HUMAN RESEARCH PROTECTION PROGRAM

JAMES H. QUILLEN VA MEDICAL CENTER
(MOUNTAIN HOME, TENNESSEE)

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Abbreviations

ACOS/R&D	Associate Chief of Staff for Research & Development
AO/R&D	Administrative Officer for Research & Development
CITI	Collaborative Institutional Training Initiative
CFR	Code of Federal Regulations
Co-I	Co-Investigator
COS	Chief of Staff
CRADA	Cooperative Research and Development Agreement
CRADO	Chief Research and Development Officer
EPA	Environmental Protection Agency
ETSU	East Tennessee State University
FDA	Food and Drug Administration
FCOI	Financial Conflict of Interest
FWA	Federal Wide Assurance
HRPP	Human Research Protection Program
IAW	In Accordance With
IO	Institutional Official
IRB	Institutional Review Board
ISSO	Information System Security Officer
JHQVAMC	James H. Quillen Veterans Affairs (VA) Medical Center
LSI	Local Site Investigator
MCD	Medical Center Director
MOU	Memorandum of Understanding
NIH	National Institutes of Health
OHRP	Office for Human Research Protection
ORO	Office of Research Oversight
ORD	Office of Research and Development
PI	Principal Investigator
PO	Privacy Officer
RCO	Research Compliance Officer
RISP	Research Information Security Program
R&D	Research and Development
R&DC	Research and Development Committee
RSO	Research Safety Officer
SRS	Subcommittee on Research Safety
SO	Signatory Official
SOP	Standard Operating Procedures
WOC	Without Compensation

1. Human Research Protection Program (HRPP) Overview

a. The HRPP is a comprehensive system to ensure the protection of human subjects participating in research. 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. The HRPP consists of a variety of individuals and committees such as:

- Medical Center Director
- Chief of Staff
- Associate Chief of Staff for Research and Development (ACOS/R&D)
- Administrative Officer for R&D (AO/R&D)
- Research Compliance Officer (RCO)
- Privacy Officer (PO)
- Information System Security Officer (ISSO)
- Research Pharmacist
- Research Safety Officer
- Radiation Safety Officer
- Principal Investigators (PI)
- Study Staff
- R&D Committee (R&DC)
- East Tennessee State University (ETSU)/ VA Institutional Review Board (IRB)
- Subcommittee on Research Safety (SRS)
- Integrated Ethics Council

2. Human Research Definitions

38 CFR 16.102; 21 CFR 50.3; 21 CFR 56.102; 21 CFR 312.3; 21 CFR 812.3; 45 CFR 46.102; VHA Directive1200.05

a. Research:

1. Research is defined by 38 CFR 16.102(d) and 45 CFR 46.102(d) as a systematic investigation (systematic investigation typically means a predetermined method for studying a specific topic, testing a specific hypothesis(es), answering a specific question or developing theory), including research development, testing and evaluation, designed to develop or contribute to generalizable knowledge (generalizable knowledge typically means that results or conclusions of the activity are intended to be extended beyond a single person or an internal program). Activities which meet this definition constitute research for purposes of this policy, whether or not they are conducted or supported under a program which is considered research for other purposes. For example, some demonstration and service programs may include research activities. The following activities are not considered research:

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

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

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

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

2. Investigation is defined by the FDA in 21 CFR 812.3(h) as a clinical investigation or research involving one or more subjects to determine the safety or effectiveness of a device.

3. Clinical Investigation is any experiment that involves a test article and one or more human subjects, and that either must meet the requirements for prior submission to the Food and Drug Administration under section 505 (i) or 520 (g) of the Federal Food, Drug, and Cosmetic Act, or need not meet the requirements for prior submission to the Food and Drug Administration under these sections of the Federal Food, Drug and Cosmetic Act, but the results of which are intended to be later submitted to, or held for inspection by, the Food and Drug Administration as part of an application for a research or marketing permit. The terms research, clinical research, clinical study, study, and clinical investigation are synonymous for purposes of FDA regulations. [21 CFR 50.3(c), 21 CFR 56.102(c)].

4. Test article is defined by the FDA in 21 CFR 50.3(j) and 56.102(i) as any drug (including a biological product for human use), medical device for human use, human food additive, color additive, electronic product, or any other article subject to FDA regulation.

5. Human subject is defined by the FDA in 21 CFR 50.3(g) and 56.102(e) as an individual who is or becomes a participant in research, either as a recipient of the test article or as a control. A subject may be either a healthy human or a patient. For device research, a subject is also an individual on whose specimen an investigational device (IDE) is used or as a control (21 CFR 812.3(p).

   Human Subject Research is defined as any research that involves humans as defined in 45 CFR 46.102(f) and 38 CFR 16.102(f) or any clinical investigation that involves humans as defined by the FDA.

6. A Clinical Trial is 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.

7. 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:

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

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

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

   (d) 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;

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

(f) 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;

(g) 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;

(h) 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);

(i) 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;

(j) 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;

(k) 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;

(l) 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;

(m) 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;

(n) 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.

b. Human Subjects

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

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

   (b) 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 policy.1a. Intervention includes both physical procedures by which data is gathered (for example, venipuncture) and manipulations of the subject or the subject's environment that is performed for research purses. 1b. Interaction includes communication or interpersonal contact between investigator and subject.*

2. De-identified Information: De-identified information is health information that is presumed not to identify an individual, and with respect to which there is no reasonable basis to believe that the information can be used to identify an individual, because the 18 Patient Identifiers described in the HIPAA Privacy Rule have been removed 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). (VHA Directive 1200.05).

3. 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.

4. 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.

c. 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.*

3. Statement of Principles Concerning Protection of Human Research Subjects

a. The Belmont Report of April 18, 1979 contains the principles upon which the HRPP is based. These principles are as follows:

   1. Respect

   2. Beneficence

   3. Justice

b. The principles of the Belmont Report are addressed in the triennial Collaborative Institutional Training Initiative (CITI) training listed on the IRB website (www.etsu.edu/irb.htm) as a reference, and shall be applied to the review and conduct of all human subject research at this facility.

c. 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 policy incorporates both the pre-2018 and the 2018 Requirements where applicable.

