research involving human subjects;

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

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

(d) Ensuring provision of adequate resources to support the operations of the HRPP;

(e) Ensuring independence of the IRB;

(f) Appointing the facility's IRB voting members in writing when the VA facility operates its own IRB;

(g) Appointing the Chair and, when applicable, Co-chair(s) or Vice Chair(s) for a term of up to 3 years when the VA facility operates its own IRB;

(3) Serving as the official representative of the institution to external agencies and oversight bodies, and providing all written communication with external departments, agencies, and oversight bodies;

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

(5) Ensuring that a documented procedure is in place for determining when a

research activity approved by the IRB, prior to January 21, 2019, can transition to the 2018 Requirements, if applicable. The documented procedure must list what individuals or groups are designated to make the determinations. **NOTE:** *Investigators may not make a determination that their studies can be transitioned to the 2018 Requirements;*

(6) Ensuring appropriate documentation of required actions and responsibilities pertaining to review, approval, conduct and oversight of research conducted at that facility set forth in this directive;

(7) Ensuring all research subject to this directive is reviewed and approved by an IRB and will be subject to oversight by the IRB. **NOTE:** *Research that meets the exempt categories is not subject to IRB review unless it is determined to meet one of the exempt categories requiring limited IRB review. All exempt research must be reviewed and approved by the R&D Committee (see Appendices A and B);*

(8) Ensuring that any IRB operated by the VA facility is established in accordance with the requirements of this directive and registered through ORO with the HHS OHRP (see VHA Handbook 1058.03);

(a) The facility's IRB(s) of Record may include the facility's own IRB(s), VHA Central Office IRB (VA Central IRB), an IRB of another VA facility, the IRB(s) of a medical or dental school, or the IRB of another Federal agency. A facility may also use an IRB for multi-site protocols that has been specifically designated by ORD as an IRB that may serve as a multi-site IRB for VA facilities.

(b) VA will permit use of a commercial IRB as an IRB of Record for VA facilities if it has been specifically designated by ORD as a commercial IRB that may serve as an IRB for cooperative research.

(c) A VA facility's own IRB, also known as an internal IRB, and the VA Central IRB, cannot serve as an IRB of Record for any non-VA entity except a Department of Defense (DoD) facility, Department of Energy laboratory, or a VA NPC;

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

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

2. Ensuring that external IRBs of Record used by the VA facility hold current IRB registrations with FDA/OHRP and provide updates to membership as required by VHA Handbook 1058.03;

(9) Requesting CRADO approval when the VA facility wants to establish a new HRPP, change its IRB(s) of Record, or wants its internal IRB to serve as an IRB of Record for a non-VA entity. **NOTE:** *All IRBs overseeing VA human subjects research*

regardless of the type described above must meet all the IRB requirements described in 38 CFR Part 16;

(10) Submitting waiver requests electronically to the CRADO for approval of research involving prisoners conducted by VA investigators while on official VA duty, in accordance with the process outlined in section 20 below; and

(11) Approving VA participation in proposed research that includes pregnant women, neonates, or children as described in this directive (see sections 19 and 21).

g. **VA Investigators.** Each VA investigator is responsible for:

(1) Giving first priority to the protection of research subjects, upholding professional and ethical standards and practices, and adhering to all applicable VA and other Federal requirements, including the local VA facility's policies and procedures, regarding the conduct of research and the protection of human subjects;

(2) Holding a current VA appointment to conduct VA research;

(a) VA investigators must have the appropriate training, education, expertise, and credentials to conduct the research according to the research protocol;

(b) PIs must ensure that all research staff are qualified (e.g., including but not limited to appropriate training, education, expertise, and credentials) to perform procedures assigned to them during the study;

(c) Investigators and their staff conducting human subjects research must be credentialed and privileged as required by current local and VA requirements (see VHA Handbook 1100.19, Credentialing and Privileging, dated October 15, 2012, and VHA Directive 2012-030, Credentialing of Health Care Professionals, dated October 11, 2012). Investigators and their research staff may only perform those activities in a research study for which they have the relevant credentials and privileges;

(d) Investigators must be identified on the IRB application and must provide credentials, conflict of interest statements or other documentation required by VA and local facility policies;

(e) VHA Program Office employees acting as Investigators, regardless of duty station, must prospectively document their research with their supervisor in writing. For more information on documentation and review requirements, see Appendix C;

(3) Developing and submitting a research protocol that is scientifically valid and ethical, describes the research objectives, background and methodology, and is relevant to the health or welfare of the Veteran population. When applicable, the protocol must include the following safety measures:

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

- (b) Frequency of safety data collection;
 - (c) Frequency or periodicity of review of cumulative safety data;
 - (d) Statistical tests for analyzing the safety data to determine if harm is occurring;
and
 - (e) Conditions that trigger an immediate suspension of the research, if applicable;
- (4) For all non-exempt human subjects research, submitting the protocol for initial review and obtaining written approvals from the IRB, other applicable committees, and from the R&D Committee. In addition, the investigator must receive written notice from the ACOS/R&D that the research may commence before initiating the research. See VHA Handbook 1200.01;
- (5) For all exempt human subjects research requiring a limited IRB review, submitting the protocol for initial limited IRB review, other applicable committees, and obtaining approval from the R&D Committee. In addition, the investigator must receive written notice from the ACOS/R&D that the research may commence before initiating the research. See VHA Handbook 1200.01. **NOTE:** *Submitting the protocol for initial limited IRB review is not applicable for all exempt categories. See Appendix B;*
- (6) Once approved by the R&D Committee and the investigator receives written notification from the ACOS/R&D that the study may be initiated, implementing the protocol as approved. All modifications to the approved research protocol or consent form must be approved by the IRB prior to initiating the changes except when necessary to eliminate apparent immediate hazards to the subject. The IRB must have a written procedure specifying when and how the IRB is notified of changes initiated by an investigator prior to IRB approval. For studies approved by an IRB, the investigator must also obtain continuing review and approval at a frequency established by the IRB, but not less than once every year except as described in section 9.e.(2) and is expected to submit all materials required for continuing review in sufficient time to assure approval prior to the expiration date. Non-exempt human subjects research activities cannot be conducted at any time without a current valid IRB approval except when stopping interventions or interactions with current participating subjects could be harmful to those subjects;
- (7) Disclosing to the IRB any potential, actual, apparent, or perceived conflict of interest of a financial, professional, or personal nature that may affect any aspect of the research, and comply with all applicable VA and other Federal requirements regarding conflict of interest;
- (8) During the recruitment process, making initial contact with potential subjects in person or by letter prior to initiating any telephone contact, unless there is written documentation that the subject is willing to be contacted by telephone about the study in question or a specific kind of research as outlined in the study. **NOTE:** *If existing information from sources such as a medical record or database (research or non-*

research) are used to identify human subjects, there must be an IRB-approved waiver of HIPAA authorization for this activity in the new protocol;

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

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

NOTE: *This section does not apply when a Veteran calls in response to an advertisement;*

(9) Obtaining and documenting legally effective informed consent of the subject or the subject's LAR prospectively that is in alignment with ethical principles that govern informed consent for research. The only exceptions are if the IRB determines the research is exempt, or approves a waiver of the informed consent process, or approves a waiver of the signed informed consent document (see sections 17 and 18);

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

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

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

(13) Obtaining a HIPAA authorization or an IRB or Privacy Board-approved waiver of HIPAA authorization prior to the use and/or disclosure of the subject's Protected Health Information (PHI) (see section 23 in this directive and VHA Directive 1605.01). PHI cannot be used or disclosed without prior authorization or a waiver of authorization unless the PHI constitutes a limited data set and there is an appropriate data use agreement (DUA). The information in the written authorization or approved waiver of authorization or DUA for use or disclosure of a limited data set must not contradict any provisions of the protocol and informed consent documents as applicable;

(14) Reporting problems, adverse events, local research deaths, and apparent serious or continuing noncompliance including, in accordance with local facility or IRB Standard Operating Procedures (SOPs) and VHA Handbook 1058.01. **NOTE:** *Current*

guidance on such reporting can be found on the ORO Web site at:
<https://www.va.gov/ORO/oropubs.asp>;

(15) Ensuring research records include all information made or received by a VA investigator over the entire lifecycle of a research activity. This includes, but is not limited to, as applicable, the research protocol and all amended versions of the protocol; the grant application; documentation on each subject including informed consent, interactions with subjects by telephone or in person, observations, interventions, and other data relevant to the research, codes and keys used to de-identify and re-identify subjects protected health information; documents related to budget and funding; and other forms required by VA policy and Federal regulations. If the investigator leaves VA, all research records must be retained for the applicable retention period by the VA facility where the research was approved.

