VA HOSPITAL RESEARCH – SPECIAL CONSIDERATIONS

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REQUIREMENTS FOR THE PROTECTION OF
HUMAN SUBJECTS IN RESEARCH WHEN RESEARCH IS VA REGULATED

1. PURPOSE

To assure knowledge and compliance by documenting the policies and procedures to be followed when conducting research involving the Harry S Truman Memorial Veterans Hospital.

2. SCOPE

The SOP applies to all human subject research falling under the purview of the Health Sciences Institutional Review Board. The Campus IRB does not review VA regulated research.

3. POLICY

The HS IRB has been appointed as the IRB of record for the Harry S Truman Memorial Veterans Hospital. The agreement has been outlined in a Memorandum of Understanding (MOU) signed by both parties. Further, the HS IRB agrees to comply with the federal regulations including 38 CFR 16 and with all applicable regulations as outlined in the VA Handbook 1200.5 “Requirements for Protection of Human Subjects Research in Department of Veterans Affairs (VA) Research. A commercial IRB is prohibited from being used to review VA research projects.

VA research will be reviewed and monitored in the same manner as all other research under the purview of the HS IRB. It will be expected to comply with the federal regulations and adhere to the HS IRB SOPs as outlined for all research. **VA regulations have some additional requirements specific to VA research and these requirements are outlined in these policies and procedures.**

For VA research, IRB approval may be granted pending approval of the R&D Committee. Research cannot commence until R&D Committee approval is granted. Therefore, research may not commence until R&D approval has been obtained. The R&D Committee will provide a written approval letter to the investigator with a copy sent to the HS IRB for inclusion in the study files.

Regulations, handbooks and forms referenced within this document can be found on the HSIRB web site [http://research.missouri.edu/hsirb/index.htm](http://research.missouri.edu/hsirb/index.htm).

4. DEFINITION

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

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

5. FACILITY DIRECTOR GENERAL RESPONSIBILITIES REGARDING HUMAN SUBJECT RESEARCH

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

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

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

(3) **Advertising.** The facility Director is responsible for ensuring that recruiting documents, flyers, and advertisements for non-VA research are not posted within or on the premises of a VA facility. Posting of such documents may give the Veteran or visitors to the VA facility the impression that the non-VA study is VA-approved research, the VA supports or endorses the research, or that VA will pay for the research expenses that are incurred. General guidance may be posted within VA indicating that Veterans may speak with their health care providers if they wish to participate in research and that information on clinical trials is available at: http://clinicaltrials.gov.

6. FACILITY DIRECTOR RESPONSIBILITIES WHEN AN EXTERNAL IRB (Affiliated IRB) OTHER THAN THE VA CENTRAL IRB IS AN IRB OF RECORD

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

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

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

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

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

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

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

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

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

### 7. VA Study Requirements

a. **Use of Social Security Numbers**

Investigators can obtain and use real Social Security numbers only when real Social Security numbers are required to meet the specific aims of the research protocol or to enter information into the subjects’ health records. The collection and use of real Social Security numbers must be approved by IRB, and the investigators must follow all applicable VA and other Federal requirements for obtaining and using real Social Security numbers.

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

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

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

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

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

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

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

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

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

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

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

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

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

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

(2) A procedure to determine when and how to notify individual subjects or their health care providers of findings that may affect the subjects’ health.
e. **Differentiating Usual Care from Research.** This means the investigator provides for usual care. If the protocol involves “usual care,” the protocol must either include a narrative section or there must be a separate document in the IRB application that clearly differentiates the research intervention(s) from “usual care” (whether the “usual care” is limited to one “arm” of the study or is being delivered to all study subjects).

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

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

(a) Explaining potential risks and benefits of the treatment or service to the subject;
(b) Providing the treatment or service;
(c) Monitoring the treatment or service, as applicable;
(d) Defining whether the adverse events result from usual care or research, as applicable;
(e) Alerting the subject if there is a problem with the treatment or service (e.g., a newly discovered risk, a product recall); and
(f) Documenting the subject’s clinical course while receiving the treatment or service, as applicable.

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

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

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

1. Whether or not individually identifiable information is to be collected or used;
2. How the data is to be collected or acquired;
3. Where the data (original and all copies) is to be stored and corresponding security systems;
4. How the data is to be transported or transmitted from one location to another;
5. Who is to have access to the data and how they are to access it (anyone who has access to the data is responsible for its security);
6. All entities or individuals outside VHA to whom the data is to be disclosed, and the justification for such disclosure and the authority (e.g., the HIPAA authorization);
7. Who is to have access and be responsible for the security of the information (e.g., the Coordinating Center, the statistician, and PI who has ultimate responsibility);
8. Mechanisms used to account for the information;
9. Security measures that must be in place to protect individually identifiable information if collected or used; and
10. How and to whom a suspected or confirmed loss of VA information is to be reported.

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

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

1. Identifies any circumstances that may warrant special safeguards to protect the rights and welfare of subjects who are likely to be vulnerable including, but not limited to, those subjects who may be susceptible to coercion or undue influence; and
2. Describes appropriate actions to provide such safeguards.