4. Institutional Official Accountable for the HRPP

a. The Medical Center Director (MCD) is the Institutional Official (IO) accountable for the James H. Quillen VA Medical Center (JHQVAMC) HRPP and the President, ETSU is accountable for the ETSU HRPP. The IO is the individual legally authorized as Signatory Official (SO) to commit the facility to a FWA. The SO 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).

5. Assurances

a. The JHQVAMC is operating under Federalwide Assurance (FWA) #00002117 issued by DHHS (OHRP) and expires on October 29, 2023.

b. The VA Medical Center Director is the responsible official.

c. The Chief Officer for the VA Office of Research Compliance and Assurance (ORCA – now Office of Research Oversight or ORO) approved the original FWA on February 22, 2002.

d. ETSU/VA IRB is operating under FWA # 00002703 issued by DHHS (OHRP) and expires December 21, 2022.

e. The Mountain Home Research & Education Corporation is operating under FWA # 00015003 issued by DHHS OHRP and expires November 21, 2023.

6. Organizational Structure

a. The key individuals responsible for the HRPP are the MCD, COS, ACOS/R&D, Chair of the VA R&DC, Chair of the ETSU/VA IRB, VA Vice-Chair of the ETSU/VA IRB, and the Chair of the VA Subcommittee on Research Safety (SRS). The HRPP is further supported by the AO/R&D, RCO, ISSO, PO, Research Pharmacist, and ETSU HRPP Director. The key entities are the VA R&DC, the ETSU/VA IRB, and the VA SRS. The policy-making process occurs through the deliberations of the 3 entities, with interaction among them being facilitated by cross-membership. Review of these policies is done using the same mechanism.

b. The VA R&DC focus is on oversight of the research program at the JHQVAMC. The R&DC reviews the membership of the ETSU/VA IRB and VA SRS to ensure appropriate VA representation and qualifications. The R&DC has assigned scientific review of studies to the ETSU/VA IRB and delegated some administrative responsibilities and compliance functions to other subcommittees and individuals.

c. The ETSU/VA IRB functions as the human subject research subcommittee of the VA R&DC. The ETSU/VA IRB reviews and approves, requires modifications to, disapproves, suspends and/or terminates all human subjects research activities in order to assure that the rights and welfare of research subjects are being protected in accordance with federal regulations. The ETSU/VA IRB conducts the scientific review of all studies involving human subjects.

d. The VA SRS is a committee formally designated by a VA facility to review the safety and security of VA research laboratories in accordance with VA and other Federal requirements. The SRS is responsible for reviewing all research activities involving biological, chemical, physical, and radiation hazards for compliance with all applicable regulations, policies, and guidelines prior to submission to the appropriate research committees and subcommittees for review.

7. Responsibilities of the MCD

a. As the IO, is responsible for the facility's research program, and is supported by the R&DC.

b. Is responsible for overseeing the creation and implementation of an HRPP for research involving human subjects or biospecimens and overseeing the R&DC, all R&DC subcommittees, the research office, and all investigators (see VHA Directive 1200.02, ¶14) and research team members who perform human research at the JHQVAMC. Ensures 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.

c. Ensures that R&DC, ETSU/VA IRB, VA SRS members, and VA research personnel have the requisite knowledge to conduct research in accordance with ethical standards and all applicable regulations. 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 an affiliated medical or dental school, or the IRB of another Federal agency. A facility may also use for multi-site protocols an IRB from a non-affiliated medical or dental school if that IRB has been specifically designated by ORD as an IRB that may serve as a multi-site IRB for VA facilities. When the facility engages the services of another entity's IRB as its IRB of Record, the IO is responsible for establishing and signing a Memorandum of Understanding (MOU) or Authorizing Agreement with other VA facilities or external organization(s) providing IRB services and 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.

NOTE: *A VA facility may not use a commercial IRB as an IRB of Record.*

d. Delegates to the R&DC the development and implementation of an educational plan for R&DC, ETSU/VA IRB, VA SRS members, and VA research personnel which includes initial and continuing education.

e. Fulfills all educational requirements mandated by the VA, ORD, and OHRP.

f. Appoints one or more research compliance officers to conduct annual research informed consent document audits and triennial regulatory audits, and to assist in the VA facility's assessments of research compliance.

g. Reports any appointment, resignation, or change in status of the research compliance officer to ORO VHA Central Office, with a copy to the relevant ORO Research Work Group, within 5 business days after the appointment, resignation, or change takes effect.

h. Ensures appropriate auditing of local human research studies to assess compliance with all applicable local, VA, and other federal requirements including, but not limited to, ORO requirements. These functions are delegated to the RCO.

i. Reports to ORO in writing within five business days after being notified of a research problem or event (including apparent serious and continuing non-compliance, unanticipated problems involving risks to participants or others, and suspensions and terminations) for which such reporting is required. The MCD's written report is required regardless of whether disposition of the event has been resolved at the time of the report. Follow-up reports detailing any additional findings and appropriate remedial actions must be provided to the relevant ORO office at intervals and in a manner specified by that office.

j. Provides a copy of any ORO compliance reports regarding the research program to the ACOS/R&D, IRB, R&DC, any relevant research review committee(s), and the RCO in a timely fashion.

k. Reports the following research events to ORO Central Office, with a simultaneous copy to ORO Human Research Protections:

    1. ETSU/VA IRB changes in membership rosters must be reported to ORO CO via email by the R&D Service within 30 days of receipt of the revised ETSU/VA IRB membership roster. The ETSU/VA IRB will notify the ACOS/R&D, R&D Service, and RCO via email to ensure ORO is notified per the requirements of VHA Handbook 1058.03.