NOTE: Please refer to VHA RCS 10-1 for a list of local research investigator records that constitute a Federal record in VA research with the applicable specified retention and disposition requirements;

(16) Creating or updating a VHA health record and creating a progress note for all research subjects (Veterans or non-Veterans) who receive research procedures or interventions as inpatients or outpatients at VA medical facilities that are either used in or may impact the medical care of the research subject at a VA medical facility or at facilities contracted by VA to provide services to Veterans (e.g., Community-Based Outpatient Clinics or community living centers). Informed consent and HIPAA authorization documents are not required to be in the health record;

(17) Conducting VA human subjects research involving investigational drugs and devices in accordance with all applicable VA policies and other Federal requirements including, but not limited to, this directive; VHA Handbook 1108.04, Investigational Drugs and Supplies, dated February 29, 2012; and applicable FDA regulations. The storage and security procedures for test articles used in research must be reviewed and approved by the IRB and follow all applicable Federal laws, regulations, and VA policies;

(18) Initiating the IRB-approved research protocol only after all applicable requirements in VHA Directive 1200.01 have been met, including obtaining R&D Committee approval and obtaining written notification from the ACOS/R&D that the research can be initiated. IRB approval is for a specified time period based on the degree of risk of the study, not to exceed 1 year except as described in section 9.e.(2). The IRB determines the expiration date based upon its date of review and communicates that date to the investigator in its written approval letter;

(19) Continuing review and requesting re-approval of research on or before the date when IRB approval expires. There is no provision for any grace period to extend the conduct of research beyond the expiration date of IRB approval. If approval expires, the investigator must:

(a) Stop all research activities including, but not limited to, enrollment of new subjects, analyses of individually identifiable data, and research interventions or interactions with currently participating subjects, except where stopping such interventions or interactions could be harmful to those subjects; and

(b) Immediately submit to the IRB Chair a list of research subjects who could be harmed by stopping specified study interventions or interactions; and

(20) If either the awardee of a clinical trial funded or supported by a Federal agency or department other than VA, or conducting a clinical trial funded or supported by a non-Federal agency or department (e.g., university, industry, nonprofit organization) or not funded, posting a copy of the IRB-approved informed consent form used to enroll subjects after the clinical trial is closed to recruitment and no later than 60 days after the last study visit by any subject as described in the IRB-approved protocol. For multi-site studies, it applies when all sites have closed subject recruitment. **NOTE:** *Additional information about posting of clinical trial informed consent forms is in section 17.j.*

6. APPLICABILITY OF 2018 REQUIREMENTS

a. Except as indicated in section 6.b below, research must comply with the pre-2018 Requirements as described in this directive if the research was initially approved by an IRB, or for which such review was waived pursuant to 38 CFR 16.101(i), or for which a determination was made that the research was exempt, before January 21, 2019.

b. Research must comply with the 2018 Requirements as described in this directive if the research meets any of the following conditions:

(1) Was approved by an IRB on or after January 21, 2019;

(2) Was approved by an IRB using the burden-reducing provision eliminating IRB review of a grant application or contract proposal between June 19, 2018, and January 20, 2019. **NOTE:** *Research in this category must comply with all 2018 Requirements as of January 21, 2019;*

(3) Was determined to be exempt on or after January 21, 2019; or

(4) Was approved by an IRB prior to January 21, 2019, where an institution still engaged in such research on or after January 21, 2019, determines that such ongoing research will transition to comply with the 2018 Requirements. **NOTE:** *The institution or an IRB must document and date such determinations. The research must comply with the 2018 Requirements as of the date of the determination. The institution must define in writing who is authorized to make determinations on behalf of the institution.*

7. IRB MEMBERSHIP

a. Each IRB must have at least five voting members with varying backgrounds to promote complete and adequate review of research activities commonly conducted by the institution(s) for which it reviews research.

(1) The IRB must be sufficiently qualified through the experience and expertise of its members (professional competence), and the diversity of its members, including 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.

(2) The IRB must be able to ascertain the acceptability of proposed research in terms of institutional commitments (including policies and resources) and regulations, applicable local, VA and other Federal requirements, and standards of government ethics and professional conduct and practice. The IRB must therefore include persons knowledgeable in these areas.

(3) If an IRB regularly reviews research that involves a category of subjects that is vulnerable to coercion or undue influence, such as children, prisoners, individuals with impaired decision-making capacity, or economically or educationally disadvantaged persons, consideration must be given to the inclusion of one or more individuals on the IRB who are knowledgeable about and are experienced in working with these subjects.

NOTE: *IRBs serving VA should also consider including a Veteran or Veteran's representative.*

b. Each IRB must include at least one voting member whose primary concerns are in scientific areas and at least one member whose primary concerns are in nonscientific areas. Members whose training, background, and occupation are within a behavioral or biomedical research discipline should be considered a scientist, while members whose training, background, and occupation are outside of a behavioral or biomedical research discipline should be considered a nonscientist.

c. Each IRB must include at least one voting member who is not otherwise affiliated with the institution and who is not part of the immediate family of a person who is affiliated with the institution. Retired VA employees who are receiving VA retirement benefits are considered affiliated for purposes of VA IRB membership. **NOTE:** *Veterans who receive their care at the facility, but have never been employed by VA, would not be considered affiliated.*

d. An IRB cannot have a member participate in the IRB's initial or continuing review of any project in which the member has a conflict of interest, except to provide information requested by the IRB.

e. An IRB may invite individuals with competence in special areas to assist in the review of issues which require expertise beyond or in addition to that available on the IRB. These individuals are not allowed to be voting members of the IRB.

f. VA facilities must maintain accurate membership rosters for their designated IRB(s) of Record and submit the roster(s) to ORO as required by VHA Handbook 1058.03. The roster must list IRB members identified by name, earned degrees, representative capacity, indications of experience such as board certifications, licenses, etc., sufficient to describe each member's primary anticipated contributions to IRB

deliberations, and any employment or other relationship between each member and the institution (e.g., full-time employee, part-time employee, member of governing panel or board, paid or unpaid consultant).

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

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

i. The Privacy Officer (PO) and the Information System Security Officer (ISSO) serve in an advisory capacity to the facility's IRB as either non-voting members or as consultants.

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

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

l. The IO appoints VA voting members to an IRB in writing. Appointment procedures for ex officio, non-voting members are made according to local SOPs and any other applicable VA requirements. Voting members of VA IRBs and VA representatives to external IRB(s) of Record and the VA Central IRB are appointed for a period of up to 3 years. They may be re-appointed to new terms of up to 3 years without a break in service at the end of each term. **NOTE:** *There is not a maximum number of terms for IRB members as long as the composition of the IRB meets all requirements. VA representation on external IRBs, such as academic IRBs, is optional and at the discretion of the IO and the external IRB.*

m. The Chair, Co-Chair(s), and Vice Chair(s) of an internal VA IRB (e.g., an IRB that is managed by the VA Facility or by a VA Program Office such as the VHA Central Office IRB) must be paid VA employees (i.e., not holding a WOC or IPA appointment at VA). **NOTE:** *This does not apply to IRBs of Record external to VA.*

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

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

8. IRB FUNCTIONS AND OPERATIONS

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

(1) Conducting initial and continuing review of research and reporting findings and actions to the investigator, the R&D Committee, and the institution that is relying upon it;

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

(3) Ensuring prompt reporting by an investigator to the IRB of proposed changes in a research activity, and for ensuring that investigators will conduct the research activity in accordance with the terms of the IRB approval until any proposed changes have been reviewed and approved by the IRB, except when necessary to eliminate apparent immediate hazards to the subject;

(4) Ensuring prompt reporting to the IRB, appropriate institutional officials, department or agency head, ORO, and OHRP of: (i) any unanticipated problems involving risks to subjects or others, or any serious or continuing noncompliance with this policy or the requirements or determinations of the IRB, and (ii) any suspension or termination of IRB approval. **NOTE:** *Requirements for reporting to ORO are discussed in VHA Handbook 1058.01. VA studies under the oversight of FDA must be reported to FDA as specified in FDA regulations;*

(5) Determining whether a study meets the criteria in Appendix B for exemption from the requirements of the Common Rule and when a study requires limited IRB review. **NOTE:** *The investigator may not self-certify that a study is exempt. The R&D Committee must be responsible for initial approval and continuing review of the exempt research unless the research is assigned to another subcommittee (see VHA Handbook 1200.01);*

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

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

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

NOTE: *When the IRB of Record is directly operated and supported by a non-VA entity, the SOPs related to the review of VA research by the non-VA entity must be consistent with this directive and all regulations applicable to VA research.*

b. **IRB Functions.** Except when an expedited review procedure is used (see section 11) or when a limited IRB review process is used (see section 11), the IRB must review proposed VA research at convened meetings at which a majority of the voting members are present (quorum), including at least one member whose primary concerns are in nonscientific areas. Meetings may be held using audio technologies (e.g., telephone conference calls) provided that each participating IRB member has received all pertinent material prior to the meeting and can actively and equally participate in the discussion of all protocols. In order for the research to be approved, it must receive the approval of a majority of those members present at the meeting.

(1) The IRB may vote to approve, require modifications in (to secure approval), or disapprove a protocol, including exempt research activities under which limited IRB review is a condition of exemption.

