REVIEWING VA RESEARCH

This document highlights specific requirements applicable to research supported by, or otherwise subject to, the Department of Veterans Affairs (VA).

Questions on VA requirements? Contact RHJVAHCS Human Research Protection Program (HRPP) Administrator.

GENERAL INFORMATION	
WHEN TO APPLY VA REGULATIONS	• **VA Research:** VA research is research that is conducted by researchers (serving on VA compensated, WOC, or IPA appointments) while on VA time or on VA property. The research may be funded by VA, by other sponsors or be unfunded. VA research must have Research and Development Committee (R&DC) approval before it is considered VA Research and before it can be initiated. All research activities approved by the R&DC are considered VA Research. **VA appointment status is confirmed by the R&D committee.** ***NOTE**: Any emergency use of a test article does not require R&D Committee approval but is VA research under this policy.* • **Nonprofit Research and Education Corporations:** VA-affiliated nonprofit research and education corporations (NPC) are authorized by Congress under 38 U.S.C. 7361-7366 to provide flexible funding mechanisms for the conduct of research and education at one or more VA facilities. Research approved by a facility R&D Committee are considered to be a VA research project or a VA education activity respectively, regardless of the source of funding, the entity administering the funds, or the research or education site (see VHA Handbook 1200.17, Department of Veterans Affairs Nonprofit Research and Education Corporations Authorized by Title 38 U.S.C. Sections 7361 Through 7366, dated April 27, 2016, and revised May 9, 2017).Individuals working under a VA contract may not serve as VA investigators while simultaneously serving as contractors. • **International Research:** VA international research is defined as any VA-approved research conducted at international sites (i.e., not within the United States (U.S.), its territories, or Commonwealths), any VA-approved research using either identifiable or de-identified human biological specimens or identifiable or de-identified human data originating from international sites, or any VA-approved research that entails sending such specimens or data out of the U.S. This definition applies regardless of the funding source (funded or unfunded) and to research conducted through any mechanism of support including MOUs, CRADAs, grants, contracts, or other agreements. ***NOTE**: Research conducted at U.S. military bases, ships, or embassies is not considered international research.*
INVESTIGATOR VA APPOINTMENT REQUIREMENT	All investigators conducting VA research — including the principal investigator, co-investigators, and sub-investigators — must hold a current VA appointment (compensated, WOC, or IPA) at the time they participate in VA research activities. Investigators who do not hold a VA appointment may not conduct VA research, regardless of their MUSC appointment status. • VA appointment types include: VA-compensated (salaried), Without Compensation (WOC), or Intergovernmental Personnel Act (IPA). • VA appointment status must be confirmed and documented in the study's IRBNet application prior to submission. • A change in a VA investigator's appointment status must be reported as a modification if it affects the investigator's ability to conduct VA research activities.

	Note: Individuals working under a contract with VA may not serve as VA investigators. Contractors may participate in research in other capacities, such as collaborators or consultants, but may not be listed as VA investigators on a VA research protocol.
VA RESEARCH TRAINING REQUIREMENTS	All individuals subject to VA regulations who participate in VA human research — including investigators, co-investigators, research coordinators, and other study personnel — must complete training in the ethical principles governing human research before they may participate in VA research activities. Training must meet requirements specified by ORD and must be completed before study initiation. Required training elements include: • Human subjects protections (Good Clinical Practice or equivalent, as required by study type) • HIPAA and VA privacy requirements • VA-specific research regulations and VHA Directive 1200.05 requirements • Any additional training modules required by ORD for specific research types Training completion must be documented in IRBNet prior to protocol submission. The RHJVAHCS HRPP Administrator can provide current ORD training requirements and acceptable training programs.
2018 REVISED COMMON RULE	VA Research must follow 2018 Common Rule (e.g., concise summary in beginning of consent, 2018 OHRP elements of consent, 2018 OHRP waiver requirements, etc.)
TYPES OF MODIFICATIONS	• HIPAA Authorization changes or requests for HIPAA waiver • Significant changes to study design • Changes impacting privacy, data sharing, or security • Changes to protocol • Change in PI • Changes to advertisements or recruitment materials/methods • Addition of new funding • Adding VA or MUSC as a site (collaborative) • Adding non-Veteran population to VA research • Adding personnel to VA-only research
EXEMPT DETERMINATIONS	Exempt determinations may be made by the IRB Chair, an experienced IRB member, or qualified administrative staff with expertise in applying human research exempt regulations. Limited IRB review for applicable exempt activities may be done by the convened IRB, the IRB Chair, or delegated to one or more experienced reviewers from among voting IRB members. ***NOTE**: If the exempt activity involves PHI, a waiver of HIPAA authorization must be approved by the appropriate authority (IRB or Privacy Board or designated member of the IRB or Privacy Board), a written HIPAA authorization must be obtained from the subject or subject's LAR or a DUA for use or disclosure of a limited data set must be obtained.*
EXEMPT CATEGORIES 2 & 3	Exempt categories 2 and 3 require use of a limited IRB review if the information obtained is recorded by the investigator in such a manner that the identity of the human subjects can readily be ascertained, directly or through identifiers linked to the subjects. a) For exempt research activities involving the researcher interacting with human participants or obtaining information by educational tests, survey or interview procedures, or behavioral interventions, the following information must be given to the prospective human participant as applicable in writing or orally: 1) The activity is research.