2. Substantive HRPP MOU changes must be reported within five business days.

3. Accreditation problems must be reported within five business days.

l. Ensures that the ETSU/VA IRB functions independently.

m. Provides direct access to the chair, vice chairs, and members of the ETSU/VA IRB for appeal if they experience undue influence or if they have concerns about the ETSU/VA IRB.

n. Ensures provision of adequate resources to support the operations of the HRPP so that those operations are in compliance with all VA and other federal requirements that govern human participant research protection.

o. Ensures the conduct of an annual evaluation of the facility's HRPP. This function is delegated to the R&DC.

p. A reliable mechanism for research participants to communicate with researchers and with an informed VA representative who is independent of the research study in question (e.g., providing contact information in the consent document).

q. 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.)

r. 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.

s. Ensuring appropriate documentation of required actions and responsibilities pertaining to review, approval, conduct and oversight of research conducted at the facility. Ensuring all research subject to this policy 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 B and C)

t. Delegates to the R&DC responsibility for ensuring that the following minimum requirement is met for all protocol reviews:

1. Funded protocols, regardless of risk level, require that both the PI and responsible Co-I have a minimum 5/8th VA appointment (unless there is an approved waiver from VA Central Office).

2. Unfunded protocols require that PI and responsible Co-I have a minimum 5/8th appointment UNLESS the protocol is identified as either a chart review or VINCI/DART database review. In these specific instances, the PI must still have a minimum 5/8th VA appointment, but the responsible Co-I need only be a minimum Without Compensation (WOC) employee.

8. Roles and Responsibilities of the R&DC in Protecting Human Subjects

a. Operational Principle: The R&DC represents the institution; the IRB represents human research subjects.

   1. ETSU/VA IRB members are human research specialists. The R&DC members include specialists who represent services that interface with research activities. There is cross-membership between the two committees.

   2. The ETSU/VA IRB meets the first Tuesday of the month. The R&DC meets the last Wednesday of the month.

   3. The JHQVAMC MCD and R&DC have full authority to disapprove items approved by the ETSU/VA IRB but cannot approve items disapproved by the IRB. The R&DC minutes are forwarded to the R&DC Chair, ACOS/R&D, COS, and MCD for review and approval.

b. The R&DC is responsible for the quality and appropriateness of all research involving human subjects.

c. The R&DC is responsible, through the COS, to the MCD, for oversight of the VA R&D Program and ensuring the highest standards of ethics and quality of all research projects. The R&D Office, ISSO, PO, RCO, voting members of the R&DC, ETSU/VA IRB and VA SRS will review all initial and continuing reviews. IRB continuing reviews of research will occur no less than once per year. After the review process, the ACOS/R&D will provide final notification to the PI of the outcome of the review. Initial studies may not be initiated until the ACOS/R&D provides the final review and communicates to the PI that the study may be initiated. All but Exempt studies are also required to have a continuing review and approval by the ETSU/VA IRB and, if applicable, by the SRS. The R&DC is responsible for conducting continuing reviews of all Exempt studies. The R&DC is responsible for annual reviews of all pre-2018 studies. The ACOS/R&D will then communicate to the PI that the study has met all R&DC contingencies to be continued. The AO/R&D is responsible for notifying the ACOS/R&D if a study has expired.

d. The R&DC evaluates the ETSU/VA IRB program and approved human research studies at least annually through the review of ETSU/VA IRB minutes and the ETSU/VA IRB annual report.

9. Guidance for Collaborative Research

a. 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. 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.

b. 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 subject 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 so long as the document clearly describes which procedures will be performed under auspice of the VA and which will be performed under the auspice of a non-VA institution.

(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.

c. 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; VA Handbook 6500, Risk Management Framework for VA Information Systems – Tier 3: VA Information Security Program; and VHA Directive 1605.01, and 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 or any superseding policies revising or replacing it.

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

10. Implementation of HRPP

a. Responsibility: The PI, ACOS/R&D, RCO, ISSO and PO are the individuals responsible for ensuring that studies are compliant and for monitoring changes in VA and federal regulations as they relate to human participant research.

b. Review and evaluation of reports and results of compliance assessments and quality improvement activities will be completed by the ACOS/R&D, R&DC, and ETSU/VA IRB

c. Implementation of needed improvements and follow-up actions as appropriate.

    1. Through mandatory quality assessment audits (informed consent and regulatory), conducted by the RCO, which are accomplished during the year and no less than annually and tri-annually, to identify areas of needed improvement.

    2. Corrective plans will be developed and reviewed by the RCO, ACOS/R&D, R&DC and sub-committees and implemented as appropriate. To ensure corrective action is taken, each area identified will be revisited and re-evaluated by the R&DC at least monthly until all corrections have taken place. All actions will be reported per VHA Handbook 1058.01.

d. PI Responsibilities:

    1. Uphold professional and ethical standards and practices; the roles of the investigators and study staff must be well defined in the protocol.

2. All documentation for studies conducted at the JHQVAMC must first be submitted electronically via IRB Manager to the R&D Office for review by the R&D Office, SRS Chair, PO, RCO and ISSO. Notification of deficiencies are sent to the PI via IRB Manager for correction and the package must be resubmitted for re-review by the appropriate individuals prior to final acceptance by the R&D Office. Once the review is completed and all R&D required documentation is complete, then the R&D Office will accept the study and forward the study submission via IRB Manager to the ETSU/VA IRB and/or outside of IRB Manager to the SRS for review. PIs may not initiate any study until after they receive notification from the ACOS/R&D.

3. If a research study is to be submitted to the VA Central Office for funding, then the study proposal will be prepared in accordance with all applicable VA Handbooks and Directives in addition to meeting all local requirements. Assistance with additional information and forms for these submissions may be obtained from the R&D Office.

4. Ensuring adequacy of resources including time, equipment, and space for the conduct of safe research.

5. Ensuring that all members of the research team are qualified by education and training to conduct the research study utilizing Scopes of Practice (as needed) and timely completion and upkeep of CITI training. (VHA Directive 1200.05 and VHA Directive 1200.02 ¶10)

6. Conducting the study according to the IRB-approved study protocol and all terms and conditions of the grant/contract. All studies will be evaluated for compliance via the ETSU/VA IRB, SRS, and R&DC as well as via audits conducted by the RCO.

7. Maintain the original ACOS/R&D notification which is sent to the PI after all approvals have been obtained.

8. Informing the ETSU/VA IRB of any potential conflict of interest as outlined in the ETSU/VA IRB Policies. The ETSU/VA IRB Policies can be obtained from the ETSU IRB web site http://www.etsu.edu/irb.