(2) The IRB determines the approval period (not to exceed 1 year) requiring review by the convened IRB or for any research it determines requires continuing review, and whether verification should be required from sources other than the investigators that no substantive modifications have occurred since previous IRB review. Continuing review is not required for study activities described in section 9.e.(2) of this directive.

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

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

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

(1) For protocols reviewed by the convened IRB, the IRB minutes must document that the IRB determined that all of the criteria for approval of the research (see section 12) were satisfied.

(2) If the IRB approves a consent procedure which does not include, or which alters, any of the elements of informed consent (see section 17.h.), or waives the requirement to obtain a signed informed consent document (see section 18.c.), it must find and document that all criteria for the waiver have been satisfied.

(3) A copy of the final IRB minutes must be submitted to the R&D Committee in accordance with local SOPs. When the IRB of Record for a VA facility is the IRB of a

non-VA entity (e.g., IRB of another Federal entity, IRB of an academic affiliate), the non-VA entity must either:

(a) Provide VA with, or access to, unredacted copies of meeting minutes in a timely manner that allows the R&D Committee to review the IRB's deliberations on VA protocols; or

(b) Provide VA with, or access to, redacted copies of meeting minutes in a timely manner that allows the R&D Committee to review the IRB's deliberations on VA protocols. The non-VA entity must permit relevant VA personnel (including, but not limited to, ORO staff, local VA research office staff, local RCOs, and R&D Committee members) to review the unredacted meeting minutes within 2 business days of a written request from VA. Such review may occur at either site during normal business hours, or as otherwise mutually acceptable to VA and the IRB. **NOTE:** *Redacted copies of meeting minutes should include the parts of the minutes related to the IRB's review of VA protocols in a timely manner.*

9. IRB REVIEW OF RESEARCH

An institution's IRB of Record must:

a. Review and have authority to approve, require modifications in (to secure approval), or disapprove all research activities covered by this directive, except as provided in the **NOTE** below, including exempt research for which limited IRB review is a condition of exemption;

b. Require that information given to subjects (or LARs as appropriate) as part of informed consent is in accordance with section 17 of this directive. The IRB may require that information, in addition to that specifically mentioned in section 17 of this directive, be given to the subjects when in the IRB's judgment the information would meaningfully add to the protection of the rights and welfare of subjects. **NOTE:** Prospective IRB approval is not required if an activity meets the requirements for use of the emergency exemption from IRB approval in 21 CFR 56.104(c); informed consent must be obtained from the subjects (or LARs) unless both the investigator and a physician who is not otherwise participating in the clinical investigation certify in writing the requirements described in 21 CFR 50.23(a).

c. Require documentation of informed consent or waive documentation of informed consent in accordance with section 18 of this directive;

d. Notify investigators and the R&D Committee in writing of its decision to approve or disapprove the proposed research activity, or of modifications required to secure IRB approval of the research activity. If the IRB decides to disapprove a research activity, it 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;

e. Conduct continuing review of research requiring review by the convened IRB at intervals appropriate to the degree of risk, not less than once per year unless it meets the criteria described in section 9.e.(2);

(1) Notify the Investigator in writing if IRB approval expires and to stop all research activities except when stopping such interventions or interactions could be harmful to subjects. A list of the research subjects who could be harmed must be submitted immediately in writing to the IRB Chair. The IRB Chair must determine within 2 business days whether or not such interventions or interactions may continue;

(2) For research subject to the 2018 Requirements, unless the IRB determines otherwise, continuing review is not required in the following circumstances:

(a) Research eligible for expedited review; or

(b) Research reviewed by the IRB in accordance with the limited IRB review; or

(c) Research that has progressed to the point that it involves only one or both of the following, which are part of the IRB-approved study:

1. Data analysis, including analysis of identifiable private information or identifiable biospecimens, or

2. Accessing follow-up clinical data from procedures that subjects would undergo as part of clinical care.

(3) For research subject to the 2018 Requirements, if the IRB requires continuing review for any of the above circumstances, it must document its rationale for requiring continuing review in its communication to the investigator and institution. The R&D Committee is not required to conduct continuing review for studies approved by the IRB for which continuing review by the IRB is not required.

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

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

10. EXEMPT REVIEW

a. Exempt activities must follow the requirements of this section and as specified in the applicable exempt category. There are eight categories of exempt research activities described in Appendix B for research that must be compliant with the 2018 Requirements. Four of the categories include a provision for use of a limited IRB

review. There are six categories of exempt research activities described in Appendix A for research that is subject to the pre-2018 Requirements. **NOTE:** *None of the exempt research categories in the pre-2018 Requirements include a provision for use of a limited IRB review.*

b. Exempt determinations may be made by the IRB Chair, an experienced IRB member, or qualified administrative staff with expertise in applying human research exempt regulations. **NOTE:** *If the exempt activity involves PHI, a waiver of HIPAA authorization must be approved by the appropriate authority (IRB or Privacy Board or designated member of the IRB or Privacy Board), a written HIPAA authorization must be obtained from the subject or subject's LAR or a DUA for use or disclosure of a limited data set must be obtained.*

c. For exempt research activities involving the Investigator interacting with human subjects or obtaining information by educational tests, survey or interview procedures, or behavioral interventions, the following information must be given to the prospective human subject as applicable in writing or orally:

- (1) The activity is research;
- (2) Participation is voluntary;
- (3) Permission to participate can be withdrawn;
- (4) Permission for use of data can be withdrawn for exempt research activities involving the collection and use of identifiable data; and
- (5) Contact information for the VA Investigator.

d. If an exempt activity requires a limited IRB review, the limited IRB review must be completed prior to approval by the R&D Committee. When a limited IRB review is conducted, the IRB is not required to evaluate whether all of the IRB approval criteria in section 12 of this directive are satisfied.

e. When a limited IRB review is required for an exempt activity as described in this directive, the IRB must review the research to ascertain whether specific IRB approval criteria are met as described in this directive.

f. Exempt categories 2 and 3 listed in Appendix B require use of a limited IRB review if the information obtained is recorded by the investigator in such a manner that the identity of the human subjects can readily be ascertained, directly or through identifiers linked to the subjects. The IRB is required to conduct a limited review to make the determinations required by section 12.a.(7) (i.e., to determine that when appropriate, there are adequate provisions to protect the privacy of subjects and to maintain the confidentiality of data).

g. Exempt categories 7 and 8 listed in Appendix B always require use of a limited IRB review and broad consent.

(1) Research activities described in exempt category 7 require that an IRB conduct a limited review and make the determination required by section 12.a(8).

(2) Research activities described in exempt category 8 require an IRB to conduct a limited review to make the determinations required by section 12.a.(7) (i.e., to determine that when appropriate, there are adequate provisions to protect the privacy of subjects and to maintain the confidentiality of data). Additionally, the exemption requires that an IRB conduct a limited review to make the determination that the research to be conducted is within the scope of the broad consent under which the identifiable private information or identifiable biospecimens were collected.

(3) The following requirements must also be satisfied and documented as part of the limited IRB review for exempt category 8:

(a) Broad consent was obtained in accordance with section 17.f.;

(b) Documentation of informed consent was obtained in accordance with section 18.

h. Limited IRB review for applicable exempt activities may be done by the convened IRB, the IRB Chair, or delegated to one or more experienced reviewers from among voting IRB members.

i. Research determined to be exempt requires approval by the R&D Committee and requires continuing review by the R&D Committee as required by VHA Directive 1200.05 unless it is under the oversight of another subcommittee (e.g., Safety Review Subcommittee).

11. EXPEDITED REVIEW

a. An IRB may use the expedited review process to review the following:

(1) Any of the categories of research appearing on the list found at <https://www.hhs.gov/ohrp/regulations-and-policy/guidance/categories-of-research-expedited-review-procedure-1998/index.html> unless the reviewer(s) determines and documents that the study involves more than minimal risk;

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

(3) Research for which limited IRB review is a condition of exemption.

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

c. The reviewers may exercise all of the authorities of the IRB except that the reviewers may not disapprove the research. A research activity may be disapproved only after review in accordance with the non-expedited procedure set forth in section 9.

d. The IRB must have a written procedure for informing all IRB members, investigators, and the R&D Committee of the decision and the expedited review eligibility category for any expedited review actions.