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

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

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

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

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

c. Suspension or Termination. IRB has authority to suspend or terminate approval of research that is not being conducted in accordance with IRB’s requirements, or that has been associated with unexpected serious harm to subjects. Any suspension or termination of approval must include a statement of the reasons for IRB’s action and must be reported promptly to the investigator, appropriate IO(s), and the department or agency head, according to applicable local, VA, and other Federal requirements (see 38 CFR 16.113, VHA Handbook 1058.01).

9. IRB COMPOSITION

a. Nonaffiliated Members

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

   2. Individuals who have retired from VA and who are receiving VA retirement benefits are considered affiliated.

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

b. Conflict of Interest. No IRB may have a member participate in the IRB’s initial or continuing review of any study in which the member has a conflicting interest, except to provide information requested by IRB (38 CFR 16.107(e)).
1. The member with a conflict of interest of a financial, professional, or personal nature must not be present during the vote or during any related IRB discussion except to answer questions; this member cannot be counted toward the quorum.

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

c. **Research Office Staff.** VA facility research office staff including, but not limited to the ACOS for R&D, the AO for R&D, and IRB administrative staff, may not serve as voting members of IRB. They may serve as ex officio, non-voting members, but they and IRB must be sensitive to and appropriately manage potential, actual, or perceived conflict of interest.

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

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

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

f. **Privacy Officer and Information Security Officer**

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

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

g. **Appointment of Members**

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

   (2) The HS IRB maintains a CV on file for all board members. These are made available to the VA R&D as requested.

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

   (4) In the event alternate members become necessary, the IRB will follow appropriate procedures with the VA to have alternate members appointed.
h. **Term of Appointment for Voting Members.** Voting members of VA IRBs and VA representatives to external IRB(s) of record are appointed for a period of up to 3 years. They may be re-appointed to new terms of up to 3 years without a lapse in service at the end of each term.

10. **IRB CONVENED MEETINGS**

IRB must observe the following requirements for convened meetings:

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

11. **EXEMPT RESEARCH**

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

   1. Review all requests for exemption in a timely manner,

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

   3. Record the determination.

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

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

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

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

12. **IRB APPROVAL CRITERIA**

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

a. **Risks and Benefits.**
(1) The IRB must ensure protocols with treatment or services that constitute “usual care” include a narrative section that clearly differentiates the research interventions from usual care, whether usual care is delivered to only some or to all research subjects.

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

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

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

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

**A. PARTICIPATION OF NON-VETERANS AS RESEARCH SUBJECTS**

VA research needs to be relevant to Veterans or active duty military personnel. The investigator must justify including non-Veterans in a VA research protocol, and the IRB must review the justification for inclusion of non-Veterans into the study before any non-Veterans can be recruited. The IRB must appropriately document in the IRB minutes or IRB protocol file its determinations regarding participation of non-Veterans in the study.

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

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

c. **Other Research.** Non-Veterans may be entered into an approved VA research study when the investigator can present a compelling argument to the IRB for the inclusion of non-Veterans (e.g., insufficient number of Veterans; survey of VA employees; study of active duty military; study involving Veterans’ family members), and the research is relevant to the care of Veterans or active duty military personnel.

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

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

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

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

13. **CONTINUING REVIEW**

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

   (1) A brief summary of the research methodology;

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

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

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

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

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

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

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

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

   (10) Summaries, recommendations, or minutes of the DMC meetings (if applicable) or findings based on information collected by the data and safety monitoring plan submitted in the initial proposal;
(11) An assurance that all identified unanticipated internal or local SAEs, whether related or unrelated to the research, have been reported as required to the IRB of record (see VHA Handbook 1058.01);

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

(13) Research findings to date, if available;

(14) Any relevant multi-center trial reports;

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

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

b) IRB Review

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

14. IRB COMMUNICATION WITH INVESTIGATORS

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

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

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

15. IRB RECORDS

a. Record Retention. The required records, including the investigator’s research records, must be retained until disposition instructions are approved by the National Archives and Records Administration and are published in VHA’s Records Control Schedule (RCS 10-1).
(1) All records must be accessible for inspection and copying by authorized representatives of VA, OHRP, FDA, and other authorized entities at reasonable times and in a reasonable manner in accordance with 38 CFR 16.115(b).

(2) Records are the property and the responsibility of the local research office. The local VA facility must designate where the records will be maintained or stored.

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

16. IRB MINUTES

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

a. **Vulnerable Populations.** Document any review of additional safeguards to protect vulnerable populations if entered as study subjects and findings related to the use of surrogate consent.

b. **Non-Veteran Subjects.** Provide a summary of the justification for including non-Veterans as subjects.

c. **Real Social Security Numbers.** Provide a summary of the discussion when real Social Security Numbers (SSNs), scrambled SSNs, or the last four digits of SSNs will be used in the study. The summary needs to include the security measures that are in place to protect the SSN instances embedded in the study. **NOTE:** This does not apply if the only use of SSNs is on the informed consent form or the HIPAA authorization as required by VHA Handbook 1907.01).