9. Completing the VA FCOI documentation as outlined in the R&D Overview and Protocol Submission Guide.

10. Ensuring that any issues regarding non-compliance are reported as soon as possible, but not later than 5 business days after discovery, to the ETSU/VA IRB Chair and ACOS/R&D per ETSU/VA IRB Policy 25 and VHA Handbook 1058.01.

11. Maintaining adequate and accurate records in accordance with all regulations and making those records available for inspection.

12. Ensuring that initial contact of potential study subjects is done in person or by letter.

13. Investigators must provide notice of privacy practices to any non-veteran enrolled in an approved VA protocol.

14. Ensuring that when study subjects are being consented that a separate stand-alone Informed Consent Document is used (VA form 10-1086; Pre-2018 requirements). For 2018 requirements, the use of VA form 10-1086 is no longer required, and HIPAA may be embedded in the consent form.

15. Ensuring that study subjects complete a separate stand-alone HIPAA Authorization for new VA studies (VA form 10-0493) effective March 12, 2015 (Pre-2018 requirements). For 2018 requirements, the VA form 10-0493 will be used when HIPAA is a standalone document.

16. Ensuring the adequacy of the informed consent process and that study subjects are contacted and informed in a timely manner about all areas of the study including participation when an investigational device and/or investigational drug is used.

17. Reporting to the ETSU/VA IRB in a timely fashion any serious adverse events using ETSU/VA IRB Form 109 in accordance with ETSU/VA IRB Policy 18. **(See Appendix A)**

18. Retaining copies of all ETSU/VA IRB, SRS, and R&D documents and correspondence per regulatory binder checklist.

19. Documentation of the subject's enrollment and subsequent study visits in the subject's electronic medical record (CPRS).

20. Acknowledging VA support and affiliation on publications and presentations.

21. Research personnel are required to disclose any inventions or discoveries to Department of Veterans Affairs through completion and submission of the required Invention Disclosure and VA Certification forms (through the ACOS/-R&D) and the OGE 0450 VA FCOI form.

22. Notifying the R&D Office of any Study Site Monitoring visit.

    (a) Flagging medical records of study subjects in CPRS, when required for more than minimal risk research. (See ETSU/VA IRB policy for establishing more than minimal risk status.)

    (b) If the investigator leaves the VA and no longer holds an appointment as an employee (compensated, WOC, or IPA), all research records, data, and data in repositories must remain at VA and under VA control. All

data and records are the property of VA. The data may not be copied or removed unless all requirements for use of VA data by non-VA investigators are met. If the investigator leaves the VA and maintains a VA appointment, the original records must remain with JHQVAMC. The investigator may request a copy of the records and/or data be transferred to another VA facility. The request for records and/or data must be reviewed and approved by the facility PO, ISSO, and ACOS/R&D.

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

10. HRPP Budgeting Process

a. The ACOS/R&D will ensure that any grant accepted by the Mountain Home Research and Education Corporation includes an amount equal to 28% of the direct cost of the study, to be applied to the costs of the HRPP incurred by the JHQVAMC. These funds will be used in support of the HRPP (i.e., personnel, supplies, equipment, training, and education).

b. The R&D Office will provide the ACOS/R&D with an annual accounting (in November) of the total amount of direct costs of Government and industry-funded studies conducted at the JHQVAMC, as well as the amount of funds that were made available from the Mountain Home Research and Education Corporation for support of HRPP costs. The R&D Office will then forward the report to the Director of Finance at the ORD along with an accounting of all expenditures in support of compliance-related activities (reference annual RDIS Part II ORD letter of request).

11. Institutional Oversight

a. ETSU/VA IRB:

1. ETSU/VA IRB is evaluated on an annual basis by the R&DC, the RCO, ACOS/R&D, COS, and MCD through auditing, and review of reports and minutes. Communication between the AO/R&D and the HRPP Director is done on an "as needed basis". VA and R&DC membership on the ETSU/VA IRB also facilitates oversight/evaluation. Additionally, the AO/R&D serves as an ex-officio member and the RCO serves as a non-voting consultant of the ETSU/VA IRB and monitors its function for compliance with VA and federal guidelines.

b. IRB Membership:

1. The membership of the IRB is reviewed/evaluated annually by both IOs accountable for the HRPP (the JHQVAMC MCD and the ETSU President).

2. The R&DC will continually review the membership of the ETSU/VA IRB to assure its appropriateness, evaluate the presence of representatives having experience with vulnerable populations (either as members or as ad hoc consultants), and determine the need for appointment of VA representatives (minimum 1/8th appointment required) to the ETSU/VA IRB.

c. ETSU/VA IRB Chair and Vice Chairs:

1. When a new candidate is considered for either the ETSU/VA IRB Chair, Vice Chair or VA Vice Chair, the ETSU/VA IRB will assess the candidate's knowledge and qualifications as presented via a current cv/resume before recommending them to the IOs for appointment.

2. The ETSU/VA IRB Chair, Vice Chair and VA Vice Chair are appointed by the IOs for a term of up to 3 years and may be re-appointed indefinitely (per VHA Directive1200.05).

12. ETSU/VA IRB Function

a. Evaluation of ETSU/VA IRB performance occurs monthly by careful review of the IRB minutes (per VHA Directive1200.05) and by review of proposals approved by ETSU/VA IRB.

b. Evaluation includes the following areas:

1. Content and accuracy of informed consent document (all elements included).

2. IRB analysis of risks and benefits including designation of minimal risk.

3. Special considerations and protections for vulnerable populations (children, pregnant women, neonates, and human fetuses): VA Research that will include the recruitment of vulnerable populations must obtain approval from the MCD prior to the conduct of research. Interventional studies on neonates continue to be prohibited in VA research.

4. VA Research that will include the recruitment of prisoners still requires a waiver from the CRADO prior to conduct of research.

5. VA international research must obtain approval from the MCD prior to the conduct of research. All international research must also be approved explicitly in a document signed by the VA MCD, except for Cooperative

Studies Program activities which must be approved by the CRADO. Secure remote use/access (VPN, etc.) to data residing on VA servers in the US or Puerto Rico is not considered international research. (see guidance at: http://www.research.va.gov/resources/policies/default.cfm).