	2) Participation is voluntary. 3) Permission to participate can be withdrawn. 4) Permission for use of data can be withdrawn for exempt research activities involving the collection and use of identifiable data. 5) Contact information for the VA researcher. b) If an exempt activity requires a limited IRB review, the limited IRB review must be completed prior to approval by the R&D Committee. c) Research that has undergone limited IRB review and determined to be exempt requires approval by the R&D Committee and requires continuing review by the R&D Committee unless it is under the oversight of another subcommittee (e.g., Safety Review Subcommittee).
EXEMPT CATEGORY 5	***NOTE**: The determination of exempt status for research and demonstration projects meeting the criteria for exempt category 5 must be made by the Under Secretary for Health on behalf of the Secretary of VA, after consultation with Office of Research and Development (ORD), Office of Research Oversight (ORO), Office of General Counsel (OGC), and other experts, as appropriate.*
IRBNET ID FOR eIRB	If anyone on the VA team needs an IRBNet ID, please contact the RHJVAHCS HRPP Administrator.
JOINT MUSC/VA STUDIES (COLLABORATIVE)	The protocol, study procedures, data storage, consent process, research setting, and recruitment methods entered into eIRB should clearly delineate which procedures will occur at MUSC facilities, and which at VA.
ICDs AND HIPAA AUTHORIZATION	The following may have multiple informed consent documents and HIPAA Authorization forms: • If the research project includes a non-Veteran or study partner • If separate procedures will be taking place at an offsite VA location (i.e. MUSC)
VA-SPECIFIC FORMS	For VA research, the following forms are required: • VA Form 10-250 (Privacy Review Checklist) for **all studies** • VA Form 1086 (Informed Consent), as applicable • VA Form 10-0493 (HIPAA Authorization), as applicable • VA Form 10-3203 (Media Consent), as applicable • VA Form 10-9012 (Investigational Drug Information Record), as applicable
RESEARCH REQUIRING ORD APPROVAL (*LINKS ONLY ACCESSABLE ON THE VA INTRANET*)	• Proactive (cold) calling • Electronic consent (DocuSign) • VA Box (data storage) • Single IRB (sIRB) When a VA investigator serves as the multi-site PI for all participating sites, the VA facility may use a designated multi-site IRB only if that IRB has been specifically approved by ORD for multi-site VA review. The following requirements apply: • ORD approval is required before MUSC may serve as the sIRB of Record for a VA-led multi-site study. Study teams should contact the RHJVAHCS HRPP Administrator to initiate the ORD designation request. • A signed reliance agreement (MOU or Authorizing Agreement) between the VA facility and MUSC must be in place before review begins. • The reliance agreement must require MUSC to comply with VHA Directive 1200.05 and all VA-applicable regulations when reviewing VA research. • VA representation requirements (including the voting member quorum rule) apply to all convened reviews of VA multi-site protocols.
DATA USAGE/SHARING/STORAGE	The protocol, addendum, and/or IRB of Record application must describe the data to be disclosed to collaborators, the entities to which the data are to be disclosed, how the data are to be transmitted, and how the transmitted data will be stored, retained, destroyed, and/or further disclosed and to whom. This includes data from individual subjects as well as other data developed during the research such as the analytic data and the aggregate data. Data use/sharing agreements must be submitted to the Office of Research Reviews (ORR).

	The protocol should include: • Where data will be stored • How data will be analyzed • Provisions for monitoring the data • Protection to the privacy of subjects and maintaining confidentiality of the data • ***NOTE**: If there is a change made for research purposes in the way the identifiable private information or identifiable biospecimens are stored or maintained, there are adequate provisions to protect the privacy of subjects and to maintain the confidentiality of the data* VA Researchers are responsible for: • Ensuring that all original or digitalized signed and dated informed consent documents are maintained in the researcher's research files, stored on a VA protected server, readily retrievable, and secure. • Creating or updating a VA health record and creating a progress note for all research participants (Veterans or non- Veterans) who receive research procedures or interventions as inpatients or outpatients at VA medical facilities that are either used in or may impact the medical care of the research participant at a VA medical facility or at facilities contracted by VA to provide services to Veterans (e.g., Community-Based Outpatient Clinics or community living centers). Informed consent documents are not required to be in the health record. • Using VA Box, not MUSC Box, for VA research data. This is captured in the HIPAA and the VA Form 10-250. DUA reviews are centralized at the VA level (including ERDSP below).
VIDEO CONFERENCING TOOLS	VA allows the use of Microsoft Teams and WebEx for video conferencing. Zoom has been discontinued.
ENTERPRISE RESEARCH DATA SECURITY PLAN (ERDSP)	VAHCS Information Safety Security Officers (ISSO) are no longer conducting local ERDSP reviews. All ERDSPs must be submitted directly to the Office of Research Review (ORR) by the study team. This is centralized at the VA level and tracked internally by the VA. An Enterprise Research Data Security Plan (ERDSP) is required for all VA research studies involving electronic data. The ERDSP documents how the study team will protect VA research data in accordance with VA Directive 6500. Submission process: • The ERDSP must be submitted and approved by ORR before research involving electronic VA data may be initiated. • ERDSPs must be updated when there are changes to data storage, transmission methods, or personnel with access to VA data. • Contact the RHJVAHCS HRPP Administrator for the current ERDSP template and ORR submission instructions.
HIPAA IDENTIFIERS	Under VA policy, a scrambled (masked) Social Security Number (SSN) is treated as a HIPAA-covered identifier and constitutes individually identifiable information. Research protocols that include scrambled SSNs as part of a dataset must include appropriate