17. AUDITS

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

a. Involvement of vulnerable populations;

b. Level of risk;

c. Phase I or Phase II studies;

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

f. Data confidentiality or security concerns.

18. GENERAL REQUIREMENTS FOR INFORMED CONSENT
   a. **Person Obtaining Informed Consent.** If someone other than the investigator conducts the informed consent process and obtains informed consent from a subject or the subject’s representative, the investigator must formally and prospectively designate in writing in the protocol or the application for IRB approval, the individual who will have this responsibility. The person so designated must have received appropriate training to perform this activity. This person must be knowledgeable about the research to be conducted and the consent process, and must be able to answer questions about the study.

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

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

       (1) All required elements must be completed as well as any additional elements required by the IRB.

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

19. REQUIRED ELEMENTS OF INFORMED CONSENT-AS REQUIRED BY THE VA
   a. **Elements of Informed Consent Required by the Common Rule**

      (1) **Research-Related Injury**

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

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

      2. An explanation as to whether any medical treatments are available if injury occurs and, if so, what they consist of, or where further information may be obtained (38 CFR 16.116(a)(6).

      (b) Although the Common Rule at 38 CFR 16.116(a)(6) only requires that the informed consent contain information on research-related injury if the study is more than minimal risk, VA regulations (38 CFR 17.85) require the VA to provide care for all research-related injuries including those studies that are considered minimal risk.
(2) **Contact Information.** An explanation of whom to contact for answers to pertinent questions about the research and research subjects' rights, and whom to contact in the event of research-related injury to the subject (38 CFR 16.116(a)(7). There must be at least one contact other than the investigator or study personnel.

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

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

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

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

20. **ADDITIONAL ELEMENTS OF INFORMED CONSENT**

a. **Additional Elements of Informed Consent Required by the Common Rule**

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

(a) Pursuant to 38 CFR 17.102, subjects in VA-approved research cannot be charged, nor can their insurance be billed, for research-related interventions or procedures (e.g., tests, drugs, clinic visits, hospital admissions, transportation) that are required by the protocol. If medical services are furnished to a person who is not eligible for medical services as a Veteran, the medical care appropriation will be reimbursed from the research appropriation.

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

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

(1) **Commercial Product.** If applicable, that the investigator believes that the human biologic specimens obtained could be part of, or lead to the development of, a commercially valuable product.
(2) **Future Use of Specimens.** If the specimens are to be retained after the end of the study for future research, where the specimens will be retained, who will have access to them, and how long they will be retained. Current applicable institutional, VA and other Federal requirements must be met for handling, use and storage of biologic specimens and data (see VHA Handbook 1200.12).

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

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

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

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

**21. DOCUMENTATION OF INFORMED CONSENT**

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

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

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

(2) To facilitate use of the 10-1086 the HS IRB provides a consent template which includes all required elements of consent and VA specific required language.

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

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

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

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

2. The person obtaining the informed consent, and

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

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

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

d. **Copies of Signed Consent Form**

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

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

22. **SURROGATE CONSENT**

Under appropriate conditions, investigators may obtain consent from the LAR of a subject (i.e., surrogate consent). **NOTE:** Check with Regional Counsel for state or local requirements for surrogate consent for research that may supersede VA requirements.
a. **Assessment of Capacity.** Before persons who lack decision-making capacity may be considered for participation in any VA research, the IRB must find that the proposed research meets all of the conditions of –Research involving persons who lack decision making capacity(p. 27).

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

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

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

c. **LARs**

(1) **Authorized Person.** The following persons are authorized to consent on behalf of persons who lack decision-making capacity in the following order of priority (38 CFR 17.32(e)):

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

(b) Legal guardian or special guardian;

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

(d) Close friend.

**NOTE:** An individual who is qualified as a LAR to provide informed consent on behalf of a prospective research subject may not always qualify as a personal representative for purposes of consent to use or disclose a human subject’s PHI (i.e., signing a HIPAA authorization). Therefore, in circumstances involving authorization for use or disclosure of a human subject’s PHI, the investigator must ensure the LAR meets the requirements of a personal representative (legal guardian or power of attorney) in HIPAA and the Privacy Act of 1974 prior to the LAR’s signing a HIPAA authorization (see VHA Handbook 1605.1).

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

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

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

(c) LARs generally assume the same rights and responsibilities as the individuals who lack decision-making capacity in the informed consent process (see 38 CFR 17.32(e)).
d. **Dissent or Assent.** If feasible, the investigator must explain the proposed research to the prospective research subject even when the surrogate gives consent. Although unable to provide informed consent, some persons may resist participating in a research (i.e., if they dissent) protocol approved by their representatives. Under no circumstances may a subject be forced or coerced to participate in a research study even if the LAR has provided consent.