6. Privacy and confidentiality protections.

7. Continuation review of approved research (Pre-2018 requirement). There is no continuation review performed by the IRB for any study approved under the 2018 requirements.

8. Ongoing review of previously approved research.

9. Use of expedited review.

10. Determination of exemption from Federal requirements for ETSU/VA IRB review.

11. Granting of waivers for documentation of informed consent requirement and HIPAA Authorization must be captured in the IRB minutes.

12. Granting of waivers of any elements of informed consent. A waiver of the signature of the individual obtaining consent is not permissible for more than minimal risk research.

13. VA Form 10-3203 is no longer required and will not be accepted for new VA studies. The consent form 10-1086 must include information describing any photographs, video, and/or audio recordings that will be obtained for research purposes.

14. 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. The VA does not issue Certificates of Confidentiality.

13. Conflict of Interest Policies

a. In accordance with VHA Directive1200.05, Section5., VA Investigators* are responsible for disclosing to the ETSU/VA IRB any potential, actual, or perceived conflict of interest of a financial, professional, or personal nature that may affect

any aspect of the research and complying with all applicable VA and other Federal requirements regarding conflict of interest.

b. In accordance with MCM 151-16-01, investigators are required to complete and sign the OGE 0450 VA FCOI form prior to initial review of a study protocol, continuing review, or if they are being added as an investigator to a study protocol. An updated FCOI is also required when there is a change in relevant information on Section I of the FCOI form (i.e., answer changed to "yes" or any change that results in a change to the reason for a "yes" answer). Any conflict of interest will first be reported to the ACOS/R&D and VA Integrated Ethics Council for review followed with a review by the ETSU/VA IRB for studies under the Pre-2018 requirement. For studies falling under the 2018 requirement, this process will be accomplished by means of an Administrative Check-in on an annual basis.

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

c. R&DC and ETSU/VA IRB:

   1. R&DC and ETSU/VA IRB members do not participate in, and will recuse themselves from, the deliberation or vote of any protocol for which a potential conflict of interest exists (this will be documented in the minutes). At the beginning of each meeting the Chair will poll the committee for any conflicts of interest. R&DC and ETSU/VA IRB members are considered to have a conflicting interest whenever any one of the following is true:

      (a) The R&DC and ETSU/VA IRB Member, Consultant, R&D staff, IRB staff, or a member of their immediate family has significant financial interest as defined in IRB Policy 17a.

      (b) The R&DC and ETSU/VA IRB Member, Consultant, R&D staff, IRB staff, or a member of their immediate family is a member of the research team designing, conducting, or reporting the research presented in the protocol (reference VA FCOI and ETSU/VA IRB COI forms).

      (c) The R&DC and ETSU/VA IRB Member, Consultant, R&D staff, IRB staff, or a member of their immediate family has any other interest of any kind that the individual believes conflicts with his or her ability to objectively review a protocol (reference VA FCOI and ETSU/VA IRB COI forms).

d. The Institution (JHQVAMC):

   1. The AO/R&D has been designated by the MCD to be the FCOI Administrator who will be responsible for the day-to-day activities related to conflicts of interest in the research program. If the institution or an institutional official

has a potential conflict of interest that is determined to be problematic, then the R&DC will review the institution's financial relationship with the sponsor. If a FCOI is confirmed, then the R&DC will report the FCOI to the JHQVAMC Integrated Ethics Council for review and action.

2. An Institutional Conflict of Interest might occur when research involves patents or royalties as the VA retains a portion of the earned income from patents and royalties. This VA facility, through the ACOS/R&D, must insure that patent and royalty applications are reviewed and approved by ORD Technology Transfer Office before they are initiated. After the Office of Research and Development notifies the ACOS/R&D of approval of patents and royalties, the ACOS/R&D will notify the IRB and R&DC through the IRB administrator and the AO/R&D of a VA protocol with a potential Institutional Financial Conflict of Interest. Referral to the Office of Regional Council or the legal representative serving as an ex-officio member of the IRB will also occur and an evaluation of whether an institutional financial conflict of interest exists will be conducted. If recommended, then consultation with the appropriate committee or subcommittee re: strategies for management of the financial conflict of interest will occur. The IRB has the final authority to grant approval of the research associated with patents and royalties.

14. Questions, Concerns, Complaints, and Allegations of Noncompliance

a. A standard element of the ICD is entitled "Contact for Questions". This paragraph states, "If you have any questions, problems, or research-related medical problems at any time you may contact (PI) at (ph#) or (name of PI-appointed second or co-PI) at (ph#). You may call the Chair of the Institutional Review Board at (ph#) for any questions you may have about your rights as a research subject." Each ICD must contain this statement in order to be approved. All issues will be addressed by the ETSU/VA IRB and reported to the VAMC IO, COS, ACOS/R&D, R&DC and appropriate subcommittees. The process by which complaints and allegations of non-compliance are managed is addressed by VHA Handbook 1058.01 and in the ETSU/VA IRB Policy 2.

b. All investigators, study personnel, and R&D Office staff are required to report to the R&D Office any undue influence by internal or external sources that would concern any study with which they are connected. The R&D Office will forward the report of undue influence to the appropriate subcommittee and the R&DC for action. Following review by the R&DC, the report of undue influence will be forwarded to the MCD for final disposition.

c. All unanticipated problems or risks to human research subjects are reported in accordance with ETSU/VA IRB Policies and Procedures: Unanticipated Problems (Policy 18) and Reporting Policy (Policy 34).

d. Ensure prompt reporting, in accordance with ORD, VISN 9 Director, the FDA, the OHRP, ORO, and ETSU/VA IRB Policies and Procedures Reporting Requirements **(see Appendix A)**

e. The JHQVAMC IO or research committees cannot alter or approve an adverse report or disapproval ruling issued by the ETSU/VA IRB.

15. Investigational Drugs, Devices and Emergency Use of Test Articles

a. The ETSU/VA IRB is responsible for initial full review of all studies which incorporate Investigational Drugs, and Devices IAW VHA Directive1200.05, ETSU/VA IRB Policies and Procedures, Full Review (Policy 9), Device Determinations (Policy 19), and Emergency Use (Policy 20).