	HIPAA authorization or an IRB-approved waiver of authorization, even when other identifying elements have been removed. NOTE: This is a VA-specific policy that exceeds standard HIPAA de-identification requirements. Study teams working with VA datasets should contact the RHJVAHCS Privacy Officer to confirm identifier status before treating data as de-identified.
RECORDS RETENTION	All VA research data should be maintained according to VHA Record Control Schedule (RCS 10-1).
FINANCIAL CONFLICT OF INTEREST	Researchers must disclose their conflicts of interest during the initial submission of their study, annually, and in the interim if changes are made outside of the annual submission window. This means disclosing to the IRB and R&DC any potential, actual, or perceived conflict of interest of a financial, professional, or personal nature that may affect any aspect of the research and complying with all applicable VA and other federal requirements regarding conflict of interest. Conflicts of interest must be submitted electronically via wizard directly into IRBNet to be reviewed and acknowledged by either the facility's Financial Conflict of Interest (FCOI) Administrator, or the Office of General Counsel (OGC).
CONSENT FORMS AND HIPAA AUTHORIZATION	
CONSENT TEMPLATE	VHA Directive 1200.05 outlines general requirements and documentation for informed consent. The Ralph H. Johnson VA and MUSC require use of VA Form 1086 – Research Consent Form, unless otherwise provided by the sponsor. The RHJVAHCS Informed Consent Template has VA specific language regarding costs, payment, research data storage in medical records, compensation, and additional optional sections. Usage of the template helps ensure all required language is present.
COLLABORATIVE RESEARCH WITH VA	When engaged in collaborative research with RHJVAHCS, each institution must use the informed consent document required by its respective institutional policies for participants recruited from that institution, or procedures requiring participation of the subject at that institution. When procedures are taking place and separate locations, the informed consent documents must clearly describe which procedures will be performed under VA's auspices, and which will be performed under a non-VA institution's auspice. • The VA informed consent document must clearly state when procedures conducted at other non-VA institutions are part of the VA's portion of the study. • The informed consent document and HIPAA authorization (for the VA portion of the collaborative study) must not contain inconsistent provisions.
DATE OF IRB APPROVAL	The informed consent document must contain the date with an IRB approval stamp. The informed consent document must be signed and dated by the participant or LAR, and the person obtaining consent.
VA FORM 10-0493, HIPAA AUTHORIZATION	The Ralph H. Johnson VAHCS requires separate informed consent documents and HIPAA Authorizations.
OBTAINING CONSENT	If the investigator does not personally obtain informed consent, the investigator must delegate this responsibility in writing (e.g., by use of a delegation log) to research staff sufficiently knowledgeable about the protocol and related concerns to answer questions from prospective participants, and about the ethical basis of the informed consent process and protocol.
ELECTRONIC CONSENT (e-CONSENT)	Consent may be obtained and documented electronically so long as there are appropriate authentication controls to provide assurance the consent is rendered by the appropriate individual, and the participant dates the consent, or software provides the current date when signed. • DocuSign is the VA-approved application for obtaining electronic-consent. Approval is required from the Office of Research and Development (ORD).
POSTING CONSENTS FOR CLINICAL TRIALS	If a VA research study is a clinical trial, the IRB-approved informed consent form must be posted after the clinical trial is closed to recruitment and no later than 60 days after the last study visit by any subject as described in the IRB-approved protocol. For multi-site studies, it applies when the entire study has closed to subject recruitment. Consent forms must be posted on either https://clinicaltrials.gov/ or a docket folder on http://Regulations.gov. (Docket ID: HHS-OPHS-2018-0021).

DATA AND MEDICAL RECORDS	VA Form 1086, Informed Consent Template, includes language regarding whether information about a participants' involvement in research will be included in their medical records, as well as whether identifiable or de-identifiable data will be shared for future studies or research. For studies in which information about the participant's participation will be included in the VA medical record, information must be provided to the prospective participants as part of the consent process.
SPECIMEN BANKING OR STORAGE FOR FUTURE RESEARCH	If specimens (e.g., blood, tissue, body fluids) will be stored for future research, describe the storage procedures in the informed consent template under "Collection of Specimens".
AUDIO, PHOTO, AND VIDEO	The informed consent for research must include information describing any photographs, video, and/or audio recordings to be taken or obtained for research purposes; how the photographs, video, and/or audio recordings will be used for the research; and whether the photographs, video, and/or audio recordings will be disclosed outside VA. • An informed consent to take a photograph, video, and/or audio recording cannot be waived by the IRB. • The consent for research does not give legal authority to disclose the photographs, video, and/or audio recordings outside VA. The disclosure of photo/audio/video must be in the HIPAA authorization. • VA Form 10-3203, Media Consent, is required to be submitted along with the ICD for review by the IRB, Privacy Officer, and R&DC.
COSTS TO PARTICIPANTS AND RESEARCH-RELATED INJURIES	Costs • If any costs to the participant or the participant's health insurance might result from the research (i.e. for tests, drugs, biologics, devices, or copayments), they must be described. • Any charges for investigational drugs or devices must be authorized. • If participants bear any additional costs (e.g. transportation, time away from work, health costs, etc.), it must be disclosed. Any such costs must be consistent with Federal laws concerning Veterans' eligibility for medical care and treatment. Research-Related Injuries • The VA will provide necessary medical treatment to a research subject injured by participation in a research project. This requirement does not apply to treatment for injuries that result from non-compliance by a research subject with study procedures. If you sustain an injury as a direct result of your study participation, medical care will be provided by the Ralph H. Johnson VA Health Care System. Required Language • You or your insurance will not be charged for any treatments or procedures that are part of this study. If you usually pay co-payments for VA care and medications, you will still pay these copayments for VA care and medications that are not part of this study.
CERTIFICATE OF CONFIDENTIALITY	When VA conducts a study that is protected by a Certificate of Confidentiality, the following requirements apply: • For studies in which information about the subject's participation will be included in the subject's VHA medical record, information must be given to the prospective subjects as part of the informed consent process that information regarding study participation will be included in the medical record; and • For studies in which the IRB requires written informed consent, the informed consent document approved by the IRB must include a statement that the study has a Certificate of Confidentiality. ***NOTE:*** *The HHS agencies that issue Certificates of Confidentiality usually have guidance specific to the issuing agency on statements that must be included in informed consent documents*