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

### 23. PRIVACY OFFICER AND INFORMATION SECURITY OFFICER RESPONSIBILITIES

The Privacy Officer and the ISO are responsible for:

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

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

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

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

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

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

e. Following up with the investigator, in a timely manner, to ensure the proposed research is in compliance with relevant privacy and confidentiality, and information security requirements, respectively, before the investigator initiates the study.
f. Providing summary reports of their review and assessment of each study according to the requirements of this paragraph. The summary report must clearly:

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

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

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

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

24. EMERGENCY USE OF A TEST ARTICLE

a. 

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

b. 

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

c. 

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

25. SERIOUS ADVERSE EVENTS (SAEs)

a. 

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

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

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

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

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

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

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

(a) When such notification must take place, and

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

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

26. **VHA HEALTH RECORD**
A VHA health record must be created or updated, and a progress note created, for all research subjects (Veterans or Non-Veterans) who are admitted to VA facilities as in-patients, treated as outpatients at VA facilities, or when research procedures or interventions are used in the medical care of the VA research subject at a VA facility or at facilities contracted by VA to provide services to Veterans (e.g., contract CBOCs or contract nursing homes) (see VHA Handbook 1907.01).

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

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

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

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

   (1) The name of the study;

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

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

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

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

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

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

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

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

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

   (11) VA Form 10-9012, Investigational Drug Information Record, or superseding forms for investigational drugs as defined in VHA Handbook 1108.04 (see VHA Handbook 1907.01);
(12) A copy of any research results that are used for medical care (see VHA Handbook 1907.01);

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

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

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

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

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

### 27. FLAGGING A VHA HEALTH RECORD

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

a. **Mandatory Flagging**

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

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

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

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

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

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

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

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

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

**28 VULNERABLE SUBJECTS**

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

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

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

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

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

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

c. **Populations Considered to be Categorically Vulnerable.** This subparagraph defines populations that are considered categorically vulnerable and specifies VA requirements for the inclusion of any of these categories of subjects in research. While all protocols need to be assessed for vulnerability of subjects within the context of the specific protocol, the populations named in this subparagraph must always have the additional protections specified in this paragraph applied. VA considers the following populations to be categorically vulnerable:
(1) **Fetuses.** Research in which the focus is either a fetus, or human fetal tissue, in-utero or ex-utero (or uses human fetal tissue), must not be conducted by VA investigators while on official duty, or at VA facilities, or at VA approved off-site facilities.

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

(3) **Pregnant Women**

(4) **Prisoners.**

(5) **Children.**

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

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

### 29. RESEARCH INVOLVING PREGNANT WOMEN

This paragraph applies to women who are pregnant at the time they are entered into a study. It does not preclude entering women of child bearing potential into studies including studies whose interventions include FDA’s Categories for Drug Use in Pregnancy’s Category C drugs. Women of child bearing potential may not be entered into studies involving the use of FDA Categories for Drug Use in Pregnancy’s Category D or X drugs unless a waiver is obtained from the CRADO.

### 30. RESEARCH INVOLVING PRISONERS

a. **Vulnerable Population.** Prisoners are considered a vulnerable population and may be under constraints because of their incarceration which could affect their ability to make a truly voluntary and uncoerced decision whether or not to participate as subjects in research (45 CFR 46.302).

b. **Waiver From CRADO.** Research involving prisoners cannot be conducted by VA investigators while on official VA duty, using VA resources, completely or partially in a VA facility or at a VA-approved off-site facility unless a waiver has been granted by the CRADO. If such a waiver is granted by the CRADO, the research must be in accordance with applicable Federal regulations pertaining to prisoners as research subjects (see 45 CFR 46, Subpart C 46.301–46.306, Additional Protections Pertaining to Biomedical and Behavioral Research Involving Prisoners as Subjects). **NOTE:** Requirements for requesting a waiver may be obtained by contacting ORD.

### 31. RESEARCH INVOLVING CHILDREN
a. **Waiver From CRADO.** VA is authorized to care for Veterans and to conduct research that supports the mission of VHA and that enhances the quality of health care delivery to Veterans. Therefore, research involving children cannot be conducted by VA investigators while on official VA duty, using VA resources, completely or partially in a VA facility or at a VA-approved off-site facility unless a waiver has been granted by the CRADO. **NOTE:** For purposes of this Handbook, research involving biological specimens or data obtained from children is considered to be research involving children.

b. **Criteria for Waiver.** Prior to requesting a waiver, the following criteria must be met:

1. The study represents no greater than minimal risk as determined by the IRB.

2. The study meets all requirements in 45 CFR 46, Subpart D, Additional Protections for Children Involved as Subjects in Research, Sections 46.401 through 46.404, and 46.408.

3. The IRB reviewing the study has appropriate membership to represent children’s interests and pediatric expertise.

4. The IRB reviewing the study has specific SOPs regarding children in research.

5. The VA facility Director certifies that the facility is able to respond to pediatric emergencies if the study includes interactions with children at the VA facility.