12. CRITERIA FOR IRB APPROVAL

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

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

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

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

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

(3) Selection of subjects is equitable. In making this assessment, the IRB must take into account the purposes of the research and the setting in which the research is to be conducted and should be particularly cognizant of the special problems of research involving categories of populations who are vulnerable to coercion or undue influence, such as children, prisoners, individuals with impaired decision-making capacity, or economically or educationally disadvantaged persons;

(4) Informed consent will be sought from each prospective subject or the subject's LAR, in accordance with, and to the extent required by section 17;

(5) Informed consent will be appropriately documented or appropriately waived, in accordance with sections 17 and 18;

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

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

(8) For purposes of conducting the limited IRB review for exempt category 7 in Appendix B, the IRB does not need to make determinations (1) thru (7) in section 12a., and must make the following determinations instead:

(a) Broad consent for storage, maintenance, and secondary research use of identifiable private information or identifiable biospecimens is obtained in accordance with the requirements of section 17. **NOTE:** *VHA does not permit a broad HIPAA authorization for use and disclosure of PHI;*

(b) Broad consent is appropriately documented in accordance with sections 17 and 18; and

(c) If there is a change made for research purposes in the way the identifiable private information or identifiable biospecimens are stored or maintained, there are adequate provisions to protect the privacy of subjects and to maintain the confidentiality of data.

b. When some or all of the subjects are likely to be vulnerable to coercion or undue influence, such as children, prisoners, individuals with limited decision-making capacity, or educationally or economically disadvantaged persons, the protocol must include additional safeguards to protect the rights and welfare of these subjects.

13. REVIEW BY INSTITUTION

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

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

c. The R&D Committee must provide the final approval before the research can be initiated in accordance with VHA Handbook 1200.01. The research cannot be initiated by the Investigator until written notification is received from the ACOS/R&D that all required approvals have obtained.

14. SUSPENSION OR TERMINATION OF IRB APPROVAL

The IRB has authority to suspend or terminate approval of research that is not being conducted in accordance with the IRB's requirements, or that has been associated with unexpected serious harm to human subjects. Any suspension or termination of approval must include a statement of the reason(s) for the IRB's action and must be reported promptly to the investigator, appropriate IO(s), ORO (in accordance with VHA Handbook 1058.01), and appropriate Federal agencies according to applicable local, VA, and other Federal requirements. **NOTE:** *The IO has the authority to suspend or*

terminate IRB approval of research. This authority can be delegated by the IO to the Chief of Staff (COS). ORD has authority to suspend or terminate any research activity it is funding.

15. COLLABORATIVE RESEARCH

This section addresses human subjects research collaborations between VA and non-VA institutions. Collaboration is encouraged when VA investigators have a substantive role in the design, conduct, and/or analysis of the research. VA may also serve as a Coordinating Center for collaborative studies.

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

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

(2) VA investigators must submit a protocol or other documentation to their VA IRB of Record that clearly delineates which research activities will be conducted as the VA portion of the overall Collaborative Research study (e.g., by VA investigators on VA time or VA property).

(3) Each institution engaged in the Collaborative Research must use the informed consent document and HIPAA authorization required by its respective institutional policies for subjects recruited from that institution, or procedures requiring participation of the subjects at that institution. The informed consent document may contain information on the project as a whole as long as the document clearly describes which procedures will be performed under VA's auspices and which will be performed under a non-VA institution's auspices.

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

(b) The informed consent document and HIPAA authorization (for the VA portion of the collaborative study) must not contain inconsistent provisions.

b. **Research Data.** The protocol, addendum, and/or IRB of Record application must describe the data to be disclosed to collaborators, the entities to which the data are to be disclosed, how the data are to be transmitted, and how the transmitted data will be stored, retained, destroyed, and/or further disclosed and to whom. This includes data from individual subjects as well as other data developed during the research such as the analytic data and the aggregate data.

(1) Each VA facility must retain a complete record of all data obtained during the VA portion of the research in accordance with privacy requirements, the Federal Records Act, and VHA RCS10-1.

(2) All disclosures and data transmission must meet privacy and security requirements per VA Directive 6500, Managing Information Security Risk: VA Information Security Program, dated September 20, 2012; VA Handbook 6500, Risk Management Framework for VA Information Systems – Tier 3: VA Information Security Program, dated March 10, 2015; and VHA Directive 1605.01, any superseding policies.

(3) Agreements regarding data use and transmission must be executed as required as applicable in VHA Handbook 1200.12, Use of Data and Data Repositories in VHA Research, dated March 9, 2009, or any superseding policies revising or replacing it.

NOTE: *This directive does not preclude other applicable agreements required for the Collaborative Research (e.g., data use agreement).*

16. IRB RECORDS

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

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

(2) Minutes of IRB meetings as described in section 8.c.;

(3) Records of continuing review activities, including the rationale for conducting continuing review of research that otherwise would not require continuing review as described in section 9.e.(2);

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

(5) A roster of IRB members in the same detail as described in section 7.f. IRB records must include a resume or Curriculum Vitae for each voting IRB member that is updated at the time of appointment or reappointment;

(6) Written procedures for the IRB in the same detail as described in section 8.a.; and

(7) Statement of significant new findings provided to subjects, as described by section 17.e.(5);

(8) For research subject to the 2018 Requirements, the rationale for an expedited reviewer's determination that particular research appearing as a category on the expedited review list located at <https://www.hhs.gov/ohrp/regulations-and-policy/guidance/categories-of-research-expedited-review-procedure-1998/index.html> is more than minimal risk, and therefore not eligible for expedited review;

(9) Documentation specifying the responsibilities that the VA facility and an organization operating as the VA facility's IRB of Record each will undertake to ensure

compliance with the requirements of this directive, such as an MOU or an IRB Authorization Agreement or IRB reliance agreement.

b. All records must be accessible for inspection and copying (by authorized representatives of VA, ORO, OHRP, FDA, and other authorized entities or Federal department or agencies at reasonable times and in a reasonable manner. Records constituting a Federal record in VA research must be retained in accordance with VHA RCS 10-1.

c. IRB records are the responsibility of the local research office. The local VA facility must designate how the records can be accessed and where the records will be maintained or stored. **NOTE:** *Records of an IRB must be addressed in the MOU for the VA Facility's use of another entity's IRB (see section 16.a.(9) and VHA Handbook 1058.03). The MOU must ensure that all applicable Federal and VA regulations are met.*

17. GENERAL REQUIREMENTS FOR INFORMED CONSENT

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

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

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

b. For research subject to the 2018 Requirements, the following general requirements for informed consent must also be applied except for broad consent obtained in accordance with section 17.f:

(1) The prospective subject or the LAR must be provided with the information that a reasonable person would want to have in order to make an informed decision about whether to participate, and an opportunity to discuss that information;

(2) Informed consent must begin with a concise and focused presentation of the key information that is most likely to assist a prospective subject or LAR in understanding the reasons why one might or might not want to participate in the research. This part of the informed consent must be organized and presented in a way that facilitates comprehension.

NOTE: For some relatively simple research studies with limited risks or benefits, the entire informed consent document may be relatively brief and still satisfy section 17; and

(3) Informed consent as a whole must present information in sufficient detail relating to the research and must be organized and presented in a way that does not merely provide lists of isolated facts, but rather facilitates the prospective subject's or LAR's understanding of the reasons why one might or might not want to participate.

c. If a VA research study's informed consent approved by the IRB prior to January 21, 2019, requires modification, the general requirements described in section 17.b are not applicable unless the research study has been transitioned to the 2018 Requirements. The IRB responsible for oversight of the study must determine and document whether all subjects previously consented must be provided the information through a re-consenting or other notification process.

d. **Basic Elements of Informed Consent.** Except as provided in section 17.g. or h., in seeking informed consent the following information must be provided to each subject or LAR:

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

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

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

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

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

(6) For research involving more than minimal risk, an explanation as to whether any compensation is available, and an explanation as to whether any medical treatments are available if injury occurs and, if so, what they consist of, or where further information may be obtained (see section 24);

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

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

(9) For any research compliant with the 2018 Requirements, a statement about any research that involves the collection of identifiable private information or identifiable biospecimens:

(a) A statement that identifiers might be removed from the identifiable private information or identifiable biospecimens and that, after such removal, the information or biospecimens could be used for future research studies or distributed to another investigator for future research studies without additional informed consent from the subject or the LAR, if this might be a possibility; or

(b) A statement that the subject's information or biospecimens collected as part of the research, even if identifiers are removed, will not be used or distributed for future research studies.