16. Monitoring, Evaluation, and Quality Improvement

a. Primary monitoring of investigator performance occurs at the ETSU/VA IRB level (both administrative and board). The following are evaluated.

1. Adherence to ETSU/VA IRB-approved protocols.

2. Reporting all unanticipated problems involving risks to subjects.

3. Reporting all protocol deviations.

4. Obtaining ETSU/VA IRB approval prior to initiating changes in the protocol or consent.

5. Using only ETSU/VA IRB-approved advertisements and subject recruitment materials for JHQVAMC R&DC-approved research.

6. Ensures that recruiting documents, flyers, and advertisements for other federally funded research may be posted on the premises of a VA facility. Review must be completed prior to advertisement. Continuing oversight functions are carried out by the PO and ISSO during environmental rounds.

7. Preparatory to Research activities involving access to PHI are limited to VA investigators only.

8. Obtaining consent prior to initiating any research-related procedures.

9. Using only ETSU/VA IRB-approved consent form VA Form 10-1086 (except in cases where the documentation of informed consent is waived by the ETSU/VA IRB) to include the following for Pre-2018 requirement studies:

(a) Purpose of study and how long it will last;

(b) Description of the study including procedures to be used;

(c) Description of any procedures that may result in discomfort or inconvenience;

(d) Expected risks of study;

(e) Expected benefits of study;

(f) Other treatment available;

(g) Use of research results;

(h) Special circumstances;

(i) Dating and signing of Informed Consent form by:

i(1). The subject or the subject's legally authorized representative,

i(2). The witness to the subject signing (if required by the IRB), and

i(3). The person obtaining the Informed Consent.

(j) The person obtaining consent ensures the subject adequately reviews the consent document and ensures that the subject initials the bottom of each page on the consent document and documents the informed consent process by entering a Research Consent note in CPRS.

10. For studies subject to the 2018 requirement, 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. Information provided the subject or representative must be language understandable to them. 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. The following general requirements for informed consent must also be applied except for broad consent:

(a) 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;

(b) 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 this section*

(c) 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.

(d) If a VA research study's informed consent approved by the IRB prior to January 21, 2019, requires modification, the general requirements described in this section 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.

(e) Except as provided for a Waiver or Alteration of Informed Consent, in seeking informed consent the following information must be provided to each subject or LAR:

e(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;

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

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

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

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

e(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;

e(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

e(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.

e(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.

e(10). A statement that VA will provide treatment for research related injury in accordance with 38 CFR 17.85

NOTE: *VA's statutory requirements in 38 CFR 17.85 apply regardless of inclusion of the information as part of the informed consent process.*

11. The ETSU/VA IRB does not have the authority to approve a HIPAA authorization per VHA Directive 1200.05. The HIPAA authorization for studies approved by the ETSU/VA IRB after March 31, 2011 must be a separate document and cannot be embedded with the VA Form 10-1086. The VAMC PO is the approving official for HIPAA authorizations subject toPre-2018 requirement. For studies subject to the 2018 requirement, 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. All HIPAA Authorizations must meet all VHA Privacy requirements detailed in VHA Directive 1605.01.

12. The ETSU/VA IRB is not authorized to approve a HIPAA Authorization but can waive the HIPAA Authorization requirement per VHA Directive1200.05. VA protocols will use VA Form 10-0521 HIPAA Waiver of Authorization for Research for this purpose.

13. The institution monitors the performance of investigators to ensure compliance with HRPP and ETSU/VA IRB requirements. The institution evaluates the following:

    (a). Adherence to HRPP policies;

    (b). Adherence to electronic record entry policy;

    (c). VA Form 10-1086 scanned into the medical record and a hard copy of the record is maintained by the PI along with all other required study documentation in accordance with the VA Records Control Schedule, RCS 10-1;

    (d). Monitoring adherence to “Stand Down” policies regarding verification of licensure, education, and background checks.

b. The following quality improvement plan goals have been established to periodically assess compliance of the HRPP:

    1. Goal - An educational compliance topic will be distributed to the PIs on a routine basis to assist the R&D program with implementing research regulations and policy and provide updates to the PIs concerning audit criteria.

    2. Goal - Track the informed consent and regulatory audit results for all human research protocols to identify trends and establish corrective measures

        (a) Objective – Ensure that all human research protocols will receive an annual informed consent audit and triennial regulatory audit for studies approved after January 1, 2008.

        (b) Measure – Informed Consent Audits and Triennial Regulatory Audits will be completed per local SOP and recorded using the audit tools provided by the VA Office of Research Oversight.

(c) Method – The facility RCO will present the annual ORO Facility Director's Certification of Research Oversight to the R&DC comparing previous year audit results to current audit results.

c. The following Quality improvement plan goals have been established to periodically assess the quality, efficiency, or effectiveness of the HRPP:

1. Goal - Track the review timelines for the submission of minor modifications, continuing reviews and/or administrative check-ins, and initial reviews.

(a) Objective and Measure – Ensure that all minor modifications, continuing reviews and initial reviews are completed by the R&D Office, SRS, ISSO, PO and RCO within time periods established by the R&DC (14 calendar days for continuing review and minor modification review and 30 calendar days for initial reviews).

(b) Method – The R&D Office and IRB will coordinate the consolidation of timeline data by running ad-hoc data reports from the IRB Manager for presentation at the monthly meeting of the R&DC.

2. Goal – Provide orientation for all new Principal Investigator's (PIs) and study staff.

(a) Objective – Ensure that all new PIs and study staff are familiar with the processes and requirements associated with the submission and maintenance of a VA research study.

d. The Research Information Security workgroup (RIS)

1. The RIS checklist will be reviewed as requested by the R&DC to coincide with the completion of the ORO Facility Director's Certification of Research Oversight.

2. Investigators and other members of the VA Research community are required to ensure that any apparent non-compliance has been reported in writing to the IRB.