6. If the sponsor of the research is not VA, the facility Director makes certain that the sponsor of the research has procured appropriate liability insurance.

c. **Waiver Application.** To request a waiver, the following information must be submitted to ORD for each protocol:

1. A cover letter signed by the VA facility Director that contains the following information:

   a. Certification by the VA facility Director that the facility is able to respond to pediatric emergencies if the study includes an interaction with children at the VA facility.

   b. Any additional safeguards that have been incorporated into the clinical site where children will be studied.

   c. Information on the study’s funding source and on liability coverage if the sponsor is not VA.

   d. Certification that the IRB has determined the study to be of no greater than minimal risk and has approved the study.

   e. A statement that the required elements of 45 CFR 46 Subpart D have been met.

   f. A description of the relevance to Veterans’ health of both the study and the inclusion of children in the study.
(2) A copy of the study protocol, the informed consent form, the assent document, and HIPAA authorization. The informed consent document signed by the parent or guardian is the vehicle for parent or guardian permission. Provisions for permission by parents or guardians must be documented in accordance with and to the extent required by 38 CFR 16.117.

(3) Minutes of the IRB meeting approving the study. The IRB minutes need to reflect the discussion regarding level of risk, the informed consent and assent forms, the investigators’ qualifications to conduct research involving children, and any additional safeguards incorporated into the protocol.

(4) If the study involves biological specimens or data collected from children, in addition to the preceding requirements, the following must be submitted:

(a) A discussion of how the biological specimens or data were, or will be, obtained and under what consents or authorization.

(b) If the biological specimens or data were, or will be, collected for research purposes, the IRB approval, the informed consent form, and the HIPAA authorization for the research.

(c) If biological specimens or data were, or will be, collected from an international site, a waiver from the CRADO for international research.

(d) Plans for future use of biological specimens or data.

32. RESEARCH INVOLVING PERSONS WHO LACK DECISION-MAKING CAPACITY

Persons who lack decision-making capacity are not to be subjects in research simply because they are readily available.

a. IRB Review and Approval. No individual who lacks decision-making capacity may participate in VA Research until the IRB has reviewed and approved that individual’s, or that class of individuals’, participation in a given study.

b. Criteria for Decision-Making Capacity

(1) An individual is presumed to have decision-making capacity unless any one or more of the following apply:

(a) It has been documented by a qualified practitioner in the individual’s medical record in a signed and dated progress note that the individual lacks capacity to make the decision to participate in the proposed study. **NOTE:** The qualified practitioner may be a member of the research team.

(b) The individual has been ruled incompetent by a court of law.
(2) If there is any question as to whether or not a potential adult subject has decision-making capacity, and there is no documentation in the medical record that the individual lacks decision-making capacity, and the individual has not been ruled incompetent by a court of law, the investigator must consult with a qualified practitioner (who may be a member of the research team) about the individual’s decision-making capacity before proceeding with the informed consent process.

c. **Temporary or Fluctuating Lack of Decision-Making Capacity.** Individuals, who because of a known condition, are at high risk for temporary (e.g., head trauma) or fluctuating (e.g., schizophrenia) lack of decision-making capacity must be evaluated by a qualified practitioner (who may be a member of the research team), to determine the individual’s ability to provide informed consent. This evaluation must be performed as described in the IRB-approved protocol. If the individual is deemed to lack decision-making capacity at the time of their participation in the study, a LAR must provide informed consent. If the subject regains decision-making capacity, the investigator or designee must repeat the informed consent process with the subject, and obtain the subject’s permission to continue with the study.

d. **Criteria for Enrollment.** Individuals who lack decision-making capacity may be enrolled in protocols if:

(1) The proposed research entails:

(a) No greater than minimal risk to the subject as determined by the IRB; or

(b) If the research presents some probability of harm, there must be at least a greater probability of direct benefit to the subject or

(c) Greater than minimal risk and no prospect of direct benefit to individual subjects, but is likely to yield generalizable knowledge about the subject’s disorder or condition that is of vital importance for the understanding or amelioration of the subject’s disorder or condition.

(2) The disorder (e.g., Alzheimer’s) leading to the individual’s lack of decision-making capacity is being studied, whether or not the lack of decision-making itself is being evaluated (e.g., an individual who lacks decision-making capacity as the result of a stroke can participate in a study of cardiovascular effects of a stroke), but only if the study cannot be performed with only persons who have decision-making capability.

(3) The subject of the study is not directly related to the individual’s lack of decision-making capacity, but the investigator can make a compelling argument for including individuals who lack decision-making capacity in the study (e.g., transmission of methicillin-resistant *Staphylococcus aureus* (MRSA) infections in a nursing home where both individuals with, and those without, decision-making capacity are affected).

e. **IRB Determination.** If the criteria are met, the IRB may approve the inclusion of individuals who lack decision-making capacity in research studies on the basis of informed consent from LARs.

(1) Before approving the study, the IRB must:
(a) Ensure the study includes appropriate procedures for respecting dissent;

(b) Consider whether or not the study needs to include procedures for obtaining assent; and

(c) Determine whether any additional safeguards need to be used (e.g., consent monitoring).

(2) The IRB must document its deliberations and the criteria used to approve inclusion of individuals who lack decision-making capacity in the IRB minutes or IRB protocol file.