(10) A statement that VA will provide treatment for research related injury in accordance with 38 CFR 17.85 (see section 24 of this directive). **NOTE:** *VA's statutory requirements in 38 CFR 17.85 apply regardless of inclusion of the information as part of the informed consent process.*

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

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

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

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

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

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

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

(7) For studies subject to the 2018 Requirements, a statement that the subject's biospecimens (even if identifiers are removed) may be used for commercial profit and whether the subject will or will not share in this commercial profit;

(8) For studies subject to the 2018 Requirements, a statement regarding whether clinically relevant research results, including individual research results, will be disclosed to subjects, and if so, under what conditions;

(9) For studies subject to the 2018 Requirements and involving biospecimens, whether the research will (if known) or might include whole genome sequencing (i.e., sequencing of a human germline or somatic specimen with the intent to generate the genome or exome sequence of that specimen); and

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

f. **Broad Consent.** For studies subject to the 2018 Requirements, an IRB may approve the use of a broad consent for storage, maintenance, and secondary research use of identifiable private information or identifiable biospecimens. Broad consent shall only be used in VA research when identifiable data or biospecimens are collected solely for research purposes. The form used to document broad consent may be standalone or combined with the informed consent for obtaining or collecting the identifiable private information or identifiable biospecimens. If a combined informed consent document is used, the information provided to subjects for broad consent must be clearly discernable from the informed consent for obtaining or collecting the identifiable private information or identifiable biospecimens. An IRB cannot waive documentation of informed consent for broad consent. The following information must be provided to each prospective subject or LAR:

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

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

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

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

(5) A statement that VA will provide treatment for research related injury in accordance with applicable Federal regulations;

(6) A general description of the types of research that may be conducted with the identifiable private information or identifiable biospecimens. This description must include sufficient information such that a reasonable person would expect that the broad consent would permit the types of research conducted;

(7) A description of the identifiable private information or identifiable biospecimens that might be used in research, whether sharing of identifiable private information or

identifiable biospecimens might occur, and the types of institutions or researchers that might conduct research with the identifiable private information or identifiable biospecimens;

(8) A description of the period of time that the identifiable private information or identifiable biospecimens may be stored and maintained (which could be indefinite), and a description of the period of time that the identifiable private information or identifiable biospecimens may be used for research purposes (which could be indefinite);

(9) Unless the subject or LAR will be provided details about specific research studies, a statement that they will not be informed of the details of any specific research studies that might be conducted using the subject's identifiable private information or identifiable biospecimens, including the purposes of the research, and that they might have chosen not to consent to some of those specific research studies;

(10) Unless it is known that clinically relevant research results, including individual research results, will be disclosed to the subject in all circumstances, a statement that such results may not be disclosed to the subject;

(11) An explanation of whom to contact for answers to questions about the subject's rights and about storage and use of the subject's identifiable private information or identifiable biospecimens, and whom to contact in the event of a research-related harm;

(12) If appropriate, a statement that informs VA research subjects that they or their insurance will not be charged for any costs related to the research;

(13) If appropriate, a statement that the subject's biospecimens (even if identifiers are removed) may be used for commercial profit and whether the subject will or will not share in this commercial profit; and

(14) If appropriate for research involving biospecimens, whether the research will (if known) or might include whole genome sequencing (i.e., sequencing of a human germline or somatic specimen with the intent to generate the genome or exome sequence of that specimen).

NOTE: *Broad consent can only be obtained for the use of information or biospecimens that are collected initially for research purposes. Subjects consented using a broad consent may withdraw their broad consent at any time. Broad consent cannot be approved by an IRB for studies subject to the pre-2018 Requirements.*

g. Waiver or Alteration of Informed Consent in Research Involving Public Benefit and Service Programs.

(1) An IRB must find and document the following to waive or alter consent in research involving public benefit and service programs conducted by or subject to the approval of State or local officials:

(a) The research or demonstration project is to be conducted by or subject to the approval of State or local government officials and is designed to study, evaluate, or otherwise examine:

1. Public benefit or service programs;
2. Procedures for obtaining benefits or services under those programs;
3. Possible changes in or alternatives to those programs or procedures; or
4. Possible changes in methods or levels of payment for benefits or services under those programs; and
5. The research could not practicably be carried out without the waiver or alteration.

(2) An IRB may waive the requirements described in section 17.a. through e. to obtain informed consent for research involving public benefit and service programs conducted by or subject to the approval of State or local officials if the IRB finds and documents the determinations described in section 17.g.(1). If an individual was asked to provide broad consent for the storage, maintenance, and secondary research use of identifiable private information or identifiable biospecimens in accordance with the requirements in section 17.f., and refused to consent, an IRB cannot waive consent for the storage, maintenance, or secondary research use of the identifiable private information or identifiable biospecimens.

(3) An IRB may approve an informed consent procedure that omits some, or alters some or all, of the elements of informed consent described in section 17.d. through 17.e. for research involving public benefit and service programs conducted by or subject to the approval of State or local officials provided the IRB finds and documents the determinations described in section 17.g.(1)(a). An IRB may not omit or alter any of the requirements described in sections 17.a. and 17.b. If a broad consent procedure is used, an IRB may not omit or alter any of the elements required under section 17.f.

h. **General Waiver or Alteration of Informed Consent in Research.** An IRB may waive consent or alter or omit the elements of informed consent.

(1) An IRB must find and document the following to waive or alter consent in research:

- (a) The research involves no more than minimal risk to the subjects;
- (b) The research could not practicably be carried out without the requested waiver or alteration;
- (c) If the research involves using identifiable private information or identifiable biospecimens, the research could not practicably be carried out without using such

information or biospecimens in an identifiable format for studies subject to the 2018 Requirements;

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

(e) Whenever appropriate, the subject or LAR will be provided with additional pertinent information after participation.

(2) An IRB may waive the requirements described in section 17.a. through 17.c. to obtain informed consent for research if the IRB finds and documents the determinations described in this section. If an individual was asked to provide broad consent for the storage, maintenance, and secondary research use of identifiable private information or identifiable biospecimens in accordance with the requirements in section 17.f., and refused to consent, an IRB cannot waive consent for the storage, maintenance, or secondary research use of the identifiable private information or identifiable biospecimens.

(3) An IRB may approve an informed consent procedure that omits some, or alters some or all, of the elements of informed consent described in section 17.d. for research provided the IRB finds and documents the determinations described in this section. An IRB may not omit or alter any of the requirements described in section 17.a. through 17.c. If a broad consent procedure is used, an IRB may not omit or alter any of the elements required under section 17.f.

i. **Screening, Recruiting, or Determining Eligibility.** For studies subject to the 2018 Requirements, the IRB may approve a research proposal in which an investigator will obtain information or biospecimens for the purpose of screening, recruiting, or determining the eligibility of prospective subjects without the informed consent of the prospective subject or the subject's LAR if either of the following conditions is met:

(1) The investigator will obtain information through oral or written communication with the prospective subject or LAR; or

(2) The investigator will obtain identifiable private information or identifiable biospecimens by accessing records or stored identifiable biospecimens.

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

j. **Posting of Clinical Trial Informed Consent Forms.** For studies subject to the 2018 Requirements, if a VA research study is a clinical trial, one IRB-approved informed consent form used to enroll subjects, unless the IRB waived documentation of informed consent, must be posted by either the investigator or the Federal department or agency conducting or supporting the study.

NOTE: *Multiple versions of the IRB-approved informed consent form are not required to be posted. If the study involves multiple sites, only one IRB-approved informed consent form for the entire clinical trial must be posted and not from separate participating sites.*

(1) The informed consent form must be posted after the clinical trial is closed to recruitment and no later than 60 days after the last study visit by any subject as described in the IRB-approved protocol. For multi-site studies, it applies when the entire study has closed to subject recruitment. Consent forms must be posted on either <https://clinicaltrials.gov> or a docket folder on <http://Regulations.gov> (Docket ID: HHS-OPHS-2018-0021).

(2) For any ORD-funded clinical trial, the applicable ORD funding service will be responsible for posting the informed consent form.

(3) For a clinical trial funded or supported by a Federal agency or department other than VA, the awardee is responsible for posting the informed consent form.

(4) For a clinical trial funded or supported by a non-Federal agency or department (e.g., university, industry, nonprofit organization) or not funded, the VA Investigator conducting the clinical trial is responsible for ensuring that the informed consent form is posted. If the clinical trial includes multiple sites engaged in the clinical trial, an agreement must exist specifying who is responsible for posting the informed consent form.

(5) Any proprietary or personal information (such as names and phone numbers) must be redacted prior to posting the informed consent form.

(6) The informed consent form must be posted on <https://clinicaltrials.gov> or a docket folder on <http://Regulations.gov> (Docket ID: HHS-OPHS-2018-0021).

(7) The informed consent requirements in this directive are not intended to preempt any applicable Federal, State, or local laws (including tribal law passed by an official governing body of an American Indian or Alaska Native tribe) that require additional information to be disclosed in order for informed consent to be legally effective.

(8) Nothing in this policy is intended to limit the authority of a physician to provide emergency medical care to the extent that the physician is permitted to do so under applicable Federal, State, or local law.

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

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

(2) The consent for research does not give legal authority to disclose the photographs, video, and/or audio recordings outside VA. A HIPAA authorization is needed to make such disclosures.

18. DOCUMENTATION OF INFORMED CONSENT

a. Except as provided in section 18.c., informed consent shall be documented by the use of a written consent form approved by the IRB and signed and dated by the subject or the subject's LAR. A physical or electronic copy must be given or made available to the person signing the form.

b. Except as provided in section 18.c., the informed consent form may be either of the following:

(1) A written consent document that meets the requirements of informed consent as described in section 17 that gives the subject or the subject's LAR adequate opportunity to read the informed consent before it is signed, or the form may be read to the subject or the subject's LAR; or

(2) A short written informed consent form stating that the elements of informed consent required in section 17 have been presented orally to the subject or the subject's LAR. If the research is subject to the 2018 Requirements, the written informed consent form must also state that key information described in section 17.b.(1) was presented first to the subject or the subject's LAR before any other information, if any, was provided. When this method is used, there must be a witness to the oral presentation. The IRB must approve a written summary of what is to be said in the oral presentation to the subject or the LAR. Only the short form itself is to be signed by the subject or the subject's LAR. However, the witness must sign both the short form and a copy of the summary, and the person actually obtaining consent must sign a copy of the summary. A copy of the summary must be given to the subject or the subject's LAR, in addition to a copy of the short form. **NOTE:** *The IRB cannot waive the requirement for a witness or witness signature when the short form consent is used.*

c. The IRB may waive the requirement for the investigator to obtain a signed informed consent form for some or all subjects if it finds any of the following:

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

(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; or

(3) For studies subject to the 2018 Requirements, if the subjects or LARs are members of a distinct cultural group or community in which signing an informed consent form is not the norm, that the research presents no more than minimal risk of harm to

subjects and provided that there is an appropriate alternative mechanism for documenting that informed consent was obtained.