3. RIS Reporting requirements per VHA Handbook 1058.01(10a)(1)- Members of the VA research community must Immediately report, within 1 hour, to the ACOS/R&D, ISSO, and PO, any unauthorized use, disclosure, transmission, removal, theft, loss, or destruction of VA research-related protected health information (PHI), individually identifiable private information, or confidential information, as defined by the HIPAA Privacy Rule, the Common Rule, the Privacy Act, or 38 U.S.C. §§5701, 5705, and 7332. The ACOS/R&D must report any incident addressed in VHA Handbook 1058.01(10a) immediately to the records management official and relevant committee for review and determination at the next scheduled meeting. Notification of information security incidents must be reviewed by each relevant research review committee

at its earliest practicable convened meeting, not to exceed 30 business days from the date of notification.

4. If the research review committee determines that the incident constitutes a serious problem:

   (a) The committee must notify the VA facility Director and the ACOS/R&D within 5 business days after the determination.

   (b) The VA facility Director must report the determination to ORO within 5 business days after receiving the committee's notification.

   (c) VHA Handbook 1058.01(10c) - VA facility Director must report the following circumstances related to research information security incidents to ORO within 5 business days after taking or becoming aware of such action(s), regardless of any determination made by the R&DC or relevant research subcommittee.

      c(1). Provision of an Issue Brief for VA Central Office regarding the incident;

      c(2). Any notification to individual(s) of an information breach or provision of credit monitoring as required by the Network Security Operations Center (NSOC);

      c(3). Any breach notification required under the Health Information Technology for Economic and Clinical Health (HITECH) Act; and/or

      c(4). Any notification to or from the Office of Inspector General (OIG) regarding the incident.

e. Independent of the reporting requirements described above, within 5 business days of discovering, receiving a credible report of, or otherwise becoming aware of findings of noncompliance, other deficiencies that substantively compromise the RIS, or any suspensions or terminations, the ACOS/R&D must report the situation directly (without intermediaries) to the facility Director, the R&D committee, and any relevant research review committees, and must ensure that the facility ISSO and the facility PO have also been notified.

f. Within five business days of identifying apparent serious or continuing non-compliance based on a consent document audit, regulatory audit, or systematic audit of VA research, the RCO must provide a written report of the apparent non-compliance directly (without intermediaries) to:

   1. The MCD

   2. The ACOS/R&D

   3. The R&D Committee

4. The IRB

5. Other relevant research Committees

g. Industry sponsored clinical trials. The following information applies:

1. Clinical Trial Site Monitors:

(a) Will not hold a VA appointment,

(b) Will not have direct access to CPRS,

(c). May only shadow the VA Study Coordinators responsible for the clinical trial for access to data for completion of regulatory documentation i.e. case report forms, serious adverse event monitoring **(see Appendix B of R&DC SOP for additional requirements)**

17. Mandatory Training

a. All Principal Investigators, Co-Principal Investigators, co-investigators, approved study personnel, VAMC R&DC members, ETSU/VA IRB members, and VAMC representatives (e.g. WOC appointments and IPAs) are required to complete mandatory HRPP training. Overview of required courses is provided at the following website: http://www.research.va.gov/programs/pride/training/all-staff.cfm . The following is a list of training requirements:

1. CITI (tri-annual requirement) website: www.citiprogram.org .

(a) In accordance with VHA Directive1200.05 CITI training is required every 3 years. The JHQVAMC defines “every 3 years” as within 1095 days after the previous training.

(b) Completion of a ‘Good Clinical Practices’ training course is required prior to conducting any clinical trial.

2. Prior to the initiation of any industry-sponsored clinical trial, both the PI and the clinical trial coordinator must complete any sponsor related training associated with the trial.

b. All personnel listed as an investigator are required to complete the mandatory Technology Transfer Program training on an annual basis as required in memo “Technology Transfer Program Training Requirement” dated July 20, 2018 and VHA Directive 1200.18. This requirement will be reported to the R&D Committee on a quarterly basis.

18 Applicability Of 2018 Requirements

a. Except as indicated in section 18b. below, research must comply with the pre-2018 Requirements as described in this policy 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.

19. The following HRPP Overview, Guidelines, and Regulations can be found on the IRB website: https://www.etsu.edu/irb/default.php

a. History of the ETSU/VA IRB and Ethical Guidelines;

b. Policies of the ETSU/VA IRB;

c. Standard Operating Procedures (IRB & R&DC);

d. VA R&D Guide and Forms;

e. Federal Regulations;

f. References (Belmont, FWA, etc.);

g. Training Guidelines/Links;

h. Contact Information.

Rescission Date: 01-21-2022. This SOP will serve as the facility policy until it is recertified or rescinded.

Owen D. Murnane, Ph.D., ACOS-R&D

Appendix A

Research Compliance Reporting Requirements

VHA Handbook 1058.01 describes the requirements for reporting compliance events in VA research to research review committees, VHA officials, and ORO. These requirements do not alter or replace any additional requirements for reporting such events to other internal or external entities as mandated by law, regulation, policy, or agreement.

All VA research personnel will report compliance events following the specific reporting requirements listed in sections (6) Human Research, (7) Animal Research, (8) Research Safety, (9) Research Laboratory Security and (10) Research Information Security. The summary table below does not list all examples of apparent serious and/or continuing noncompliance, but is a reference tool for research personnel. The IRB (423-439-6054) and RCO (423-979-4325) are available for consultation for any questions research personnel may have.

- Guidance on reporting such determinations to the OHRP
- Guidance on reporting such determination to the FDA for FDA regulated clinical investigations
- Adverse Event Reporting to IRBs—Improving Human Subject Protection (FDA, June 2009)

SUMMARY OF REQUIREMENTS FOR REPORTING RESEARCH INCIDENTS UNDER VHA HANDBOOK 1058.01

Reports should be directed to ORO as specified on the ORO SharePoint and Web sites at https://vaww.vha.vaco.portal.va.gov/sites/ORO/RCO/default.aspx and http://www1.va.gov/oro/

Note: This Table provides a CONDENSED SUMMARY of reporting requirements. See VHA Handbook 1058.01 for complete details.

Unless otherwise indicated,
#1. VA employees (including WOC and IPA employees) must notify the relevant research review committee in writing within 5 BUSINESS DAYS (BD) after becoming aware of reportable incidents.
#2. Research review committee must notify the Facility Director (FD) and Associate Chief of Staff for Research (ACOS/R) within 5 BUSINESS after making certain required determinations (DTMs).
#3. FD must report to ORO within 5 BUSINESS DAYS after receiving notification.