	describing Certificates of Confidentiality. See Office of Research Development FAQs on CoCs
LEGALLY AUTHORIZED REPRESENTATIVE (LAR)	The signature block for Legally Authorized Representatives (LAR) is only used for populations unable to provide informed consent. Only use the LAR signature block in place of the participant's signature block if it has been explained in the study application (subject to approval by the IRB) that these types of populations are going to be used in the study. • A copy of the signed and dated consent document must be given to the person signing the consent document.
Employee and Student Coercion Disclosure	When VA research involves employees or students as potential participants, the informed consent document must include language that explicitly discloses: (a) participation is completely voluntary; (b) a decision not to participate, or withdrawal from the study, will not affect the individual's employment, academic standing, grades, or working relationship; and (c) the individual's supervisor or instructor will not know whether they participated unless the participant discloses this themselves.
HIPAA AUTHORIZATION	The Ralph H. Johnson VA Health Care System does not accept combined ICDs and HIPAA Authorizations. VA Form 10-0493, HIPAA Authorization, is required.
MAINTENANCE	The investigator must ensure that all original or digitalized signed and dated informed consent documents are maintained in the investigator's research files, readily retrievable, and secure.
WAIVERS AND ALTERATIONS	
VA WAIVERS	A waiver of HIPAA authorization must be approved by the IRB or Privacy Board prior to accessing any PHI for screening, recruiting, or determining eligibility. Informed consent, or an IRB-approved waiver thereof is required before any research interventions occur after eligibility is determined.

WAIVER OR ALTERATION OF INFORMED CONSENT	• An IRB may waive consent or alter or omit the elements of informed consent.
	• The IRB must find and document the following to waive or alter consent in research:
	  ○ The research involves no more than minimal risk to the subjects;
	  ○ The research could not practicably be carried out without the requested waiver or alteration;
	  ○ If the research involves using identifiable private information or identifiable biospecimens, the research could not practicably be carried out without using such information or biospecimens in an identifiable format for studies subject to the 2018 Requirements;
	  ○ The waiver or alteration will not adversely affect the rights and welfare of the subjects; and
	  ○ Whenever appropriate, the subject or LAR will be provided with additional pertinent information after participation.
	If the IRB approves a consent procedure which does not include, or which alters, any of the elements of informed consent, or waives the requirement to obtain a signed informed consent document, it must find and document that all criteria for the waiver have been satisfied.

WAIVER OF HIPAA AUTHORIZATION FOR RECRUITMENT	If existing information from sources such as a medical record or database (research or non-research) are used to identify human participants, there must be an IRB-approved waiver of HIPAA authorization for this activity in the new protocol.
RECRUITMENT	
RECRUITMENT	During the recruitment process, the investigator is responsible for making initial contact with potential subjects in person or by letter prior to initiating any telephone contact, unless there is written documentation that the subject is willing to be contacted by telephone about the study in question or a specific kind of research as outlined in the study. ***NOTE***: *This does not apply when a Veteran calls in response to an advertisement*.
COLD/PROACTIVE CALLING	Calling potential VA subjects without first sending a notification in person or through mail or email for the purpose of VA research recruitment is NOT permitted outside of the ORD

	approval process unless there is written documentation that the subject is willing to be contacted by telephone about the study in question or a specific kind of research as outlined in the study as per VHA Office of Research and Development (ORD) policy in VHA Directive 1200.05, Requirements for the Protection of Human Subjects in Research. • Specific criteria must be met as evaluated by ORD for approval to a VA study requesting proactive calling.
NON-VETERAN RECRUITMENT	If recruiting and enrolling non-Veterans to a VA-only study (i.e., non-Veterans will complete procedures at the VA), study teams must submit a "Request for Non-Veteran Approval". This form can be found in IRBNet, VA's internal IRB system.
PROMPT REPORTING	
GENERAL INFORMATION	If the study is a VA research protocol, prompt reporting to the IRB, appropriate institutional officials, department or agency heads, the Office of Research Oversight (ORO), and the Office of Human Research Protections (OHRP) are required for: 1) any unanticipated problems involving risks to subjects or others, or any serious or continuing noncompliance according to requirements or determinations made by the IRB, and 2) any suspension or termination of IRB approval. This includes: 1) the Associate Chief of Staff/Research & Development, and 2) the VA Privacy Office (when the report involves unauthorized use, loss, or disclosure of individually identifiable patient information). The ACOS/R and the Research Compliance Officer will follow local and federal policies and reporting guidelines.
DEATH OF HUMAN SUBJECTS	The VA Medical Center Director must notify ORO within 1 business day after VA medical facility personnel first become aware of the death of a human subject enrolled in a study approved by the VA medical facility that is believed to be both unexpected and unrelated or possibly related to participation in a VA human subjects research study. In the event of a local research participant death: • VA personnel must ensure that the appropriate IRB of Record and VA ACOS/R are orally notified immediately (i.e., within one hour) upon becoming aware of any local research death of a human participant that is believed to be both unexpected and related or possibly related to a participant in a VA non-exempt human participant study. • VA personnel must also provide follow-up written notification to the IRB within one (1) business day of becoming aware of such a death. • The ACOS/R, or designee, must alert the VA Medical Center Director and appropriate ORO workgroup by email or telephone within one (1) business day after receiving the initial oral notification and provide relevant information as requested. • The VA Medical Center Director, or designee, must report the IRB's determinations to the appropriate ORO workgroup within five (5) business days after receiving the IRB's written notification. • If the IRB is unable to make a determination on the matter within 30 calendar days of the convened IRB's initial review due to insufficient information or due to a lack of sufficient time to complete its review, the IRB must notify the VA medical facility Director, the RCO, and the ACOS/R&D in writing no later than five (5) business days after the determination was due. Within one (1) business day after receiving written notification of the death, the IRB Chair or another qualified IRB member must assess and document whether any actions are warranted to eliminate apparent immediate hazards to participants and, if so, initiate those actions. • Determine and document within 30 calendar days of the convened IRB's initial review: ○ Whether the death was both unexpected and related or possibly related to participation in the research; and ○ What, if any, protocol or informed consent modifications are warranted. If modifications are warranted, the convened IRB must determine and document whether or not researchers must notify or solicit renewed/revised consent from previously enrolled participants; and if so, when such notification or consent must take place and how