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

e. Documentation of consent may be obtained electronically so long as the informed consent process meets all requirements in section 18 of this directive and VA requirements for use of electronic signatures.

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

a. Research that involves provision of in vitro fertilization services can be conducted by VA investigators while on official VA duty, at VA facilities, or at VA-approved off-site facilities. This includes prospective and retrospective research involving provision of or the enhancement of FDA-approved methods of in vitro fertilization for studies involving consenting subjects, both male and female, undergoing or who have undergone in vitro fertilization for the treatment of certain forms of human infertility. In vitro fertilization is any fertilization of human ova that occurs outside the body of a female, either through a mixture of donor human sperm and ova or by any other means.

b. Prospective and retrospective studies that enroll or include pregnant subjects who conceived through in vitro fertilization or other artificial reproductive technologies are permitted.

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

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

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

(1) Where scientifically appropriate, preclinical studies, including studies on pregnant animals, and clinical studies, including studies on non-pregnant women, have been conducted and provide data for assessing potential risks to pregnant women and fetuses;

(2) The risk to the fetus is caused solely by interventions or procedures that hold out the prospect of direct benefit for the woman or fetus. If there is no such prospect of benefit, then the risk to the fetus is not greater than minimal and the purpose of the research is the development of important biomedical knowledge that cannot be obtained by any other means;

(3) Any risk is the least possible for achieving the objectives of the research;

(4) If the research holds out the prospect of direct benefit to the pregnant woman, the prospect of a direct benefit both to the pregnant woman and the fetus, or no prospect of benefit for the woman nor the fetus when risk to the fetus is not greater than minimal and the purpose of the research is the development of important biomedical knowledge that cannot be obtained by any other means, her consent is obtained in accord with the informed consent provisions of this directive;

(5) Each individual providing consent under (2) or (4) of this section is fully informed regarding the reasonably foreseeable impact of the research on the fetus or neonate;

(6) For children who are pregnant, assent and permission are obtained in accordance with the provisions of 45 CFR Part 46, Subpart D. Research involving clinical interventions with the potential of greater than minimal risk cannot be conducted by VA for children who are pregnant;

(7) No inducements, monetary or otherwise, will be offered to terminate a pregnancy;

(8) Individuals engaged in the research will have no part in any decisions as to the timing, method, or procedures used to terminate a pregnancy; and

(9) Individuals engaged in the research will have no part in determining the viability of a neonate.

f. VA investigators cannot conduct interventions in research that include neonates while on official VA duty, at VA facilities, or at VA-approved off-site facilities. VA investigators may conduct research involving noninvasive monitoring of neonates if the research is determined by the IRB to be minimal risk. Prospective observational and retrospective record review studies that involve neonates or neonatal outcomes are permitted.

g. The reviewing IRB must have the appropriate expertise to evaluate any VA research involving neonates and must comply with the requirements of 45 CFR 46.205. The VA medical facility Director must certify that the medical facility has sufficient expertise in neonatal health to conduct the proposed research.

20. RESEARCH INVOLVING PRISONERS AS SUBJECTS

a. Research involving prisoners cannot be conducted by VA investigators while on official VA duty, at VA facilities, or at VA-approved off-site facilities unless a waiver has been granted by the CRADO. Waiver requests must be submitted electronically to the CRADO by the VA medical facility Director with the following documents:

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

b. If such a waiver is granted, the research must comply with the requirements of 45 CFR 46.301 - 46.306.

21. RESEARCH INVOLVING CHILDREN AS RESEARCH SUBJECTS

a. VA is authorized to care for Veterans and to conduct research that supports the mission of VHA and that enhances the quality of health care delivery to Veterans. Therefore, research involving children must be reviewed carefully by the IRB for its relevance to VA and must not present greater than minimal risk to the children. The VA medical facility Director must approve participation in the proposed research that includes children (see guidance at: <http://www.research.va.gov/resources/policies/default.cfm>).

NOTE: For purposes of this directive, research involving biological specimens or data obtained from children is considered to be research involving children even if de-

identified. If the biological specimens or data were previously collected, they must have been collected under applicable Federal policies and ethical guidelines.

b. The IRB must have the appropriate expertise to evaluate any VA research involving children and must comply with the requirements of 45 CFR 46.401 - 46.404 and 46.408.

NOTE: *For purposes of this directive, research involving children does not include neonates. VA research involving neonates must follow section 19 of this directive.*

22. CERTIFICATES OF CONFIDENTIALITY

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

b. Disclosure of identifiable information outside of the research team is prohibited, except:

(1) When there is a Federal, State or local law requiring disclosure of information, such as for reporting child or elder abuse or communicable diseases;

(2) When the subject consents for such disclosure;

(3) For medical treatment of the individual made with consent of the subject; or

(4) When the information is used for other scientific research that is in compliance with applicable Federal regulations governing the protection of human subjects in research.

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

(1) For studies in which information about the subject's participation will be included in the subject's VHA medical record, information must be given to the prospective

subjects as part of the informed consent process that information regarding study participation will be included in the medical record; and

(2) For studies in which the IRB requires a written informed consent, the informed consent document approved by the IRB must include a statement that the study has a Certificate of Confidentiality. **NOTE:** *The HHS agencies that issue Certificates of Confidentiality usually have guidance specific to the issuing agency on statements that must be included in informed consent documents describing Certificates of Confidentiality.*

d. As of June 13, 2017, all previously issued Certificates of Confidentiality are subject to the requirements of Section 2012 of the 21st Century Cures Act, which amends Subsection (d) of section 301 of the Public Health Service Act (42 U.S.C. 241). (See section 22.a.)

23. HIPAA AUTHORIZATION

a. **Written Authorization.** In accordance with the HIPAA Privacy Rule at 45 CFR 164.508, a written authorization signed by the individual to whom the information or record pertains is required when VA medical facilities need to access, collect, develop, use, or disclose individually-identifiable health information for a purpose other than treatment, payment, or health care operations (e.g., research) unless there is legal authority (e.g., waiver, limited data set with data use agreement, etc.) to use and/or disclose such information (see VHA Directive 1605.01).

(1) Authorization must meet all VHA Privacy requirements detailed in VHA Directive 1605.01. The written HIPAA authorization may either be a standalone document or combined with the research informed consent approved by the IRB. If a standalone document is used as the written HIPAA authorization, VA Form 10-0493: Authorization for Use and Release of Individually Identifiable Health Information Collected for VHA Research located at <http://vaww.va.gov/vaforms/medical/pdf/10-0493-fill.pdf> must be used (**NOTE:** *This is an internal VA Web site that is not available to the public.*);

(2) All potential disclosures to a non-VHA entity must be listed within the written authorization;

(3) The PO must review the written HIPAA authorization to ensure it contains all required elements and is consistent with all privacy requirements before the PI can begin to use or collect the individual's information based on an approved research protocol (see VHA Directive 1605.01); and

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

b. **Waiver of HIPAA Authorization.** An investigator requesting a waiver of HIPAA authorization must provide information sufficient to allow the IRB or Privacy Board to make the required determination. In accordance with the HIPAA Privacy Rule at 45 CFR 164.512(i)(2), the IRB must document the following:

- (1) Identification of the IRB of Record;
- (2) Date of IRB approval of waiver of HIPAA authorization;
- (3) Statement that the waiver of HIPAA authorization satisfies the following criteria:
 - (a) The use or disclosure of PHI involves no more than a minimal risk to the privacy of individuals based on the presence of the following elements:
 1. An adequate plan to protect the identifiers from improper use and disclosure;
 2. An adequate plan to destroy the identifiers at the earliest opportunity consistent with conduct of research, unless there is a health or research justification for retaining the identifiers or such retention is otherwise required by law (e.g., to satisfy records retention requirements). **NOTE:** *Records are required to be disposed in accordance with VHA RCS 10-1; and*
 3. Adequate written assurances that the PHI will not be reused or disclosed except as required by law, for authorized oversight of the research for which the use or disclosure of PHI 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) Identification of the IRB review procedure used to approve the waiver of HIPAA authorization (either convened IRB review procedures or expedited review procedures); and
- (6) Signature of the Chair of the IRB, or a qualified voting member of the IRB designated by the Chair, on the HIPAA authorization waiver document. **NOTE:** *Signatures may be electronic if they meet VA requirements for electronic signatures.*

NOTE: *If the IRB does not document the waiver or alteration of authorization as required, the waiver or alteration of authorization is not valid. If the IRB of record cannot provide a waiver or alteration of authorization, a properly constituted Privacy Board may be used to review and approve the waiver request in accordance with 45 CFR 164.512(i) (see VHA Directive 1605.01).*

NOTE: *PHI obtained in research for which the IRB of Record or Privacy Board has waived the requirements to obtain a HIPAA authorization may not be disclosed outside VA unless the VA facility PO ensures and documents VA's authority to disclose the PHI to another institution. A waiver of HIPAA authorization by itself is not sufficient to fulfill*

the requirements of other applicable privacy regulations and statutes such as the Privacy Act of 1974 (5 U.S.C. 552a).

c. **Activities Preparatory to Research.** VA investigators may use individually-identifiable health information to prepare a research protocol prior to submission of the protocol to the IRB for approval without obtaining a HIPAA authorization or waiver of authorization.