HUMAN RESEARCH – Report to ORO Regional Office (or ORO RCEP[1] where indicated)	LABORATORY ANIMAL WELFARE – Report to ORO RSAW[2]	RESEARCH SAFETY – Report to ORO RSAW[2]	RESEARCH LABORATORY SECURITY – Report to ORO RSAW[2]	RESEARCH INFORMATION SECURITY – Report to ORO RISP[3]
§6a. Local Research Deaths that are unanticipated and related to the research. ●Immediate oral notice to IRB. ●IRB alert to ORO, FD, and ACOS/R within 2 BD. ●Written notice to IRB per #1. ●IRB Chair DTMs within 5 BD of written notice. ●Convened IRB DTMs. ●IRB notice of all DTMs to FD and ACOS/R per #2. ●FD report to ORO per #3. **§6b-d. Local SAEs and Serious Problems that are both unanticipated and related to the research.** ●Written notice to IRB per #1. ●IRB Chair DTMs within 5 BD of written notice. ●Convened IRB DTMs. ●IRB notice of DTMs to FD and ACOS/R per #2. ●FD report to ORO per #3. **§6f. Apparent Serious or Continuing Noncompliance.** ●Written notice to IRB per #1. ●Convened IRB DTMs. ●IRB notice of DTMs to FD AND ACOS/R per #2. ●FD report to ORO per #3. ●Notification of, and tracking by RCO, if from RCO audit. ●IRB tracking for Facility Director Certification. **§6h. Suspension/Termination by VA.** ●Notice to FD, ACOS/R, & RCO within 5 BD. ●FD report to ORO per #3. **§6i. Suspension/Termination by External Entity.** ●Written notice to IRB per #1. ●Convened IRB DTMs. ●IRB notice of DTMs to FD AND ACOS/R per #2. ●FD report to ORO per #3. **§6j. Program Changes.** ●FD report to ORO per #3.	**§7c. Human Deaths.** ●Immediate oral notice to IACUC. ●IACUC alert to ORO, FD, and ACOS/R within 2 BD. ●Written notice to IACUC per #1. **§7a. Unanticipated Deaths of Research Animals.** **§7b. Animal Theft, Escape, or Unexplained Disappearance.** **§7d. Human Accident, Injury, Illness, or Exposure.** **§7e. Reportable Incidents Under Federal Standards.** ●Written notice to IACUC per #1. **§7f. IACUC Review of Incidents Reported under §§7a-7e.** ● DTMs by convened IACUC. ●Notice of IACUC DTMs to FD AND ACOS/R per #2. ●Notice to FD of DTMs by other officials of a reportable event. ●FD report to ORO per #3. **§7h. Delayed Determinations.** **§7i. Memoranda of Understanding.** **§7j. Public Health Service Assurances.** **§7k. Accreditation Status Change.** ●FD report to ORO per #3.	**§8a. Human Deaths.** ●Immediate oral notice to SRS. ●SRS alert to ORO, FD, and ACOS/R within 2 BD. ●Written notice to SRS per #1. **§8b. Human Accident, Injury, Illness, or Exposure.** **§8c. Reportable Incidents Under Federal Standards.** ●Written notice to SRS per #1. **§8d. Review of Incidents.** ●DTMs by convened SRS. ●Notice of SRS DTMs to FD AND ACOS/R per #2. ●Notice to FD of DTMs by other officials of a reportable event. ●FD report to ORO per #3. **§8e. Delayed Determinations.** **§8g. Memoranda of Understanding.** ●FD report to ORO per #3. **§8h. Lab Decommissions and Reassignments.** ●Written request to SRS and ACOS/R 1 month prior to implementation ●SRS DTMs. ●Notice to facility Safety Officer from ACOS/R. ●Notice to FD from ACOS/R of unauthorized decommissions or reassignments within 5 BD. ●FD report to ORO of unauthorized decommissions or reassignments per #3.	**§9a. Research Laboratory Security Incidents.** (1) Intrusion, physical security breach, break-in, or other security violations in dedicated research areas. (2) Noncompliance findings by any entity other than ORO. (3) Unplanned suspensions or terminations of research due to security concerns. (4) Other deficiencies that substantively compromise the research laboratory security program. ●Written notice to ACOS/R within 5 BD. ●Immediate notice to VA Police Service. **§9b. Reporting.** ●Notice to FD and VA Police Service from ACOS/R within 5 BD. ●FD report to ORO per #3.	**§10a. Research Information Security Incidents.** ●Immediate notice to ACOS/R, ISSO, and PO of information security incidents related to research including inappropriate access, loss, theft of PHI; noncompliant storage, transmission, removal, or destruction of PHI; theft, loss, noncompliant destruction of equipment containing PHI. ●Immediate ACOS/R&D notice to relevant research review committee(s). ●Immediate ACOS/R&D notice to Records Management Officer if VA records destroyed. ●Written notice to ACOS/R within 5 BD. **§10b. Review of Incidents Reported under §10a.** ●Review and DTMs by relevant research review committee(s) within 30 BD. ●Notice of serious problem DTM to FD AND ACOS/R per #2. ●FD report to ORO of serious problem DTM per #3 . **§10c. FD report to ORO within 5 business days of**: ●An Issue Brief on the incident for VA central office ●An NSOC requirement to notify individuals of an information breach or to provide credit monitoring ●Breach notification required under the Health Information Technology for Economic and Clinical Health (HITECH) Act ●Notification to or from the OIG regarding the incident.

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Appendix B

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.

Appendix C

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 that there are adequate provisions to protect the privacy of subjects and to maintain the confidentiality of data.

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 that there are adequate provisions to protect the privacy of subjects and to maintain the confidentiality of data.

(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 VHA Directive 1200.05.

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 VHA Directive 1200.05;

(2) Documentation of informed consent or waiver of documentation of consent was obtained in accordance with section 17 of VHA directive 1200.05;

(3) An IRB conducts a limited IRB review and makes the determination to protect the privacy of subjects and to maintain the confidentiality of data 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.