	it must be documented. • The IRB must notify the VA Medical Facility Director, the RCO, and the ACOS/R&D in writing of its determinations within five (5) business days after making those determinations.
UNANTICIPATED PROBLEMS INVOLVING RISKS TO SUBJECTS OR OTHERS	The VA Medical Center Director must notify the Office of Research Oversight (ORO) promptly, but no later than 60 days after VA medical facility personnel first become aware of the occurrence of an unanticipated problem involving risks to subjects or others (UPIRTSO). In the event of any apparent UPIRTSO, VA personnel must ensure that the appropriate IRB of Record is notified, in writing, within five (5) business days after becoming aware of any apparent UPIRTSO involving a VA non-exempt human participants research study. • An apparent UPIRTSO is an apparent incident, experience or outcome that is: unexpected and related or possibly related to participation in the research and indicative of the research placing participants or others at substantively greater risk of harm than was previously known or recognized. • The VA Medical Center Director, or designee, must report the IRB's determinations to the appropriate ORO workgroup within five (5) business days after receiving the IRB's written notification. • The VA Medical Center Director, or designee, must notify the appropriate ORO workgroup within five (5) business days after receiving the IRB's written notification that it is unable to make a UPIRTSO determination. • Within five (5) business days after receiving written notification of an apparent UPIRTSO, the IRB Chair or another qualified IRB member must assess and document whether any actions are warranted to eliminate apparent immediate hazards to participants and, if so, initiate those actions. In response to the written notification, the IRB must: o Review the written notification, the immediate hazard assessment of the IRB Chair or other qualified IRB member, and the actions taken to date at its next convened meeting, not to exceed 30 calendar days after the date of written notification. ***NOTE**: Incidents covered by this paragraph may call for immediate attention and require the IRB to convene an emergency session prior to its next scheduled meeting*. o Determine and document within 30 calendar days of the convened IRB's initial review: ▪ Whether the incident, experience, or outcome was unexpected and related to or possibly related to participation in the research and indicative of the research placing participants or others at substantively greater risk of harm than was previously known or recognized (i.e., whether the incident, experience, or outcome constituted an actual UPIRTSO); and ▪ What, if any, protocol or informed consent modifications are warranted. If modifications are warranted, the convened IRB must determine and document whether or not researchers must notify or solicit renewed or revised consent from previously enrolled participants; and if so, when such notification or consent must take place and how it must be documented. o If the IRB determines that the incident, experience, or outcome constituted an actual UPIRTSO, it must notify the VA medical facility Director, the RCO, and the ACOS/R&D in writing of its determinations within five (5) business days after making those determinations. o If the IRB is unable to make a determination on the matter within 30 calendar days of the convened IRB's initial review due to insufficient information or due to a lack of sufficient time to complete its review, the IRB must notify the VA Medical Center Director, the RCO, and the ACOS/R in writing no later than five (5) business days after the determination was due.

SERIOUS UNANTICIPATED AND UNEXPECTED PROBLEMS AND UNANTICIPATED SERIOUS ADVERSE EVENTS	• The terms "unanticipated" and "unexpected" refer to an event or problem in VA research that is new or greater than previously known in terms of nature, severity, or frequency, given the procedures described in protocol-related documents and the characteristics of the study population. • The unfounded classification of a serious adverse event as "anticipated" constitutes serious non-compliance. • For serious unanticipated problems involving risks to subjects or others, within five business days of becoming aware of any serious unanticipated problem involving risks to subjects or others in VA research, members of the VA research community are required to ensure that the problem has been reported in writing to the IRB. Serious unanticipated problems involving risks to subjects or others include: o Interruptions of subject enrollments or other research activities due to concerns about the safety, rights, or welfare of human research subjects, research staff, or others. o Any work-related injury to personnel involved in human research, or any research - related injury to any other person, that requires more than minor medical intervention (i.e., basic first aid), requires extended surveillance of the affected individuals, or leads to serious complications or death. o Any VA National Pharmacy Benefits Management (PBM) Bulletins or Communications (sometimes referred to as PBM Safety Alerts) relevant to one or more of the VA facility's research projects. o Any data monitoring committee, data and safety monitoring board or data and safety monitoring committee report describing a safety problem. o Any sponsor analysis describing a safety problem for which action at the VA facility might be warranted. o Any unanticipated problem involving substantive harm, or a genuine risk of substantive harm, to the safety, rights, or welfare of human research subjects, research staff, or others. o Any problem reflecting a deficiency that substantively compromises the effectiveness of the VA facility's HRPP. • IRB review of serious unanticipated problems and unanticipated serious adverse events in VA research: o Within five business days after a report of a serious unanticipated problem involving risks to subjects or others, or of a local unanticipated serious adverse event, the convened IRB or a the chair or designee must determine and document whether the reported incident was serious and unanticipated and related to the research. o "Related" means the event or problem may reasonably be regarded as caused by, or probably caused by, the research. o If the convened IRB or the IRB chair or designee determines that the problem or event was serious, unanticipated, and related to the research, the IRB chair or designee must report in writing the unanticipated problem or event within five business days after the determination to: ▪ Medical Center Director (responsible for reporting to the Office of Research and Development, the Office of Research Oversight and, if the report involves violations of information security requirements, the Information Safety Security Officer), ▪ Associate Chief of Staff for Research, and ▪ The Research and Development Committee o If the convened IRB or the IRB reviewer determines that the problem or event was serious, unanticipated, and related to the research, a simultaneous determination is required regarding the need for any action (e.g., suspension of activities; notification of subjects) necessary to prevent an immediate hazard to subjects in accordance with VA regulations. o All determinations of the IRB reviewer (regardless of outcome) must be reported to the IRB at its next convened meeting. o If it was determined that the problem or event is serious, unanticipated,