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

- (a) Access to PHI is only to prepare a protocol;
- (b) No PHI will be removed from the covered entity (i.e., VHA); and
- (c) Access to PHI is necessary for preparation of the research protocol.

(2) Non-VA researchers may not obtain VA information for preparatory to research activities (see VHA Directive 1605.01).

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

(a) Must only record aggregate data. The aggregate data may only be used for background information to justify the research or to show that there are adequate numbers of potential subjects to allow the investigator to meet enrollment requirements for the research study;

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

(c) Must not use any individually identifiable information to recruit research subjects.

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

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

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

24. TREATMENT OF RESEARCH-RELATED INJURIES

a. VA medical facilities, including joint VA-DoD Federal health care centers, must provide necessary medical treatment (i.e., not just emergency treatment) to a research

subject injured as a result of participation in a research study approved by a VA R&D Committee and conducted under the supervision of one or more VA employees (38 CFR 17.85). This requirement does not apply to:

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

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

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

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

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

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

25. INTERNATIONAL RESEARCH

a. VA international research is defined as any VA-approved research conducted at international sites (i.e., not within the United States (U.S.), its territories, or Commonwealths), any VA-approved research using either identifiable or de-identified human biological specimens or identifiable or de-identified human data originating from international sites, or any VA-approved research that entails sending such specimens or data out of the U.S. This definition applies regardless of the funding source (funded or unfunded) and to research conducted through any mechanism of support including MOUs, CRADAs, grants, contracts, or other agreements. **NOTE:** *For the purposes of this directive, research conducted at U.S. military bases, ships, or embassies is not considered international research.*

(1) Sending specimens or data to individuals with VA appointments at international sites (e.g., a WOC appointment, a VA investigator on sabbatical at an international site) is considered international research. Remote use of data that is maintained on VA computers within the U.S. or Puerto Rico and U.S. territories accessed via a secure connection is not considered international research.

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

(3) International research does not include studies in which VA is only one of multiple participating sites where the overall study-wide PI is not a VA investigator (i.e., the PI for the study as a whole is not a VA investigator).

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

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

26. TRAINING REQUIREMENTS

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

27. RECORDS MANAGEMENT

All records regardless of format (paper, electronic, electronic systems) created in this directive must be managed per the National Archives and Records Administration (NARA) approved records schedules found in VHA RCS 10-1. Any questions regarding any aspect of records management should be directed to the VA medical facility Records Manager or Records Liaison.

28. REFERENCES

- a. 5 U.S.C. 552a, The Privacy Act of 1974.
- b. 21 U.S.C. 321-60, Federal Food, Drug, and Cosmetic Act.
- c. 38 U.S.C. 501, Rules and Regulations.
- d. 38 U.S.C. 1710, Eligibility For Hospital, Nursing Home, and Domiciliary Care.
- e. 38 U.S.C. 5701, Confidential Nature of Claims.
- f. 38 U.S.C. 5705, Confidentiality of Medical Quality-Assurance Records.

- g. 38 U.S.C. 7331, Informed Consent.
- h. 38 U.S.C. 7332, Confidentiality of certain medical records.
- i. 38 U.S.C. 7334, Regulations.
- j. 42 U.S.C. 241, 21st Century Cures Act.
- k. 42 U.S.C. 262, Regulation of Biological Products.
- l. 10 CFR Part 20, Standards for Protection Against Radiation.
- m. 10 CFR Part 35, Medical Use of Byproduct Material.
- n. 21 CFR Part 11, Electronic Records; Electronic Signatures.
- o. 21 CFR Part 50, Protection of Human Subjects.
- p. 21 CFR Part 56, IRBs.
- q. 21 CFR Part 312, Investigational New Drug Application.
- r. 21 CFR Part 812, Investigational Device Exemptions.
- s. 38 CFR Part 16, Protection of Human Subjects.
- t. 38 CFR Part 17, Medical.
- u. 45 CFR Part 46, Protection of Human Subjects, Subpart A – Basic HHS Policy for Protection of Human Subjects; Subpart B – Additional Protections for Pregnant Women, Human Fetuses and Neonates Involved in Research; Subpart C – Additional Protections Pertaining to Biomedical and Behavioral Research Involving Prisoners as Subjects; and Subpart D – Additional Protections for Children Involved as Subjects in Research.
- v. 45 CFR Part 160, General Administrative Requirements.
- w. 45 CFR Part 164, Security and Privacy, Subpart E –Privacy of Individually Identifiable Health Information.
- x. Expedited Review Categories, 63 FR 60364, dated November 9, 1998.
- y. VA Directive 6500, Managing Information Security Risk: VA Information Security Program dated September 20, 2012.
- z. VA Handbook 6500, Risk Management Framework for VA Information Systems - Tier 3: VA Information Security Program, dated March 10, 2015.
- aa. VHA Directive 1200, Research and Development Program, dated May 13, 2016.

- bb. VHA Directive 1200.02(1), Research Business Operations, dated March 10, 2017.
- cc. VHA Directive 1605.01, Privacy and Release of Information, dated August 31, 2016.
- dd. VHA Directive 2012-030, Credentialing of Health Care Professionals, dated October 11, 2012.
- ee. VHA Handbook 1004.01, Informed Consent for Clinical Treatments and Procedures, dated August 14, 2009.
- ff. VHA Handbook 1058.01, Research Compliance Reporting Requirements, dated June 17, 2015.
- gg. VHA Handbook 1058.03, Assurance of Protection for Human Subjects in Research, dated November 21, 2014.
- hh. VHA Handbook 1100.19, Credentialing and Privileging, dated October 15, 2012.
- ii. VHA Handbook 1108.04, Investigational Drugs and Supplies, dated February 29, 2012.
- jj. VHA Handbook 1200.01, Research and Development (R&D) Committee, dated June 16, 2009.
- kk. VHA Handbook 1200.08, Safety of Personnel Engaged in Research, dated March 6, 2009.
- ll. VHA Handbook 1200.12, Use of Data and Data Repositories in VHA Research, dated March 9, 2009.
- mm. VHA Handbook 1200.16, Off Site Research, dated November 18, 2018.
- nn. VHA Handbook 1200.17, Department of Veterans Affairs (VA) Nonprofit Research and Education Corporations Authorized By Title 38 U.S.C. Sections 7361 Through 7366, dated April 27, 2016.
- oo. VHA Handbook 1605.02, Minimum Necessary Standard for Protected Health Information, dated January 23, 2013.
- pp. VHA Handbook 1605.04, Notice of Privacy Practices, dated October 7, 2015.
- qq. VHA Handbook 1907.01, Health Information Management and Health Records, dated March 19, 2015.

CATEGORIES OF EXEMPT RESEARCH: PRE-2018 REQUIREMENTS

1. USE OF CATEGORIES

Use of the exemption categories for research subjects who are pregnant women, prisoners, or children is as follows:

a. **Pregnant Women.** Each of the exemption categories may be applied to research involving pregnant women if the conditions of the exemption are met.

b. **Prisoners.** The exemptions in this Appendix do not apply to research involving prisoners.

c. **Children.** The exemptions for Categories 1, 4, 5, and 6 may be applied to research subjects who are children if the conditions of the exemption are met. Exempt category 2 of this section may only apply to research subject to 45 CFR 46, Subpart D involving educational tests or the observation of public behavior when the investigator(s) do not participate in the activities being observed.

2. CATEGORIES OF EXEMPT RESEARCH

a. **Category 1.** Research conducted in established or commonly accepted educational settings, involving normal educational practices, such as:

(1) Research on regular and special education instructional strategies, or

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

b. **Category 2.** Research involving the use of educational tests (cognitive, diagnostic, aptitude, achievement), survey procedures, interview procedures or observation of public behavior, unless:

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

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

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

(1) The human subjects are elected or appointed public officials or candidates for public office; or

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

d. **Category 4.** Research involving the collection or study of existing data, documents, records, pathological specimens, or diagnostic specimens, if these sources are publicly available or if the information is recorded by the investigator in such a manner that subjects cannot be identified, directly or through identifiers linked to the subjects.

e. **Category 5.** Research and demonstration projects which are conducted by or subject to the approval of Federal department or agency heads, and which are designed to study, evaluate, or otherwise examine:

(1) Public benefit or service programs;

(2) Procedures for obtaining benefits or services under those programs;

(3) Possible changes in or alternatives to those programs or procedures; or

(4) Possible changes in methods or levels of payment for benefits or services under those programs.