33. MULTI_SITE STUDIES

a. **Local VA Facility’s IRB of Record’s Responsibilities for Multi-Site Research When the VA Facility’s Investigator is the Multi-Site Study PI for All Participating Facilities and the VA Central IRB is Not Being Used**. In addition to other IRB responsibilities delineated in this Handbook, when the VA facility’s investigator is the multi-site study PI or study sponsor for all participating facilities, and VA Central IRB is not being used, the PI’s or study sponsor’s local VA facility’s IRB of record is responsible for:

   (1) When a participating site is added to the study, determining:

      (a) Whether or not that site will be engaged in human subjects research.

      (b) If the site will be engaged in research, then reviewing and confirming that it:

         1. Has an active FWA, and

         2. Has provided documentation of all relevant approvals, including approval of its IRB of record.

   (2) Approving the study-wide protocol and sample informed consent document to be provided to each LSI at engaged facilities.

   (3) Ensuring the study-wide protocol contains a mechanism for ensuring that any differences in the protocol or informed consent at engaged local participating sites are justified by the LSI, and that they are approved by the PI before being implemented.

   (4) Ensuring there are clear AE reporting requirements, a data monitoring committee if applicable (or other reliable monitoring mechanism) with clear procedures and requirements, and a clearly defined feedback loop to the PI’s or study sponsor’s IRB.

   (5) Reviewing the PI’s plan for communicating appropriate critical information (e.g., reports of data and safety monitoring) to engaged participating sites.

   (6) Ensuring, when relevant, confidentiality and information security requirements are met for information storage at and transmission to statistical or coordinating centers.
(7) Reviewing reports from applicable DMCs.

34. RESEARCH INVOLVING HUMAN BIOLOGICAL SPECIMENS

All activities involving the collection of human biological specimens for research purposes, as well as the research use of specimens collected for clinical care, must be conducted under the terms of an approved research protocol. The collection and use of human biological specimens (either identifiable or de-identified) must comply with all applicable VA and other Federal requirements including, but not limited to: 21 CFR 50, 21 CFR 312, 38 CFR 16, 45 CFR 46 D (if research involves specimens from children), 45 CFR 160 and 164 (HIPAA), VHA Handbook 1200.8, and current VA requirements for research involving human biological specimens or superseding requirements. *NOTE: ORD can be contacted for questions regarding research involving stem cells or cord blood.*

35. RESEARCH INVOLVING HUMAN DATA

Use of VA or non-VA human data and data repositories (whether developed for health care, administration of VA programs, or research) for research purposes must be consistent with the mission of VA including:

a. Having relevance to the health of Veterans,

b. Protecting the privacy of the individuals from whom the data were collected, and

c. Being consistent with all applicable ethical and regulatory standards, and all applicable VA and other Federal requirements (see VHA Handbook 1200.12).

*NOTE: The information from DNA sequencing is considered human subjects data (see subpar. 3n and VHA Handbook 1200.12).*

36. RESEARCH INVOLVING COLLECTION OF DATA FROM VOICE, VIDEO, OR PHOTOGRAPHS MADE FOR RESEARCH PURPOSES

a. **Informed Consent for Research**

   (1) Informed consent for research must be obtained from each research subject before taking photographs or making voice or video recordings that will be used for research purposes.

   (2) Unless IRB grants a waiver of documentation of informed consent for research, the informed consent form for research (i.e., VA Form 10-1086) must include a discussion of why photographs, or voice or video recordings are being taken for the research, who will have access to them, and what their disposition will be after the research is completed.

b. **VA Form 10-3203, Consent for Use of Picture and/or Voice.** VA Form 10-3203 documents permission for pictures, video, and voice recordings to be made or taken. In the conduct of research, VA Form 10-3203 must be used in accordance with applicable VA and VHA policy.
(1) When the research subject is a patient (either an inpatient or outpatient), the subject must sign VA Form 10-3203 to permit photographs or video and voice recordings that will be used for research purposes even if the IRB has waived the requirement for documentation of informed consent for research (VA Form 10-1086). Photography or recordings cannot occur prior to the patient’s granting such permission (VHA Handbook 1907.01).

(2) When the research subject is a patient, the subject’s signed and dated VA Form 10-3203 must be placed into the medical record along with, if applicable, the signed and dated research informed consent form (i.e., VA Form 10-1086). The signed VA Form 10-3203 must be obtained and placed in the subject’s medical record, even if the IRB has waived documentation of informed consent for research.

c. **VA Form 10-5345, Request for and Authorization to Release Medical Records or Health Information.** VA Form 10-5345 documents permission for the disclosure of medical records or health information, including pictures, video, and voice recordings to another individual. In the conduct of research, VA Form 10-5345 must be used in accordance with applicable VA and VHA policy.

37. INTERNATIONAL RESEARCH

**NOTE:** For the purposes of this Handbook, research conducted at U.S. military bases, ships, or embassies is not considered international research.