	and related to the research, the convened IRB must determine and document whether a protocol or consent document modification is warranted. o If the convened IRB determines that a protocol or consent document modification is warranted, the IRB must also determine and document: ▪ Whether previously enrolled subjects must be notified of the modification. ▪ When such notification must take place and how such notification must be documented.
SERIOUS OR CONTINUING NONCOMPLIANCE INVOLVING HUMAN SUBJECTS RESEARCH	The VA Medical Center Director must notify ORO promptly, but no later than 60 calendar days after VA medical facility personnel first become aware, of the occurrence of serious or continuing noncompliance with applicable laws, regulations, policies, and agreements pertaining to VA human subjects research. This includes, but is not limited to, serious or continuing noncompliance with 38 C.F.R. § 16, VHA Directive 1200.05, Requirements for the Protection of Human Subjects in Research, dated January 7, 2019, VA medical center policies, standard operating procedures (SOPs), and MOUs (or equivalent) related to human subjects research, Institutional Review Board (IRB)-approved protocols, and the requirements or determinations of the IRB. Serious Noncompliance: Any failure to adhere to requirements for conducting human research that may reasonably be regarded as (a) presenting a genuine risk of substantive harm to the safety, rights, or welfare of human research participants, research staff, or others, including privacy and confidentiality rights; (b) presenting a genuine risk of substantive reputational harm to VA; or (c) substantively compromising a VA facility's HRPP. Continuing Noncompliance: A persistent or repeated failure to adhere to applicable laws, regulations, or policies governing human research, where prior corrective actions have not been effective.
OTHER EVENTS INVOVLING VA HUMAN RESEARCH PROTECTION PROGRAM REPORTABLE TO ORO	The VA Medical Center Director must notify ORO promptly, but no later than 5 business days after VA medical facility personnel first became aware, of any of the following: • The suspension or early termination of a VA human research study by the IRB, R&DC, or institutional official due to the study not being conducted in accordance with applicable regulations, policies, agreements, or IRB requirements or due to concerns about the safety, rights, or welfare of human subjects or others. NOTE: The notification of suspension or early termination of a VA study by the IRB, R&DC, or institutional official must include a statement of the reason for the IRB's or institutional official's action. • The termination or non-renewal of the HHS-OHRP registration of any IRB relied upon by the VA medical facility for review and oversight of VA research. • The issuance of a research-related citation or determination of noncompliance by a state or Federal entity (including the VA Office of Inspector General) or an accrediting organization, pertaining to the VA medical facility's HRPP and human subjects portfolio. • Media Attention or Congressional Interest: The VA Medical Center Director must report to ORO within two (2) business days after being notified of any situation related to VA research that has generated media attention or Congressional interest, regardless of whether the event involves noncompliance. • RCO Appointment/Change: The VA Medical Center Director must report to ORO within ten (10) business days after any appointment, resignation, or change in status of the Research Compliance Officer (RCO), with a copy to the relevant ORO research officer.
IRB AND VA STRUCTURE, CONDITIONAL APPROVALS, AND DOCUMENTATION	
APPROVAL WITH CONDITIONS	When approval is contingent on specific minor modifications: • Review and approval must be by the IRB Chair, or experienced IRB voting member designated by the Chair

	• The designated reviewer may verify only that minor modifications have been made as required. The designated reviewer may not make substantive changes to the study or impose new conditions beyond what was specified by the convened IRB. • If the modifications requested are substantive in nature, the study must return to the convened IRB.
RISK LEVEL DOCUMENTATION	The IRB must document its determination on the level of risk either in the IRB minutes or the written communication to the researcher.
VA INSTITUTIONAL OFFICIAL (IO)	**VHA Directive 1200.05**: The Institutional Official (IO) is the individual legally authorized as Signatory Official to commit an institution to an FWA. The Signatory Official assures that human subjects research to which the FWA applies is conducted in accordance with the terms of the assurance (see VHA Handbook 1058.03). The Principal Deputy Under Secretary for Health or designee is the IO for VHA Central Office, and VA facility Directors are the IOs for local VA facilities. **VHA Directive 1058**: The VA Medical Facility Director serves as the Institutional Official (IO) responsible for the VA medical facility's research program.
IRB INDEPENDENCE	The MUSC IRB operates independently in its review and oversight of VA research. The following requirements apply: • In addition to IRB approval, the VA Privacy Officer, Information System Security Officer (ISSO), and the Research and Development Committee (R&DC) must provide their respective approvals before VA research may be initiated. • If the IRB disapproves a VA research study, or requires modifications as a condition of approval, that disapproval or requirement for modifications cannot be overruled by any other authority — including the VA Facility Director, R&DC, or ORD. • The R&DC reviews the scientific merit of VA research and the outcomes of IRB review. The R&DC may not approve research that the IRB has disapproved or that remains subject to unresolved IRB conditions.
IRB MEMBERSHIP	VA facilities must maintain accurate membership rosters for their designated IRB(s) of Record and submit the roster(s) to ORO as required by VHA Handbook 1058.03. The roster must list IRB members identified by name, earned degrees, representative capacity, indications of experience such as board certifications, licenses, etc., sufficient to describe each member's primary anticipated contributions to IRB deliberations, and any employment or other relationship between each member and the institution (e.g., full-time employee, part-time employee, member of governing panel or board, paid or unpaid consultant). The IO appoints VA voting members to an IRB in writing. Appointment procedures for ex officio, non-voting members are made according to local SOPs and any other applicable VA requirements. Voting members and VA representatives to the external IRB of Record are appointed for a period of up to 3 years. They may be re-appointed to new terms of up to 3 years without a break in service at the end of each term. ***NOTE****: There is not a maximum number of terms for IRB members as long as the composition of the IRB meets all requirements. VA representation on external IRBs, such as academic IRBs, is optional and at the discretion of the IO and the external IRB*.
IRB MEMBERSHIP RESTRICTIONS FOR VA PERSONNEL	• Facility Directors, their administrative staff, COS, other facility senior administrators such as Associate or Assistant Directors or Chief Nurse, and NPC Administrative Staff may observe IRB meetings, but may not serve as members of the IRB. • VA facility research office staff including, but not limited to, the ACOS/R&D, the AO for R&D, and IRB administrative staff may not serve as members of the IRB. They may serve as ex officio, non-voting members or attendees; however, they and the IRB must be sensitive to any potential, actual, apparent, or perceived conflicts of interest and appropriately manage such conflicts • Research Compliance Officers (RCOs) may act as consultants to the IRB but may not serve as members of the IRB. RCOs may attend IRB meetings when requested by the IRB or as specified by the IRB's SOPs. RCOs must be aware of and manage any potential, actual, apparent, or perceived conflicts of interest that arise because of their role.