NOTE: *The determination of exempt status for research and demonstration projects meeting the criteria for exempt category 5 in paragraph e. in this Appendix must be made by the Under Secretary for Health on behalf of the Secretary of VA, after consultation with Office of Research and Development (ORD), Office of Research Oversight (ORO), Office of General Counsel (OGC), and other experts, as appropriate.*

f. **Category 6.** Taste and food quality evaluation and consumer acceptance studies:

(1) If wholesome foods without additives are consumed; or

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

CATEGORIES OF EXEMPT RESEARCH: 2018 REQUIREMENTS**1. USE OF CATEGORIES**

Use of the exemption categories for research subjects who are pregnant women, prisoners, or children is as follows:

a. **Pregnant Women.** Each of the exemptions in this Appendix may be applied to research involving pregnant women if the conditions of the exemption are met.

b. **Prisoners.** The exemptions in this Appendix do not apply to research involving prisoners, except for research aimed at involving a broader subject population that only incidentally includes prisoners.

c. **Children.** The exemptions for Categories 1, 4, 5, 6, 7, and 8 may be applied to research subjects who are children if the conditions of the exemption are met. Exempt category 2a. and b. of this section may only apply to research subject to 45 CFR 46, Subpart D involving educational tests or the observation of public behavior when the investigator(s) do not participate in the activities being observed. Paragraph 2.b.(3) of this section may not be applied to research subject to 45 CFR 46, Subpart D.

2. CATEGORIES OF EXEMPT RESEARCH

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

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

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

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

(3) The information obtained is recorded by the investigator in such a manner that the identity of the human subjects can readily be ascertained, directly or through identifiers linked to the subjects, and an IRB conducts a limited IRB review to make the determination required by section 12.a.(7) of this directive.

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

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

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

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

(3) The information obtained is recorded by the investigator in such a manner that the identity of the human subjects can readily be ascertained, directly or through identifiers linked to the subjects, and an IRB conducts a limited IRB review to make the determination required by section 12.a.(7) of this directive.

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

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

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

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

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

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

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

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

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

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

NOTE: *The determination of exempt status for research and demonstration projects meeting the criteria for exempt category 5 in section e. in this Appendix must be made by the Under Secretary for Health on behalf of the Secretary of VA, after consultation*

with Office of Research and Development (ORD), Office of Research Oversight (ORO), Office of General Counsel (OGC), and other experts, as appropriate.

f. **Category 6.** Taste and food quality evaluation and consumer acceptance studies:

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

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

g. **Category 7.** Storage or maintenance for secondary research for which broad consent is required: Storage or maintenance of identifiable private information or identifiable biospecimens for potential secondary research use if an IRB conducts a limited IRB review and makes the determinations required by section 12.a.(8) of this directive.

h. **Category 8.** Secondary research for which broad consent is required: Research involving the use of identifiable private information or identifiable biospecimens for secondary research use, if the following criteria are met:

(1) Broad consent for the storage, maintenance, and secondary research use of the identifiable private information or identifiable biospecimens was obtained in accordance with section 17.f of this directive;

(2) Documentation of informed consent or waiver of documentation of consent was obtained in accordance with section 17 of this directive;

(3) An IRB conducts a limited IRB review and makes the determination required by section 12.a.(7) and makes the determination that the research to be conducted is within the scope of the broad consent referenced in paragraph h.(1) of this section; and

(4) The investigator does not include returning individual research results to subjects as part of the study plan. This provision does not prevent an investigator from abiding by any legal requirements to return individual research results.

**DOCUMENTATION AND REVIEW OF HUMAN SUBJECTS RESEARCH
CONDUCTED BY VHA PROGRAM OFFICE EMPLOYEES****1. PURPOSE**

This Appendix sets forth procedures for oversight of human subjects research conducted by individuals acting as Veterans Health Administration (VHA) Program Office employees, regardless of duty station. The requirements set forth in this Appendix do not apply to research activities conducted in any capacity other than as an employee of a VHA Program Office. **NOTE:** *VHA Veterans Integrated Services Network (VISN) employees wishing to conduct research must secure oversight from an appropriate VHA research facility within their VISN and obtain written approval of the arrangement from the relevant VA medical facility Director and VISN Director.*

2. PROGRAM OFFICE RESEARCH PROJECT DOCUMENTATION

a. **Documentation Requirement.** All human subjects research conducted by individuals acting as Program Office employees must be prospectively documented in writing by the employee's supervisor (see Appendix D). If and as applicable, all individuals conducting research as Program Office employees must provide a copy of the supervisor's documentation to the research review committees responsible for oversight of their research (see section 3 below).

b. **Documentation Content.** The Program Office documentation must include:

(1) The title of the research project, which must match the title of the research project to be reviewed by the research review committee(s);

(2) A brief description of the research project, which must match the description of the research project to be reviewed by the research review committee(s);

(3) The expiration date, not to exceed 36 months. (**NOTE:** *Documentation may be renewed as necessary for continuation of ongoing research*);

(4) The signature of the employee's Program Office supervisor.

3. REVIEW OF RESEARCH

a. **Human Research Protection Program.** Research conducted by Program Office employees that requires review, whether limited or otherwise, by an Institutional Review Board (IRB) in accordance with the Common Rule for the Protection of Human Subjects in 38 CFR Part 16 (as effective while this directive is in force) must be performed under the oversight of a VA Human Research Protection Program (HRPP), except as described in section 3b. below.

(1) **Clinical Research at VA Facilities.** Program Office employees conducting clinical research at a VA facility must:

(a) Secure the required appointment, privileges, and scope of practice from the VA facility in which the activities are to be conducted; and

(b) Conduct the research under the oversight of that facility's HRPP.

(2) **Non-Clinical Research.** Individuals acting as Program Office employees in the conduct of research, which does not require clinical privileges but does require IRB review, must secure oversight of their research from a VA facility HRPP, except as described in subparagraph 3(b) below.

(a) Program Office employees who hold an appointment (and applicable research scope of practice) at a VA facility may routinely receive oversight of their human research by the HRPP of that facility. Such oversight must be acknowledged by the HRPP and documented in writing, either separately or by specific reference in the approved study protocol.

(b) Program Office employees who do not hold a research appointment at a VA facility may secure oversight of individual human research studies from the HRPP of another VA facility. This would necessitate obtaining an appointment (such as a WOC) at that facility. Such oversight must be acknowledged by the HRPP and documented in writing, either separately or by specific reference in the approved study protocol.

b. **Research at a Non-VA Facility.** Under special circumstances, individuals acting as Program Office employees may be approved to conduct human research at a non-VA facility that holds a Federalwide Assurance.

(1) In lieu of oversight being provided through a VA HRPP described in section 3a above, the Program Office employee conducting such research must do so under a written agreement signed by the employee's Program Office Director (or Chief Officer) and the IO of the entity operating the facility. The agreement must ensure:

(a) Appropriate review, approval, and continuing oversight of the research in accordance with applicable Federal requirements; and

(b) Notification of the employee's Program Office Director (or Chief Officer) and the VHA Office of Research Oversight (ORO) of any and all events reportable to ORO as required by, and within the timelines specified, by VHA Handbook 1058.01, Research Compliance Reporting Requirements, dated June 15, 2015.

(2) A copy of the agreement must be provided to the ORO Executive Director within 5 business days of execution.

c. **Notification of Noncompliance.** In addition to any other required notifications, the IO of any VA HRPP exercising oversight of a Program Office employee's research must notify the employee's Program Office Director (or Chief Officer) and ORO of any and all events reportable to ORO as required by, and within the timelines specified, by VHA Handbook 1058.01.

SAMPLE FORMAT FOR DOCUMENTATION OF PROGRAM OFFICE RESEARCH

Title of Research Project: *(NOTE: Title must match submission to IRB or other research review committee, if and as applicable.)*

Description of Research Project: *(NOTE: Description must be consistent with submission to IRB or other research review committee, if and as applicable.)*

Investigator(s): *(List Program Office investigators)*

Verification of Program Office Supervisor

As the Supervisor of the employee(s) listed above, I verify that the research project described above is an authorized Program Office activity.

Signature of Supervisor

Date:

Name:

Title:

Program Office:

Expiration Date: *(Not to exceed 36 months from Supervisor Signature date. May be renewed as necessary for continuation of ongoing research).*

NOTE: *Each Program Office investigator must retain a copy of this documentation for a minimum of 5 years after completion of the project and in accordance with any applicable Federal records retention schedules.*