All individuals who participate as subjects in research at international sites must be provided appropriate protections that are in accord with those given to research subjects within the U.S., as well as protections considered appropriate by local authority and custom at the international site (38 CFR 16.101(g)).

a. **Definition of VA International Research.** VA international research is defined as any VA-approved research conducted at international sites (not within the U.S., its territories, or Commonwealths); any VA-approved research using either human biological specimens (identified, de-identified, or coded) or human data (identified, de-identified, or coded) originating from international sites; or any VA-approved research that entails sending such specimens or data out of the U.S. **NOTE:** This includes sending such specimens or data to individuals with VA appointments at international sites (e.g., a WOC appointment, a VA investigator on sabbatical at an international site). It also includes a VA’s serving as a coordinating center for an international research project.

b. **Multi-Site Trials.** Multi-site trials are covered under this definition if any of the following apply:

   (1) VA is a sponsor;

   (2) VA functions as the coordinating center;

   (3) VA subcontracts to a foreign site;
(4) The PI for the total study is a VA investigator; or

(5) The VA investigator is specifically collaborating with an international investigator and the VA investigator sends data or human biological specimens outside the U.S., or receives them from outside the U.S.

**NOTE:** This requirement does not apply if VA is only one of the participating sites and the trial does not meet the preceding conditions.

c. **CRADO Permission.** Permission must be obtained from the CRADO, or designee, prior to initiating any VA-approved international research. This applies regardless of the funding source (funded or unfunded) and to research conducted through any mechanism of support including agreements, MOU, Cooperative Research and Development Agreements (CRADA), grants, or contracts. The CRADO, or designee, will not grant permission for an international research study involving prisoners as research subjects.

d. **FWA and Approval.** All international sites must hold an international FWA, and the research must be approved by the IRB or Research Ethics Board of the participating site(s) that are listed on the international FWA.

e. **VA Facility Director’s Responsibilities.** In addition to VA facility Director responsibilities delineated elsewhere in this Handbook, the facility Director is responsible for:

   1. Approving the request for permission to conduct international research prior to forwarding it to the CRADO for action.

   2. Ensuring permission has been obtained from the CRADO, or designee, for the international research prior to its initiation by an investigator at the facility. **NOTE:** Information on how to request permission may be referenced on the following Web site at: [http://www.research.va.gov/resources/policies/docs/instructions-intl-research.pdf](http://www.research.va.gov/resources/policies/docs/instructions-intl-research.pdf)

f. **PI Responsibilities.** In addition to the PI responsibilities delineated elsewhere in this Handbook, the PI is responsible for:

   1. Obtaining approval from the facility Director.

   2. Obtaining permission from the CRADO, or designee, in writing before initiating an international research study.

   3. Conducting research in compliance with this Handbook, and all other applicable VA and other Federal requirements including those for protecting human subjects, tissue banking, use of databases, Federal criminal laws, and the Standards of Ethical Conduct for Employees of the Executive Branch.

**38. USE PREPARATORY TO RESEARCH**

Data repositories (including VA medical records) may be used (i.e., accessed) by VA investigators for activities that are preparatory to VA research without the requirement to obtain
either a HIPAA authorization from the subject or waiver of HIPAA authorization by an IRB or Privacy Board. This includes use of PHI for the preparation of a research protocol prior to submission to the IRB(s). “Preparatory to research” activity is the only instance of access for research purposes allowed in VHA without a written HIPAA authorization signed by the individual, a waiver of HIPAA authorization by an IRB or Privacy Board, or approval by the IRB(s). This access is granted only to VHA researchers. Non-VHA researchers may not access VHA data for reviews preparatory to research. Additionally, the following holds true:

a. **Representations by the Investigator.** The investigator must make the representations necessary for preparatory access as required by the HIPAA Privacy Rule and document it in the investigator's research files. The representations required by the HIPAA Privacy Rule are:

   (1) The access to PHI is only to prepare a protocol;
   
   (2) No PHI will be removed from the covered entity (i.e., VHA); and
   
   (3) The PHI accessed is necessary for preparation of the research proposed.

b. **Aggregate Data.** Only aggregate data may be recorded in the researcher’s files, and these aggregate data may be used only for background information, to justify the research, or to show that there are adequate numbers of potential subjects to allow the investigator to meet enrollment targets or sample size requirements.

c. **No Recording of Individually Identifiable Health Information.** Individually identifiable health information may not be recorded.

d. **No Recruiting From Data.** Data or information reviewed may not be used for contacting or recruiting subjects.

e. **Repository Requirements.** Investigators must comply with all other access requirements set by the repository of interest.

f. **Agreements.** See VHA Handbook 1200.12 regarding requirements for Data Use Agreements (DUA) or Data Transfer Agreements (DTA).

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

   **NOTE:** No formal IRB determination of exemption from human subject protection requirements is needed if all of the conditions listed in paragraph 57 are satisfied.

### 39. PAYMENT TO SUBJECTS

a. **Payment Permitted.** Payment to subjects may be permitted, with IRB approval, in the following circumstances:
(1) **No Direct Subject Benefit.** When the study to be performed is not directly intended to enhance the diagnosis or treatment of the condition for which the volunteer subject is being treated, when the standard of practice in affiliated non-VA institutions is to pay subjects in this situation.