	• The Privacy Officer (PO) and the Information System Security Officer (ISSO) serve in an advisory capacity to the facility's IRB as either non-voting members or as consultants
SERVING AS IRB FOR VA RESEARCH	The responsibilities that the Ralph H. Johnson VA Health Care System and MUSC, operating as the VA's IRB of Record, each will undertake to ensure compliance with requirements for maintaining records is described in an MOU. • All IRBs overseeing VA human participants research must meet all the IRB requirements described in 38 CFR Part 16. • When the IRB of Record is directly operated and supported by a non-VA entity, the policies and procedures related to the review of VA research by the non-VA entity must be consistent with VHA Directive 1200.05 and all regulations applicable to VA research. • When a VA facility engages the services of another entity's IRB as its IRB of Record, a Memorandum of Understanding (MOU) or Authorizing Agreement must be established and signed with the external organization providing IRB services. • IRBs of Record used by a VA facility must hold current IRB registrations with FDA/OHRP and provide updates to membership as required by VHA Directive 1058. • At least one VA member must be present for the discussion and vote whenever VA research is discussed.
RESEARCH AND DEVELOPMENT COMMITTEE	R&D reviews VA research by performing scientific reviews and reviewing outcomes of other committee reviews (e.g., IRB, IACUC, biosafety, etc.). All other committee approvals occur before the project goes to R&D. VA Research Office staff attend the meetings. Any emergency use of a test article does not require R&D Committee approval but is considered VA research under VHA Directive 1200.05.
VA IRB RECORDS ACCESS	Since MUSC is the IRB of Record for Ralph H. Johnson VAHCS, MUSC must either: • Provide VA with, or access to, unredacted copies of meeting minutes in a timely manner that allows the R&D Committee to review the IRB's deliberations on VA protocols; or • Provide VA with, or access to, redacted minutes in a timely manner that allows the R&D Committee to review the IRB's deliberations on VA protocols. MUSC must permit relevant VA personnel (including, but not limited to, ORO staff, local VA research office staff, local RCOs, and R&D Committee members) to review the unredacted meeting minutes within 2 business days of a written request from VA. Such review may occur at either site during normal business hours, or as otherwise mutually acceptable to VA and the IRB. ***NOTE****: Redacted copies of meeting minutes should include the parts of the minutes related to the IRB's review of VA protocols*.
COLLABORATING WITH THE VA	Collaboration is encouraged when VA investigators have a substantive role in the design, conduct, and/or analysis of the research. Each institution is responsible for safeguarding the rights and welfare of human subjects and providing oversight of the research activities conducted by that institution. • Investigators must submit a protocol or other documentation to the IRB that clearly delineates which research activities will be conducted as the VA portion of the overall Collaborative Research study. • Each institution engaged in the Collaborative Research must use the informed consent document and HIPAA authorization required by its respective institutional policies for subjects recruited from that institution, or procedures requiring participation of the subjects at that institution. • The protocol, addendum, and/or IRB of Record application must describe the data to be disclosed to collaborators, the entities to which the data are to be disclosed, how the data are to be transmitted, and how the transmitted data will be stored, retained, destroyed, and/or further disclosed and to whom. This includes data from individual subjects as well as other data developed during the research such as the analytic data and the aggregate data.
VULNERABLE POPULATIONS	
GENERAL INFORMATION	If an IRB regularly reviews research that involves a category of subjects that is vulnerable

	to coercion or undue influence, such as children, prisoners, individuals with impaired decision-making capacity, or economically or educationally disadvantaged persons, consideration must be given to the inclusion of one or more individuals on the IRB who are knowledgeable about and are experienced in working with these subjects. When some or all of the subjects are likely to be vulnerable to coercion or undue influence, such as children, prisoners, individuals with limited decision-making capacity, or educationally or economically disadvantaged persons, the protocol must include additional safeguards to protect the rights and welfare of these subjects.
CHILDREN	Research involving children must be reviewed carefully by the IRB for its relevance to VA and must not present greater than minimal risk to the children. The VA medical facility Director must approve participation in the proposed research that includes children. The IRB must have the appropriate expertise to evaluate any VA research involving children. ***NOTE**: Research involving biological specimens or data obtained from children is considered to be research involving children even if deidentified.* ***NOTE**: For purposes of this directive, research involving children does not include neonates.*
IN VITRO FERTILIZATION	The provision of in vitro fertilization (IVF) services as a research intervention cannot be conducted by VA investigators while on official VA duty, at VA facilities, or at VA-approved off-site facilities. The following research activities involving IVF are permitted: • Prospective and retrospective observational studies that enroll or include subjects who have undergone or are undergoing IVF for the treatment of certain forms of infertility, where the research does not involve provision or enhancement of IVF services. • Prospective and retrospective studies that enroll or include pregnant subjects who conceived through IVF or other assisted reproductive technologies. NOTE: Any proposed VA research involving IVF must be submitted to the IRB and reviewed carefully. Contact the RHJVAHCS HRPP Administrator if there are questions about whether a specific study meets permissible criteria.
PREGNANT WOMEN, HUMAN FETUSES, AND NEONATES	• Research that uses human fetal tissue or that focuses on either a fetus, or human fetal tissue, in-utero or ex-utero cannot be conducted by VA investigators while on official VA duty, at VA facilities, or at VA-approved off-site facilities. Use of stem cells shall be governed by the policy set by NIH for recipients of NIH research funding • Research involving the creation of a human embryo or embryos solely for research purposes or research in which a human embryo or embryos are destroyed, discarded, or knowingly subjected to risk of injury or death greater than that allowed for research on fetuses in utero under 45 CFR 46.208(a)(2) and Section 498B of the Public Health Service Act (42 U.S.C. 289g(b)) cannot be conducted by VA Investigators, at VA facilities, or at VA approved off-site facilities. • Women who are known to be pregnant and their fetuses may be involved in research if all the requirements are met and the VA medical facility Director certifies that the VA medical facility has sufficient expertise in women's or reproductive health to conduct the proposed research if the research includes interventional studies or invasive monitoring of pregnant women as subjects. • VA investigators cannot conduct interventions in research that include neonates while on official VA duty, at VA facilities, or at VA-approved off-site facilities. VA investigators may conduct research involving noninvasive monitoring of neonates if the research is determined by the IRB to be minimal risk. Prospective observational and retrospective record review studies that involve neonates or neonatal outcomes are permitted. • The reviewing IRB must have the appropriate expertise to evaluate interventional and invasive VA research involving neonates and must comply with the requirements of 45 CFR 46.205. The Medical Center Director must certify that the

	medical facility has sufficient expertise in neonatal health to conduct the proposed research.
PRISONERS	Research involving prisoners cannot be conducted by VA investigators while on official VA duty, at VA facilities, or at VA-approved off-site facilities unless a waiver has been granted by the Chief Research and Development Officer (CRADO). Waiver requests must be submitted electronically to the CRADO by the VA Medical Center Director.
SPECIAL CIRCUMSTANCES	
PLANNED EMERGENCY OR CLASSIFIED RESEARCH	VHA does not conduct planned emergency research or classified research involving human subjects.
INTERNATIONAL RESEARCH	• VA international research is defined as any VA-approved research conducted at international sites (i.e., not within the United States (U.S.), its territories, or Commonwealths), any VA-approved research using either identifiable or de-identified human biological specimens or identifiable or de-identified human data originating from international sites, or any VA-approved research that entails sending such specimens or data out of the U.S. This definition applies regardless of the funding source (funded or unfunded) and to research conducted through any mechanism of support including MOUs, CRADAs, grants, contracts, or other agreements. NOTE: For the purposes of this directive, research conducted at U.S. military bases, ships, or embassies is not considered international research. • Sending specimens or data to individuals with VA appointments at international sites (e.g., a WOC appointment, a VA investigator on sabbatical at an international site) is considered international research. Remote use of data that is maintained on VA computers within the U.S. or Puerto Rico and U.S. territories accessed via a secure connection is not considered international research. • International research includes multi-site trials involving non-U.S. sites where VA is the study sponsor, a VA investigator is the overall study-wide PI, VA holds the Investigational New Drug (IND), or the VA manages the data collection and the data analyses. • International research does not include studies in which VA is only one of multiple participating sites where the overall study-wide PI is not a VA investigator (i.e., the PI for the study as a whole is not a VA investigator). • Before approving international research involving human subjects research, the IRB must ensure that human subjects outside of the U.S. who participate in research projects in which VA is a collaborator receive equivalent protections as research participants inside the U.S. if the activity involves human subjects research requiring IRB approval or limited IRB review. • All international research must also be approved explicitly in a document signed by the VA medical facility Director, except for Cooperative Studies Program activities which must be approved by the CRADO.
SURVEY RESEARCH FIRMS	If the investigator contracts with a firm (e.g., a survey research firm) to obtain consent from subjects, collect private individually identifiable information from human subjects, or be involved in activities that would institutionally engage the firm in human subjects research, the firm must have its own IRB oversight of the activity. In addition, the Privacy Officer (PO) must determine that there is appropriate authority to allow the disclosure of individual names and other information to the contracted firm.
RESEARCH COMPLIANCE OFFICER (RCO) AUDITS	The Research Compliance Officer (RCO) at Ralph H. Johnson VAHCS conducts mandatory audits of VA research studies to assess compliance with all applicable local, VA, and federal requirements. Mandatory audit requirements include: • Annual consent document audits: The RCO conducts consent document audits on all active VA research studies at least annually. • Triennial regulatory audits: The RCO conducts comprehensive regulatory audits on all active VA research protocols at least once every three years. • The RCO reports directly to the VA Medical Center Director. The activities of the RCO may not be determined or managed by the Research Service, researchers, or any other research personnel.

	IRB authority over audits: The IRB may accept audits conducted by the RCO to fulfill its own auditing requirements. The IRB may also require: • More frequent audits beyond the mandatory minimum, based on factors including: involvement of vulnerable populations, level of risk, Phase I or Phase II studies, FDA safety warnings on study drugs, data confidentiality concerns, or prior noncompliance findings. • Focused audits of specific aspects of a study. • Audits by a third party or by IRB observation of the consent process. The IRB determines appropriate corrective actions based on audit findings and evaluates the effectiveness of any corrective actions taken.

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