(2) **Others Being Paid.** In multi-institutional studies, when human subjects at a collaborating VA or non-VA institution are to be paid for the same participation in the same study, subjects may be paid at a rate comparable to that proposed at the other sites, if deemed reasonable by the local IRB.

(3) **Comparable Situations.** In other comparable situations in which, in the opinion of the IRB, payment of subjects is appropriate.

(4) **Transportation Expenses.** When transportation expenses are incurred by the subject that would not be incurred in the normal course of receiving treatment and that are not reimbursed by any other mechanism.

**NOTE:** Investigators must not pay human subjects to participate in research when the research is integrated with a patient’s medical care and when it makes no special demands on the patient beyond those of usual care.

b. **Protocol Provisions for Payment.** Prospective investigators who wish to pay research subjects must include in the protocol:

1. Substantiation that proposed payments are reasonable and commensurate with the expected contributions of the subject;

2. The terms of the payment and the amount of payment are in the informed consent form.

3. Substantiation that subject payments are fair and appropriate, and that they do not constitute (or appear to constitute) undue pressure or influence on the prospective research subjects to volunteer for, or to continue to participate in, the research study. In addition, the payments do not constitute (or appear to constitute) coercion to participate in, or continue to participate in, the research study.

c. **IRB Review.** The IRB must review all proposals for payment of subjects to ensure conformity with VA requirements.

d. **Source of Funding.** The VA facility research office must ensure IRB-approved payment to subjects is made from a VA-approved source for funding research activities.

**NOTE:** Due to limitations in the Financial Management System, payments to subjects made through Austin Financial Services Center generate Internal Revenue Service (IRS) Form 1099 regardless of amount. This information, and the fact that the SSN will be used for this purpose, must be included in the informed consent form. Gift cards are not subject to these reporting requirements.

40. TREATMENT OF RESEARCH-RELATED INJURIES TO HUMAN SUBJECTS
a. **VA Facilities’ Responsibilities.** VA medical facilities must provide necessary medical treatment to a research subject injured as a result of participation in a research study approved by a VA R&D Committee and conducted under the supervision of one or more VA employees (38 CFR 17.85). This does not apply to:

1. Treatment for injuries due to non-compliance by a subject with study procedures (38 CFR 17.85(a)(1)); or

2. Research conducted for VA under a contract with an individual or a non-VA institution (38 CFR 17.85(a)(2)).

b. **Provision of Care Outside VA Facilities.** Care for VA research subjects under this Paragraph must be provided in VA medical facilities, except in the following situations:

1. If VA facilities are not capable of furnishing economical care or are not capable of furnishing the care or services required. Under these circumstances, VA facility Directors may contract for such care (38 CFR 17.85(b)(1)).

2. If inpatient care must be provided to a non-Veteran under this paragraph, VA facility Directors may contract for such care (38 CFR 17.85(b)(2)).

3. The sponsor cannot bill the injured subject’s insurance company for the injury; however, the sponsor is responsible for reasonable and customary costs incurred for treatment of injury reasonably related to the subject’s participation in the study described in the scope of work except to the extent that:
   a. The injury is attributable to the negligence or willful misconduct of an indemnitee; or
   b. The injury is attributable to failure to administer the test article as required in the protocol or to otherwise substantially follow the protocol.

4. If a research subject needs treatment in a medical emergency in a non-VA facility for a condition covered by this paragraph, VA facility directors must provide reasonable reimbursement for the emergency treatment in a non-VA facility (38 CFR 17.85(b)(3)).

41. **STUDENT AND OTHER TRAINEE RESEARCH**

a. **Research Conducted by Students and Other Trainees to Fulfill Academic Requirements.** Only students and other trainees (including residents and fellows), including VA employees, from schools with an academic affiliation agreement consistent with current VHA policy, may serve as investigators within a VA facility, or use data, or human biological specimens that have been collected within VA for clinical, administrative, or research purposes. **NOTE:** A waiver may be obtained from the CRADO under special circumstances.

1. A VA investigator sufficiently experienced in the area of the trainee’s research interest must serve as PI or co-PI and is responsible for oversight of the research and the trainee. The PI
or co-PI is responsible for ensuring the trainee complies with all applicable local, VA and other Federal requirements.

(2) In conducting the research, the trainee must comply with all VA and other Federal and local institutional requirements, including those related to research, information security, and privacy.

(3) If the trainee does not complete all aspects of the research prior to leaving VA, the VA employee serving as the PI or co-PI must ensure the protocol is completed or terminated in an orderly fashion, and in accordance with all applicable local, VA, and other Federal requirements.

(4) When the trainee leaves VA, the VA employee serving as the PI or co-PI is responsible for ensuring all research records are retained by VA.

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

43 **Planned Emergency Research.** Planned emergency research must not be granted approval by a VA IRB or R&D Committee and cannot be conducted by VA.